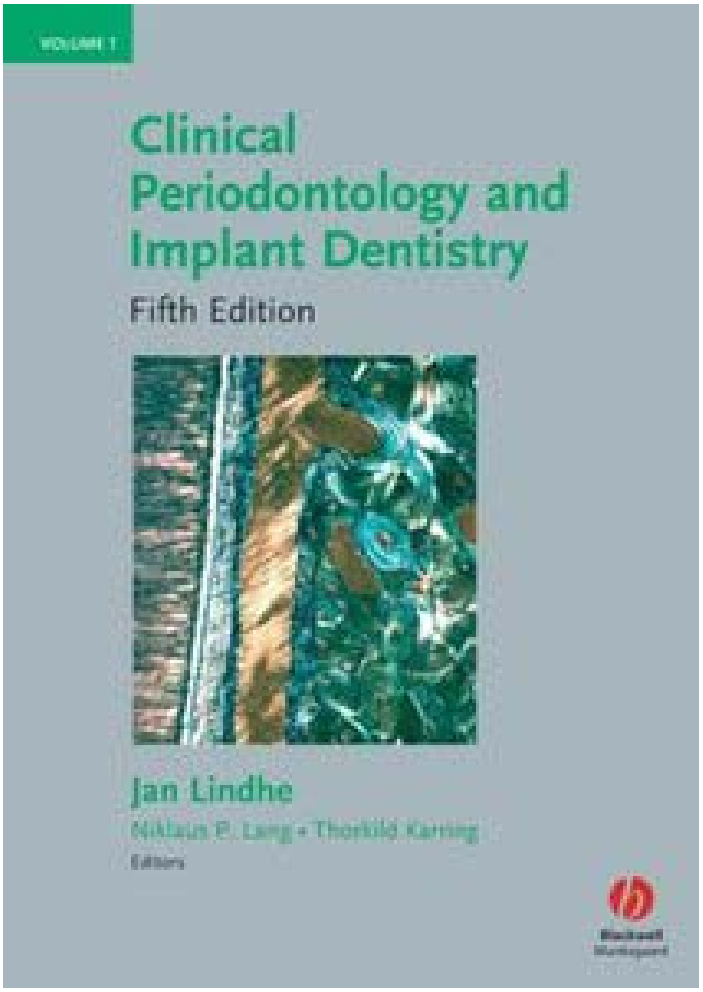

Clinical Periodontology and Implant Dentistry

Fifth Edition

Edited by

Jan Lindhe
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Blackwell Munksgaard

Volume 1
BASIC CONCEPTS

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Preface

When the groundwork for the fifth edition of *Clinical Periodontology and Implant Dentistry* began in early 2007, it became clear that we had reached a fork in the road. It has always been my intention that each successive edition of this work should reflect the state of the art of clinical periodontology and, in doing such, should run the gamut of topics within this subject area. However, thorough coverage of an already large and now rapidly expanding specialty has resulted in a book of commensurate size and therefore for the fifth edition, the decision was taken to divide the book into two volumes: basic concepts and clinical concepts. The decision to make the split a purely physical one, and not an intellectual one, reflects the realization that over the past decade, implant dentistry has become a basic part of periodontology. The integrated structure of this latest edition of the textbook mirrors this merger.

In order for the student of dentistry, whatever his or her level, to learn how teeth and implants may function together as separate or connected units in the same dentition, a sound knowledge of the tissues that surround the natural tooth and the dental implant, as well as an understanding of the various lesions that may occur in the supporting tissues, is imperative. Hence, in both volumes of the textbook, chapters dealing with traditional periodontal issues, such as anatomy, pathology and treatment, are followed by similar topics related to tissues surrounding dental implants. In the first volume of the fifth edition, "basic concepts" as they relate to anatomy, microbiology and pathology, for example, are presented, while in the second volume ("clinical concepts"), various aspects of often evidence-based periodontal and restorative examination and treatment procedures are outlined.

It is my hope that the fifth edition of *Clinical Periodontology and Implant Dentistry* will challenge the reader intellectually, provide elucidation and clarity of information, and also impart an understanding of how the information presented in the text can, and should, be used in the practice of contemporary dentistry.

Jan Lindhe

Part 1: Anatomy

Chapter 1

The Anatomy of Periodontal Tissues

Jan Lindhe, Thorkild Karring, and Maurício Araújo

Introduction

This chapter includes a brief description of the characteristics of the normal periodontium. It is assumed that the reader has prior knowledge of oral embryology and histology. The periodontium (peri = around, odontos = tooth) comprises the following tissues (Fig. 1-1): (1) the *gingiva* (G), (2) the *periodontal ligament* (PL), (3) the *root cementum* (RC), and (4) the *alveolar bone* (AP). The alveolar bone consists of two components, the *alveolar bone proper* (ABP) and the alveolar process. The alveolar bone proper, also called "bundle bone", is continuous with the alveolar process and forms the thin bone plate that lines the alveolus of the tooth.

The main function of the periodontium is to attach the tooth to the bone tissue of the jaws and to maintain the integrity of the surface of the masticatory mucosa of the oral cavity. The periodontium, also called "the attachment apparatus" or "the supporting tissues of the teeth", constitutes a developmental, biologic, and functional unit which undergoes certain changes with age and is, in addition, subjected to morphologic changes related to functional alterations and alterations in the oral environment.

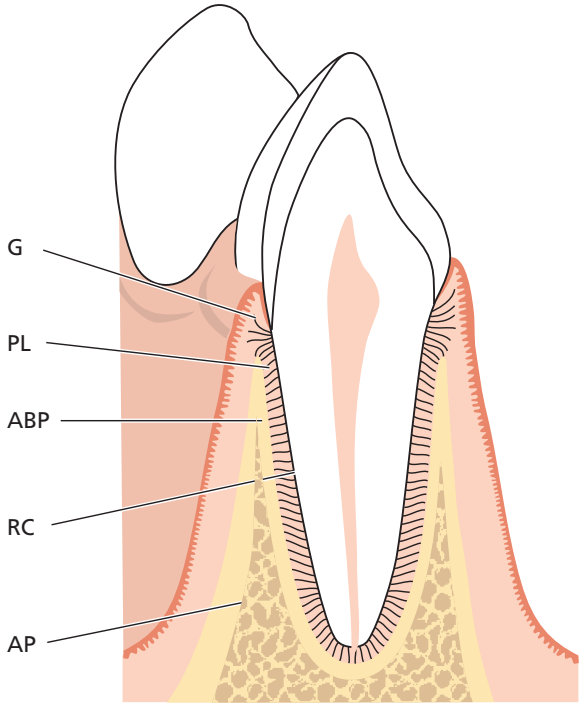


Fig. 1-1

The development of the periodontal tissues occurs during the development and formation of teeth. This process starts early in the embryonic phase when cells from the neural crest (from the neural tube of the embryo) migrate into the first branchial arch. In this position the neural crest cells form a band of *ectomesenchyme* beneath the epithelium of the stomatodeum (the primitive oral cavity). After the uncommitted neural crest cells have reached their location in the jaw space, the epithelium of the stomatodeum releases factors which initiate epithelial–ectomesenchymal interactions. Once these interactions have occurred, the ectomesenchyme takes the dominant role in the further development. Following the formation of the *dental lamina*, a series of processes are initiated (bud stage, cap stage, bell stage with root development) which result in the formation of a tooth and its surrounding periodontal tissues, including the alveolar bone proper. During the cap stage, condensation of ectomesenchymal cells appears in relation to the dental epithelium (the dental organ (DO)),

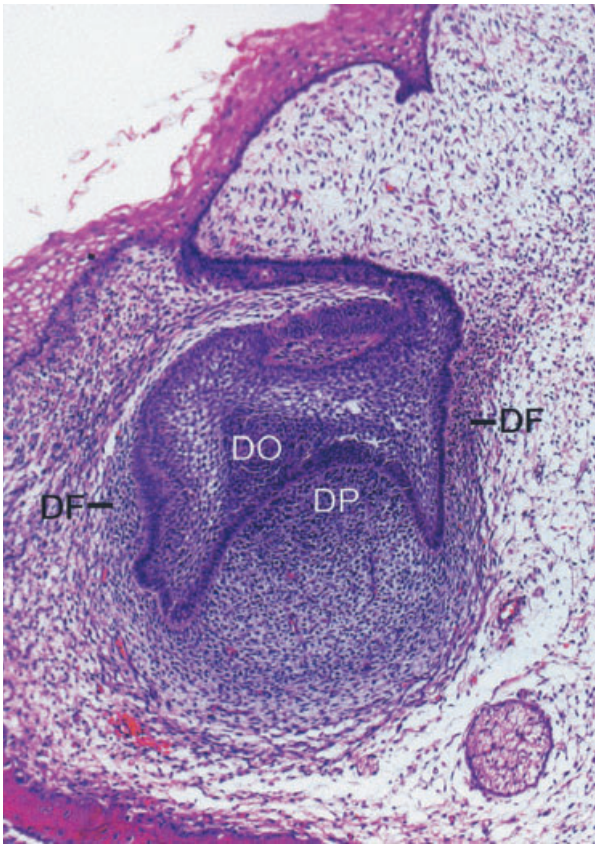


Fig. 1-2

forming the *dental papilla* (DP) that gives rise to the dentin and the pulp, and the *dental follicle* (DF) that gives rise to the periodontal supporting tissues (Fig. 1-2). The decisive role played by the ectomesenchyme in this process is further established by the fact that the tissue of the dental papilla apparently also determines the shape and form of the tooth.

If a tooth germ in the bell stage of development is dissected and transplanted to an ectopic site (e.g. the connective tissue or the anterior chamber of the eye), the tooth formation process continues. The crown and the root are formed, and the supporting structures, i.e. cementum, periodontal ligament, and a thin lamina of alveolar bone proper, also develop. Such experiments document that all information necessary for the formation of a tooth and its attachment apparatus obviously resides within the tissues of the dental organ and the surrounding ectomesenchyme. The dental organ is the formative organ of enamel, the dental papilla is the formative organ of the dentin–pulp complex, and the dental follicle is the formative organ of the attachment apparatus (the cementum, the periodontal ligament, and the alveolar bone proper).

The development of the root and the periodontal supporting tissues follows that of the crown. Epithelial cells of the external and internal dental epithelium (the dental organ) proliferate in an apical direction forming a double layer of cells named *Hertwig's epithelial root sheath* (RS). The odontoblasts (OB) forming the dentin of the root differentiate from ecto-

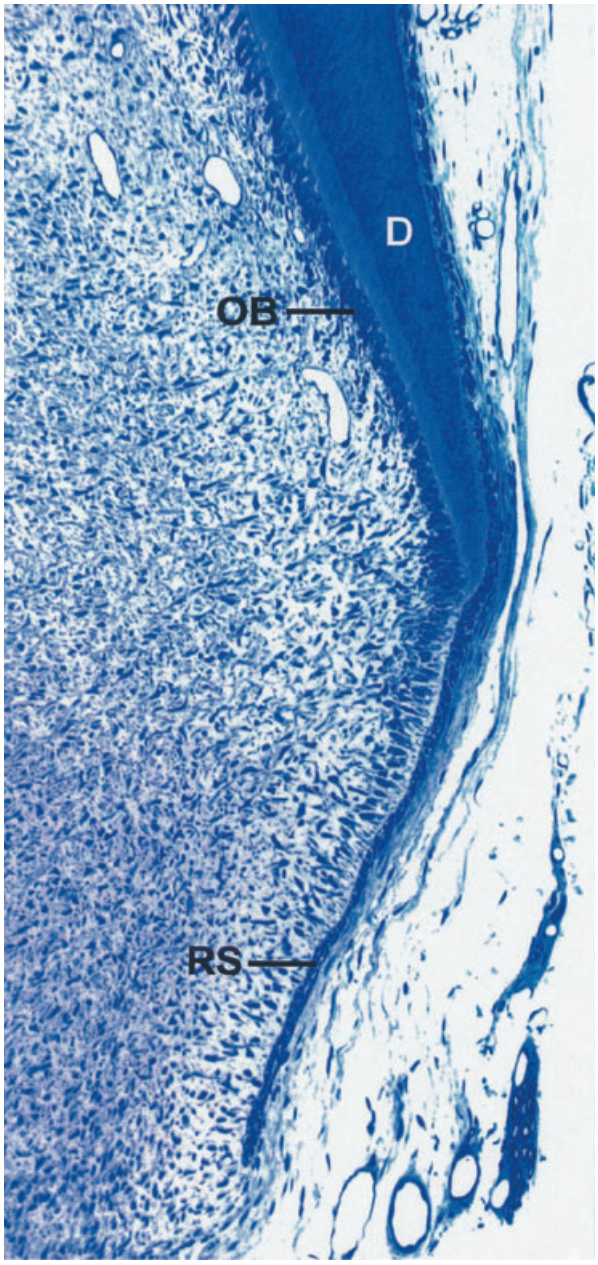


Fig. 1-3

mesenchymal cells in the dental papilla under inductive influence of the inner epithelial cells (Fig. 1-3). The dentin (D) continues to form in an apical direction producing the framework of the root. During formation of the root, the periodontal supporting tissues, including acellular cementum, develop. Some of the events in the cementogenesis are still unclear, but the following concept is gradually emerging.

At the start of dentin formation, the inner cells of Hertwig's epithelial root sheath synthesize and secrete enamel-related proteins, probably belonging to the amelogenin family. At the end of this period, the epithelial root sheath becomes fenestrated and ectomesenchymal cells from the dental follicle penetrate through these fenestrations and contact the root surface. The ectomesenchymal cells in contact with the enamel-related proteins differentiate into cementoblasts and start to form cementoid. This cementoid

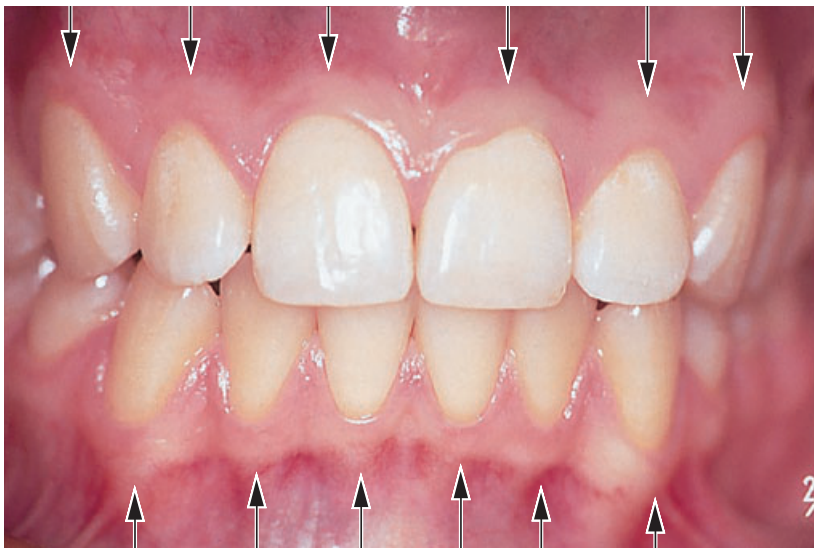


Fig. 1-4

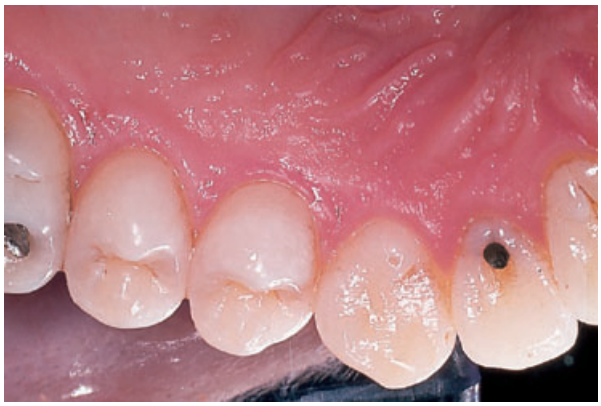


Fig. 1-5

represents the organic matrix of the cementum and consists of a ground substance and collagen fibers, which intermingle with collagen fibers in the not yet fully mineralized outer layer of the dentin. It is assumed that the cementum becomes firmly attached to the dentin through these fiber interactions. The formation of the cellular cementum, which covers the apical third of the dental roots, differs from that of acellular cementum in that some of the cementoblasts become embedded in the cementum.

The remaining parts of the periodontium are formed by ectomesenchymal cells from the dental follicle lateral to the cementum. Some of them differentiate into periodontal fibroblasts and form the fibers of the periodontal ligament while others become osteoblasts producing the alveolar bone proper in which the periodontal fibers are anchored. In other words, the primary alveolar wall is also an ectomesenchymal product. It is likely, but still not conclusively documented, that ectomesenchymal cells remain in the mature periodontium and take part in the turnover of this tissue.

Gingiva

Macroscopic anatomy

The oral mucosa (mucous membrane) is continuous with the skin of the lips and the mucosa of the soft palate and pharynx. The oral mucosa consists of (1) the *masticatory mucosa*, which includes the gingiva and the covering of the hard palate, (2) the *specialized mucosa*, which covers the dorsum of the tongue, and (3) the remaining part, called the *lining mucosa*.

Fig. 1-4 The gingiva is that part of the masticatory mucosa which covers the alveolar process and surrounds the cervical portion of the teeth. It consists of an epithelial layer and an underlying connective tissue layer called the *lamina propria*. The gingiva obtains its final shape and texture in conjunction with eruption of the teeth.

In the coronal direction the coral pink gingiva terminates in the *free gingival margin*, which has a scalloped outline. In the apical direction the gingiva is continuous with the loose, darker red *alveolar mucosa* (lining mucosa) from which the gingiva is separated by a usually easily recognizable borderline called

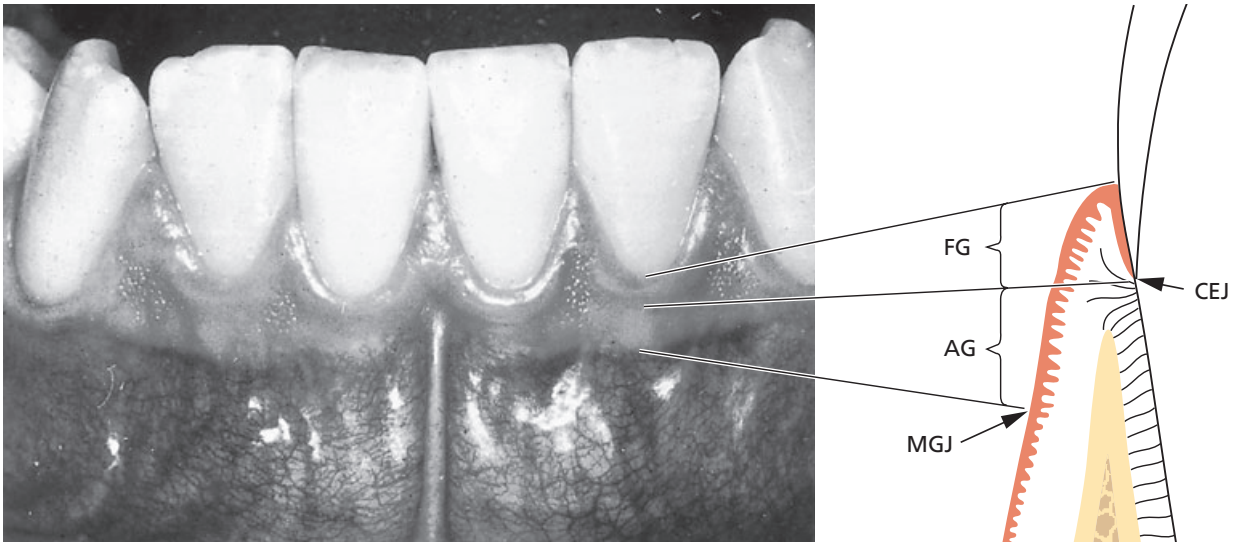


Fig. 1-6

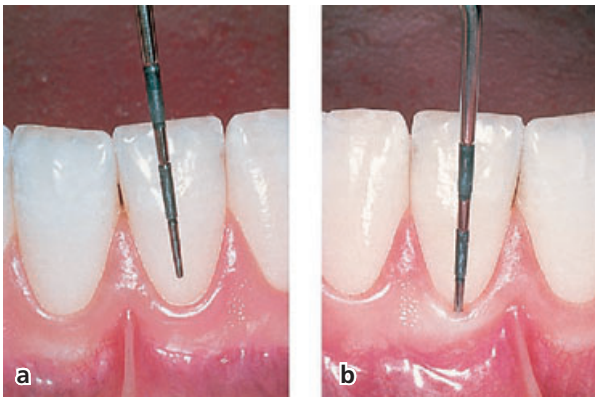


Fig. 1-7

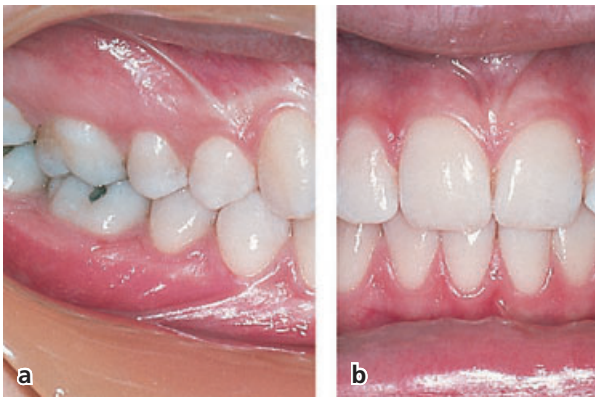


Fig. 1-8

either the mucogingival junction (arrows) or the mucogingival line.

Fig. 1-5 There is no mucogingival line present in the palate since the hard palate and the maxillary alveolar process are covered by the same type of masticatory mucosa.

Fig. 1-6 Two parts of the gingiva can be differentiated:

1. The free gingiva (FG)
2. The attached gingiva (AG).

The free gingiva is coral pink, has a dull surface and firm consistency. It comprises the gingival tissue at the vestibular and lingual/palatal aspects of the teeth, and the *interdental gingiva* or the *interdental papillae*. On the vestibular and lingual side of the teeth, the free gingiva extends from the gingival margin in apical direction to the *free gingival groove* which is positioned at a level corresponding to the level of the *cemento-enamel junction* (CEJ). The attached gingiva is demarcated by the mucogingival junction (MGJ) in the apical direction.

Fig. 1-7 The free gingival margin is often rounded in such a way that a small invagination or sulcus is formed between the tooth and the gingiva (Fig. 1-7a).

When a periodontal probe is inserted into this invagination and, further apically, towards the cemento-enamel junction, the gingival tissue is separated from the tooth, and a "*gingival pocket*" or "*gingival crevice*" is artificially opened. Thus, in normal or clinically healthy gingiva there is in fact no "gingival pocket" or "gingival crevice" present but the gingiva is in close contact with the enamel surface. In the illustration to the right (Fig. 1-7b), a periodontal probe has been inserted in the tooth/gingiva interface and a "gingival crevice" artificially opened approximately to the level of the cemento-enamel junction.

After completed tooth eruption, the free gingival margin is located on the enamel surface approximately 1.5–2 mm coronal to the cemento-enamel junction.

Fig. 1-8 The shape of the interdental gingiva (the interdental papilla) is determined by the contact relationships between the teeth, the width of the approximal tooth surfaces, and the course of the cemento-enamel junction. In anterior regions of the

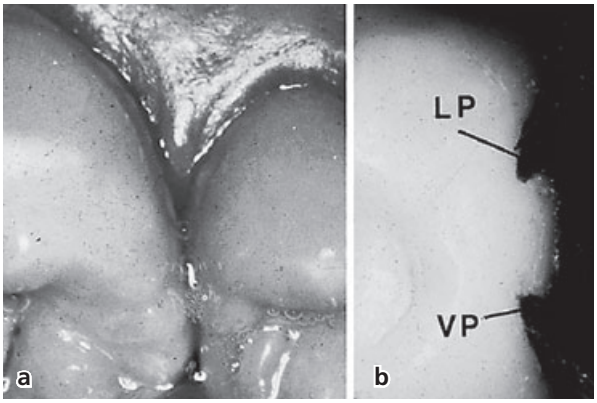


Fig. 1-9

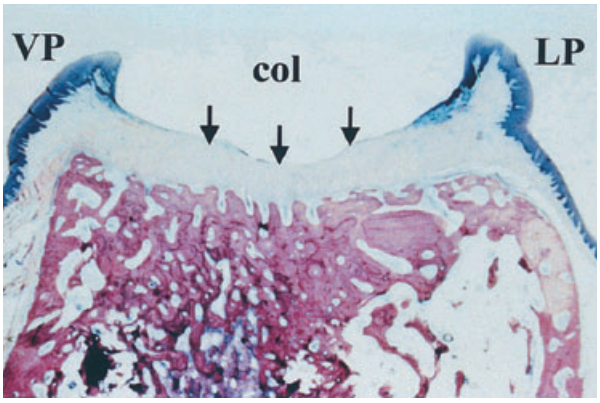


Fig. 1-9c

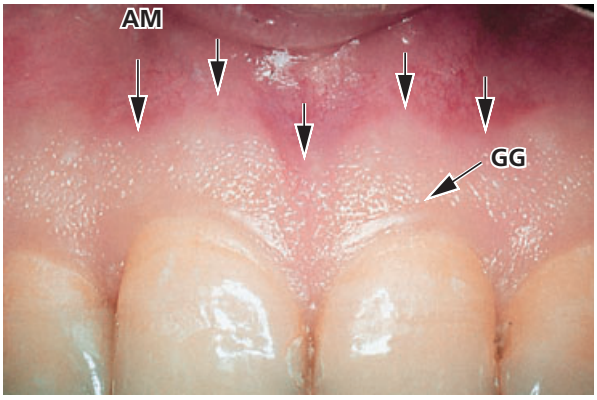


Fig. 1-10

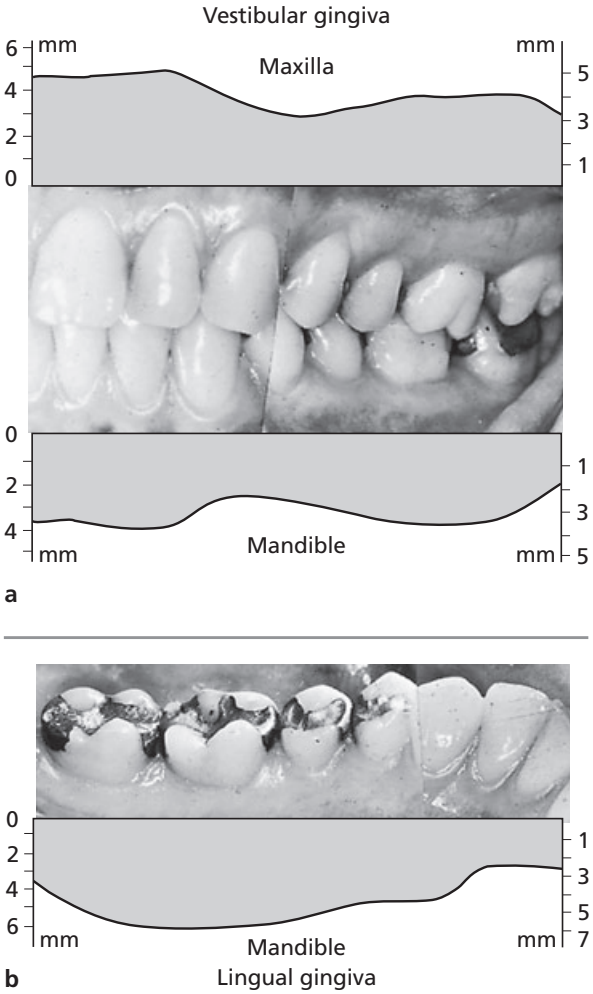


Fig. 1-11

dentition, the interdental papilla is of pyramidal form (Fig. 1-8b) while in the molar regions, the papillae are more flattened in the buccolingual direction (Fig. 1-8a). Due to the presence of interdental papillae, the free gingival margin follows a more or less accentuated, scalloped course through the dentition.

Fig. 1-9 In the premolar/molar regions of the dentition, the teeth have approximal contact surfaces (Fig. 1-9a) rather than contact points. Since the interdental papilla has a shape in conformity with the outline of the interdental contact surfaces, a concavity – *a col* – is established in the premolar and molar regions, as demonstrated in Fig. 1-9b, where the distal tooth has been removed. Thus, the interdental papillae in these areas often have one vestibular (VP) and one lingual/palatal portion (LP) separated by the col region. The col region, as demonstrated in the histological section (Fig. 1-9c), is covered by a thin non-keratinized epithelium (arrows). This epithelium has many features in common with the junctional epithelium (see Fig. 1-34).

Fig. 1-10 The attached gingiva is demarcated in the coronal direction, by the free gingival groove (GG) or, when such a groove is not present, by a horizontal plane placed at the level of the cemento-enamel junction. In clinical examinations it was observed that a free gingival groove is only present in about 30–40% of adults.

The free gingival groove is often most pronounced on the vestibular aspect of the teeth, occurring most frequently in the incisor and premolar regions of the mandible, and least frequently in the mandibular molar and maxillary premolar regions.

The attached gingiva extends in the apical direction to the mucogingival junction (arrows), where it becomes continuous with the alveolar (lining) mucosa (AM). It is of firm texture, coral pink in color, and often shows small depressions on the surface. The depressions, named “stippling”, give the appearance

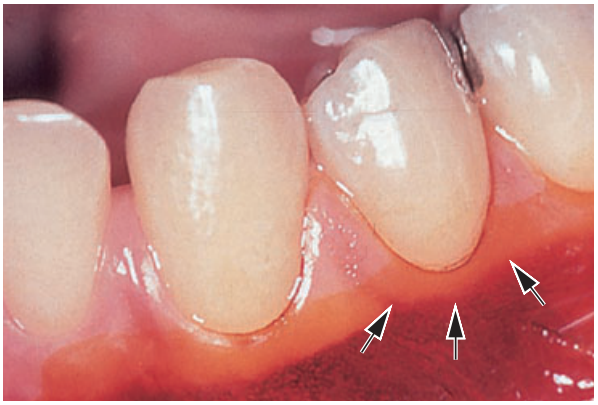


Fig. 1-12

of orange peel. It is firmly attached to the underlying alveolar bone and cementum by connective tissue fibers, and is, therefore, comparatively immobile in relation to the underlying tissue. The darker red alveolar mucosa (AM) located apical to the mucogingival junction, on the other hand, is loosely bound to the underlying bone. Therefore, in contrast to the attached gingiva, the alveolar mucosa is mobile in relation to the underlying tissue.

Fig. 1-11 describes how the width of the gingiva varies in different parts of the mouth. In the maxilla (Fig. 1-11a) the vestibular gingiva is generally widest in the area of the incisors and most narrow adjacent to the premolars. In the mandible (Fig. 1-11b) the gingiva on the lingual aspect is particularly narrow in the area of the incisors and wide in the molar region. The range of variation is 1–9 mm.

Fig. 1-12 illustrates an area in the mandibular premolar region where the gingiva is extremely narrow. The arrows indicate the location of the mucogingival junction. The mucosa has been stained with an iodine solution in order to distinguish more accurately between the gingiva and the alveolar mucosa.

Fig. 1-13 depicts the result of a study in which the width of the attached gingiva was assessed and related to the age of the patients examined. It was found that the gingiva in 40–50-year-olds was significantly wider than that in 20–30-year-olds. This observation indicates that the width of the gingiva tends to increase with age. Since the mucogingival junction remains stable throughout life in relation to the lower border of the mandible, the increasing width of the gingiva may suggest that the teeth, as a result of occlusal wear, erupt slowly throughout life.

Microscopic anatomy

Oral epithelium

Fig. 1-14a A schematic drawing of a histologic section (see Fig. 1-14b) describing the composition of the

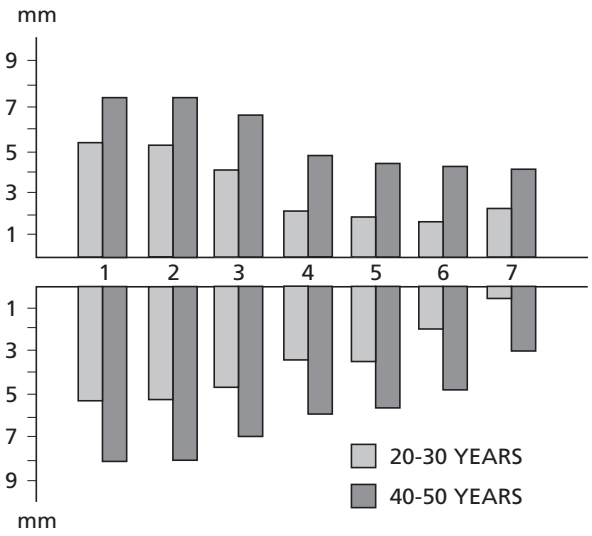


Fig. 1-13

gingiva and the contact area between the gingiva and the enamel (E).

Fig 1-14b The free gingiva comprises all epithelial and connective tissue structures (CT) located coronal to a horizontal line placed at the level of the cemento-enamel junction (CEJ). The epithelium covering the free gingiva may be differentiated as follows:

- *Oral epithelium* (OE), which faces the oral cavity
- *Oral sulcular epithelium* (OSE), which faces the tooth without being in contact with the tooth surface
- *Junctional epithelium* (JE), which provides the contact between the gingiva and the tooth.

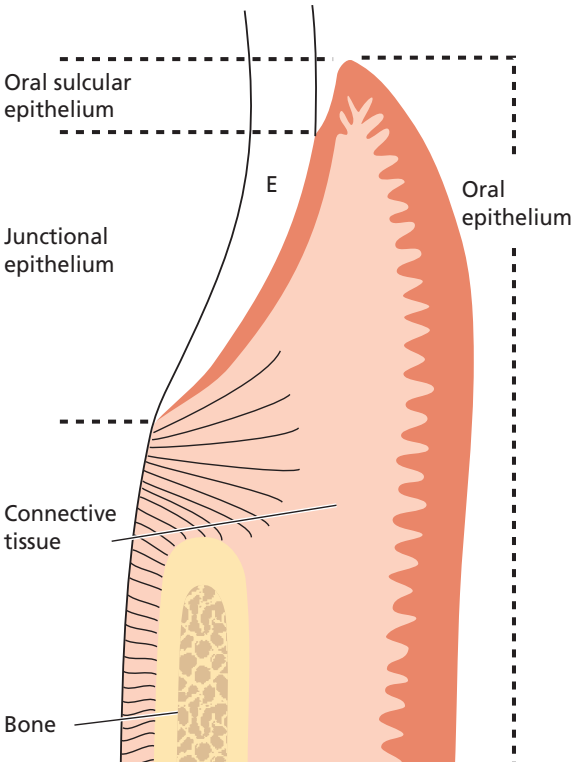


Fig. 1-14a

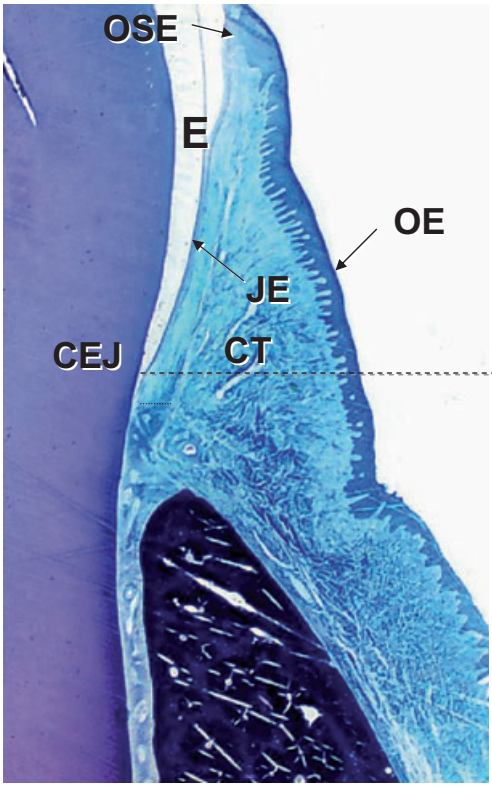


Fig. 1-14b

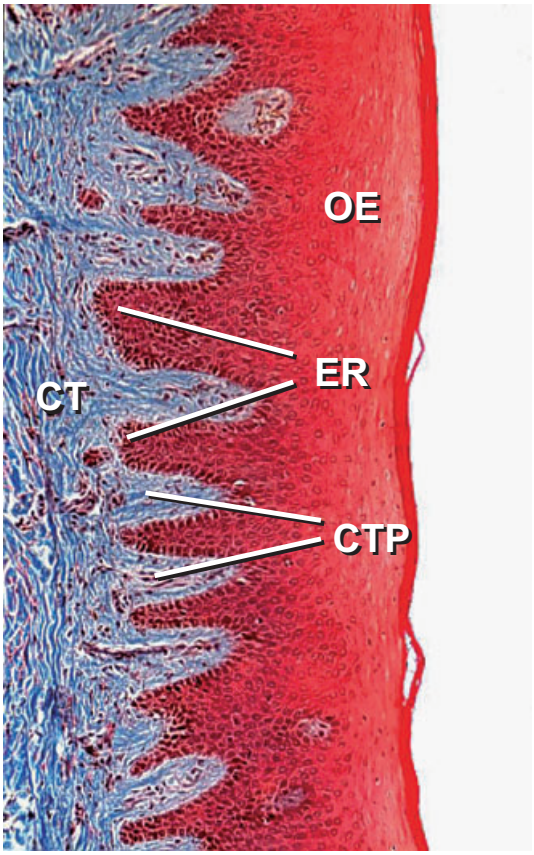


Fig. 1-14c

Fig. 1-15

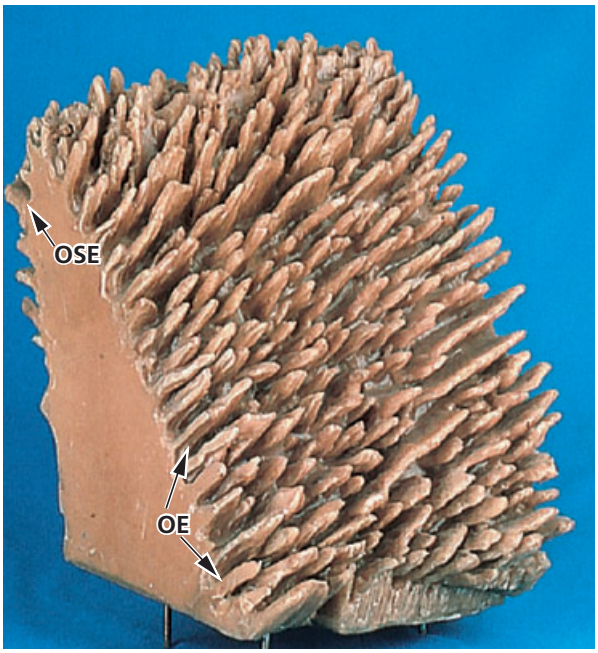
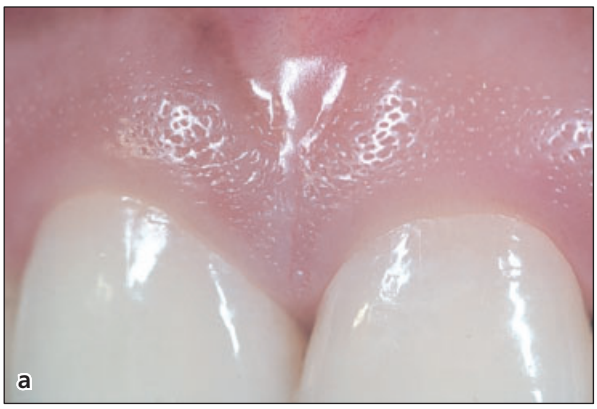
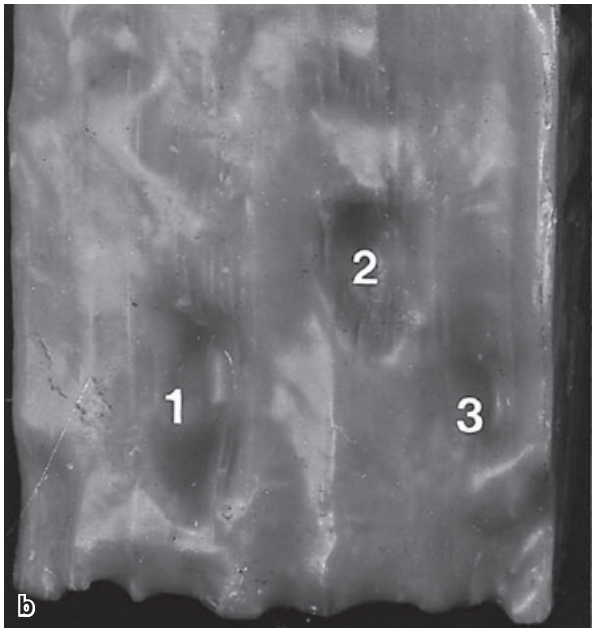


Fig. 1-16

Fig. 1-14c The boundary between the oral epithelium (OE) and underlying connective tissue (CT) has a wavy course. The connective tissue portions which project into the epithelium are called *connective tissue papillae* (CTP) and are separated from each other by





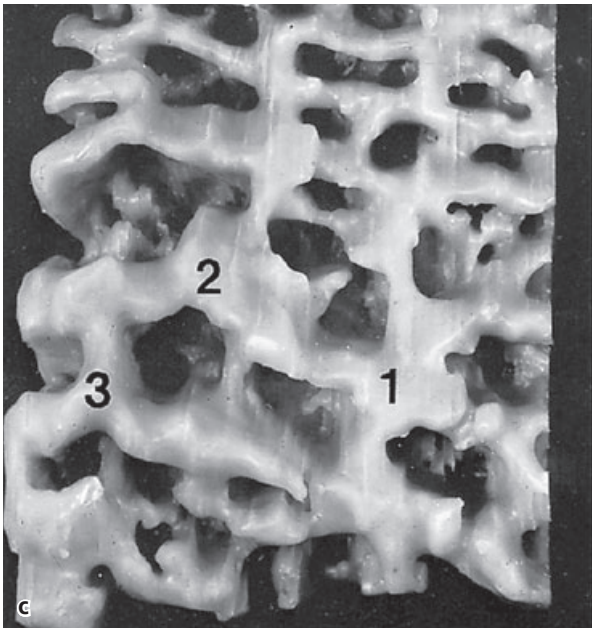


Fig. 1-17

epithelial ridges – so-called *rete pegs* (ER). In normal, non-inflamed gingiva, rete pegs and connective tissue papillae are lacking at the boundary between the junctional epithelium and its underlying connective tissue (Fig. 1-14b). Thus, a characteristic morphologic feature of the oral epithelium and the oral sulcular epithelium is the presence of rete pegs, while these structures are lacking in the junctional epithelium.

Fig. 1-15 presents a model, constructed on the basis of magnified serial histologic sections, showing the subsurface of the oral epithelium of the gingiva after the connective tissue has been removed. The subsurface of the oral epithelium (i.e. the surface of the epithelium facing the connective tissue) exhibits several depressions corresponding to the connective tissue papillae (in Fig. 1-16) which project into the epithelium. It can be seen that the epithelial projections, which in histologic sections separate the connective tissue papillae, constitute a continuous system of epithelial ridges.

Fig. 1-16 presents a model of the connective tissue, corresponding to the model of the epithelium shown in Fig. 1-15. The epithelium has been removed, thereby making the vestibular aspect of the gingival connective tissue visible. Notice the connective tissue papillae which project into the space that was occupied by the oral epithelium (OE) in Fig. 1-15 and by the oral sulcular epithelium (OSE) on the back of the model.

Fig. 1-17a In 40% of adults the attached gingiva shows a stippling on the surface. The photograph shows a case where this stippling is conspicuous (see also Fig. 1-10).

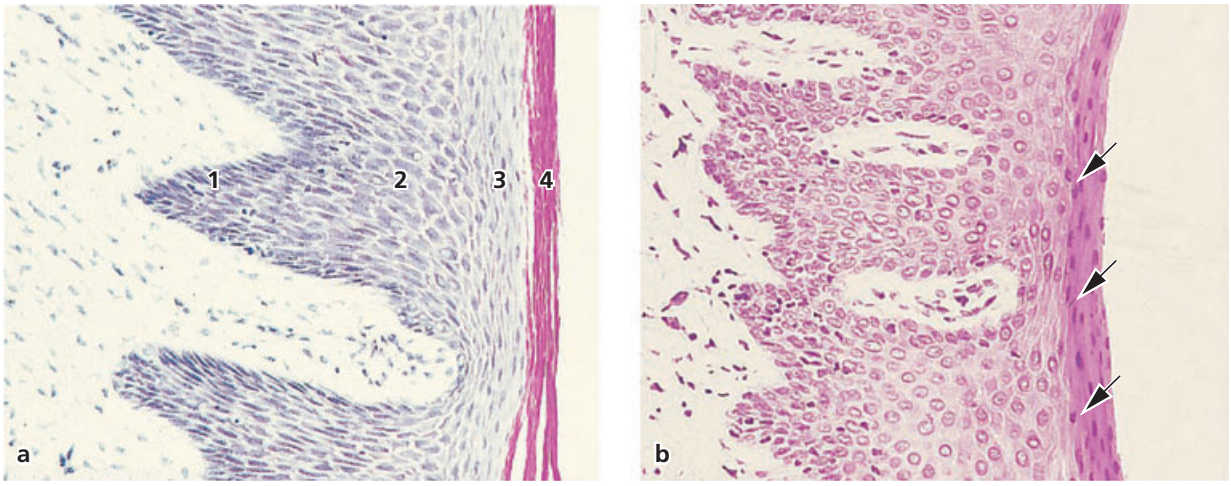


Fig. 1-18

Fig. 1-17b presents a magnified model of the outer surface of the oral epithelium of the attached gingiva. The surface exhibits the minute depressions (1–3) which, when present, give the gingiva its characteristic stippled appearance.

Fig. 1-17c shows a photograph of the subsurface (i.e. the surface of the epithelium facing the connective tissue) of the same model as that shown in Fig. 1-17b. The subsurface of the epithelium is characterized by the presence of epithelial ridges which merge at various locations (1–3). The depressions (1–3) seen on the outer surface of the epithelium (shown in Fig. 1-17b) correspond with the fusion sites (1–3) between epithelial ridges. Thus, the depressions on the surface of the gingiva occur in the areas of fusion between various epithelial ridges.

Fig. 1-18 (a) A portion of the oral epithelium covering the free gingiva is illustrated in this photomicrograph. The oral epithelium is a *keratinized*, *stratified*, *squamous epithelium* which, on the basis of the degree to which the keratin-producing cells are differentiated, can be divided into the following cell layers:

1. *Basal layer* (stratum basale or stratum germinativum)
2. *Prickle cell layer* (stratum spinosum)
3. *Granular cell layer* (stratum granulosum)
4. *Keratinized cell layer* (stratum corneum).

It should be observed that in this section, cell nuclei are lacking in the outer cell layers. Such an epithelium is denoted *orthokeratinized*. Often, however, the cells of the stratum corneum of the epithelium of human gingiva contain remnants of the nuclei (arrows) as seen in Fig. 1-18b. In such a case, the epithelium is denoted *parakeratinized*.

Fig. 1-19 In addition to the keratin-producing cells which comprise about 90% of the total cell population, the oral epithelium contains the following types of cell:

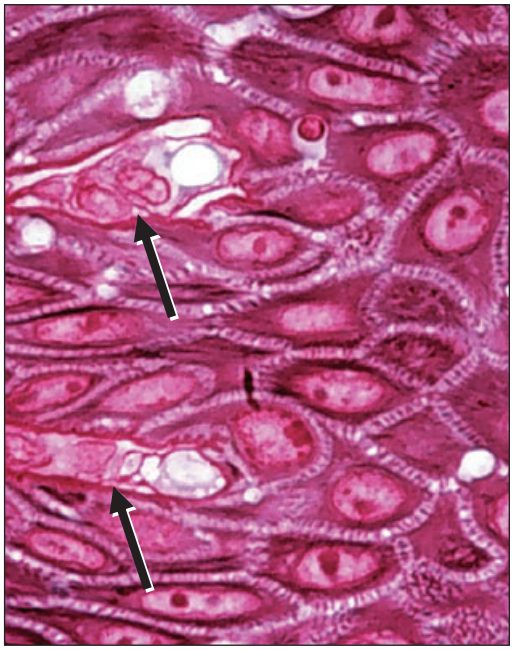


Fig. 1-19

- *Melanocytes*
- *Langerhans cells*
- *Merkel's cells*
- *Inflammatory cells.*

These cell types are often stellate and have cytoplasmic extensions of various size and appearance. They are also called "clear cells" since in histologic sections, the zone around their nuclei appears lighter than that in the surrounding keratin-producing cells.

The photomicrograph shows "clear cells" (arrows) located in or near the stratum basale of the oral epithelium. Except the Merkel's cells, these "clear cells", which do not produce keratin, lack desmosomal attachment to adjacent cells. The melanocytes are

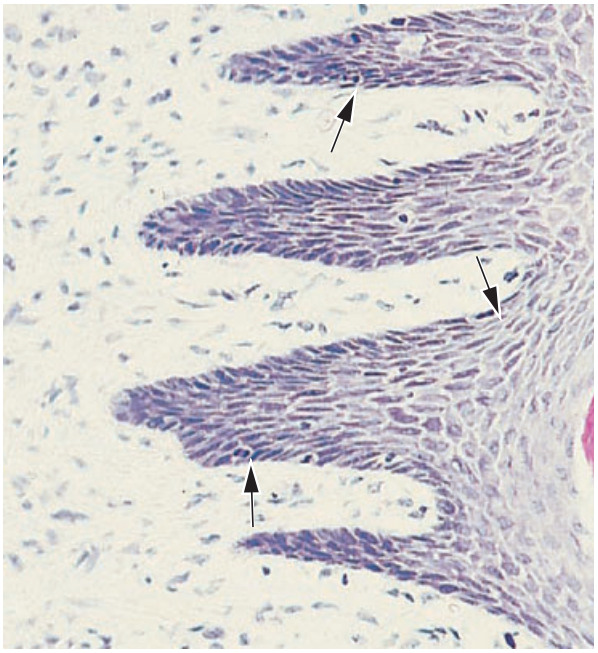


Fig. 1-20

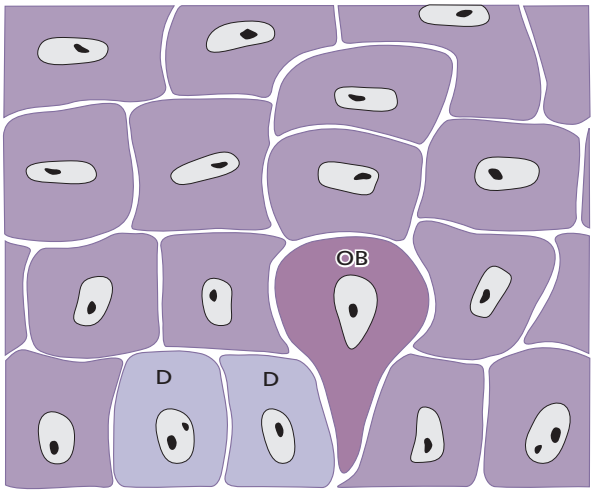


Fig. 1-21

pigment-synthesizing cells and are responsible for the melanin pigmentation occasionally seen on the gingiva. However, both lightly and darkly pigmented individuals present melanocytes in the epithelium.

The Langerhans cells are believed to play a role in the defense mechanism of the oral mucosa. It has been suggested that the Langerhans cells react with antigens which are in the process of penetrating the epithelium. An early immunologic response is thereby initiated, inhibiting or preventing further antigen penetration of the tissue. The Merkel's cells have been suggested to have a sensory function.

Fig. 1-20 The cells in the basal layer are either cylindric or cuboid, and are in contact with the *basement membrane* that separates the epithelium and the connective tissue. The basal cells possess the ability to divide, i.e. undergo mitotic cell division. The cells marked with arrows in the photomicrograph are in the process of dividing. It is in the basal layer that the epithelium is renewed. Therefore, this layer is also termed *stratum germinativum*, and can be considered the *progenitor cell compartment* of the epithelium.

Fig. 1-21 When two daughter cells (D) have been formed by cell division, an adjacent "older" basal cell (OB) is pushed into the spinous cell layer and starts, as a *keratinocyte*, to traverse the epithelium. It takes approximately 1 month for a keratinocyte to reach the outer epithelial surface, where it becomes shed from the stratum corneum. Within a given time, the number of cells which divide in the basal layer equals the number of cells which become shed from the surface. Thus, under normal conditions there is complete equilibrium between cell renewal and cell loss so that the epithelium maintains a constant thickness. As the basal cell migrates through the epithelium, it becomes flattened with its long axis parallel to the epithelial surface.

Fig. 1-22 The basal cells are found immediately adjacent to the connective tissue and are separated from this tissue by the basement membrane, probably produced by the basal cells. Under the light microscope this membrane appears as a structureless zone approximately 1–2 µm wide (arrows) which reacts positively to a PAS stain (periodic acid-Schiff stain). This positive reaction demonstrates that the basement membrane contains carbohydrate (glycoproteins). The epithelial cells are surrounded by an extracellular substance which also contains protein–polysaccharide complexes. At the ultrastructural level, the basement membrane has a complex composition.

Fig. 1-23 is an electronmicrograph (magnification ×70 000) of an area including part of a basal cell, the basement membrane, and part of the adjacent connective tissue. The basal cell (BC) occupies the upper portion of the picture. Immediately beneath the basal cell an approximately 400 Å wide electron-lucent zone can be seen which is called *lamina lucida* (LL). Beneath the lamina lucida an electron-dense zone of approximately the same thickness can be observed. This zone is called *lamina densa* (LD). From the lamina densa so-called *anchoring fibers* (AF) project in a fan-shaped fashion into the connective tissue. The anchoring fibers are approximately 1 µm in length and terminate freely in the connective tissue. The basement membrane, which appeared as an entity under the light microscope, thus, in the electronmicrograph, appears to comprise one lamina lucida and one lamina densa with adjacent connective tissue fibers (anchoring fibers). The cell membrane of the epithelial cells facing the lamina lucida harbors a number of electron-dense, thicker zones appearing at various intervals along the cell membrane. These structures are called *hemidesmosomes* (HD). The cytoplasmic

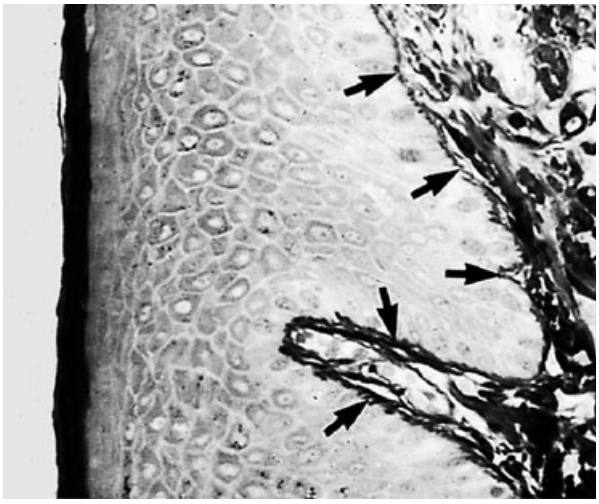


Fig. 1-22

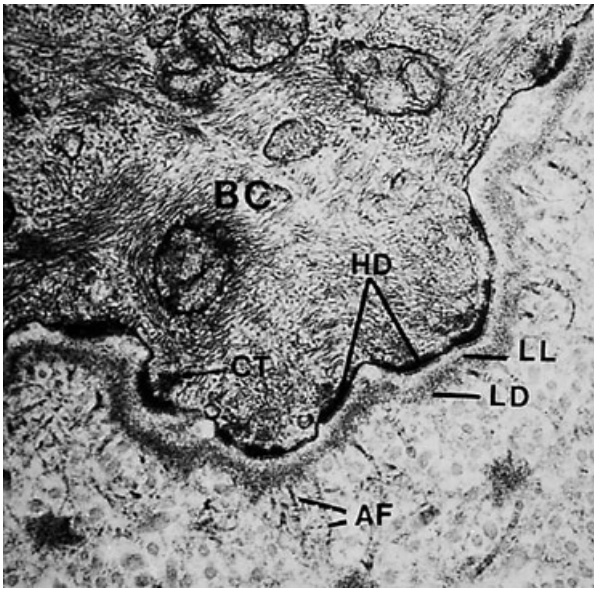


Fig. 1-23

tonofilaments (CT) in the cell converge towards the hemidesmosomes. The hemidesmosomes are involved in the attachment of the epithelium to the underlying basement membrane.

Fig. 1-24 illustrates an area of stratum spinosum in the gingival oral epithelium. Stratum spinosum consists of 10–20 layers of relatively large, polyhedral cells, equipped with short cytoplasmic processes resembling spines. The cytoplasmic processes (arrows) occur at regular intervals and give the cells a prickly appearance. Together with intercellular protein–carbohydrate complexes, cohesion between the cells is provided by numerous "desmosomes" (pairs of hemidesmosomes) which are located between the cytoplasmic processes of adjacent cells.

Fig. 1-25 shows an area of stratum spinosum in an electronmicrograph. The dark-stained structures between the individual epithelial cells represent the *desmosomes* (arrows). A desmosome may be considered to be two hemidesmosomes facing one another. The presence of a large number of desmosomes indicates that the cohesion between the epithelial cells is solid. The light cell (LC) in the center of the illustration harbors no hemidesmosomes and is, therefore, not a keratinocyte but rather a "clear cell" (see also Fig. 1-19).

Fig. 1-26 is a schematic drawing describing the composition of a desmosome. A desmosome can be

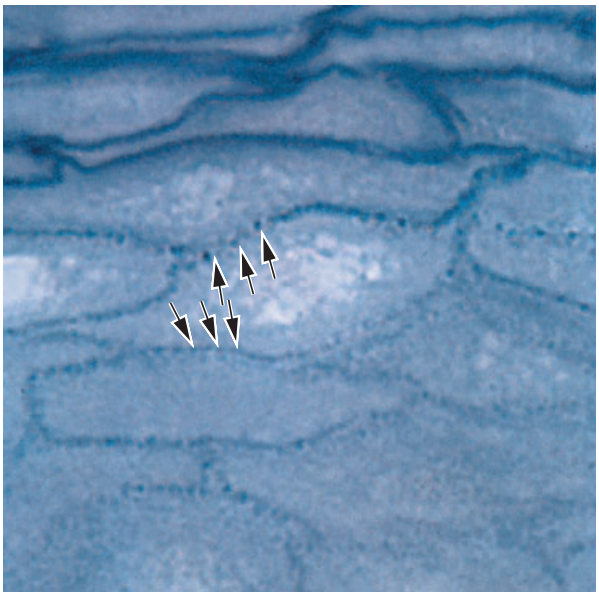


Fig. 1-24

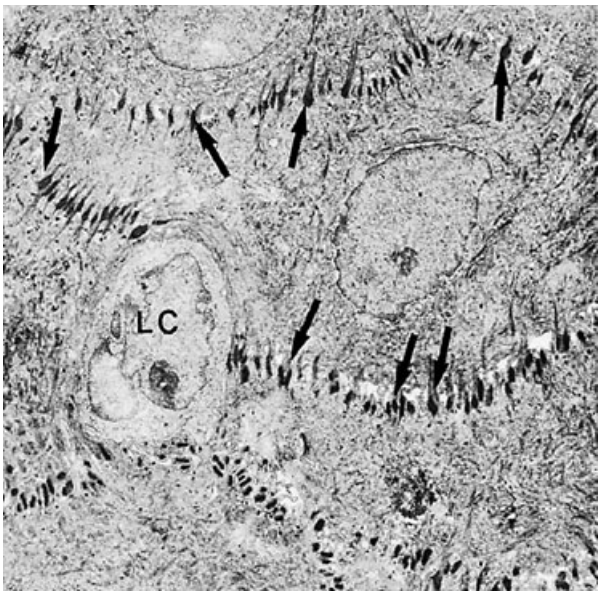


Fig. 1-25

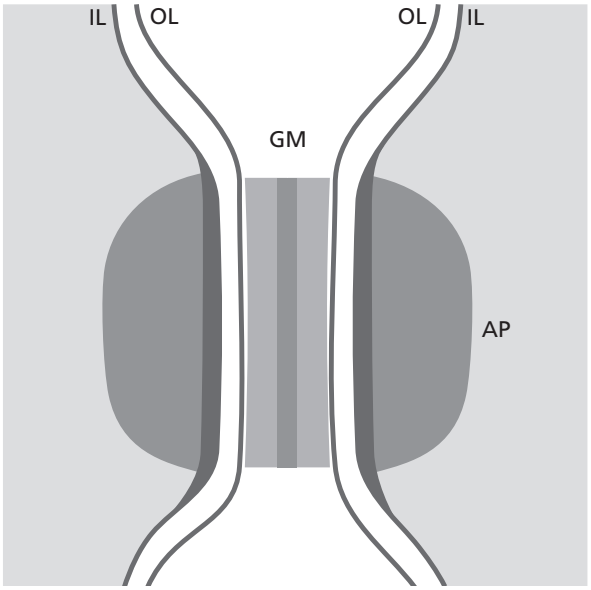


Fig. 1-26

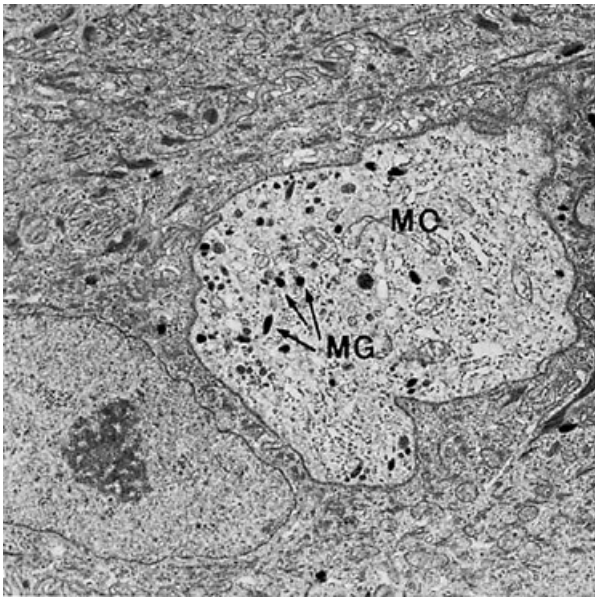


Fig. 1-27

considered to consist of two adjoining hemidesmosomes separated by a zone containing electron-dense granulated material (GM). Thus, a desmosome comprises the following structural components: (1) the *outer leaflets* (OL) of the cell membrane of two adjoining cells, (2) the thick *inner leaflets* (IL) of the cell membranes and (3) the *attachment plaques* (AP), which represent granular and fibrillar material in the cytoplasm.

Fig. 1-27 As mentioned previously, the oral epithelium also contains melanocytes, which are responsible for the production of the pigment melanin. Melanocytes are present in individuals with marked pigmentation of the oral mucosa as well as in individuals where no clinical signs of pigmentation can be seen. In this electronmicrograph a melanocyte (MC) is present in the lower portion of the stratum spinosum. In contrast to the keratinocytes, this cell contains melanin granules (MG) and has no tonofilaments or hemidesmosomes. Note the large amount of tonofilaments in the cytoplasm of the adjacent keratinocytes.

Fig. 1-28 When traversing the epithelium from the basal layer to the epithelial surface, the keratinocytes undergo continuous differentiation and specialization. The many changes which occur during this process are indicated in this diagram of a keratinized stratified squamous epithelium. From the basal layer (stratum basale) to the granular layer (stratum granulosum) both the number of tonofilaments (F) in the cytoplasm and the number of desmosomes (D) increase. In contrast, the number of organelles, such as mitochondria (M), lamellae of rough endoplasmic reticulum (E) and Golgi complexes (G), decrease in the keratinocytes on their way from the basal layer towards the surface. In the stratum granulosum, electron-dense *keratohyalin bodies* (K) and clusters of

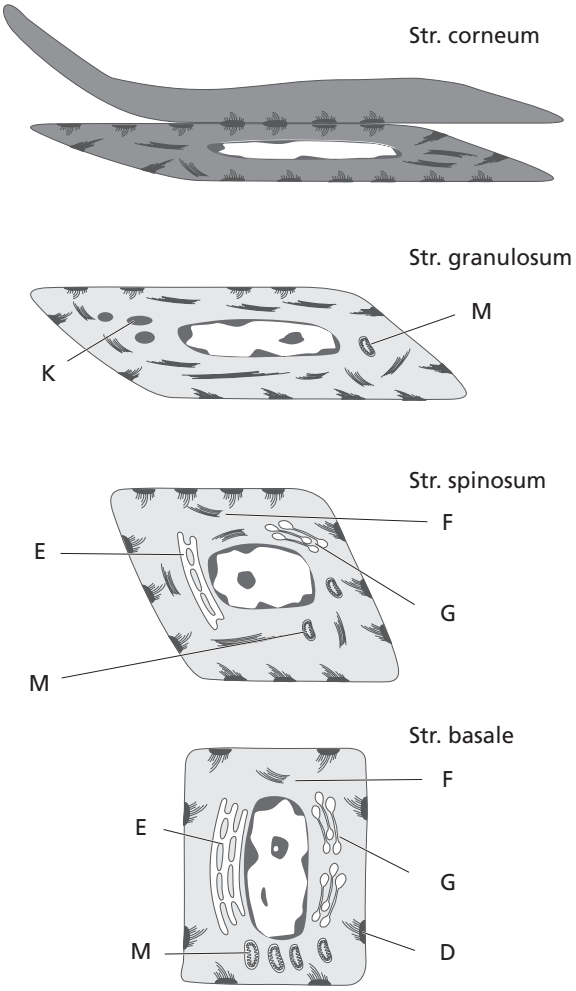


Fig. 1-28

glycogen-containing granules start to occur. Such granules are believed to be related to the synthesis of keratin.

Fig. 1-29 is a photomicrograph of the stratum granulosum and stratum corneum. Keratohyalin granules (arrows) are seen in the stratum granulosum. There is an abrupt transition of the cells from the stratum granulosum to the stratum corneum. This is indicative of a very sudden keratinization of the cytoplasm of the keratinocyte and its conversion into a horny squame. The cytoplasm of the cells in the stratum corneum (SC) is filled with keratin and the entire apparatus for protein synthesis and energy production, i.e. the nucleus, the mitochondria, the endoplasmic reticulum, and the Golgi complex, is lost. In a parakeratinized epithelium, however, the cells of the stratum corneum contain remnants of nuclei. Keratinization is considered a process of differentiation rather than degeneration. It is a process of protein synthesis which requires energy and is dependent on functional cells, i.e. cells containing a nucleus and a normal set of organelles.

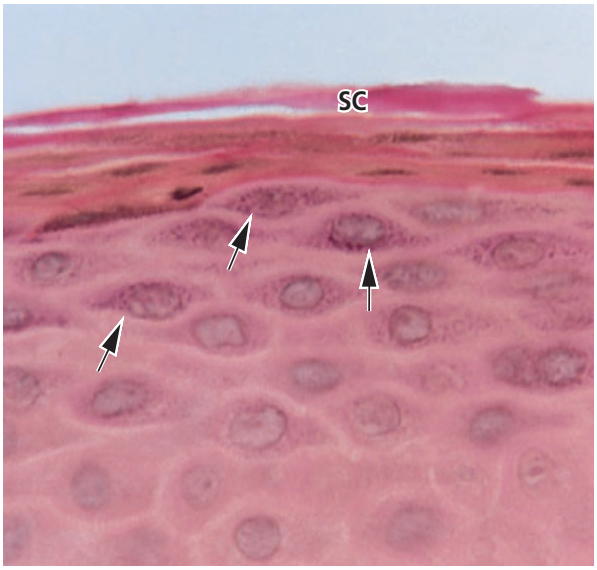


Fig. 1-29

Summary: The keratinocyte undergoes continuous differentiation on its way from the basal layer to the surface of the epithelium. Thus, once the keratinocyte has left the basement membrane it can no longer divide but maintains a capacity for production of protein (tonofilaments and keratohyalin granules). In the granular layer, the keratinocyte is deprived of its energy- and protein-producing apparatus (probably by enzymatic breakdown) and is abruptly converted into a keratin-filled cell which, via the stratum corneum, is shed from the epithelial surface.

Fig. 1-30 illustrates a portion of the epithelium of the alveolar (lining) mucosa. In contrast to the epithelium of the gingiva, the lining mucosa has no stratum corneum. Notice that cells containing nuclei can be identified in all layers, from the basal layer to the surface of the epithelium.

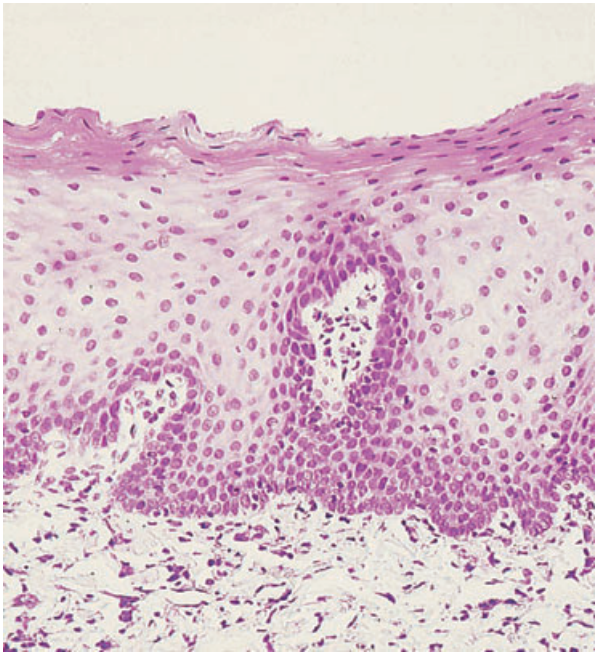


Fig. 1-30

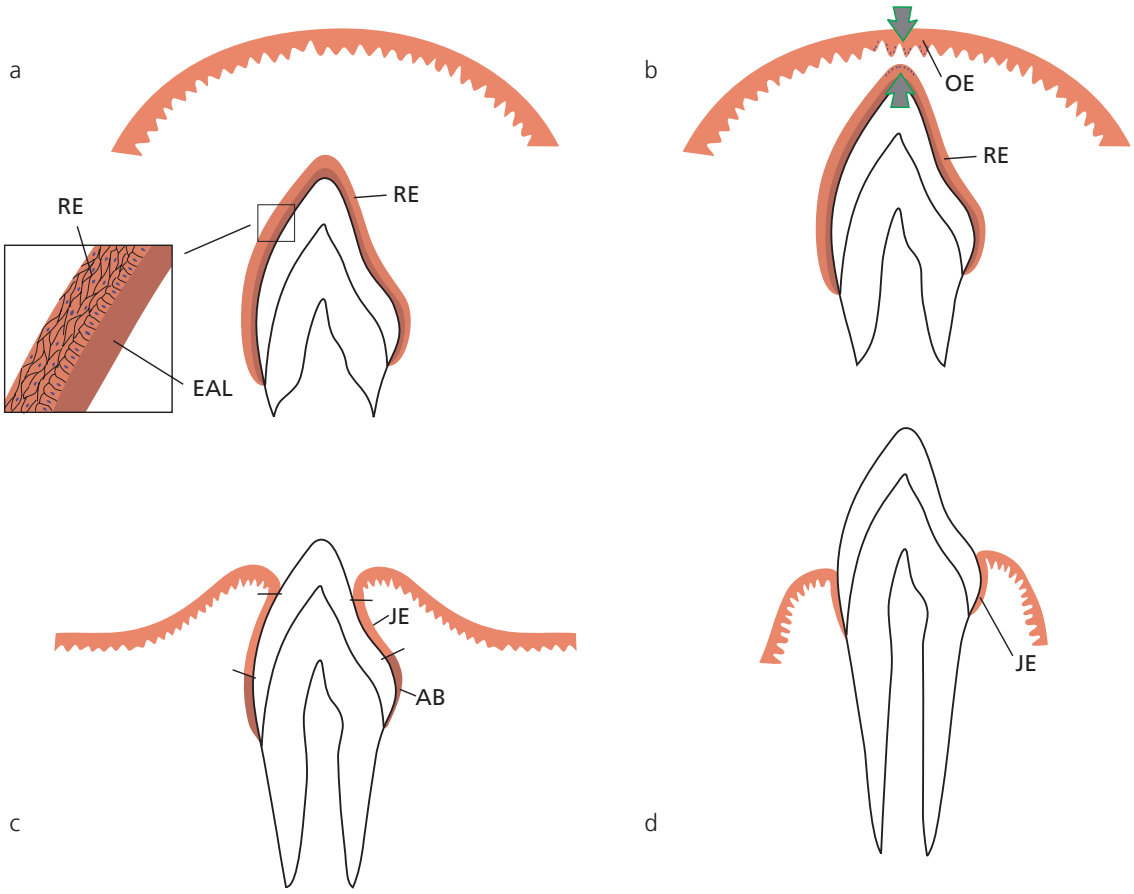


Fig. 1-31

Dento-gingival epithelium

The tissue components of the dento-gingival region achieve their final structural characteristics in conjunction with the eruption of the teeth. This is illustrated in Fig. 1-31a–d.

Fig. 1-31a When the enamel of the tooth is fully developed, the enamel-producing cells (ameloblasts) become reduced in height, produce a basal lamina and form, together with cells from the outer enamel epithelium, the so-called reduced dental epithelium (RE). The basal lamina (epithelial attachment lamina: EAL) lies in direct contact with the enamel. The contact between this lamina and the epithelial cells is maintained by hemidesmosomes. The reduced enamel epithelium surrounds the crown of the tooth from the moment the enamel is properly mineralized until the tooth starts to erupt.

Fig. 1-31b As the erupting tooth approaches the oral epithelium, the cells of the outer layer of the reduced dental epithelium (RE), as well as the cells of the basal layer of the oral epithelium (OE), show increased mitotic activity (arrows) and start to migrate into the underlying connective tissue. The migrating epithelium produces an epithelial mass between the oral epithelium and the reduced dental epithelium so that the tooth can erupt without bleeding. The former ameloblasts do not divide.

Fig. 1-31c When the tooth has penetrated into the oral cavity, large portions immediately apical to the incisal area of the enamel are covered by a junctional epithelium (JE) containing only a few layers of cells. The cervical region of the enamel, however, is still covered by ameloblasts (AB) and outer cells of the reduced dental epithelium.

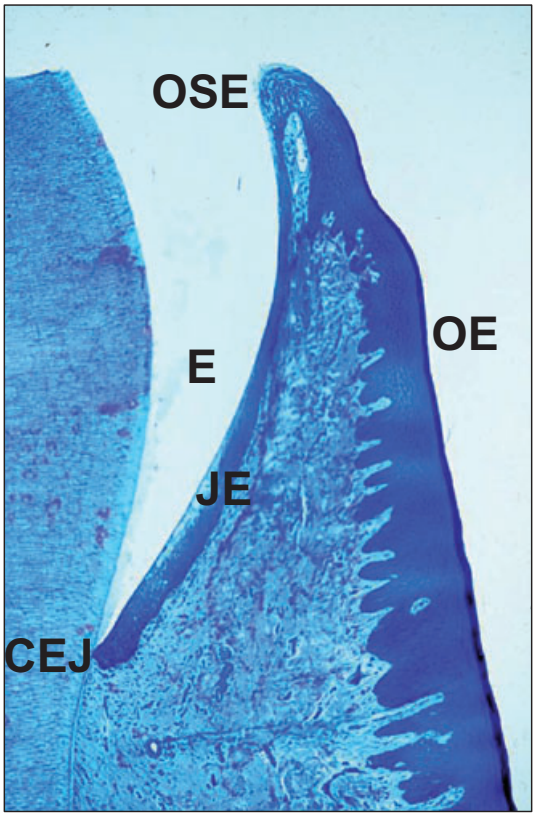


Fig. 1-32

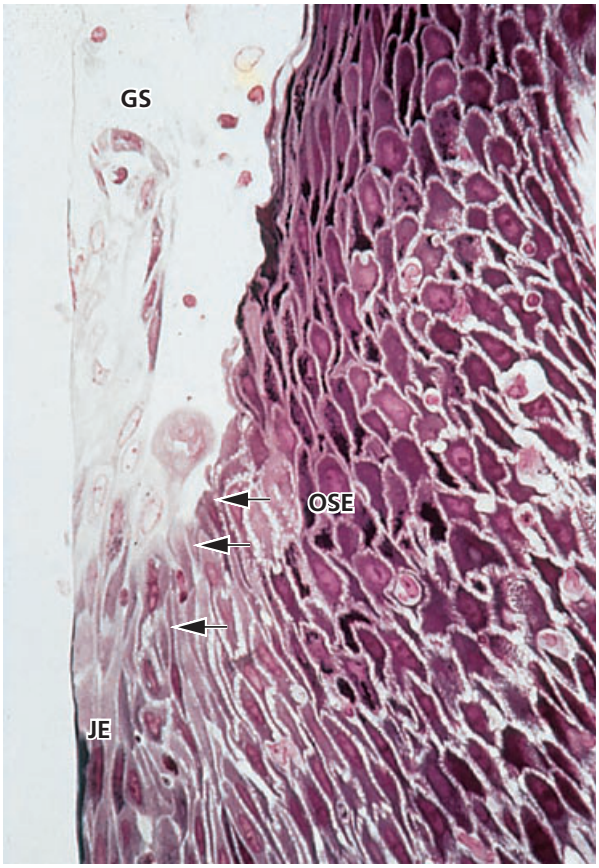


Fig. 1-33

Fig. 1-31d During the later phases of tooth eruption, all cells of the reduced enamel epithelium are replaced by a junctional epithelium. This epithelium is continuous with the oral epithelium and provides the attachment between the tooth and the gingiva. If the free gingiva is excised after the tooth has fully erupted, a new junctional epithelium, indistinguishable from that found following tooth eruption, will develop during healing. The fact that this new junctional epithelium has developed from the oral epithelium indicates that the cells of the oral epithelium possess the ability to differentiate into cells of junctional epithelium.

Fig. 1-32 is a histologic section cut through the border area between the tooth and the gingiva, i.e. the *dentogingival region*. The enamel (E) is to the left. To the right are the *junctional epithelium* (JE), the *oral sulcular epithelium* (OSE), and the *oral epithelium* (OE). The oral sulcular epithelium covers the shallow groove, the gingival sulcus, located between the enamel and the top of the free gingiva. The junctional epithelium differs morphologically from the oral sulcular epithelium and oral epithelium, while the two latter are structurally very similar. Although individual variation may occur, the junctional epithelium is usually widest in its coronal portion (about 15–20 cell layers), but becomes thinner (3–4 cells) towards the cementoenamel junction (CEJ). The borderline between the junctional epithelium and the underlying connective tissue does not present epithelial rete pegs except when inflamed.

Fig. 1-33 The junctional epithelium has a free surface at the bottom of the *gingival sulcus* (GS). Like the oral sulcular epithelium and the oral epithelium, the junctional epithelium is continuously renewed through cell division in the basal layer. The cells migrate to the base of the gingival sulcus from where they are shed. The border between the junctional epithelium (JE) and the oral sulcular epithelium (OSE) is indicated by arrows. The cells of the oral sulcular epithelium are cuboidal and the surface of this epithelium is keratinized.

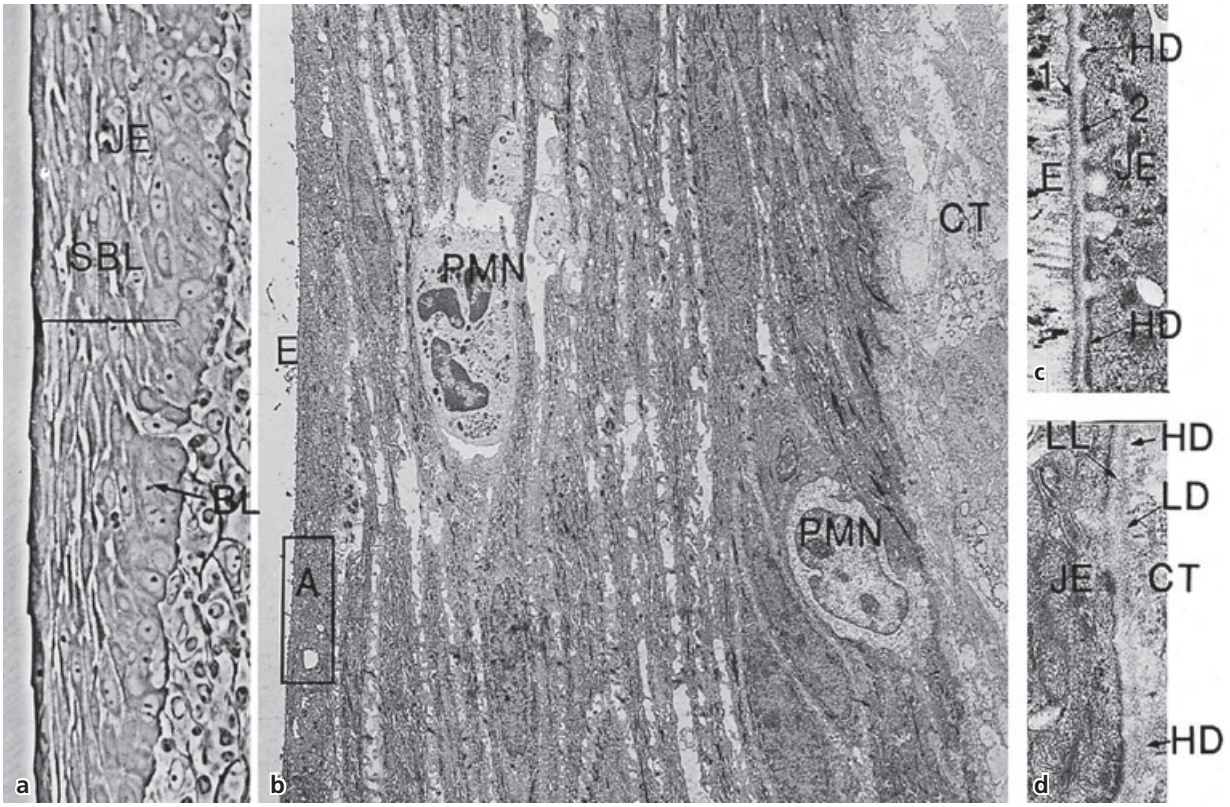


Fig. 1-34

Fig. 1-34 illustrates different characteristics of the junctional epithelium. As can be seen in Fig. 1-34a, the cells of the junctional epithelium (JE) are arranged into one basal layer (BL) and several suprabasal layers (SBL). Fig. 1-34b demonstrates that the basal cells as well as the suprabasal cells are flattened with their long axis parallel to the tooth surface. (CT = connective tissue, E = enamel space.)

There are distinct differences between the oral sulcular epithelium, the oral epithelium and the junctional epithelium:

1. The size of the cells in the junctional epithelium is, relative to the tissue volume, larger than in the oral epithelium.
2. The intercellular space in the junctional epithelium is, relative to the tissue volume, comparatively wider than in the oral epithelium.
3. The number of desmosomes is smaller in the junctional epithelium than in the oral epithelium.

Note the comparatively wide intercellular spaces between the oblong cells of the junctional epithelium, and the presence of two neutrophilic granulocytes (PMN) which are traversing the epithelium.

The framed area (A) is shown in a higher magnification in Fig. 1-34c, from which it can be seen that the basal cells of the junctional epithelium are not in direct contact with the enamel (E). Between the enamel and the epithelium (JE) one electron-dense zone (1) and one electron-lucent zone (2) can be seen. The electron-lucent zone is in contact with the cells of the junctional epithelium (JE). These two zones have a structure very similar to that of the lamina densa (LD) and lamina lucida (LL) in the basement membrane area (i.e. the epithelium (JE)–connective tissue (CT) interface) described in Fig. 1-23. Furthermore, as seen in Fig. 1-34d, the cell membrane of the junctional epithelial cells harbors hemidesmosomes (HD) towards the enamel as it does towards the connective tissue. Thus, the interface between the enamel and the junctional epithelium is similar to the interface between the epithelium and the connective tissue.

Fig. 1-35 is a schematic drawing of the most apically positioned cell in the junctional epithelium. The enamel (E) is depicted to the left in the drawing. It can be seen that the electron-dense zone (1) between the junctional epithelium and the enamel can be considered a continuation of the lamina densa (LD) in the basement membrane of the connective tissue side. Similarly, the electron-lucent zone (2) can be considered a continuation of the lamina lucida (LL). It should be noted, however, that at variance with the epithelium–connective tissue interface, there are no anchoring fibers (AF) attached to the lamina densa-like structure (1) adjacent to the enamel. On the other hand, like the basal cells adjacent to the basement membrane (at the connective tissue interface), the cells of the junctional epithelium facing the lamina lucida-like structure (2) harbor hemidesmosomes. Thus, the interface between the junctional epithelium and the enamel is structurally very similar to the

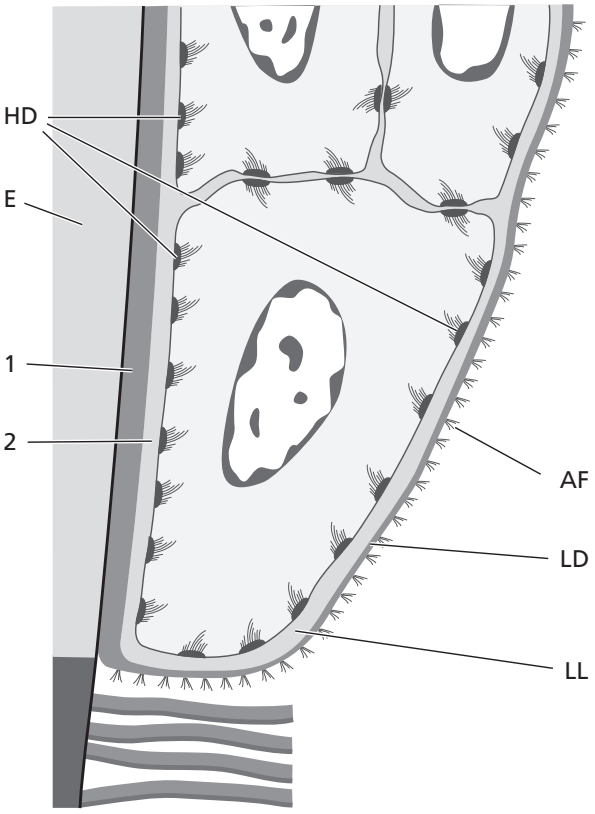


Fig. 1-35

epithelium–connective tissue interface, which means that the junctional epithelium is not only in contact with the enamel but is actually physically attached to the tooth via hemidesmosomes.

Lamina propria

The predominant tissue component of the gingiva is the connective tissue (lamina propria). The major components of the connective tissue are *collagen fibers* (around 60% of connective tissue volume), *fibroblasts* (around 5%), *vessels and nerves* (around 35%) which are embedded in an amorphous ground substance (matrix).

Fig. 1-36 The drawing illustrates a fibroblast (F) residing in a network of connective tissue fibers (CF). The intervening space is filled with matrix (M), which constitutes the "environment" for the cell.

Cells

The different types of cell present in the connective tissue are: (1) *fibroblasts*, (2) *mast cells*, (3) *macrophages*, and (4) *inflammatory cells*.

Fig. 1-37 The *fibroblast* is the predominant connective tissue cell (65% of the total cell population). The fibroblast is engaged in the production of various types of fibers found in the connective tissue, but is also instrumental in the synthesis of the connective tissue matrix. The fibroblast is a spindle-shaped or stellate cell with an oval-shaped nucleus containing one or

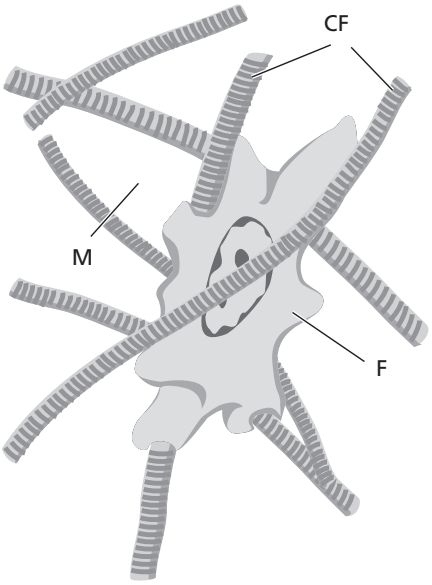


Fig. 1-36

more nucleoli. A part of a fibroblast is shown in electron microscopic magnification. The cytoplasm contains a well developed granular endoplasmic reticulum (E) with ribosomes. The Golgi complex (G) is usually of considerable size and the mitochondria (M) are large and numerous. Furthermore, the cytoplasm contains many fine tonofilaments (F). Adjacent to the cell membrane, all along the periphery of the cell, a large number of vesicles (V) can be found.

Fig. 1-38 The *mast cell* is responsible for the production of certain components of the matrix. This cell also produces vasoactive substances, which can affect the function of the microvascular system and control the flow of blood through the tissue. A mast cell is presented in electron microscopic magnification. The cytoplasm is characterized by the presence of a large number of vesicles (V) of varying size. These vesicles

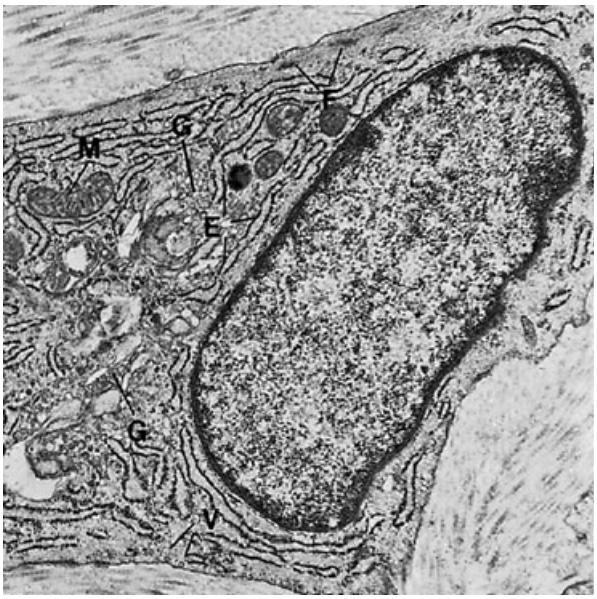


Fig. 1-37

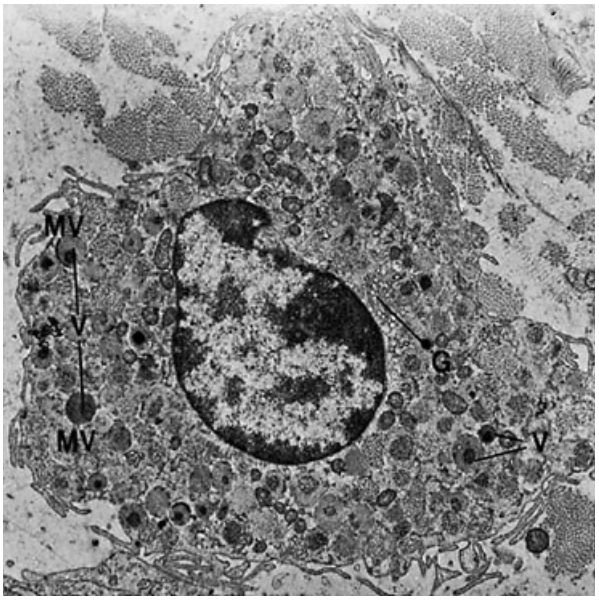


Fig. 1-38

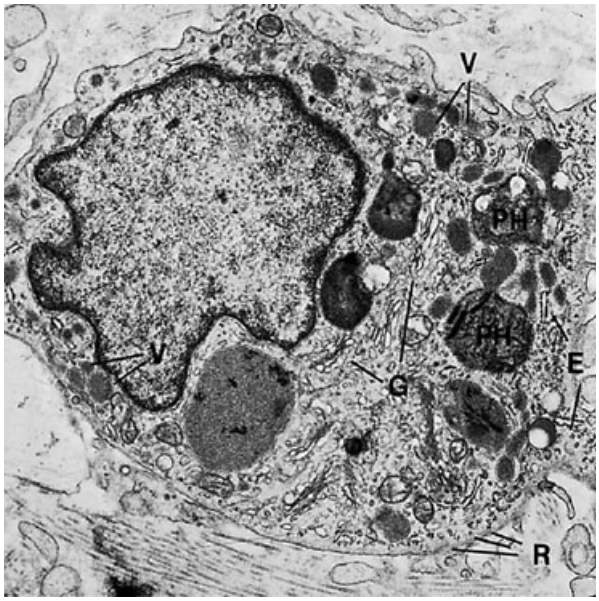


Fig. 1-39

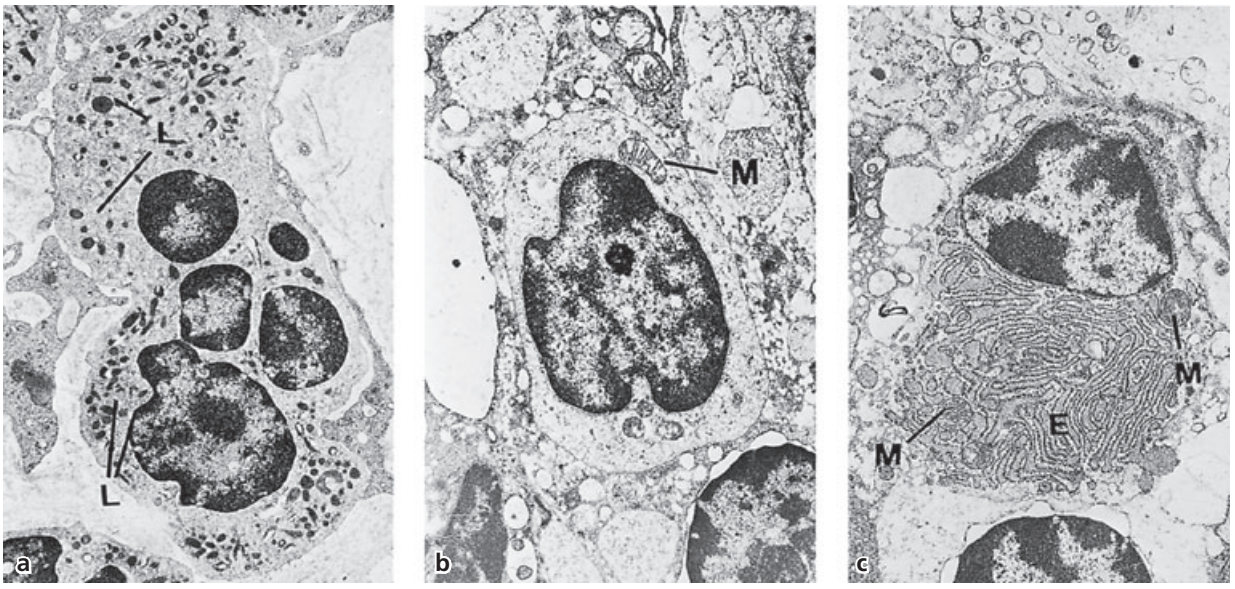


Fig. 1-40

contain biologically active substances such as proteolytic enzymes, histamine and heparin. The Golgi complex (G) is well developed, while granular endoplasmic reticulum structures are scarce. A large number of small cytoplasmic projections, i.e. microvilli (MV), can be seen along the periphery of the cell.

Fig. 1-39 The *macrophage* has a number of different phagocytic and synthetic functions in the tissue. A macrophage is shown in electron microscopic magnification. The nucleus is characterized by numerous invaginations of varying size. A zone of electron-dense chromatin condensations can be seen along the periphery of the nucleus. The Golgi complex (G) is well developed and numerous vesicles (V) of varying size are present in the cytoplasm. Granular endoplasmic reticulum (E) is scarce, but a certain number of free ribosomes (R) are evenly distributed in the cytoplasm. Remnants of phagocytosed material are often found in lysosomal vesicles: phagosomes (PH). In the periphery of the cell, a large number of microvilli of varying size can be seen. Macrophages are particularly numerous in inflamed tissue. They are derived from circulating blood monocytes which migrate into the tissue.

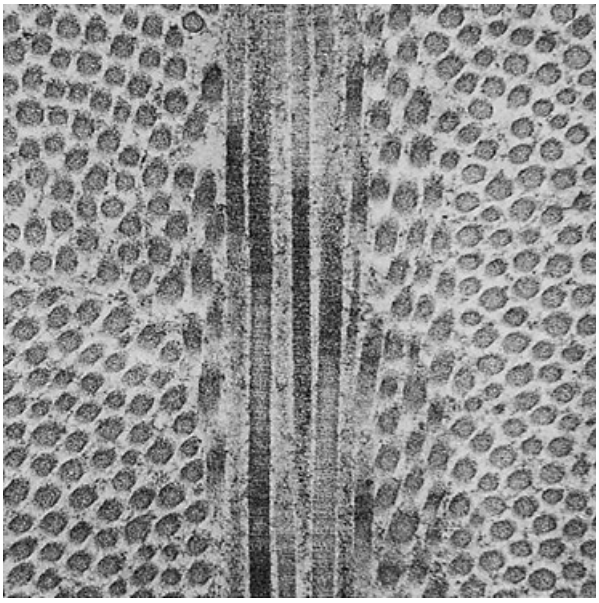


Fig. 1-41

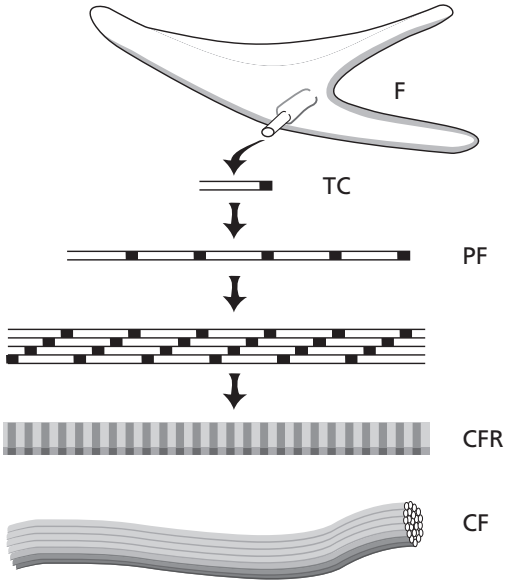


Fig. 1-42

Fig. 1-40 Besides fibroblasts, mast cells and macrophages, the connective tissue also harbors *inflammatory cells* of various types, for example neutrophilic granulocytes, lymphocytes, and plasma cells.

The *neutrophilic granulocytes*, also called *polymorphonuclear leukocytes*, have a characteristic appearance (Fig. 1-40a). The nucleus is lobulate and numerous lysosomes (L), containing lysosomal enzymes, are found in the cytoplasm.

The *lymphocytes* (Fig. 1-40b) are characterized by an oval to spherical nucleus containing localized areas of electron-dense chromatin. The narrow border of cytoplasm surrounding the nucleus contains numerous free ribosomes, a few mitochondria (M), and, in localized areas, endoplasmic reticulum with fixed ribosomes. Lysosomes are also present in the cytoplasm.

The *plasma cells* (Fig. 1-40c) contain an eccentrically located spherical nucleus with radially deployed electron-dense chromatin. Endoplasmic reticulum (E) with numerous ribosomes is found randomly distributed in the cytoplasm. In addition, the cytoplasm contains numerous mitochondria (M) and a well developed Golgi complex.

Fibers

The connective tissue fibers are produced by the fibroblasts and can be divided into: (1) *collagen fibers*, (2) *reticulin fibers*, (3) *oxytalan fibers*, and (4) *elastic fibers*.

Fig. 1-41 The *collagen fibers* predominate in the gingival connective tissue and constitute the most essential components of the periodontium. The electronmicrograph shows cross sections and longitudinal sections of collagen fibers. The collagen fibers have a characteristic cross-banding with a periodicity of 700 Å between the individual dark bands.

Fig. 1-42 illustrates some important features of the synthesis and the composition of collagen fibers produced by fibroblasts (F). The smallest unit, the collagen molecule, is often referred to as *tropocollagen*. A tropocollagen molecule (TC) which is seen in the upper portion of the drawing is approximately 3000 Å long and has a diameter of 15 Å. It consists of three polypeptide chains intertwined to form a helix. Each chain contains about 1000 amino acids. One third of these are glycine and about 20% proline and hydroxyproline, the latter being found practically only in collagen. Tropocollagen synthesis takes place inside the fibroblast from which the tropocollagen molecule is secreted into the extracellular space. Thus, the polymerization of tropocollagen molecules to collagen fibers takes place in the extracellular compartment. First, tropocollagen molecules are aggregated longitudinally to *protofibrils* (PF), which are subsequently laterally aggregated parallel to *collagen fibrils* (CFR), with an overlapping of the tropocollagen molecules by about 25% of their length. Due to the fact that special refraction conditions develop after staining at the sites where the tropocollagen molecules adjoin, a cross-banding with a periodicity of approximately 700 Å occurs under light microscopy. The *collagen fibers* (CF) are bundles of collagen fibrils, aligned in such a way that the fibers also exhibit a cross-banding with a periodicity of 700 Å. In the tissue, the fibers are usually arranged in bundles. As the collagen fibers mature, covalent crosslinks are formed between the tropocollagen molecules, resulting in an age-related reduction in collagen solubility.

Cementoblasts and *osteoblasts* are cells which also possess the ability to produce collagen.

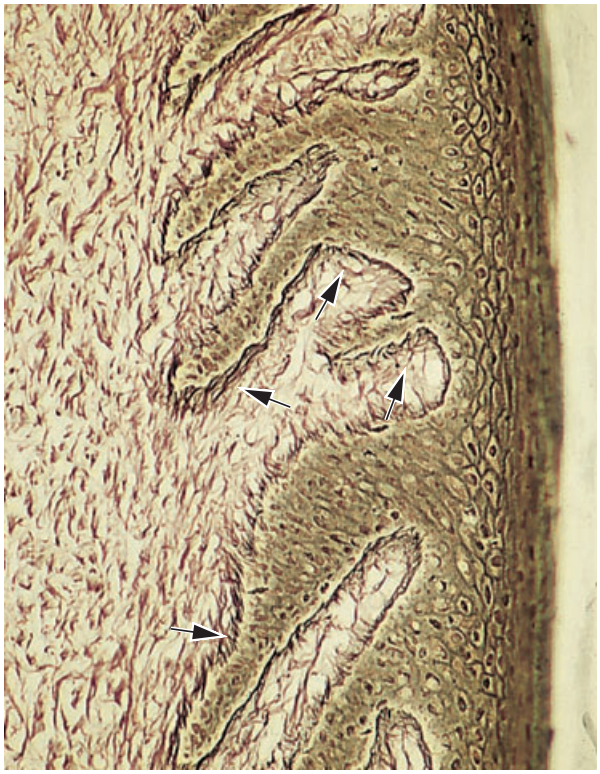


Fig. 1-43

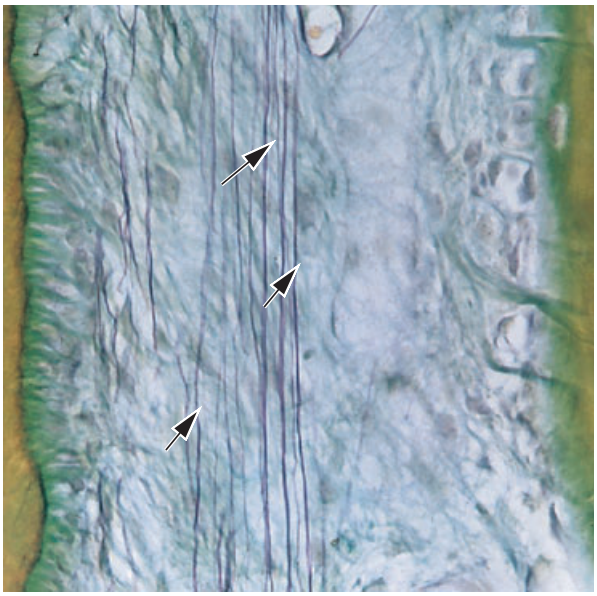


Fig. 1-44

Fig. 1-43 *Reticulin fibers*, as seen in this photomicrograph, exhibit argyrophilic staining properties and are numerous in the tissue adjacent to the basement membrane (arrows). However, reticulin fibers also occur in large numbers in the loose connective tissue surrounding the blood vessels. Thus, reticulin fibers are present at the epithelium–connective tissue and the endothelium–connective tissue interfaces.

Fig 1-44 *Oxytalan fibers* are scarce in the gingiva but numerous in the periodontal ligament. They are composed of long thin fibrils with a diameter of approximately 150 Å. These connective tissue fibers can be demonstrated light microscopically only after previous oxidation with peracetic acid. The photomicrograph illustrates oxytalan fibers (arrows) in the periodontal ligament, where they have a course mainly parallel to the long axis of the tooth. The function of these fibers is as yet unknown. The cementum is seen to the left and the alveolar bone to the right.

Fig. 1-45 *Elastic fibers* in the connective tissue of the gingiva and periodontal ligament are only present in association with blood vessels. However, as seen in this photomicrograph, the lamina propria and submucosa of the alveolar (lining) mucosa contain numerous elastic fibers (arrows). The gingiva (G) seen coronal to the mucogingival junction (MGJ) contains no elastic fibers except in association with the blood vessels.

Fig. 1-46 Although many of the collagen fibers in the gingiva and the periodontal ligament are irregularly or randomly distributed, most tend to be arranged in groups of bundles with a distinct orientation. According to their insertion and course in the tissue, the oriented bundles in the gingiva can be divided into the following groups:

1. *Circular fibers* (CF) are fiber bundles which run their course in the free gingiva and encircle the tooth in a cuff- or ring-like fashion.
2. *Dento-gingival fibers* (DGF) are embedded in the cementum of the supra-alveolar portion of the root and project from the cementum in a fan-like configuration out into the free gingival tissue of the facial, lingual and interproximal surfaces.
3. *Dento-periosteal fibers* (DPF) are embedded in the same portion of the cementum as the dento-gingival fibers, but run their course apically over the vestibular and lingual bone crest and terminate in the tissue of the attached gingiva. In the border area between the free and attached gingiva, the epithelium often lacks support by underlying oriented collagen fiber bundles. In this area the free gingival groove (GG) is often present.
4. *Trans-septal fibers* (TF), seen on the drawing to the right, extend between the supra-alveolar cementum of approximating teeth. The trans-septal fibers run straight across the interdental septum and are embedded in the cementum of adjacent teeth.

Fig. 1-47 illustrates in a histologic section the orientation of the trans-septal fiber bundles (arrows) in the supra-alveolar portion of the interdental area. It should be observed that, besides connecting the cementum (C) of adjacent teeth, the trans-septal fibers also connect the supra-alveolar cementum (C) with the crest of the alveolar bone (AB). The four groups

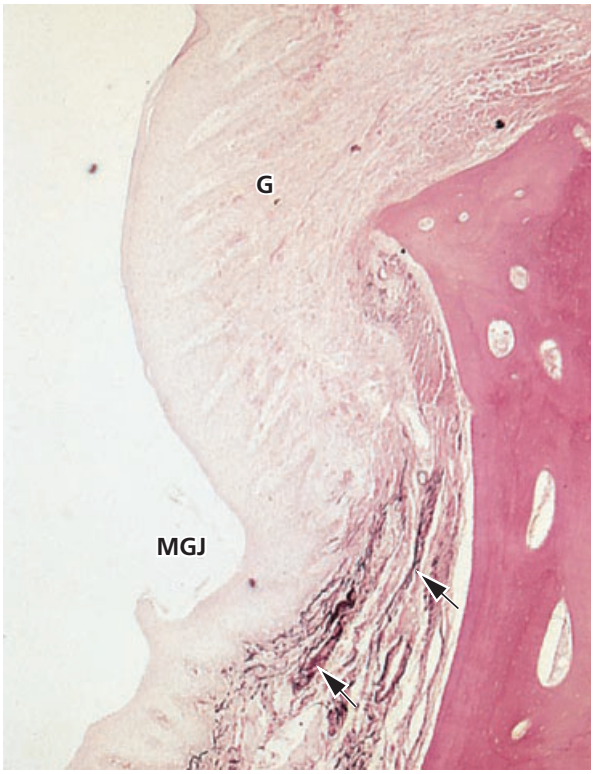


Fig. 1-45

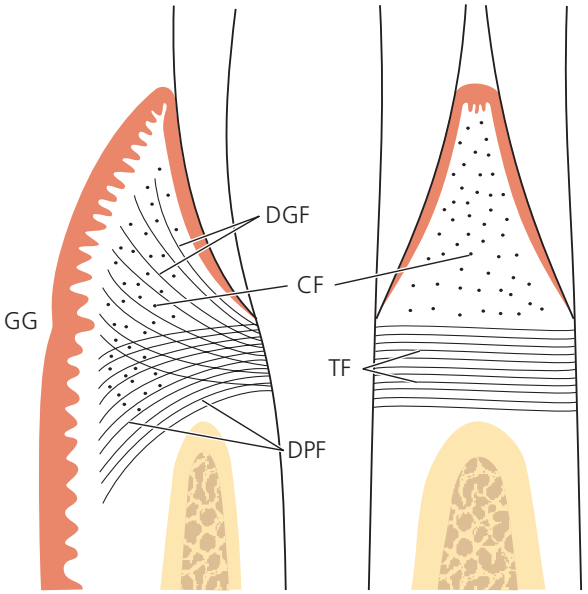


Fig. 1-46

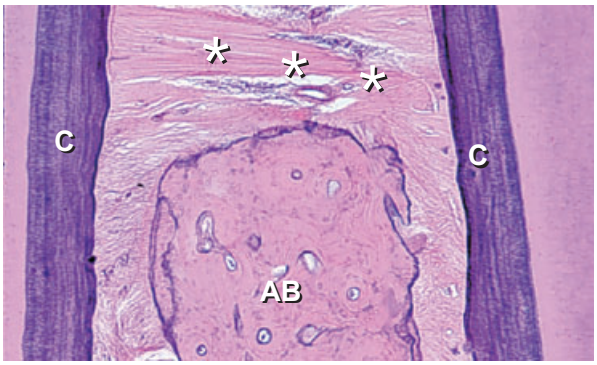


Fig. 1-47

of collagen fiber bundles presented in Fig. 1-46 reinforce the gingiva and provide the resilience and tone which is necessary for maintaining its architectural form and the integrity of the dento-gingival attachment.

Matrix

The *matrix* of the connective tissue is produced mainly by the fibroblasts, although some constituents are produced by mast cells, and other components are derived from the blood. The matrix is the medium in which the connective tissue cells are embedded and it is essential for the maintenance of the normal function of the connective tissue. Thus, the transportation of water, electrolytes, nutrients, metabolites, etc., to and from the individual connective tissue cells occurs within the matrix. The main constituents of the connective tissue matrix are protein–carbohydrate macromolecules. These complexes are normally divided into *proteoglycans* and *glycoproteins*. The proteoglycans contain *glycosaminoglycans* as the carbohydrate units (hyaluronan sulfate, heparan sulfate, etc.), which are attached to one or more protein chains via covalent bonds. The carbohydrate component is always predominant in the proteoglycans. The glycosaminoglycan called hyaluronan or "hyaluronic acid" is probably not bound to protein. The glycoproteins (fibronectin, osteonectin, etc.) also contain polysaccharides, but these macromolecules are different from glycosaminoglycans. The protein component is predominating in glycoproteins. In the macromolecules, mono- or oligosaccharides are connected to one or more protein chains via covalent bonds.

Fig. 1-48 Normal function of the connective tissue depends on the presence of proteoglycans and gly-

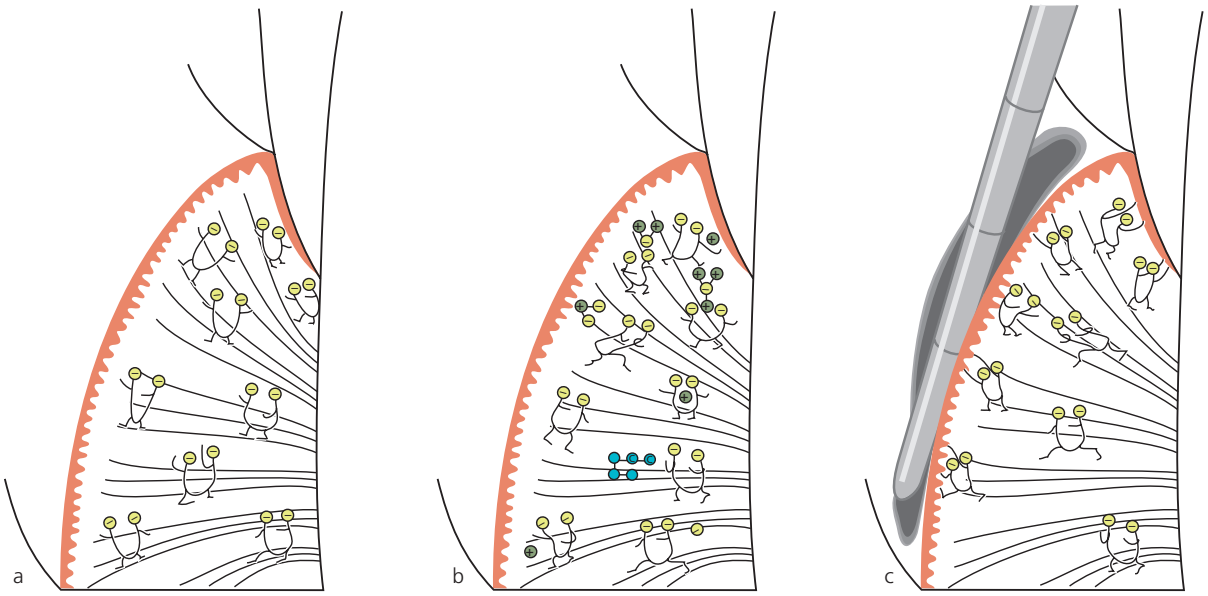


Fig. 1-48

cosaminoglycans. The carbohydrate moiety of the proteoglycans, the glycosaminoglycans (), are large, flexible, chain formed, negatively charged molecules, each of which occupies a rather large space (Fig. 1-48a). In such a space, smaller molecules, e.g. water and electrolytes, can be incorporated while larger molecules are prevented from entering (Fig. 1-48b). The proteoglycans thereby regulate diffusion and fluid flow through the matrix and are important determinants for the fluid content of the tissue and the maintenance of the osmotic pressure. In other words, the proteoglycans act as a molecule filter and, in addition, play an important role in the regulation of cell migration (movements) in the tissue. Due to their structure and hydration, the macromolecules exert resistance towards deformation, thereby serving as regulators of the consistency of the connective tissue (Fig. 1-48c). If the gingiva is suppressed, the macromolecules become deformed. When the pressure is eliminated, the macromolecules regain their original form. Thus, the macromolecules are important for the resilience of the gingiva.

Epithelial mesenchymal interaction

There are many examples of the fact that during the embryonic development of various organs, a mutual inductive influence occurs between the epithelium and the connective tissue. The development of the teeth is a characteristic example of such phenomena. The connective tissue is, on the one hand, a determining factor for normal development of the tooth bud while, on the other, the enamel epithelia exert a definite influence on the development of the mesenchymal components of the teeth.

It has been suggested that tissue differentiation in the adult organism can be influenced by environmental factors. The skin and mucous membranes, for instance, often display increased keratinization and hyperplasia of the epithelium in areas which are exposed to mechanical stimulation. Thus, the tissues seem to adapt to environmental stimuli. The presence of keratinized epithelium on the masticatory mucosa has been considered to represent an adaptation to mechanical irritation released by mastication. However, research has demonstrated that the char-

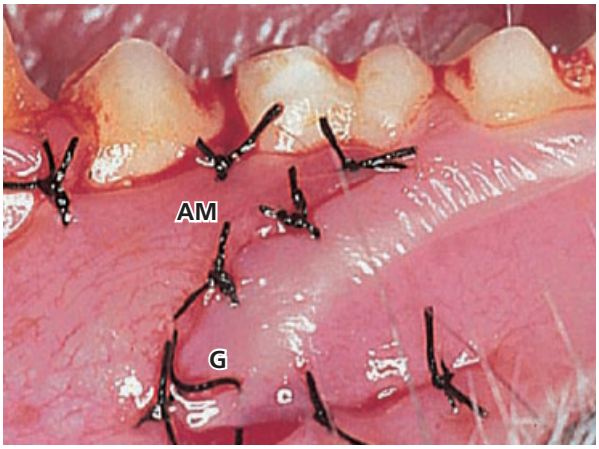


Fig. 1-49

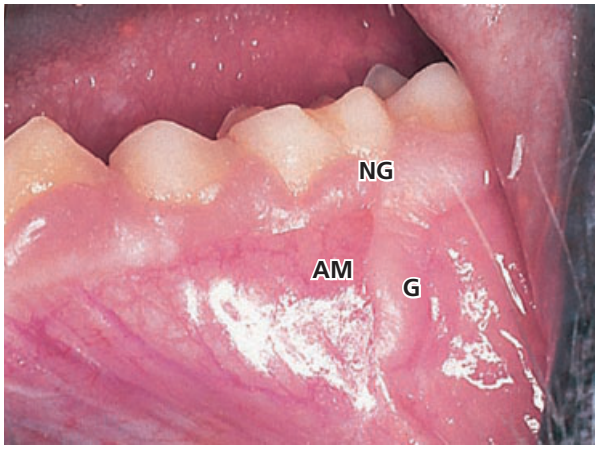


Fig. 1-50

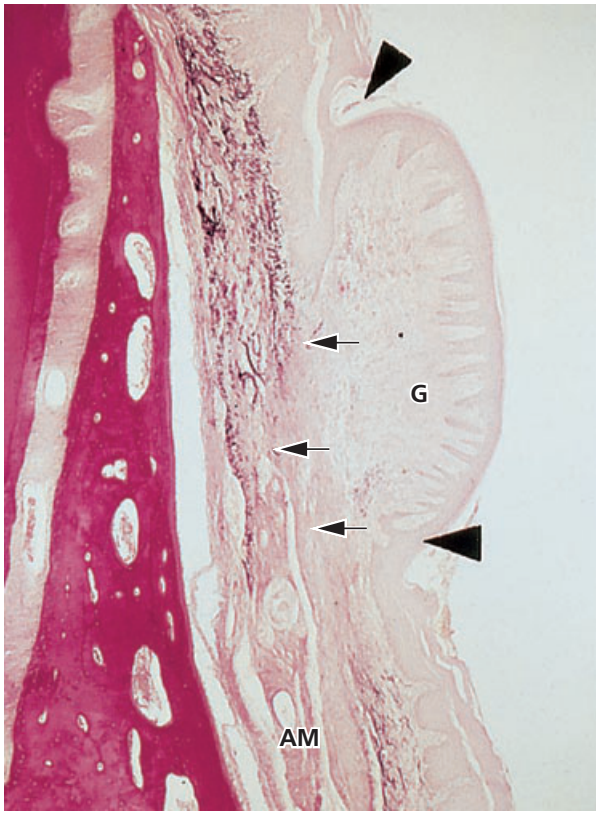


Fig. 1-51

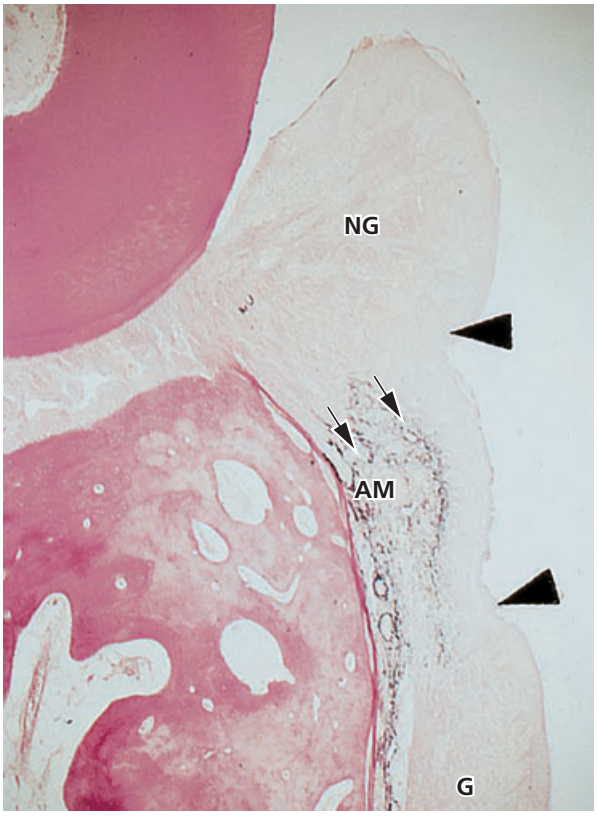


Fig. 1-52

acteristic features of the epithelium in such areas are genetically determined. Some pertinent observations are reported in the following:

Fig. 1-49 shows an area in a monkey where the gingiva (G) and the alveolar mucosa (AM) have been transposed by a surgical procedure. The alveolar mucosa is placed in close contact with the teeth while the gingiva is positioned in the area of the alveolar mucosa.

Fig. 1-50 shows the same area, as seen in Fig. 1-49, 4 months later. Despite the fact that the transplanted gingiva (G) is mobile in relation to the underlying bone, like the alveolar mucosa, it has retained its characteristic, morphologic features of a masticatory mucosa. However, a narrow zone of new keratinized gingiva (NG) has regenerated between the transplanted alveolar mucosa (AM) and the teeth.

Fig. 1-51 presents a histologic section cut through the transplanted gingiva seen in Fig. 1-50. Since elastic fibers are lacking in the gingival connective tissue (G), but are numerous (small arrows) in the connective tissue of the alveolar mucosa (AM), the transplanted gingival tissue can readily be identified. The epithelium covering the transplanted gingival tissue exhibits a distinct keratin layer (between large arrows) on the surface, and also the configuration of the epithelium–connective tissue interface (i.e. rete pegs and connective tissue papillae) is similar to that of normal non-transplanted gingiva. Thus, the heterotopically located gingival tissue has maintained its original specificity. This observation demonstrates that the characteristics of the gingiva are genetically determined rather than being the result of functional adaptation to environmental stimuli.

Fig. 1-52 shows a histologic section cut through the coronal portion of the area of transplantation (shown in Fig. 1-50). The transplanted gingival tissue (G) shown in Fig. 1-51 can be seen in the lower portion of the photomicrograph. The alveolar mucosa transplant (AM) is seen between the large arrows in the middle of the illustration. After surgery, the alveolar mucosa transplant was positioned in close contact with the teeth as seen in Fig. 1-49. After healing, a narrow zone of keratinized gingiva (NG) developed coronal to the alveolar mucosa transplant (see Fig. 1-50). This new zone of gingiva (NG), which can be seen in the upper portion of the histologic section, is covered by keratinized epithelium and the connective tissue contains no purple-stained elastic fibers. In addition, it is important to notice that the junction between keratinized and non-keratinized epithelium (large arrows) corresponds exactly to the junction between "elastic" and "inelastic" connective tissue (small arrows). The connective tissue of the new gingiva has regenerated from the connective tissue of the supra-alveolar and periodontal ligament compartments and has separated the alveolar mucosal transplant (AM) from the tooth (see Fig. 1-53). However, it is most likely that the epithelium which covers the new gingiva has migrated from the adjacent epithelium of the alveolar mucosa.

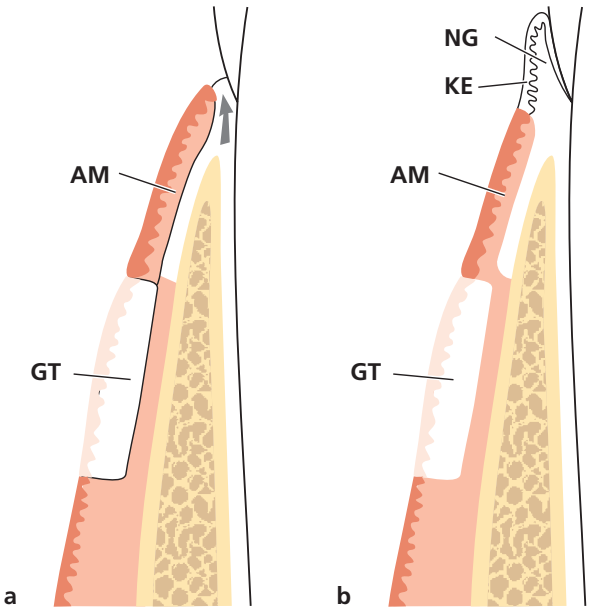


Fig. 1-53

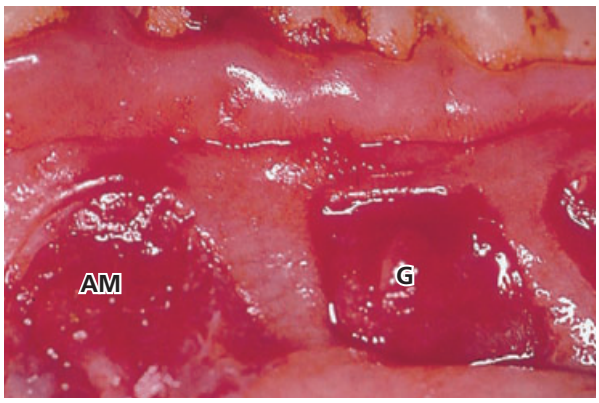


Fig. 1-54

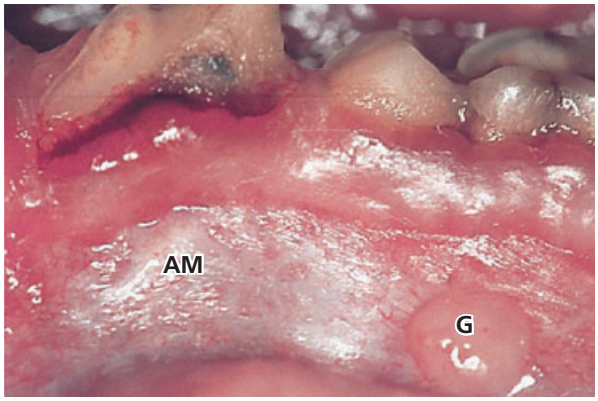


Fig. 1-55

Fig. 1-53 presents a schematic drawing of the development of the new, narrow zone of keratinized gingiva (NG) seen in Figs. 1-50 and 1-52.

Fig. 1-53a Granulation tissue has proliferated coronally along the root surface (arrow) and has separated the alveolar mucosa transplant (AM) from its original contact with the tooth surface.

Fig. 1-53b Epithelial cells have migrated from the alveolar mucosal transplant (AM) on to the newly formed gingival connective tissue (NG). Thus, the newly formed gingiva has become covered with a keratinized epithelium (KE) which originated from the non-keratinized epithelium of the alveolar mucosa (AM). This implies that the newly formed gingival connective tissue (NG) possesses the ability to induce changes in the differentiation of the epithelium originating from the alveolar mucosa. This epithelium, which is normally non-keratinized, apparently differentiates to keratinized epithelium because of stimuli arising from the newly formed gingival connective tissue (NG). (GT: gingival transplant.)

Fig. 1-54 illustrates a portion of gingival connective tissue (G) and alveolar mucosal connective tissue (AM) which, after transplantation, has healed into wound areas in the alveolar mucosa. Epithelialization of these transplants can only occur through migration of epithelial cells from the surrounding alveolar mucosa.

Fig. 1-55 shows the transplanted gingival connective tissue (G) after re-epithelialization. This tissue portion has attained an appearance similar to that of the normal gingiva, indicating that this connective tissue is now covered by keratinized epithelium. The transplanted connective tissue from the alveolar mucosa (AM) is covered by non-keratinized epithelium, and has the same appearance as the surrounding alveolar mucosa.

Fig. 1-56 presents two histologic sections through the area of the transplanted gingival connective tissue. The section shown in Fig. 1-56a is stained for elastic fibers (arrows). The tissue in the middle without elastic fibers is the transplanted gingival connective tissue (G). Fig. 1-56b shows an adjacent section stained with hematoxylin and eosin. By comparing Figs. 1-56a and 1-56b it can be seen that:

1. The transplanted gingival connective tissue is covered by keratinized epithelium (between arrowheads)
2. The epithelium–connective tissue interface has the same wavy course (i.e. rete pegs and connective tissue papillae) as seen in normal gingiva.

The photomicrographs seen in Figs. 1-56c and 1-56d illustrate, at a higher magnification, the border area between the alveolar mucosa (AM) and the transplanted gingival connective tissue (G). Note the distinct relationship between keratinized epithelium (arrow) and "inelastic" connective tissue (arrowheads), and between non-keratinized epithelium and

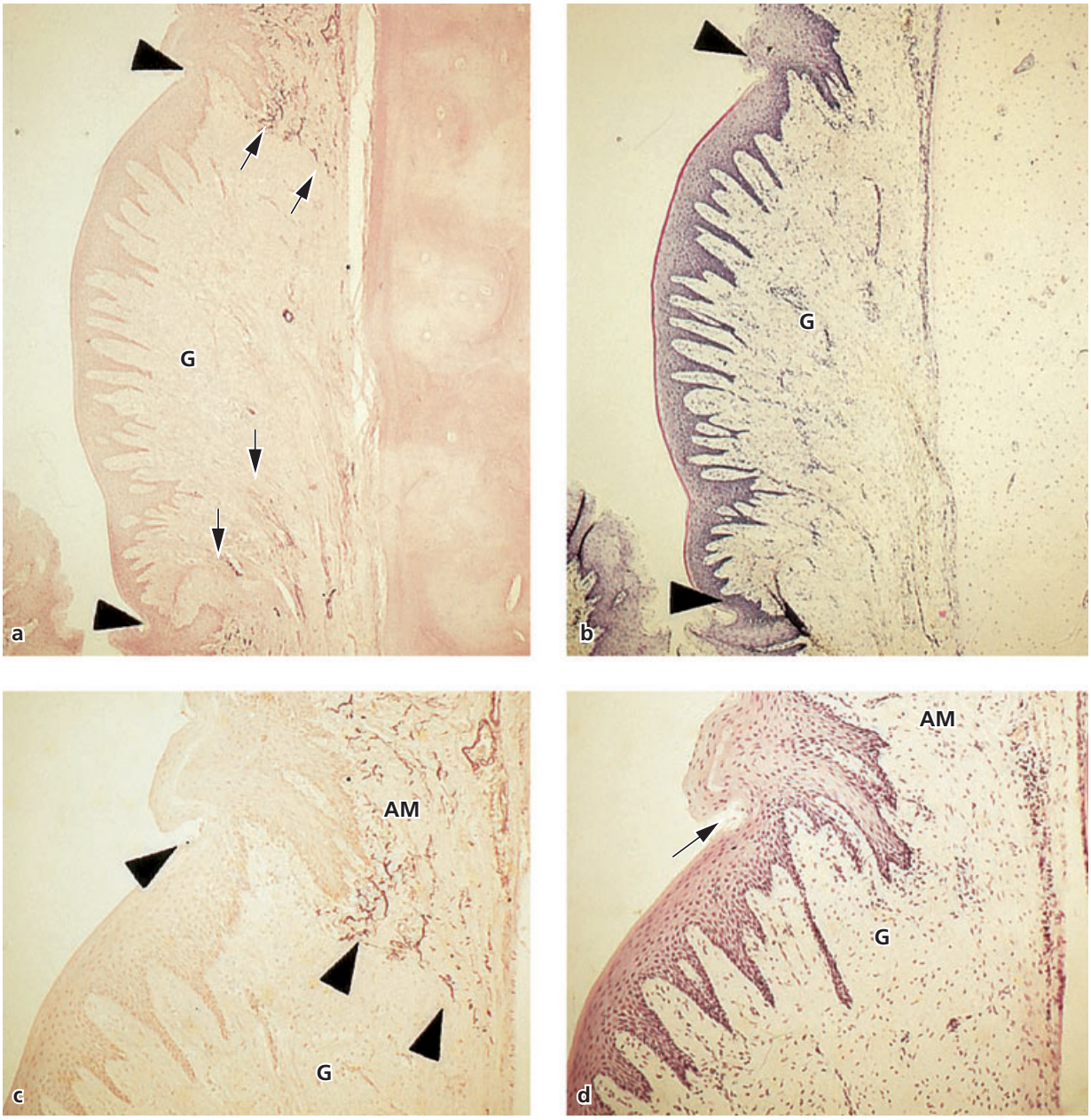


Fig. 1-56

"elastic" connective tissue. The establishment of such a close relationship during healing implies that the transplanted gingival connective tissue possesses the ability to alter the differentiation of epithelial cells as previously suggested (Fig. 1-53). From being non-keratinizing cells, the cells of the epithelium of the alveolar mucosa have evidently become keratinizing cells. This means that the specificity of the gingival epithelium is determined by genetic factors inherent in the connective tissue.

Periodontal ligament

The periodontal ligament is the soft, richly vascular and cellular connective tissue which surrounds the roots of the teeth and joins the root cementum with the socket wall. In the coronal direction, the periodontal ligament is continuous with the lamina propria of the gingiva and is demarcated from the gingiva by the collagen fiber bundles which connect the alveolar bone crest with the root (the alveolar crest fibers).

Fig. 1-57 is a radiograph of a mandibular premolar–molar region. In radiographs two types of alveolar bone can be distinguished:

1. The part of the alveolar bone which covers the alveolus, called "lamina dura" (arrows)
2. The portion of the alveolar process which, in the radiograph, has the appearance of a meshwork. This is called the "spongy bone".

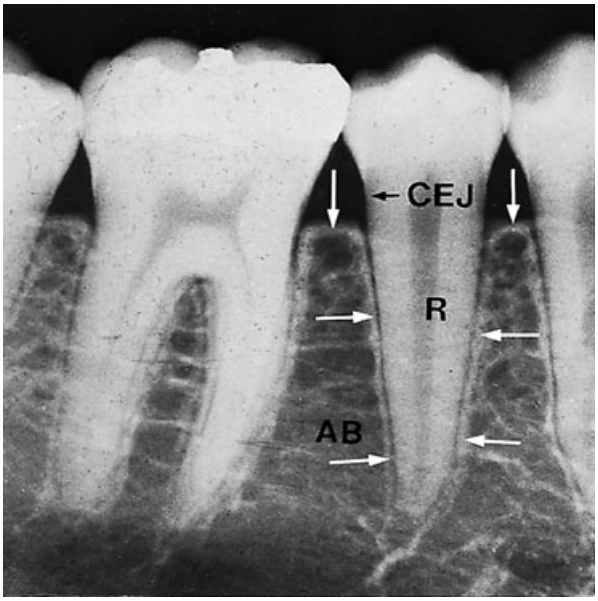


Fig. 1-57

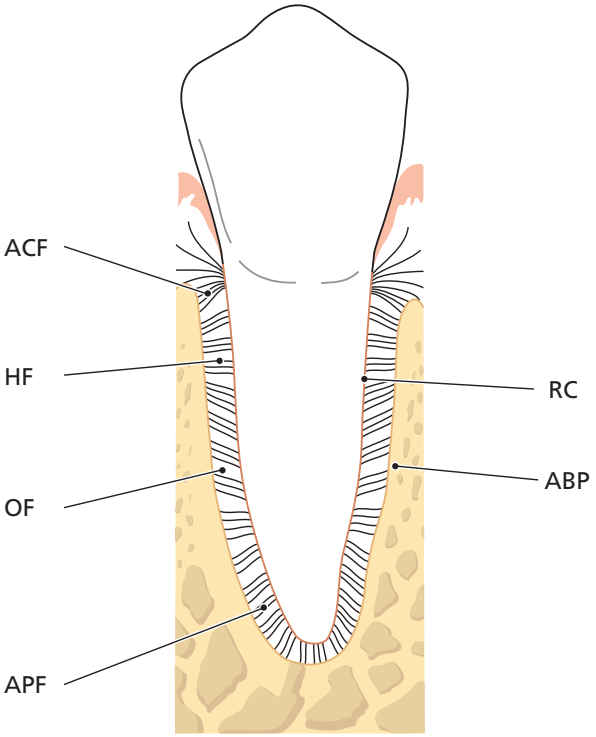


Fig. 1-58

The periodontal ligament is situated in the space between the roots (R) of the teeth and the lamina dura or the alveolar bone proper (arrows). The alveolar bone (AB) surrounds the tooth to a level approximately 1 mm apical to the cemento-enamel junction (CEJ). The coronal border of the bone is called the *alveolar crest* (arrows).

The periodontal ligament space has the shape of an hourglass and is narrowest at the mid-root level. The width of the periodontal ligament is approximately 0.25 mm (range 0.2–0.4 mm). The presence of a periodontal ligament permits forces, elicited during masticatory function and other tooth contacts, to be distributed to and resorbed by the alveolar process via the alveolar bone proper. The periodontal ligament is also essential for the mobility of the teeth. Tooth mobility is to a large extent determined by the width, height, and quality of the periodontal ligament (see Chapters 14 and 51).

Fig. 1-58 illustrates in a schematic drawing how the periodontal ligament is situated between the alveolar bone proper (ABP) and the root cementum (RC). The tooth is joined to the bone by bundles of collagen fibers which can be divided into the following main groups according to their arrangement:

1. *Alveolar crest fibers* (ACF)
2. *Horizontal fibers* (HF)
3. *Oblique fibers* (OF)
4. *Apical fibers* (APF).

Fig. 1-59 The periodontal ligament and the root cementum develop from the loose connective tissue (the follicle) which surrounds the tooth bud. The schematic drawing depicts the various stages in the organization of the periodontal ligament which forms concomitantly with the development of the root and the eruption of the tooth.

Fig. 1-59a The tooth bud is formed in a crypt of the bone. The collagen fibers produced by the fibroblasts in the loose connective tissue around the tooth bud are embedded, during the process of their maturation, into the newly formed cementum immediately apical to the cemento-enamel junction (CEJ). These fiber bundles oriented towards the coronal portion of the bone crypt will later form the dento-gingival fiber group, the dento-periosteal fiber group and the transseptal fiber group which belong to the oriented fibers of the gingiva (see Fig. 1-46).

Fig. 1-59b The true periodontal ligament fibers, the *principal fibers*, develop in conjunction with the eruption of the tooth. First, fibers can be identified entering the most marginal portion of the alveolar bone.

Fig. 1-59c Later, more apically positioned bundles of oriented collagen fibers are seen.

Fig. 1-59d The orientation of the collagen fiber bundles alters continuously during the phase of tooth eruption. First, when the tooth has reached contact in occlusion and is functioning properly, the fibers of the periodontal ligament associate into groups of

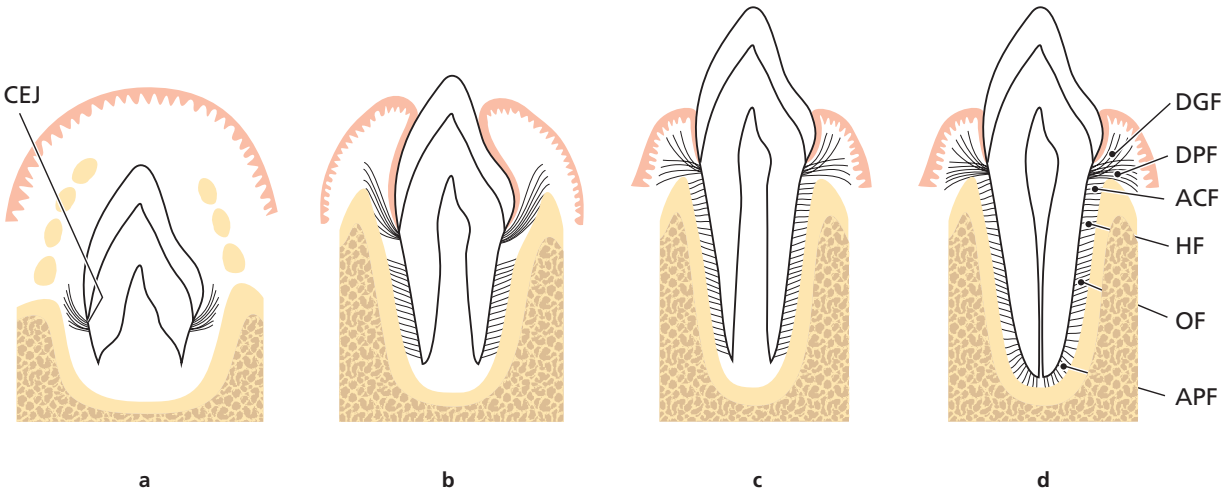


Fig. 1-59

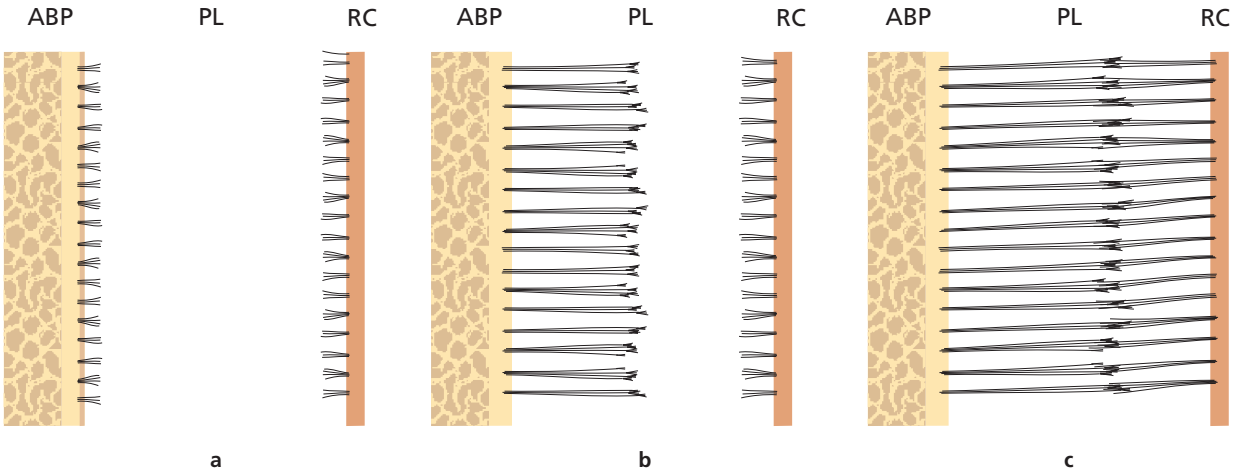


Fig. 1-60

well oriented dentoalveolar collagen fibers demonstrated in Fig. 1-58. These collagen structures undergo constant remodeling (i.e. resorption of old fibers and formation of new ones).

Fig. 1-60 This schematic drawing illustrates the development of the principal fibers of the periodontal ligament. The alveolar bone proper (ABP) is seen to the left, the periodontal ligament (PL) is depicted in the center and the root cementum (RC) is seen to the right.

Fig. 1-60a First, small, fine, brush-like fibrils are detected arising from the root cementum and projecting into the PL space. At this stage the surface of the bone is covered by osteoblasts. From the surface of the bone only a small number of radiating, thin collagen fibrils can be seen.

Fig. 1-60b Later on, the number and thickness of fibers entering the bone increase. These fibers radiate towards the loose connective tissue in the mid-portion of the periodontal ligament area (PL), which contains more or less randomly oriented collagen fibrils. The fibers originating from the cementum are still short while those entering the bone gradually become longer. The terminal portions of these fibers carry finger-like projections.

Fig. 1-60c The fibers originating from the cementum subsequently increase in length and thickness and fuse in the periodontal ligament space with the fibers originating from the alveolar bone. When the tooth, following eruption, reaches contact in occlusion and starts to function, the principal fibers become organized in bundles and run continuously from the bone to the cementum.

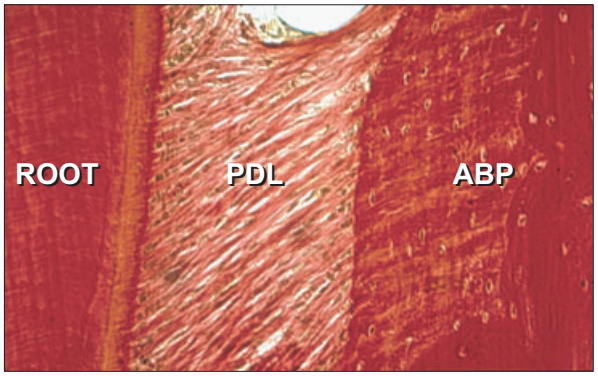


Fig. 1-61a

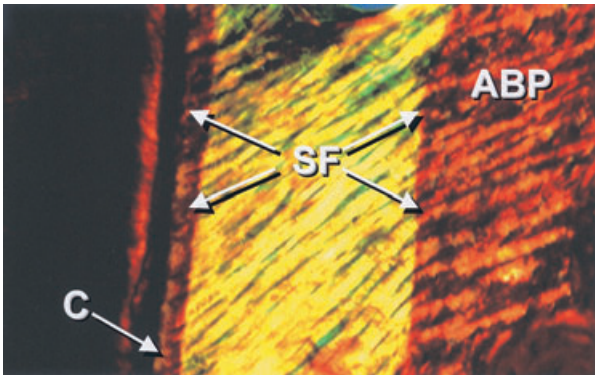


Fig. 1-61b

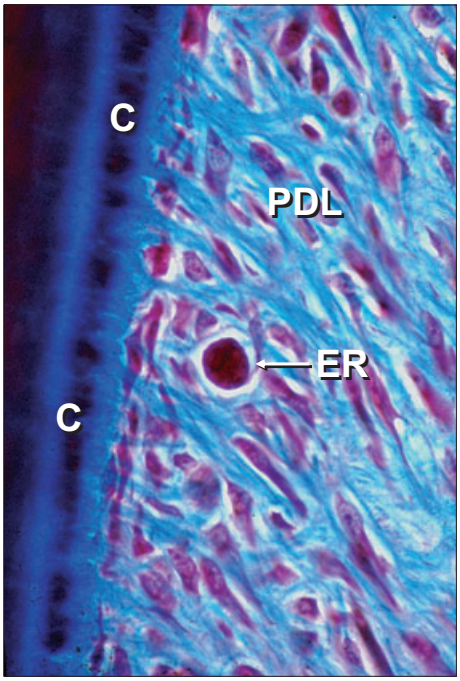


Fig. 1-62a

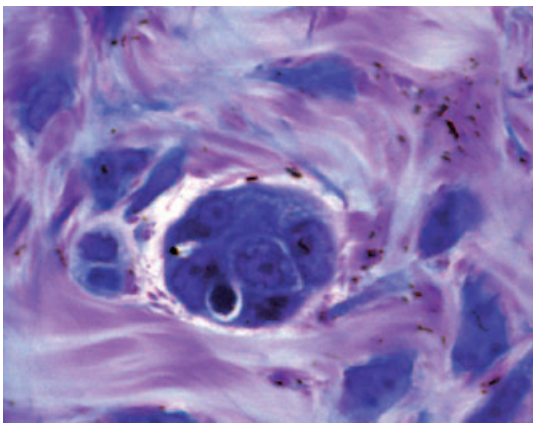


Fig. 1-62b

Fig. 1-61a illustrates how the principal fibers of the periodontal ligament (PDL) run continuously from the root cementum to the alveolar bone proper (ABP). The principal fibers embedded in the cementum (Sharpey's fibers) have a smaller diameter but are more numerous than those embedded in the alveolar bone proper (Sharpey's fibers).

Fig. 1-61b presents a polarized version of Fig. 1-61a. In this illustration the Sharpey's fibers (SF) can be seen penetrating not only the cementum (C) but also the entire width of the alveolar bone proper (ABP). The periodontal ligament also contains a few elastic fibers associated with the blood vessels. Oxytalan fibers (see Fig. 1-44) are also present in the periodontal ligament. They have a mainly apico-occlusal orientation and are located in the ligament closer to the tooth than to the alveolar bone. Very often they insert into the cementum. Their function has not been determined.

The cells of the periodontal ligament are: *fibroblasts*, *osteoblasts*, *cementoblasts*, *osteoclasts*, as well as *epithelial cells* and *nerve fibers*. The fibroblasts are aligned along the principal fibers, while cementoblasts line the surface of the cementum, and the osteoblasts line the bone surface.

Fig. 1-62a shows the presence of clusters of epithelial cells (ER) in the periodontal ligament (PDL). These cells, called the *epithelial cell rests of Mallassez*, represent remnants of the Hertwig's epithelial root sheath. The epithelial cell rests are situated in the periodontal ligament at a distance of 15–75 µm from the cementum (C) on the root surface. A group of such epithelial cell rests is seen in a higher magnification in Fig. 1-62b.

Fig. 1-63 Electron microscopically it can be seen that the epithelial cell rests are surrounded by a basement membrane (BM) and that the cell membranes of the epithelial cells exhibit the presence of desmosomes (D) as well as hemidesmosomes (HD). The epithelial cells contain only few mitochondria and have a poorly developed endoplasmic reticulum. This means that they are vital, but resting, cells with minute metabolism.

Fig. 1-64 is a photomicrograph of a periodontal ligament removed from an extracted tooth. This

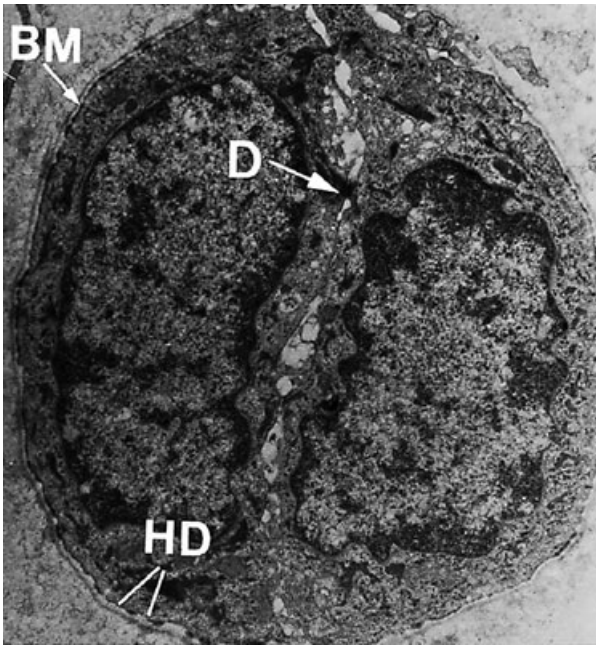


Fig. 1-63

specimen, prepared tangential to the root surface, shows that the epithelial cell rests of Mallassez, which in ordinary histologic sections appear as isolated groups of epithelial cells, in fact form a continuous network of epithelial cells surrounding the root. Their function is unknown at present.

Root cementum

The cementum is a specialized mineralized tissue covering the root surfaces and, occasionally, small portions of the crown of the teeth. It has many features in common with bone tissue. However, the cementum contains no blood or lymph vessels, has no innervation, does not undergo physiologic resorption or remodeling, but is characterized by continuing deposition throughout life. Like other mineralized tissues, it contains collagen fibers embedded in an organic matrix. Its mineral content, which is mainly hydroxyapatite, is about 65% by weight; a little more than that of bone (i.e. 60%). Cementum serves different functions. It attaches the periodontal ligament fibers to the root and contributes to the process of repair after damage to the root surface.

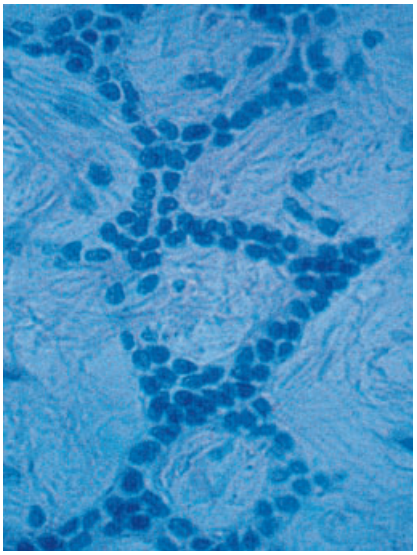


Fig. 1-64

Different forms of cementum have been described:

1. *Acellular, extrinsic fiber cementum* (AEFC) is found in the coronal and middle portions of the root and contains mainly bundles of Sharpey's fibers. This type of cementum is an important part of the attachment apparatus and connects the tooth with the alveolar bone proper.
2. *Cellular, mixed stratified cementum* (CMSC) occurs in the apical third of the roots and in the furcations. It contains both extrinsic and intrinsic fibers as well as cementocytes.
3. *Cellular, intrinsic fiber cementum* (CIFC) is found mainly in resorption lacunae and it contains intrinsic fibers and cementocytes.

Fig. 1-65a shows a portion of a root with adjacent periodontal ligament (PDL). A thin layer of acellular, extrinsic fiber cementum (AEFC) with densely packed extrinsic fibers covers the peripheral dentin. Cementoblasts and fibroblasts can be observed adjacent to the cementum.

Fig. 1-65b represents a scanning electron micrograph of AEFC. Note that the extrinsic fibers attach to the dentin (left) and are continous with the collagen fiber

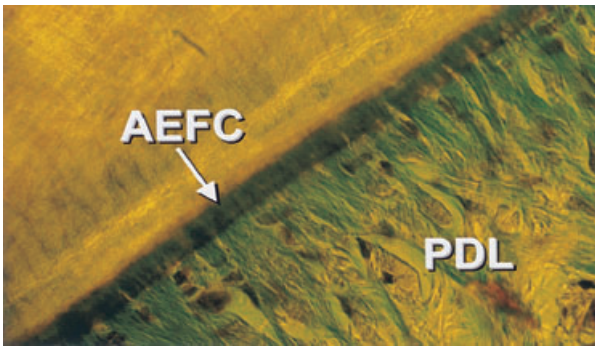


Fig. 1-65a

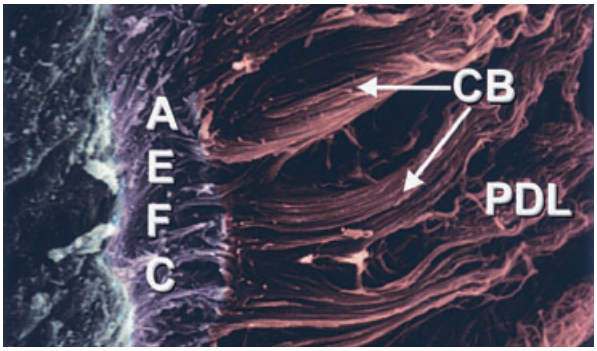


Fig. 1-65b

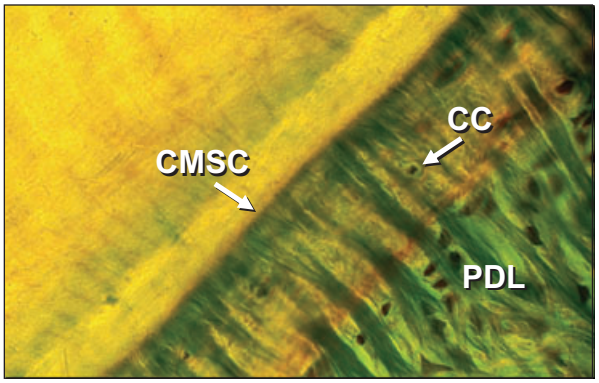


Fig. 1-66

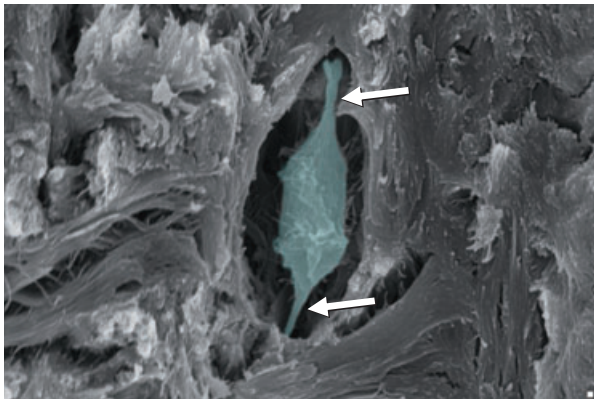


Fig. 1-67

bundles (CB) of the periodontal ligament (PDL). The AEFC is formed concomitantly with the formation of the root dentin. At a certain stage during tooth formation, the epithelial sheath of Hertwig, which lines the newly formed predentin, is fragmented. Cells from the dental follicle then penetrate the epithelial sheath of Hertwig and occupy the area next to the predentin. In this position, the ectomesenchymal cells from the dental follicle differentiate into cementoblasts and begin to produce collagen fibers at right angles to the surface. The first cementum is deposited on the highly mineralized superficial layer of the mantle dentin called the "hyaline layer" which contains enamel matrix proteins and the initial collagen fibers of the cementum. Subsequently, cementoblasts drift away from the surface resulting in increased thickness of the cementum and incorporation of principal fibers.

Fig. 1-66 demonstrates the structure of cellular, mixed stratified cementum (CMSC) which, in contrast to AEFC, contains cells and intrinsic fibers. The CMSC is laid down throughout the functional period of the tooth. The various types of cementum are produced by cementoblasts or periodontal ligament (PDL) cells lining the cementum surface. Some of these cells become incorporated into the cementoid, which subsequently mineralizes to form cementum. The cells which are incorporated in the cementum are called *cementocytes* (CC).

Fig. 1-67 illustrates how cementocytes (blue cell) reside in lacunae in CMSC or CIFC. They communicate with each other through a network of cytoplasmic processes (arrows) running in canaliculi in the cementum. The cementocytes also communicate with

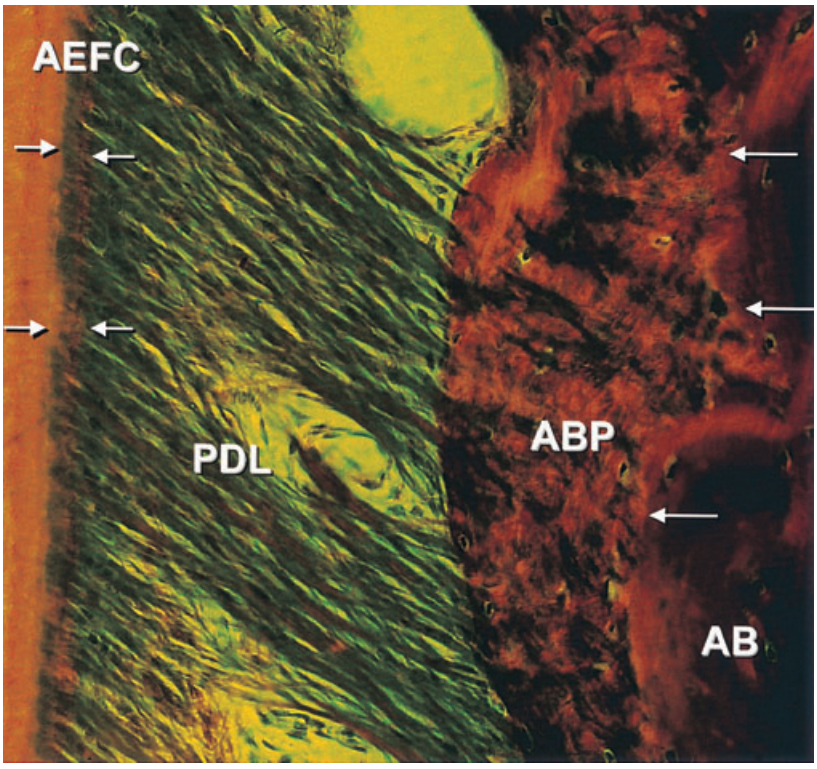


Fig. 1-68a

the cementoblasts on the surface through cytoplasmic processes. The presence of cementocytes allows transportation of nutrients through the cementum, and contributes to the maintenance of the vitality of this mineralized tissue.

Fig. 1-68a is a photomicrograph of a section through the periodontal ligament (PDL) in an area where the root is covered with acellular, extrinsic fiber cementum (AEFC). The portions of the principal fibers of the periodontal ligament which are embedded in the root cementum (arrows) and in the alveolar bone proper (ABP) are called *Sharpey's fibers*. The arrows to the right indicate the border between ABP and the alveolar bone (AB). In AEFC the Sharpey's fibers have a smaller diameter and are more densely packed than their counterparts in the alveolar bone. During the continuous formation of AEFC, portions of the periodontal ligament fibers (principal fibers) adjacent to the root become embedded in the mineralized tissue. Thus, the Sharpey's fibers in the cementum are a direct continuation of the principal fibers in the periodontal ligament and the supra-alveolar connective tissue.

Fig. 1-68b The Sharpey's fibers constitute the *extrinsic fiber system* (E) of the cementum and are produced by fibroblasts in the periodontal ligament. The *intrinsic fiber system* (I) is produced by cementoblasts and is composed of fibers oriented more or less parallel to the long axis of the root.

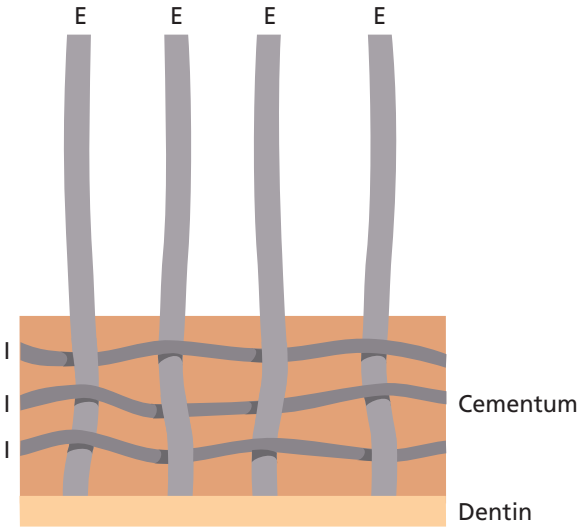


Fig. 1-68b

Fig. 1-69 shows extrinsic fibers penetrating acellular, extrinsic fiber cementum (AEFC). The characteristic cross-banding of the collagen fibers is masked in the cementum because apatite crystals have become deposited in the fiber bundles during the process of mineralization.

Fig. 1-70 In contrast to the bone, the cementum (C) does not exhibit alternating periods of resorption and apposition, but increases in thickness throughout life by deposition of successive new layers. During this

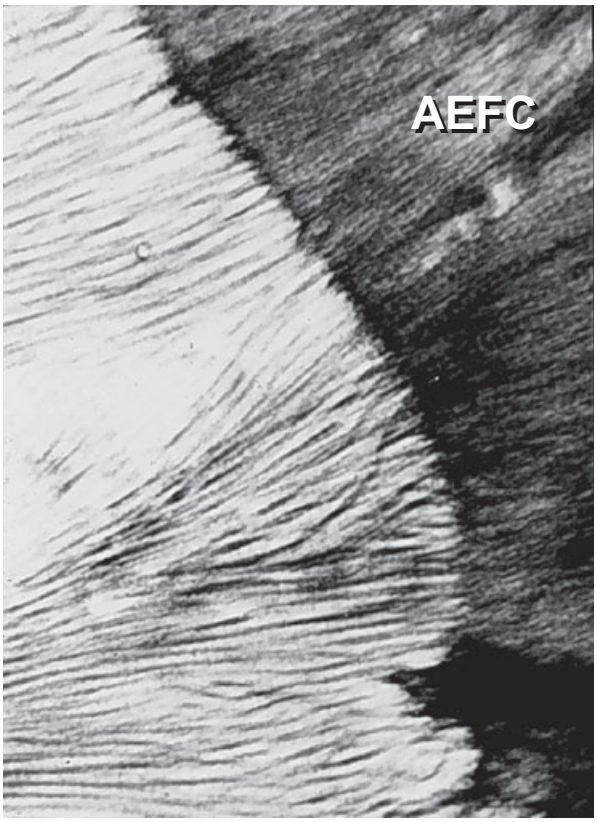


Fig. 1-69

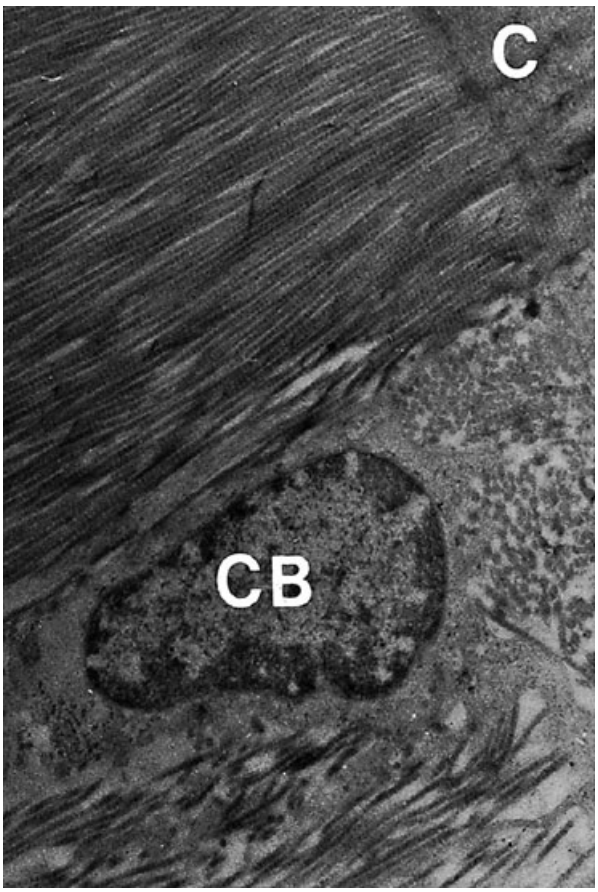


Fig. 1-70

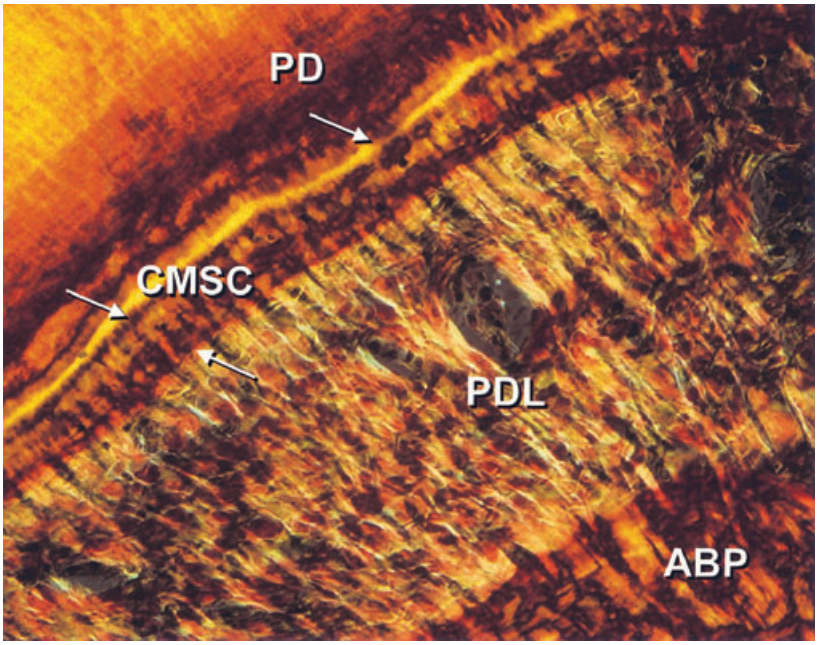


Fig. 1-71

process of gradual apposition, the particular portion of the principal fibers which resides immediately adjacent to the root surface becomes mineralized. Mineralization occurs by the deposition of hydroxyapatite crystals, first within the collagen fibers, later upon the fiber surface, and finally in the interfibrillar matrix. The electronphotomicrograph shows a cementoblast (CB) located near the surface of the cementum (C) and between two inserting principal fiber bundles. Generally, the AEFC is more mineralized than CMSC and CIFC. Sometimes only the periphery of the Sharpey's fibers of the CMSC is mineralized, leaving an unmineralized core within the fiber.

Fig. 1-71 is a photomicrograph of the periodontal ligament (PDL) which resides between the cementum (CMSC) and the alveolar bone proper (ABP). The CMSC is densely packed with collagen fibers oriented parallel to the root surface (intrinsic fibers) and Sharpey's fibers (extrinsic fibers), oriented more or less perpendicularly to the cementum–dentin junction (predentin (PD)). The various types of cementum increase in thickness by gradual apposition throughout life. The cementum becomes considerably wider in the apical portion of the root than in the cervical portion, where the thickness is only 20–50 µm. In the apical root portion the cementum is often 150–250 µm wide. The cementum often contains incremental lines indicating alternating periods of formation. The CMSC is formed after the termination of tooth eruption, and after a response to functional demands.

Alveolar bone

The alveolar process is defined as the parts of the maxilla and the mandible that form and support the sockets of the teeth. The alveolar process develops in conjunction with the development and eruption of the teeth. The alveolar process consists of bone which is formed both by cells from the dental follicle (alveolar bone proper) and cells which are independent of tooth development. Together with the root cementum and the periodontal membrane, the alveolar bone constitutes the attachment apparatus of the teeth, the main function of which is to distribute and resorb forces generated by, for example, mastication and other tooth contacts.

Fig. 1-72 illustrates a cross section through the alveolar process (pars alveolaris) of the maxilla at the mid-root level of the teeth. Note that the bone which covers the root surfaces is considerably thicker at the palatal than at the buccal aspect of the jaw. The walls of the sockets are lined by *cortical bone* (arrows), and the area between the sockets and between the compact jaw bone walls is occupied by *cancellous bone*. The cancellous bone occupies most of the interdental septa but only a relatively small portion of the buccal and palatal bone plates. The cancellous bone contains *bone trabeculae*, the architecture and size of which are partly genetically determined and partly the result of the forces to which the teeth are exposed during function. Note how the bone on the buccal and palatal aspects of the alveolar process varies in thickness from one region to another. The bone plate is thick at the palatal aspect and on the buccal aspect of the molars but thin in the buccal anterior region.

Fig. 1-73 shows cross sections through the mandibular alveolar process at levels corresponding to the coronal (Fig. 1-73a) and apical (Fig. 1-73b) thirds of the roots. The bone lining the wall of the sockets (alveolar bone proper) is often continuous with the compact or cortical bone at the lingual (L) and buccal

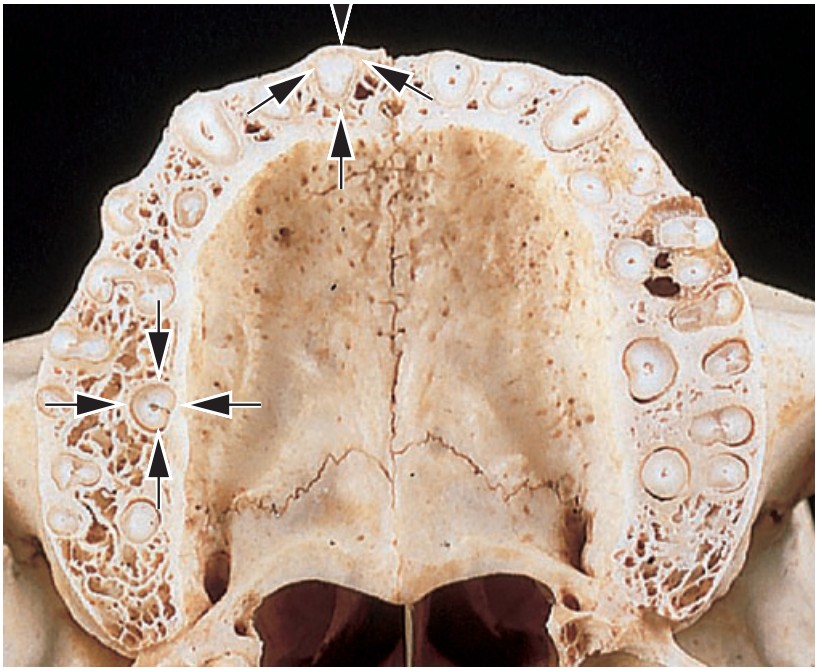
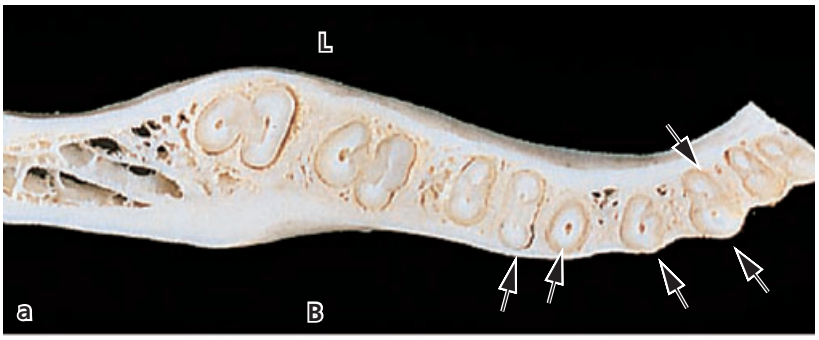


Fig. 1-72



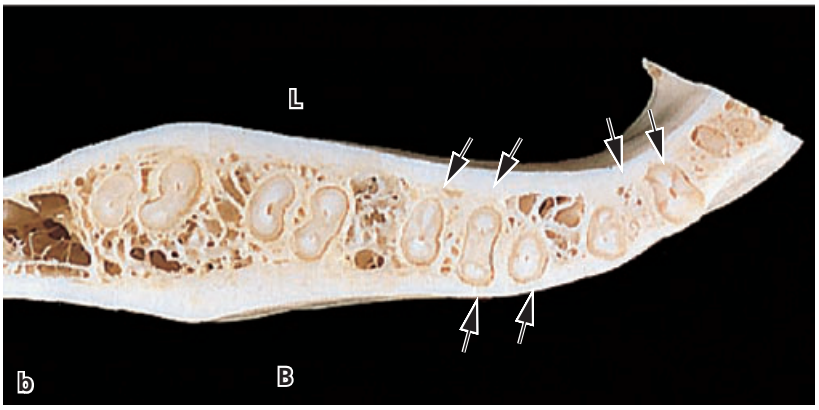


Fig. 1-73

(B) aspects of the alveolar process (arrows). Note how the bone on the buccal and lingual aspects of the alveolar process varies in thickness from one region to another. In the incisor and premolar regions, the bone plate at the buccal aspects of the teeth is considerably thinner than at the lingual aspect. In the molar region, the bone is thicker at the buccal than at the lingual surfaces.

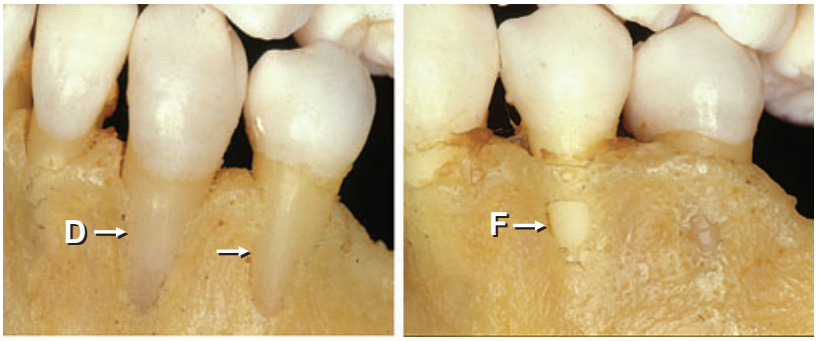


Fig. 1-74

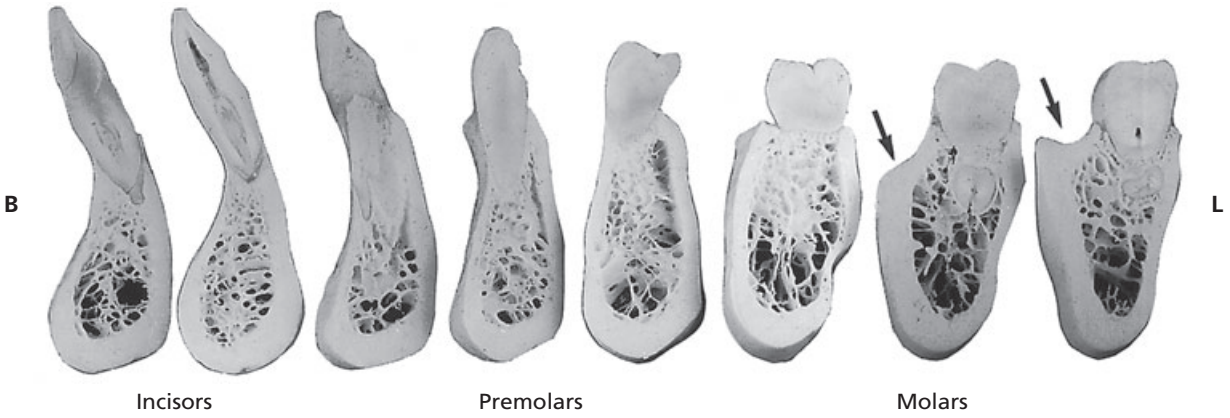


Fig. 1-75

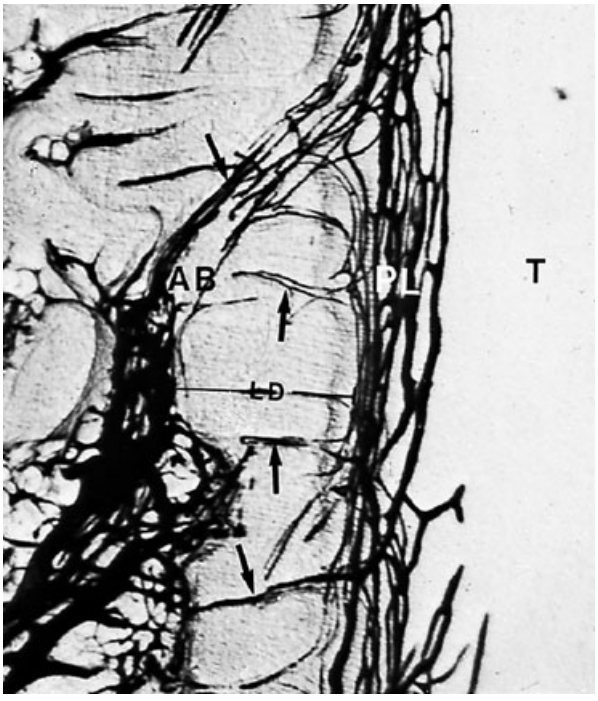


Fig. 1-76

Fig. 1-74 At the buccal aspect of the jaws, the bone coverage is sometimes missing at the coronal portion of the roots, forming a so-called *dehiscence* (D). If some bone is present in the most coronal portion of such an area the defect is called a *fenestration* (F). These defects often occur where a tooth is displaced out of the arch and are more frequent over anterior than posterior teeth. The root in such defects is covered only by periodontal ligament and the overlying gingiva.

Fig. 1-75 presents vertical sections through various regions of the mandibular dentition. The bone wall at the buccal (B) and lingual (L) aspects of the teeth varies considerably in thickness, e.g. from the premolar to the molar region. Note, for instance, how the presence of the oblique line (*linea obliqua*) results in a shelf-like bone process (arrows) at the buccal aspect of the second and third molars.

Fig. 1-76 shows a section through the periodontal ligament (PL), tooth (T), and the alveolar bone (AB). The blood vessels in the periodontal ligament and the alveolar bone appear black because the blood system was perfused with ink. The compact bone (alveolar bone proper) which lines the tooth socket, and in a radiograph (Fig. 1-57) appears as "lamina dura" (LD), is perforated by numerous *Volkmann's canals* (arrows) through which blood vessels, lymphatics, and nerve fibers pass from the alveolar bone (AB) to the periodontal ligament (PL). This layer of bone into which the principal fibers are inserted (Sharpey's fibers) is sometimes called "bundle bone". From a functional and structural point of view, this "bundle bone" has many features in common with the cementum layer on the root surfaces.

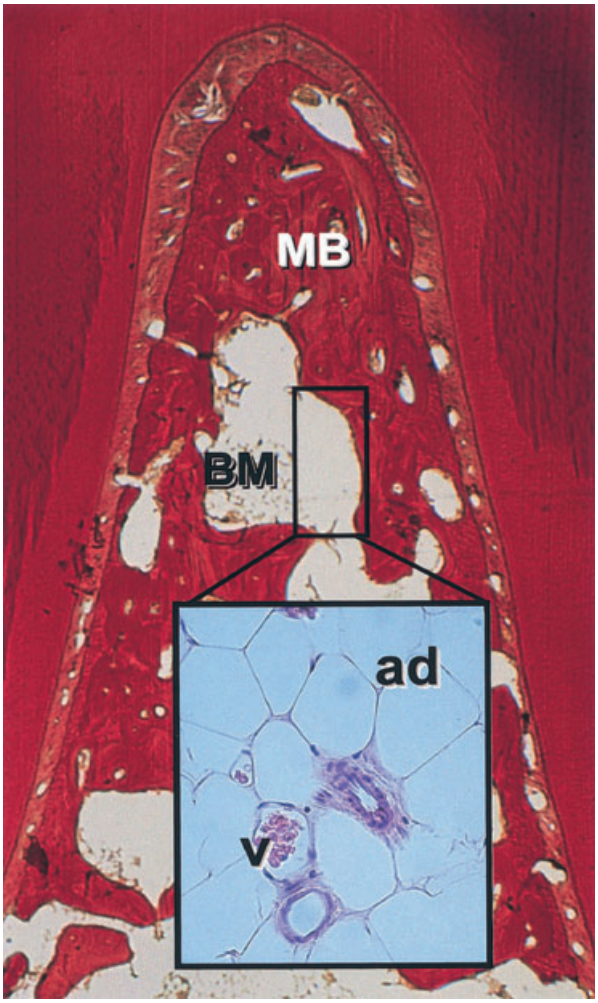


Fig. 1-77

Fig. 1-77 The alveolar process starts to form early in fetal life, with mineral deposition at small foci in the mesenchymal matrix surrounding the tooth buds. These small mineralized areas increase in size, fuse, and become resorbed and remodeled until a continuous mass of bone has formed around the fully erupted teeth. The mineral content of bone, which is mainly hydroxyapatite, is about 60% on a weight basis. The photomicrograph illustrates the bone tissue within the furcation area of a mandibular molar. The bone tissue can be divided into two compartments: mineralized bone (MB) and bone marrow (BM). The mineralized bone is made up of lamellae – lamellar bone – while the bone marrow contains adipocytes (ad), vascular structures (v), and undifferentiated mesenchymal cells (see insertion).

Fig. 1-78 The mineralized, lamellar bone includes two types of bone tissue: the bone of the alveolar process (AB) and the alveolar bone proper (ABP), which covers the alveolus. The ABP or the bundle bone has a varying width and is indicated with white arrows. The alveolar bone (AB) is a tissue of mesenchymal origin and it is not considered as part of the genuine attachment apparatus. The alveolar bone proper (ABP), on the other hand, together with the periodontal ligament (PDL) and the cementum (C), is responsible for the attachment between the tooth and the skeleton. AB and ABP may, as a result of altered functional demands, undergo adaptive changes.

Fig. 1-79 describes a portion of lamellar bone. The lamellar bone at this site contains *osteons* (white

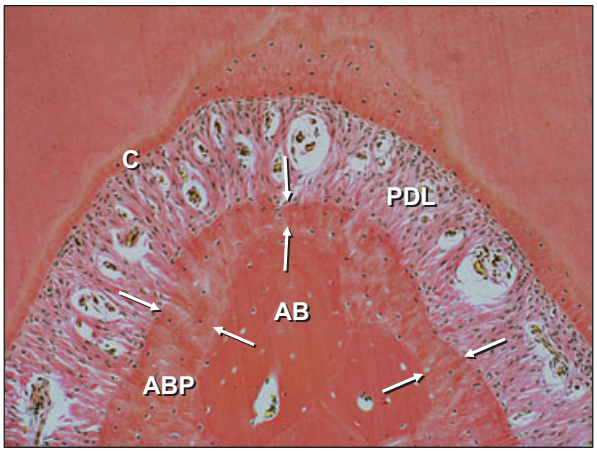


Fig. 1-78

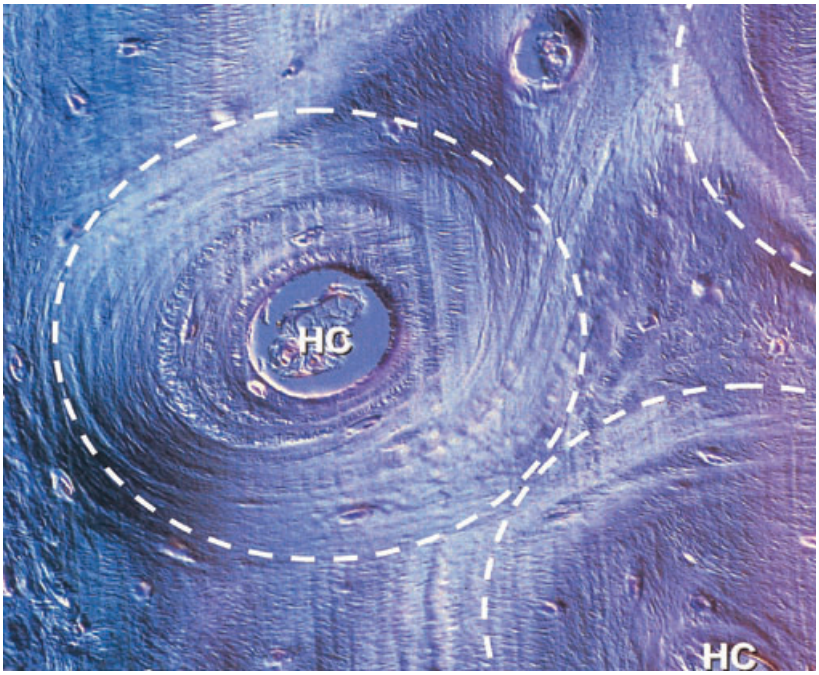


Fig. 1-79

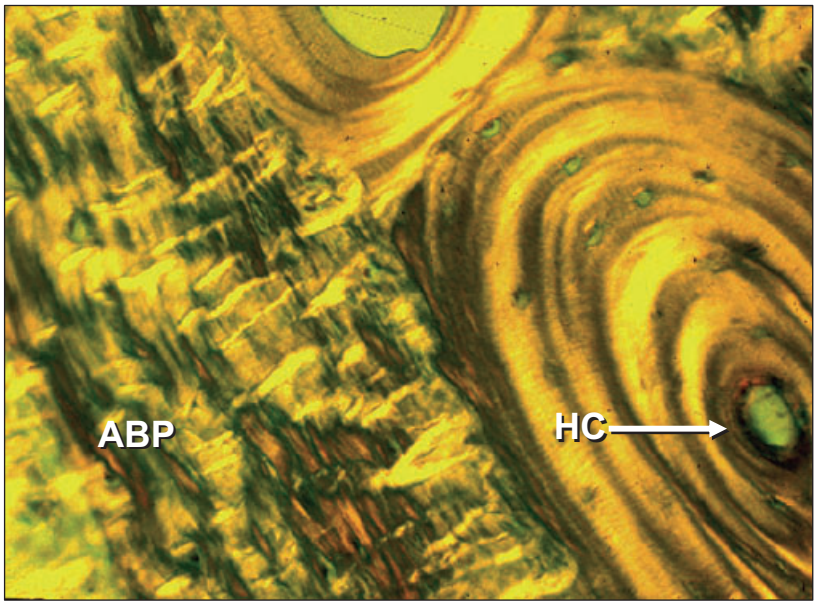


Fig. 1-80a

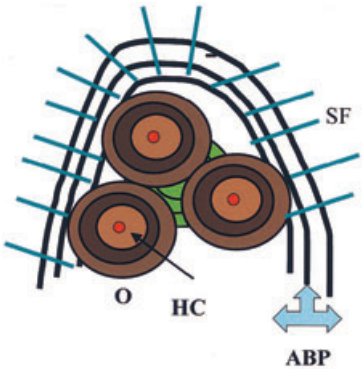


Fig. 1-80b

circles) each of which harbors a blood vessel located in a Haversian canal (HC). The blood vessel is surrounded by concentric, mineralized lamellae to form the osteon. The space between the different osteons is filled with so-called interstitial lamellae. The osteons in the lamellar bone are not only structural units but also metabolic units. Thus, the nutrition of the bone is secured by the blood vessels in the Haversian canals and connecting vessels in the Volkmann canals.

Fig. 1-80 The histologic section (Fig. 1-80a) shows the borderline between the alveolar bone proper (ABP) and lamellar bone with an osteon. Note the presence of the Haversian canal (HC) in the center of the osteon. The alveolar bone proper (ABP) includes circumferential lamellae and contains Sharpey's fibers which extend into the periodontal ligament. The schematic drawing (Fig. 1-80b) is illustrating three active osteons (brown) with a blood vessel (red) in the Haversian canal (HC). Interstitial lamella (green) is located between the osteons (O) and represents an old and partly remodelled osteon. The alveolar bone proper (ABP) is presented by the dark lines into which the Sharpey's fibers (SF) insert.

Fig. 1-81 illustrates an osteon with osteocytes (OC) residing in osteocyte lacunae in the lamellar bone. The osteocytes connect via canaliculi (can) which

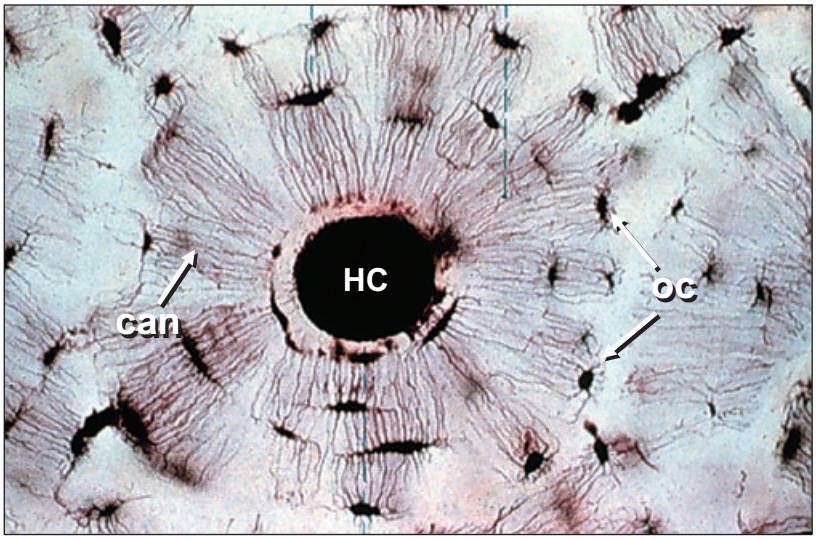


Fig. 1-81

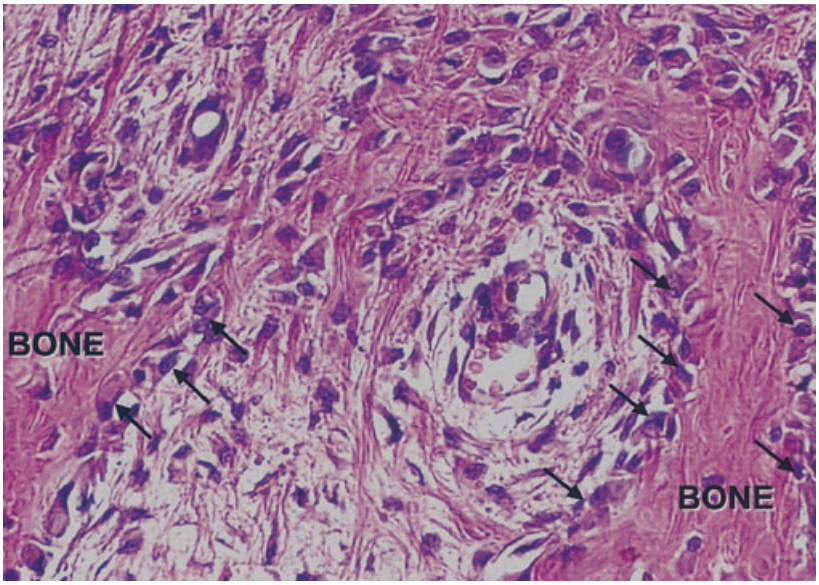


Fig. 1-82

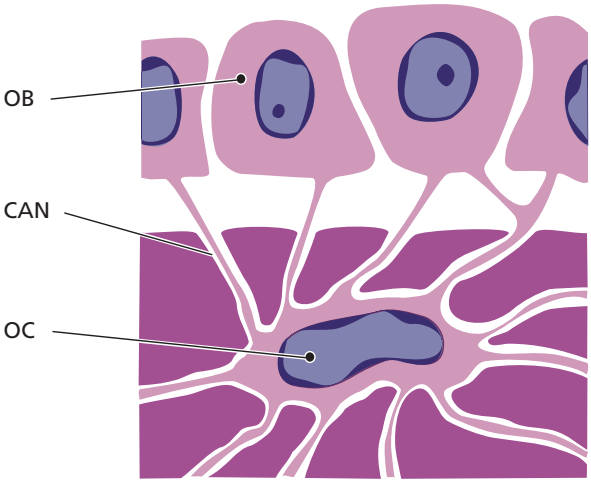


Fig. 1-83

contain cytoplasmatic projections of the osteocytes. A Haversian canal (HC) is seen in the middle of the osteon.

Fig. 1-82 illustrates an area of the alveolar bone in which bone formation occurs. The osteoblasts (arrows), the bone-forming cells, are producing bone matrix (osteoid) consisting of collagen fibers, glycoproteins, and proteoglycans. The bone matrix or the osteoid undergoes mineralization by the deposition of minerals such as calcium and phosphate, which are subsequently transformed into hydroxyapatite.

Fig. 1-83 The drawing illustrates how osteocytes, present in the mineralized bone, communicate with osteoblasts on the bone surface through canaliculi.

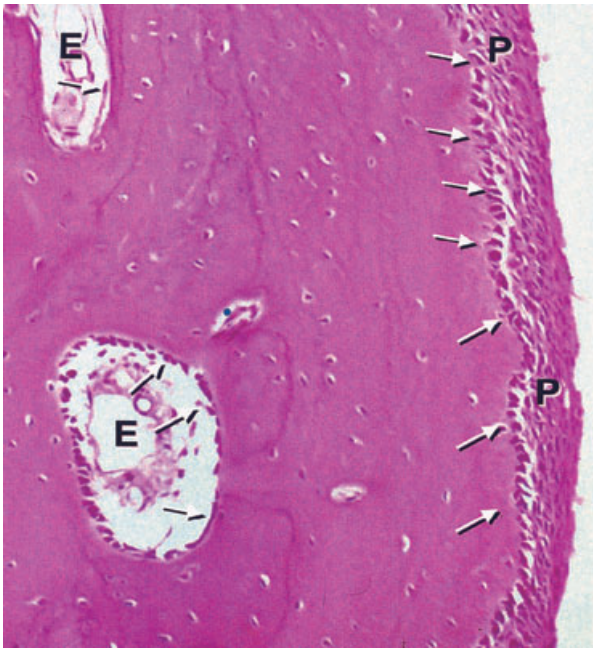


Fig. 1-84

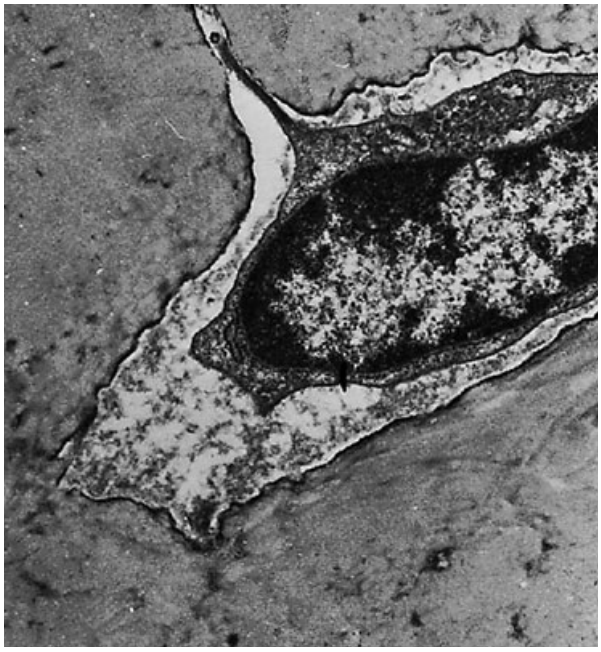


Fig. 1-85

Fig. 1-84 All active bone-forming sites harbor osteoblasts. The outer surface of the bone is lined by a layer of such osteoblasts which, in turn, are organized in a periosteum (P) that contains densely packed collagen fibers. On the "inner surface" of the bone, i.e. in the bone marrow space, there is an endosteum (E), which presents similar features as the periosteum.

Fig. 1-85 illustrates an osteocyte residing in a lacuna in the bone. It can be seen that cytoplasmic processes radiate in different directions.

Fig. 1-86 illustrates osteocytes (OC) and how their long and delicate cytoplasmic processes communicate through the canaliculi (CAN) in the bone. The resulting canalicular–lacunar system is essential for cell metabolism by allowing diffusion of nutrients and waste products. The surface between the osteocytes with their cytoplasmic processes on the one

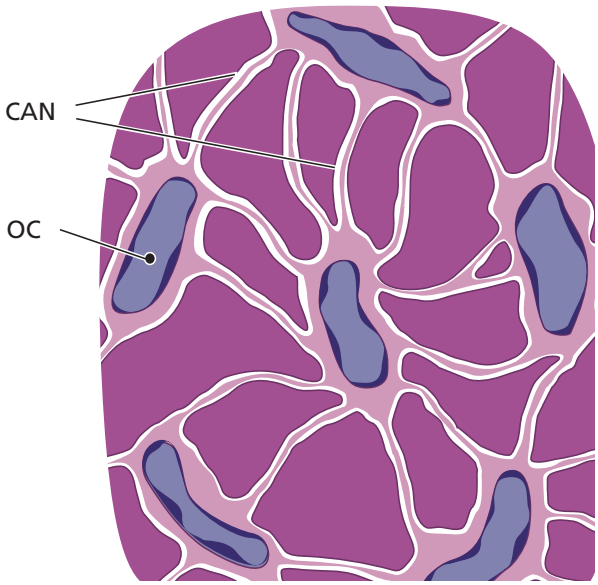


Fig. 1-86

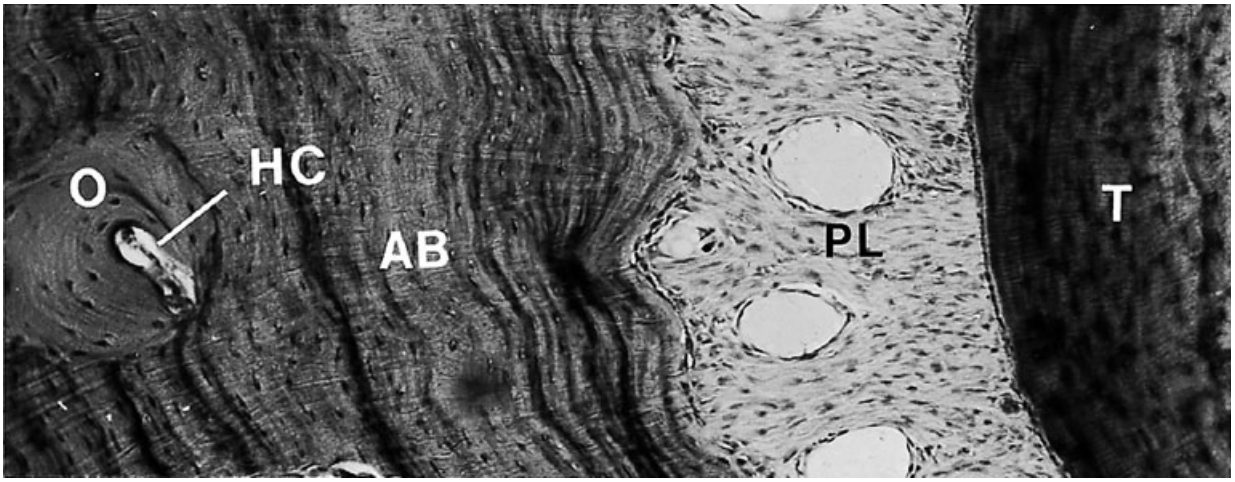


Fig. 1-87

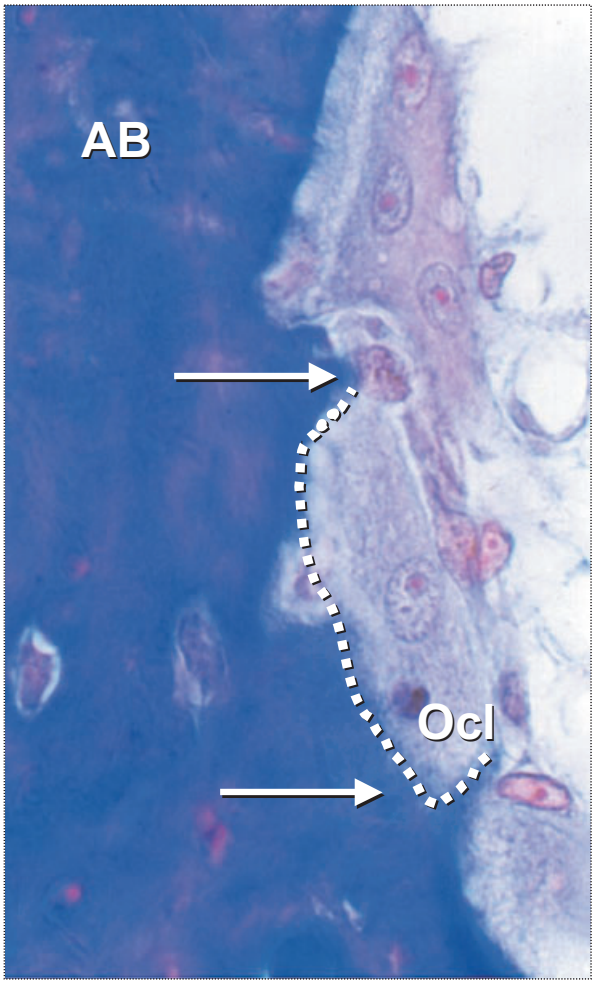


Fig. 1-88

side, and the mineralized matrix on the other, is very large. It has been calculated that the interface between cells and matrix in a cube of bone, 10 × 10 × 10 cm, amounts to approximately 250 m^2. This enormous surface of exchange serves as a regulator, e.g. for serum calcium and serum phosphate levels via hormonal control mechanisms.

Fig. 1-87 The alveolar bone is constantly renewed in response to functional demands. The teeth erupt and migrate in a mesial direction throughout life to compensate for attrition. Such movement of the teeth implies remodeling of the alveolar bone. During the process of remodeling, the bone trabeculae are continuously resorbed and reformed and the cortical bone mass is dissolved and replaced by new bone. During breakdown of the cortical bone, resorption canals are formed by proliferating blood vessels. Such canals, which contain a blood vessel in the center, are subsequently refilled with new bone by the formation of lamellae arranged in concentric layers around the blood vessel. A new Haversian system (O) is seen in the photomicrograph of a horizontal section through the alveolar bone (AB), periodontal ligament (PL), and tooth (T).

Fig. 1-88 The resorption of bone is always associated with *osteoclasts* (Ocl). These cells are giant cells specialized in the breakdown of mineralized matrix (bone, dentin, cementum) and are probably developed from blood monocytes. The resorption occurs by the release of acid substances (lactic acid, etc.) which form an acidic environment in which the mineral salts of the bone tissue become dissolved. Remaining organic substances are eliminated by enzymes and osteoclastic phagocytosis. Actively resorbing osteoclasts adhere to the bone surface and produce lacunar pits called *Howship's lacunae* (dotted line). They are mobile and capable of migrating over the bone surface. The photomicrograph demonstrates osteoclastic activity at the surface of alveolar bone (AB).

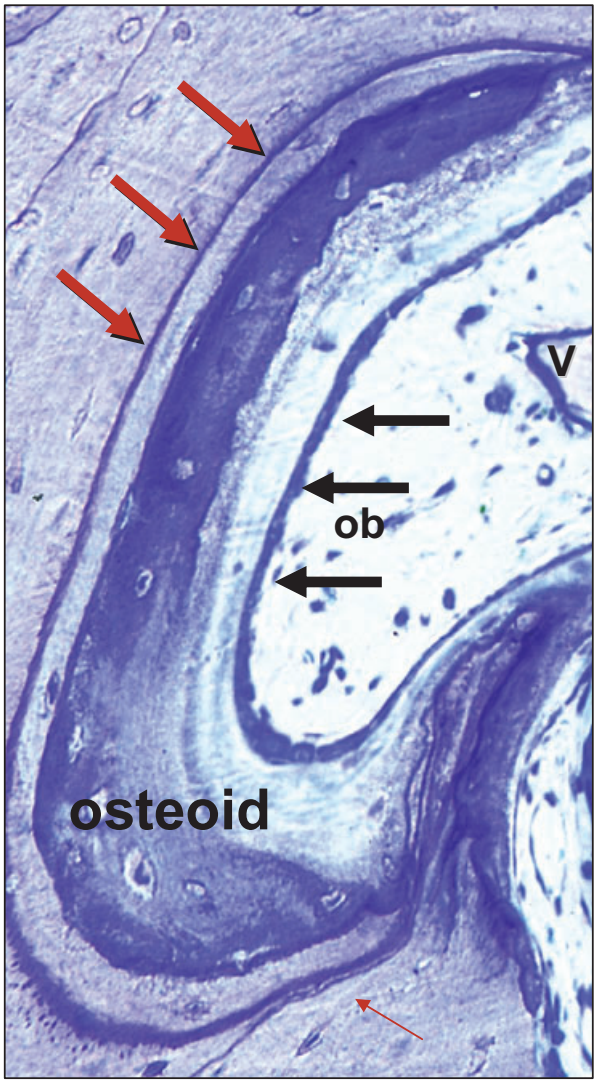


Fig. 1-89

Fig. 1-89 illustrates a so-called bone multicellular unit (BMU), which is present in bone tissue undergoing active remodeling. The reversal line, indicated by red arrows, demonstrates the level to which bone resorption has occurred. From the reversal line new bone has started to form and has the character of osteoid. Note the presence of osteoblasts (ob) and vascular structures (v). The osteoclasts resorb organic as well as inorganic substances.

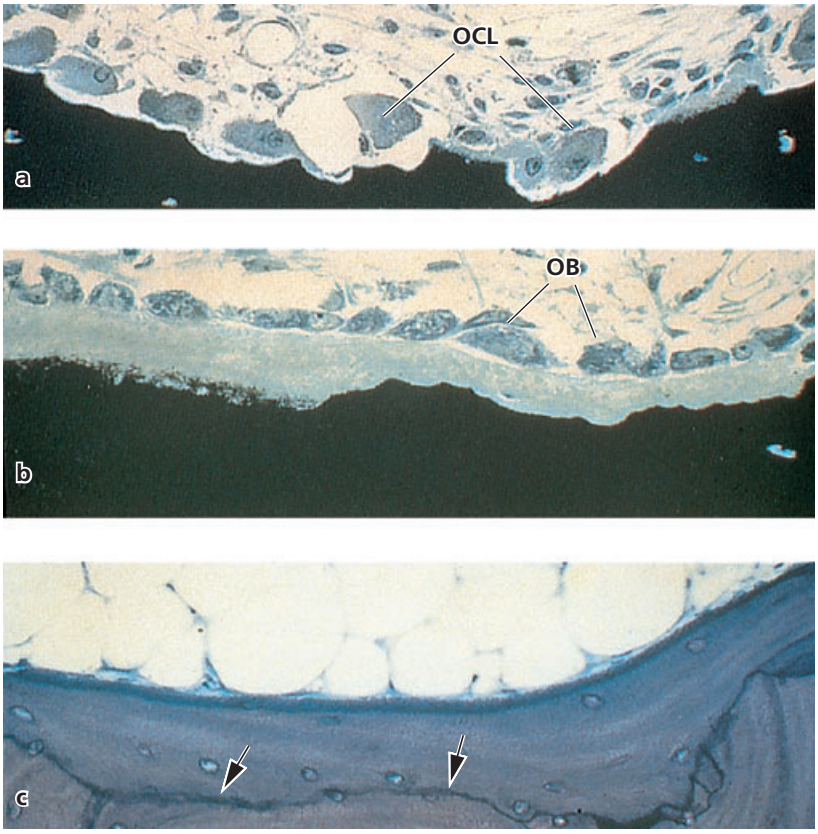


Fig. 1-90

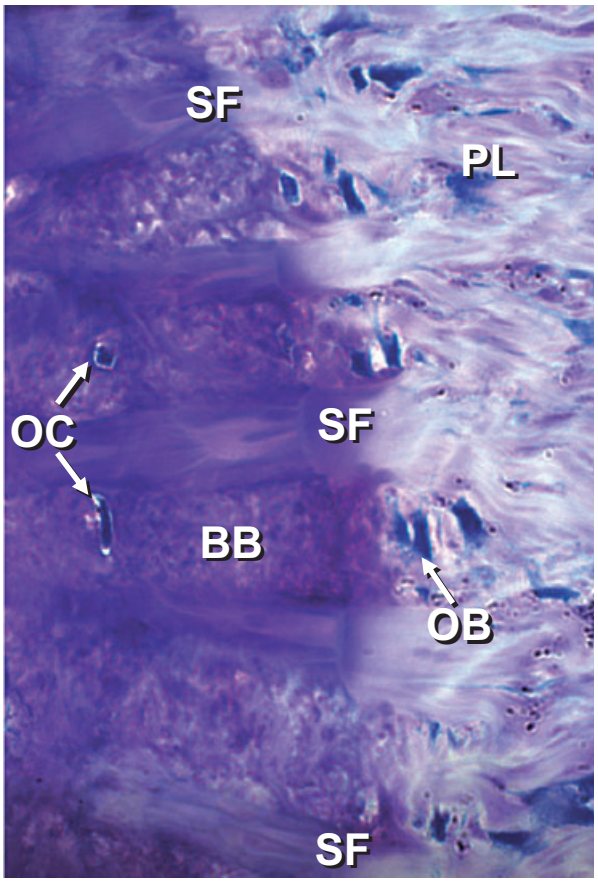


Fig. 1-91

Fig. 1-90 Both the cortical and cancellous alveolar bone are constantly undergoing remodeling (i.e. resorption followed by formation) in response to tooth drifting and changes in functional forces acting on the teeth. Remodeling of the trabecular bone starts with resorption of the bone surface by osteoclasts (OCL) as seen in Fig. 1-90a. After a short period, osteoblasts (OB) start depositing new bone (Fig. 1-90b) and finally a new bone multicellular unit is formed, clearly delineated by a reversal line (arrows) as seen in Fig. 1-90c.

Fig. 1-91 Collagen fibers of the periodontal ligament (PL) insert in the mineralized bone which lines the wall of the tooth socket. This bone, called alveolar bone proper or bundle bone (BB), has a high turnover rate. The portions of the collagen fibers which are inserted inside the bundle bone are called Sharpey's fibers (SF). These fibers are mineralized at their periphery, but often have a non-mineralized central core. The collagen fiber bundles inserting in the bundle bone generally have a larger diameter and are less numerous than the corresponding fiber bundles in the cementum on the opposite side of the periodontal ligament. Individual bundles of fibers can be followed all the way from the alveolar bone to the cementum. However, despite being in the same bundle of fibers, the collagen adjacent to the bone is always less mature than that adjacent to the cementum. The collagen on the tooth side has a low turnover rate. Thus, while the collagen adjacent to the bone is renewed relatively rapidly, the collagen adjacent to the root surface is renewed slowly or not at all. Note the occurrence of osteoblasts (OB) and osteocytes (OC).

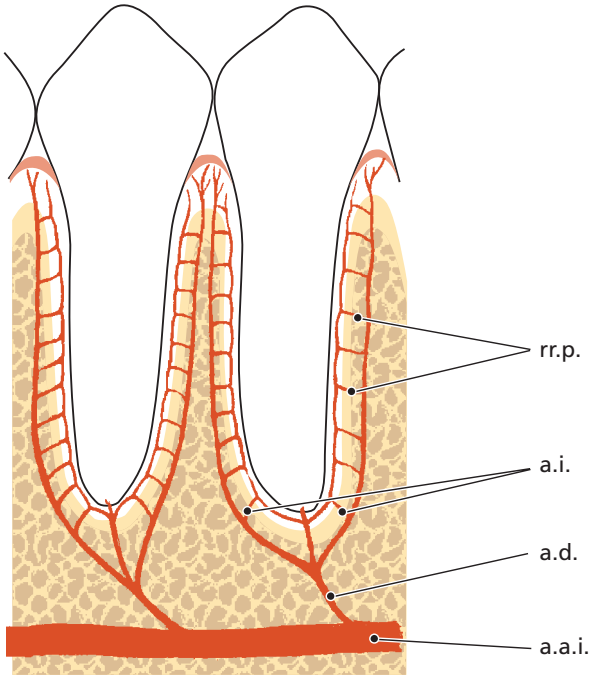


Fig. 1-92

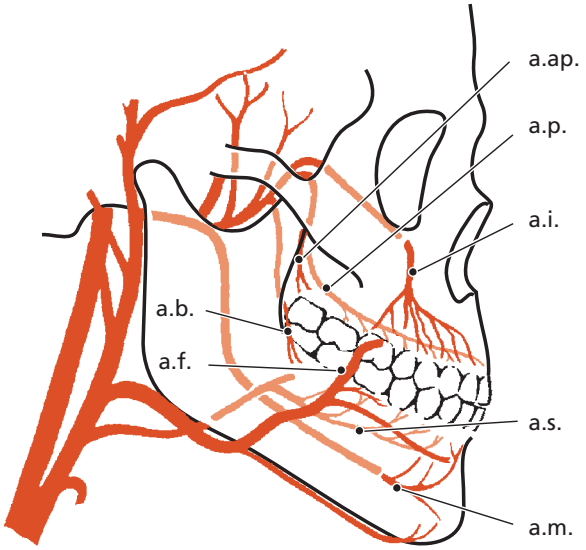


Fig. 1-93

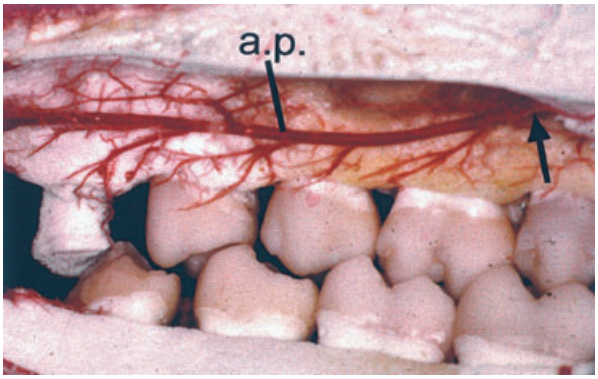


Fig. 1-94

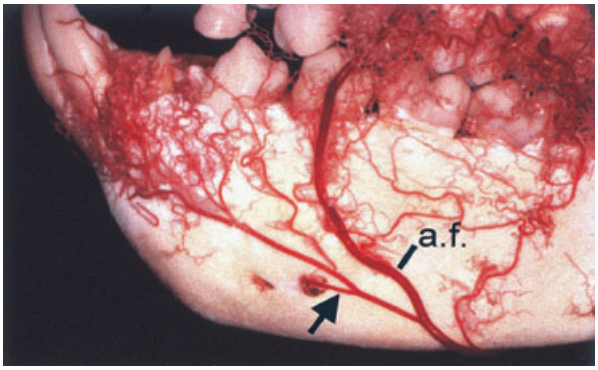


Fig. 1-95

Blood supply of the periodontium

Fig. 1-92 The schematic drawing depicts the blood supply to the teeth and the periodontal tissues. The *dental artery* (a.d.), which is a branch of the *superior* or *inferior* alveolar artery (a.a.i.), dismisses the *intraseptal artery* (a.i.) before it enters the tooth socket. The terminal branches of the *intraseptal artery* (*rami perforantes*, rr.p.) penetrate the alveolar bone proper in canals at all levels of the socket (see Fig. 1-76). They anastomose in the periodontal ligament space, together with blood vessels originating from the apical portion of the periodontal ligament and with other terminal branches, from the intraseptal artery (a.i.). Before the dental artery (a.d.) enters the root canal it puts out branches which supply the apical portion of the periodontal ligament.

Fig. 1-93 The gingiva receives its blood supply mainly through *supraperiosteal* blood vessels which are terminal branches of the *sublingual artery* (a.s.), the *mental artery* (a.m.), the *buccal artery* (a.b.), the *facial artery* (a.f.), the *greater palatine artery* (a.p.), the *infra orbital artery* (a.i.), and the *posterior superior dental artery* (a.ap.).

Fig. 1-94 depicts the course of the greater palatine artery (a.p.) in a specimen of a monkey which was perfused with plastic at sacrifice. Subsequently, the soft tissue was dissolved. The greater palatine artery (a.p.), which is a terminal branch of the *ascending palatine artery* (from the *maxillary*, "internal maxillary", artery), runs through the *greater palatine canal* (arrow) to the palate. As this artery runs in a frontal direction it puts out branches which supply the gingiva and the masticatory mucosa of the palate.

Fig. 1-95 The various arteries are often considered to supply certain well defined regions of the dentition. In reality, however, there are numerous anastomoses

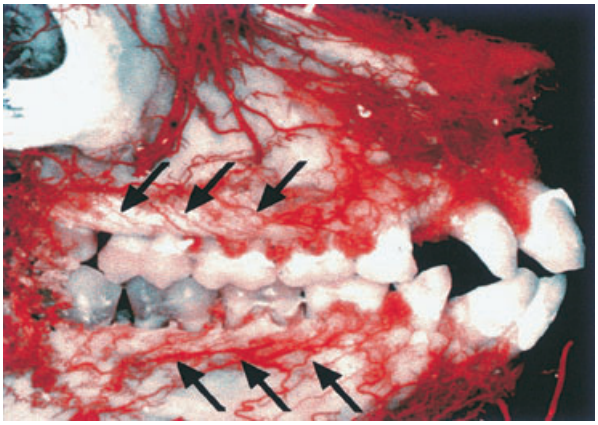


Fig. 1-96

present between the different arteries. Thus, the *entire system of blood vessels*, rather than individual groups of vessels, should be regarded as the unit supplying the soft and hard tissue of the maxilla and the mandible, e.g. in this figure there is an anastomosis (arrow) between the *facial artery* (a.f.) and the blood vessels of the mandible.

Fig. 1-96 illustrates a vestibular segment of the maxilla and mandible from a monkey which was perfused with plastic at sacrifice. Notice that the vestibular gingiva is supplied with blood mainly through *supraperiosteal* blood vessels (arrows).

Fig. 1-97

Fig. 1-97 As can be seen, blood vessels (arrows) originating from vessels in the periodontal ligament pass the alveolar bone crest and contribute to the blood supply of the free gingiva.

Fig. 1-98 shows a specimen from a monkey which was perfused with ink at the time of sacrifice. Subsequently, the specimen was treated to make the tissue transparent (cleared specimen). To the right, the supraperiosteal blood vessels (sv) can be seen. During

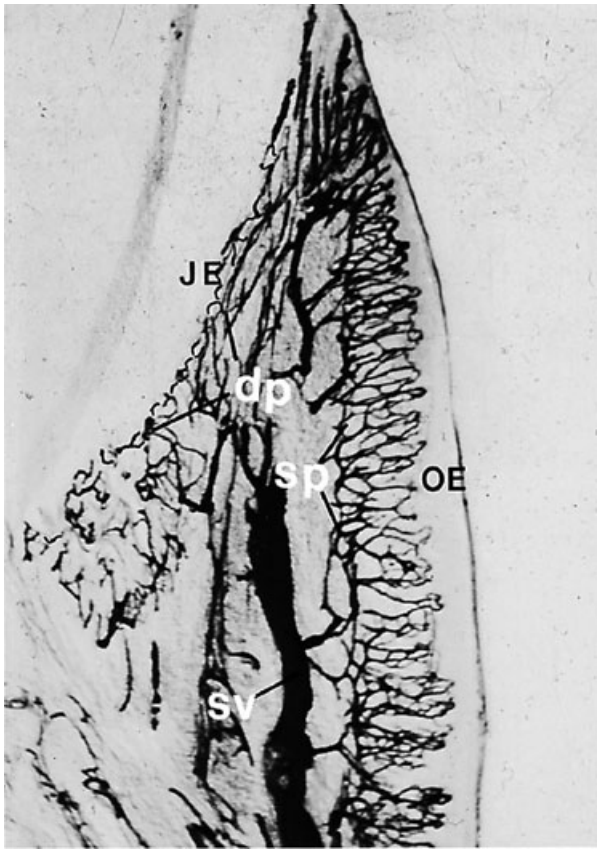


Fig. 1-98

Fig. 1-99

their course towards the free gingiva they put forth numerous branches to the *subepithelial plexus* (sp), located immediately beneath the oral epithelium of the free and attached gingiva. This subepithelial plexus in turn yields thin *capillary loops* to each of the connective tissue papillae projecting into the oral epithelium (OE). The number of such capillary loops is constant over a very long time and is not altered by application of epinephrine or histamine to the gingival margin. This implies that the blood vessels of the lateral portions of the gingiva, even under normal circumstances, are fully utilized and that the blood flow to the free gingiva is regulated entirely by velocity alterations. In the free gingiva, the supraperiosteal blood vessels (sv) anastomose with blood vessels from the periodontal ligament and the bone. Beneath the junctional epithelium (JE) seen to the left, is a plexus of blood vessels termed the *dento-gingival plexus* (dp). The blood vessels in this plexus have a thickness of approximately 40 µm, which means that they are mainly venules. In healthy gingiva, no capillary loops occur in the dento-gingival plexus.

Fig. 1-99 This specimen illustrates how the subepithelial plexus (sp), beneath the oral epithelium of the free and attached gingiva, yields thin capillary loops to each connective tissue papilla. These capillary loops have a diameter of approximately 7 µm, which means they are the size of true capillaries.

Fig. 1-100 illustrates the dento-gingival plexus in a section cut parallel to the subsurface of the junctional epithelium. As can be seen, the dento-gingival plexus consists of a fine-meshed network of blood vessels. In the upper portion of the picture, capillary loops can be detected belonging to the subepithelial plexus beneath the oral sulcular epithelium.

Fig. 1-101 is a schematic drawing of the blood supply to the free gingiva. As stated above, the main blood supply of the free gingiva derives from the *supraperiosteal* blood vessels (SV) which, in the gingiva, anastomose with blood vessels from the *alveolar bone* (ab) and *periodontal ligament* (pl). To the right in the drawing, the oral epithelium (OE) is depicted with its underlying subepithelial plexus of vessels (sp). To the left beneath the junctional epithelium (JE), the dento-gingival plexus (dp) can be seen, which, under normal conditions, comprises a fine-meshed network without capillary loops.

Fig. 1-100

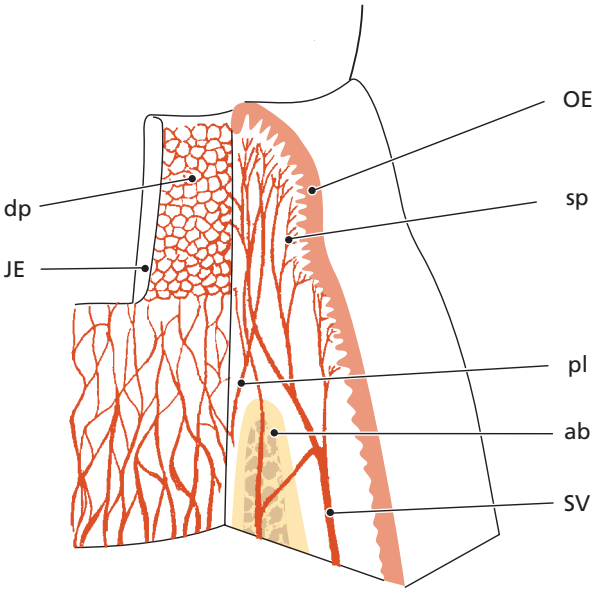


Fig. 1-101

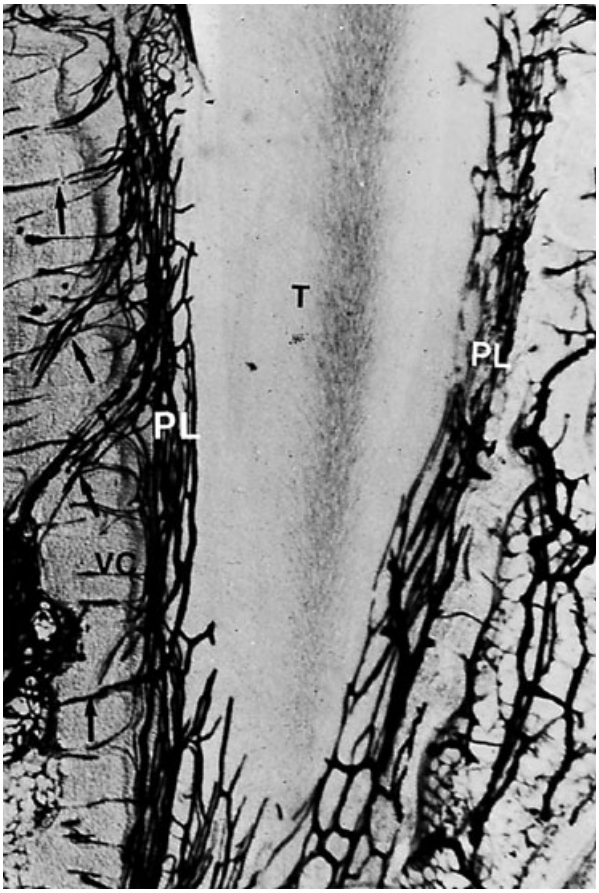


Fig. 1-102

Fig. 1-103

Fig. 1-102 shows a section prepared through a tooth (T) with its periodontium. Blood vessels (perforating rami; arrows) arising from the intraseptal artery in the alveolar bone run through canals (Volkmann's canals) in the socket wall (VC) into the periodontal ligament (PL), where they anastomose.

Fig. 1-103 shows blood vessels in the periodontal ligament in a section cut parallel to the root surface. After entering the periodontal ligament, the blood vessels (perforating rami; arrows) anastomose and form a polyhedral network which surrounds the root like a stocking. The majority of the blood vessels in the periodontal ligament are found close to the alveolar bone. In the coronal portion of the periodontal ligament, blood vessels run in coronal direction, passing the alveolar bone crest, into the free gingiva (see Fig. 1-97).

Fig. 1-104 is a schematic drawing of the blood supply of the periodontium. The blood vessels in the periodontal ligament form a polyhedral network surrounding the root. Note that the free gingiva receives its blood supply from (1) supraperiosteal blood vessels, (2) the blood vessels of the periodontal ligament, and (3) the blood vessels of the alveolar bone.

Fig. 1-105 illustrates schematically the so-called *extravascular* circulation through which nutrients and other substances are carried to the individual cells and metabolic waste products are removed from the tissue. In the arterial (A) end of the capillary, to the left in the drawing, a hydraulic pressure of approximately 35 mmHg is maintained as a result of the pumping function of the heart. Since the hydraulic pressure is higher than the osmotic pressure (OP) in the tissue (which is approximately 30 mmHg), transportation of substances will occur from the blood vessels to the extravascular space (ES). In the venous (V) end of the capillary system, to the right in the drawing, the hydraulic pressure has decreased to approximately 25 mmHg (i.e. 5 mmHg lower than the osmotic pressure in the tissue). This allows transportation of substances from the extravascular space to the blood vessels. Thus, the difference between the hydraulic pressure and the osmotic pressure (OP) results in transportation of substances from the blood vessels to the extravascular space in the arterial part of the capillary while, in the venous part, transportation of substances occurs from the extravascular space to the blood vessels. An extravascular circulation is hereby established (small arrows).

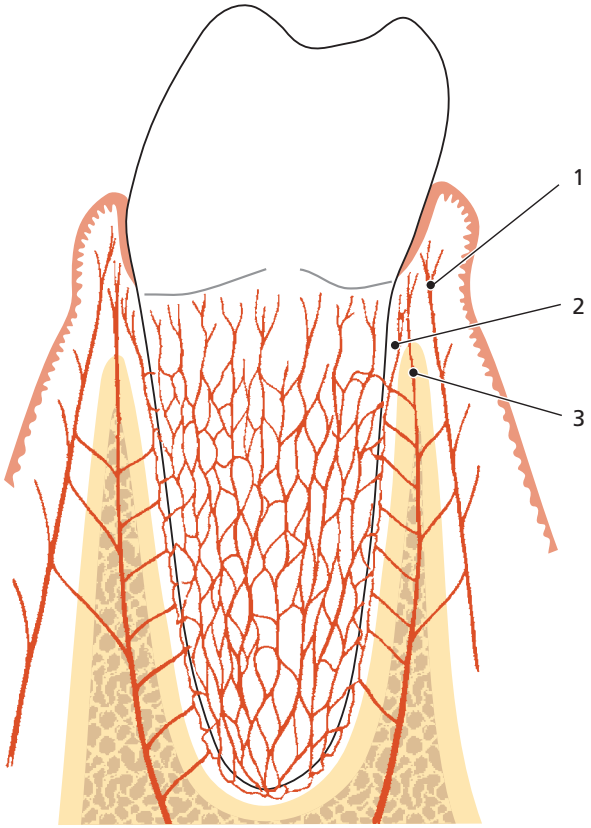


Fig. 1-104

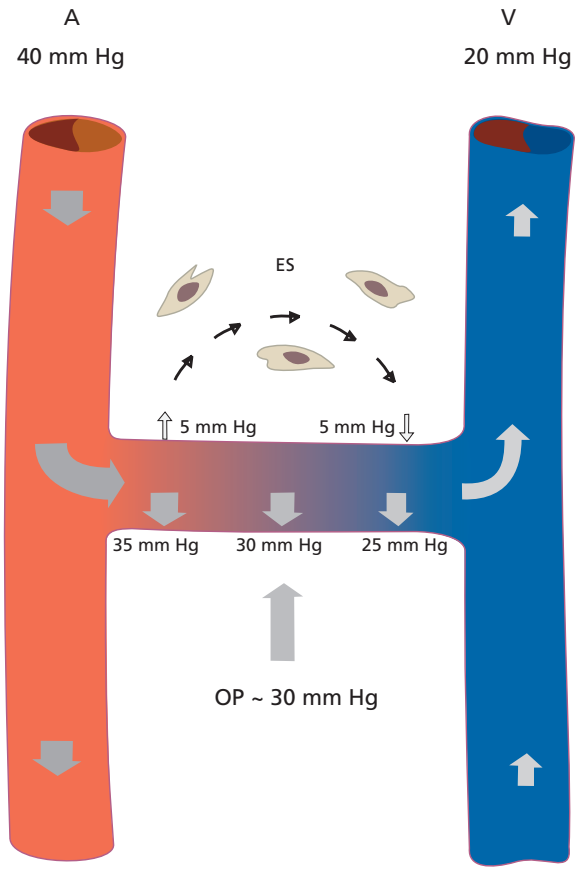


Fig. 1-105

Lymphatic system of the periodontium

Fig. 1-106 The smallest lymph vessels, the *lymph capillaries*, form an extensive network in the connective tissue. The wall of the lymph capillary consists of a single layer of endothelial cells. For this reason such capillaries are difficult to identify in an ordinary histologic section. The lymph is absorbed from the tissue fluid through the thin walls into the lymph capillaries. From the capillaries, the lymph passes into larger lymph vessels which are often in the vicinity of corresponding blood vessels. Before the lymph enters the blood stream it passes through one or more *lymph nodes* in which the lymph is filtered and supplied with lymphocytes. The lymph vessels are like veins provided with valves. The lymph from the periodontal tissues drains to the lymph nodes of the head and the neck. The labial and lingual gingiva of the mandibular incisor region is drained to the *submental lymph nodes* (sme). The palatal gingiva of the maxilla is drained to the *deep cervical lymph nodes* (cp). The buccal gingiva of the maxilla and the buccal and lingual gingiva in the mandibular premolar–molar region are drained to *submandibular lymph nodes* (sma). Except for the third molars and mandibular incisors, all teeth with their adjacent periodontal tissues are drained to the submandibular lymph nodes (sma). The third molars are drained to the *jugulodigastric lymph node* (jd) and the mandibular incisors to the *submental lymph nodes* (sme).

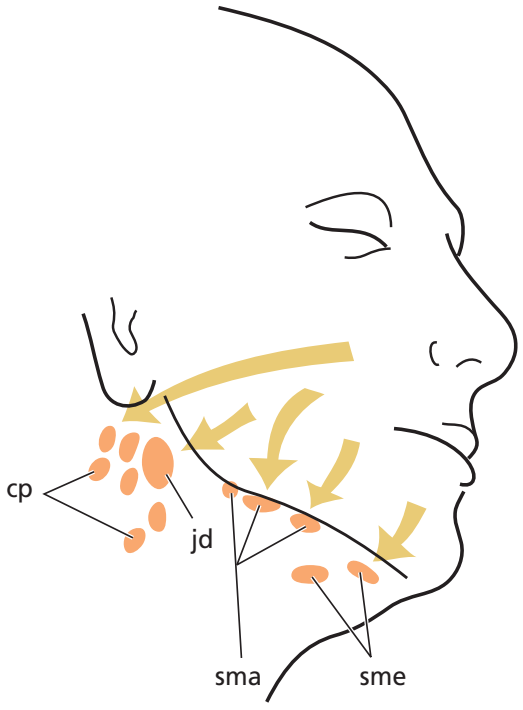


Fig. 1-106

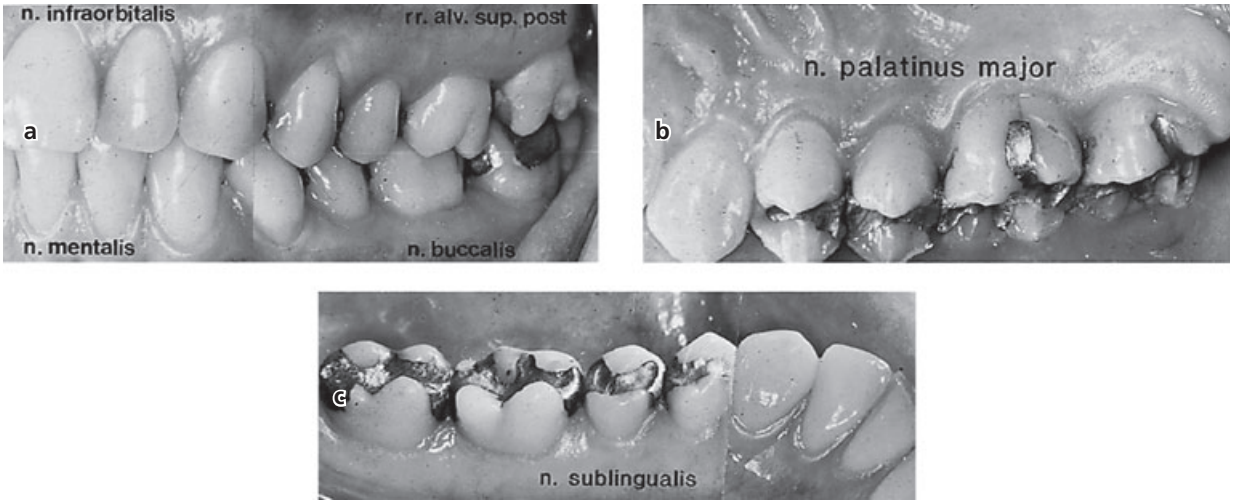


Fig. 1-107

Nerves of the periodontium

Like other tissues in the body, the periodontium contains receptors which record pain, touch, and pressure (*nociceptors* and *mechanoreceptors*). In addition to the different types of sensory receptors, nerve components are found innervating the blood vessels of the periodontium. Nerves recording pain, touch, and pressure have their trophic center in the *semilunar ganglion* and are brought to the periodontium via the *trigeminal nerve* and its end branches. Owing to the presence of receptors in the periodontal ligament, small forces applied on the teeth may be identified. For example, the presence of a very thin (10–30 µm) metal foil strip placed between the teeth during occlusion can readily be identified. It is also well known that a movement which brings the teeth of the mandible in contact with the occlusal surfaces of the maxillary teeth is arrested reflexively and altered into an opening movement if a hard object is detected in the chew. Thus, the receptors in the periodontal ligament, together with the proprioceptors in muscles and tendons, play an essential role in the regulation of chewing movements and chewing forces.

Fig. 1-107 shows the various regions of the gingiva which are innervated by end branches of the trigeminal nerve. The gingiva on the labial aspect of maxillary incisors, canines, and premolars is innervated by *superior labial branches* from the *infraorbital nerve* (n. infraorbitalis) (Fig. 1-107a). The buccal gingiva in the maxillary molar region is innervated by branches from the *posterior superior dental nerve* (rr. alv. sup. post) (Fig. 1-107a). The palatal gingiva is innervated by the *greater palatal nerve* (n. palatinus major) (Fig. 1-107b), except for the area of the incisors, which is innervated by the *long sphenopalatine nerve* (n. pterygopalatini). The lingual gingiva in the mandible is innervated by the *sublingual nerve* (n. sublingualis) (Fig. 1-107c), which is an end branch of the *lingual nerve*. The gingiva at the labial aspect of mandibular

Fig. 1-108

incisors and canines is innervated by the *mental nerve* (n. mentalis), and the gingiva at the buccal aspect of the molars by the *buccal nerve* (n. buccalis) (Fig. 1-107a). The innervation areas of these two nerves frequently overlap in the premolar region. The teeth in the mandible, including their periodontal ligament, are innervated by the *inferior alveolar nerve* (n. alveolaris inf.), while the teeth in the maxilla are innervated by the *superior alveolar plexus* (n. alveolares sup).

Fig. 1-108 The small nerves of the periodontium follow almost the same course as the blood vessels. The nerves to the gingiva run in the tissue superficial to the periosteum and put out several branches to the oral epithelium on their way towards the free gingiva. The nerves enter the periodontal ligament through the perforations (Volkmann's canals) in the socket wall (see Fig. 1-102). In the periodontal ligament, the nerves join larger bundles which take a course parallel to the long axis of the tooth. The photomicrograph illustrates small nerves (arrows) which have emerged from larger bundles of ascending nerves in order to supply certain parts of the periodontal ligament tissue. Various types of neural terminations such as free nerve endings and Ruffini's corpuscles have been identified in the periodontal ligament.

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Chapter 2

The Edentulous Alveolar Ridge

Maurício Araújo and Jan Lindhe

Clinical considerations

The alveolar process forms in harmony with the development and eruption of the teeth and it gradually regresses when the teeth are lost. In other words, the formation as well as the continued preservation of the alveolar process is dependent on the continued presence of teeth. Furthermore, the morphologic characteristics of the alveolar process are related to the size and shape of the teeth, events occurring during tooth eruption as well as the inclination of the erupted teeth. Thus, subjects with long and narrow teeth, compared with subjects who have short and wide teeth, appear to have a more delicate alveolar process and, in particular, a thin, sometimes fenestrated buccal bone plate (Fig. 2-1).

The tooth and its surrounding attachment tissues – the root cementum, the periodontal ligament and the bundle bone – establish a functional unit (Fig. 2-2). Hence, forces elicited, for example during mastication, are transmitted from the crown of the tooth via the root and the attachment tissues to the load-carrying hard tissue structures in the alveolar process, where they are dispersed. The loss of teeth, and the loss or change of function within and around the socket will result in a series of adaptive alterations of the now edentulous portion of the ridge. Thus, it is well documented that following *multiple tooth* extractions and the subsequent restoration with removable dentures, the size of the alveolar ridge will become markedly reduced, not only in the horizontal but also in the vertical dimension (Figs. 2-3, 2-4); in addition, the arch will be shortened (Atwood 1962, 1963; Johnson 1963, 1969; Carlsson *et al*. 1967).

Also following the removal of *single* teeth the alveolar ridge will be markedly diminished (Fig. 2-5). The magnitude of this change was studied and reported in a publication by Pietrokovski and Massler (1967). The authors had access to 149 dental cast models (72 maxillary and 77 mandibular) in which one tooth was missing (and not replaced) on one side of the jaw. The outer contours of the buccal and lingual (palatal) portions of the ridge at a tooth site and at

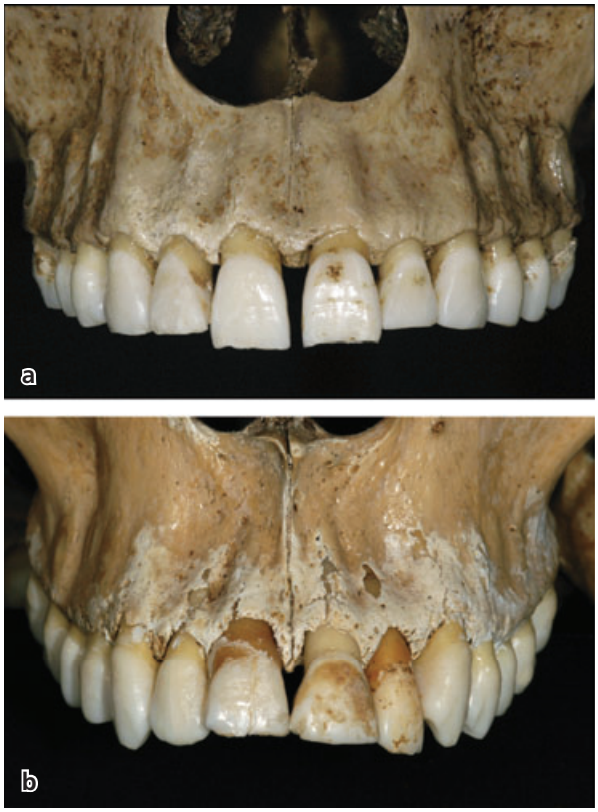

Fig. 2-1 Buccal aspect of adult skull preparations illustrating a dentate maxilla of one subject with a thick (a) and another subject with a thin (b) periodontal biotype.

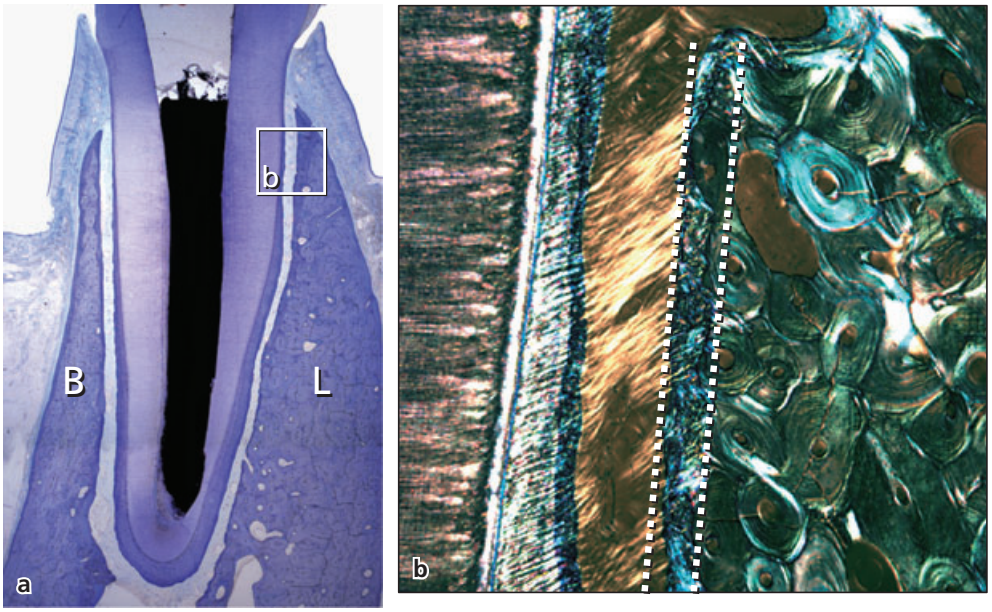

Fig. 2-2 Buccal–lingual section of a dentate portion of the alveolar process. B = buccal aspect; L = lingual aspect. (a) The tooth is surrounded by its attachment tissues. (b) Larger magnification of the attachment tissues. Note that the dentin is connected to the alveolar bone via the root cementum, the periodontal ligament and the alveolar bone. The inner portion of the alveolar bone (dotted line) is called the alveolar bone proper or the bundle bone.

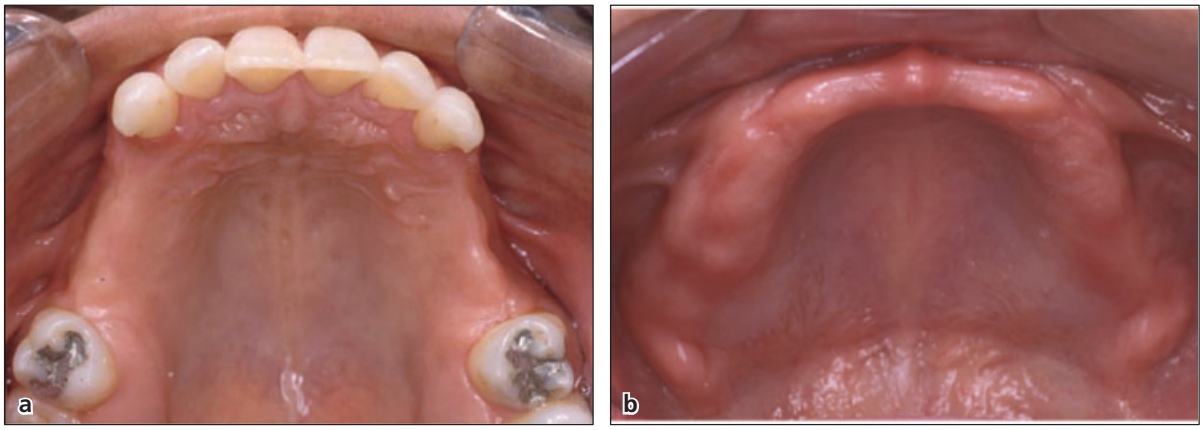

Fig. 2-3 (a) Clinical view of a partially edentulous maxilla. Note that the crest of the edentulous portions of the ridge is narrow in the buccal–palatal direction. (b) Clinical view of a fully edentulous and markedly resorbed maxilla. Note that *papilla incisiva* is located in the center of the ridge. This indicates that the entire buccal but also a substantial portion of the palatal ridge are missing.

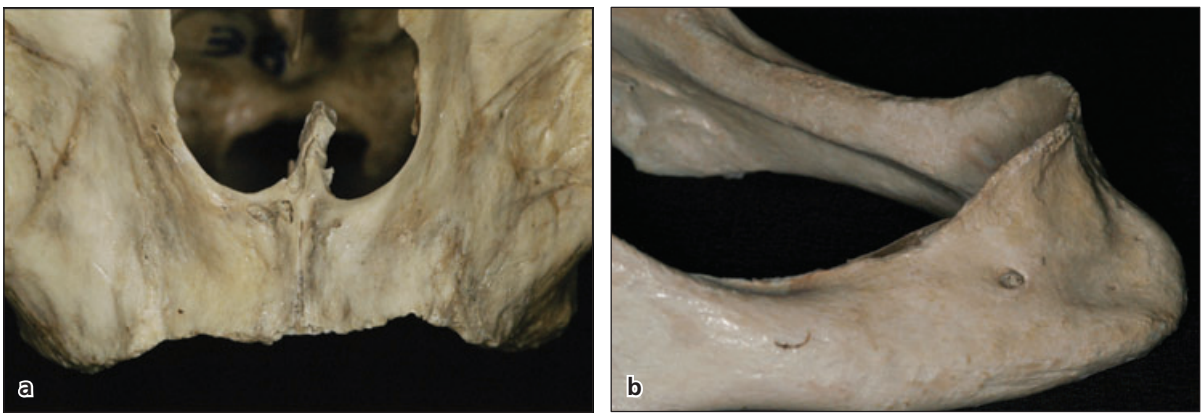

Fig. 2-4 Buccal aspect of a skull preparation illustrating a fully edentulous maxilla (a) and mandible (b). The small segments of the alveolar ridge that still remain are extremely thin in the buccal–palatal/lingual direction.

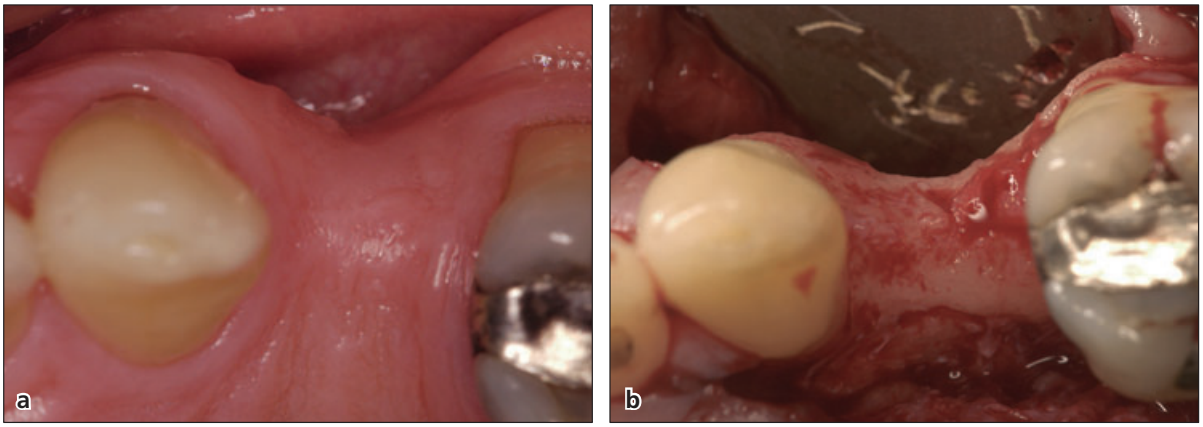

Fig. 2-5 Clinical view of an edentulous ridge in the maxillary premolar region. The premolar was extracted several years before the clinical documentation was made. (a) Note the presence of a buccal invagination of the ridge. (b) Following flap elevation, the crest region of the severely resorbed buccal portion of alveolar process is disclosed.

the contralateral edentulous site were determined by the use of a profile stylus and an imaging technique. Their findings are reported in Table 2-1.

It was concluded that the amount of tissue resorption (hard and soft tissues combined) following the loss of a single tooth was substantial and that the reduction of the ridge was greater along the buccal surface than along the lingual and palatal surfaces in every specimen examined, although the absolute amounts and differences varied from one group of teeth to the next. As a result of this tissue modeling, the center of the edentulous site shifted toward the lingual or palatal aspect of the ridge. The observations made by Pietrokovski and Massler (1967) were supported by recent findings presented by Schropp *et al*. (2003). They studied bone and soft tissue volume changes that took place during a 12-month period following the extraction of single premolars and molars. Clinical as well as cast model measurements were made immediately after tooth extraction and subsequently after 3, 6, and 12 months of healing. It was observed that the buccal–lingual/palatal dimension during the first 3 months was reduced about 30%, and after 12 months the edentulous site had lost at least 50% of its original width. Furthermore, the height of the buccal bone plate was reduced and after 12 months of healing the buccal prominence was located 1.2 mm apical of its lingual/palatal counterpart.

Conclusion: The extraction of single as well as multiple teeth induces a series of adaptive changes in the soft and hard tissues that result in an overall regress of the edentulous site(s). Resorption appears to be more pronounced at the buccal than at lingual/palatal aspects of the ridge.

In this context it should be observed that the alveolar process might also undergo change as the result of tooth-related disease processes, such as aggressive, chronic and necrotizing forms of marginal periodontitis as well as periapical periodontitis. Furthermore, traumatic injuries may cause marked alterations of the maxilla and mandible including their alveolar processes.

Table 2-1 Average amount of resorption of tooth extraction in different tooth areas*

Tooth	Average amount of resorption (mm)		Difference
	Buccal surface	Lingual/palatal surface	
Mandibular teeth			
Central incisor	2.08	0.91	1.17
Lateral incisor	3.54	1.41	2.13
Canine	3.25	1.59	1.66
First premolar	3.45	1.40	2.05
Second premolar	3.28	0.75	2.53
First molar	4.69	2.79	1.90
Second molar	4.30	3.00	1.30
Maxillary teeth			
Central incisor	3.03	1.46	1.57
Lateral incisor	3.47	0.86	2.61
Canine	3.33	1.91	1.42
First premolar	3.33	2.04	1.29
Second premolar	2.58	1.62	0.96
First molar	5.25	3.12	2.13

* "The amount of resorption was greater along the buccal surface than along the lingual or palatal surface in every specimen examined, although the absolute amounts and differences varied very widely. This caused a shift in the center of the edentulous ridge toward the lingual or palatal side of the ridge with a concomitant *decrease* in arch length in the mandible as well as the maxillae." (Pietrokovski & Massler 1967)

Remaining bone in the edentulous ridge

In the publication by Schropp *et al*. (2003) bone tissue formation in extraction sockets was studied by means of subtraction radiography. Thus, radiographs of the study sites were obtained using a standardized technique immediately after tooth extraction and then

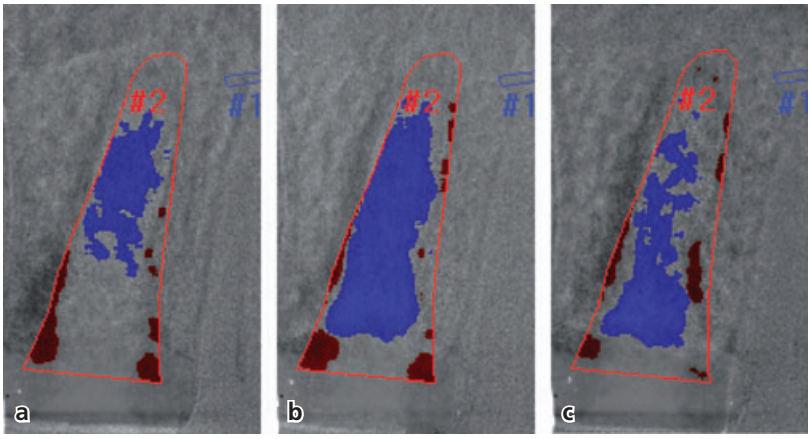

Fig. 2-6 Radiographic (subtraction radiography) images of an extraction site obtained after (a) 3 months, (b) 6 months, and (c) 12 months of healing. The blue color represents areas of new bone formation. During the first 6 months, the deposition of new bone was intense. Between 6 and 12 months, some of the newly formed bone was remodeled. (Courtesy of Dr. L. Schropp.)

after 3, 6, and 12 months of healing (Fig. 2-6). It was observed that in the first few months some bone loss (height) took place in the alveolar crest region. Most of the bone gain in the socket occurred in the first 3 months. There was additional gain of bone in the socket between 3 and 6 months. In the interval between 6 and 12 months, the newly formed bone obviously remodeled and the amount of mineralized tissue was reduced. In other words, towards the end of socket healing small amounts of mineralized tissue may have remained in the center of the edentulous site.

Classification of remaining bone

Based on the volume of remaining mineralized bone, the edentulous sites may, according to Lekhom and Zarb (1985), be classified into five different groups (Fig. 2-7). In groups A and B substantial amounts of the alveolar process still remain, whereas in groups C, D, and E, there are only minute remnants of the alveolar process present. Lekholm and Zarb (1985) also classified the "quality" of the bone in the edentulous site. Class 1 and class 2 characterized a location in which the walls – the cortical plates – of the site are thick and the volume of bone marrow is small. Sites that belong to class 3 and class 4, however, are bordered by relatively thin walls of cortical bone, while the amount of cancellous bone (spongiosa), including trabeculae of lamellar bone and marrow, is large.

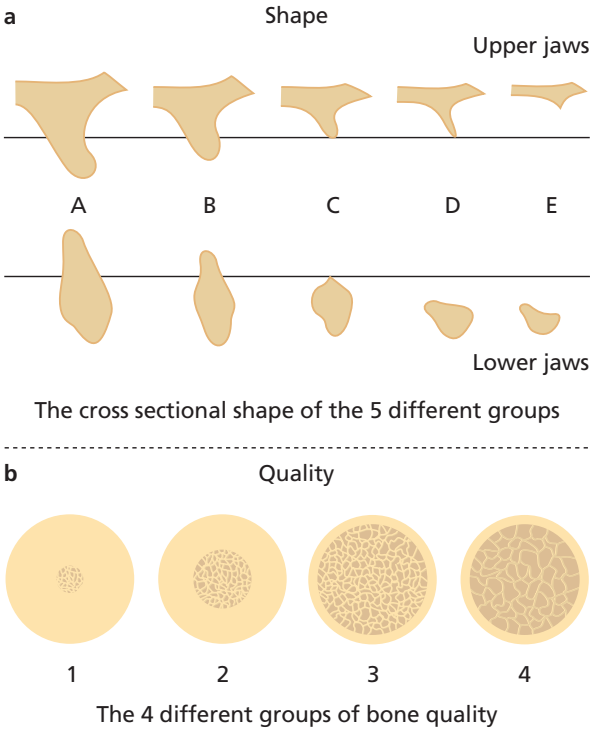

Fig. 2-7 Schematic drawings showing (a) a classification of residual jaw shape, and (b) jaw bone quality, according to Lekholm and Zarb (1985).

Topography of the alveolar process

The dentate alveolar process is defined as the portion of the mandible or maxilla that contains the sockets of the teeth (Fig. 2-8). There is, however, no distinct boundary between the alveolar process and the basal bone of the jaws.

The alveolar process (Fig. 2-9) is comprised of the outer walls – buccal and lingual/palatal cortical plates – and a central portion of spongy bone (anatomic term) – or trabecular bone (radiographic term) or cancellous bone (histologic term) – that contains bone trabeculae as well as marrow. The cortical plates are continuous with the bone that lines the sockets, i.e. the alveolar bone proper (Fig. 2-10). The alveolar bone proper can also be identified as the cribriform plate (anatomic term; Fig. 2-11), or the lamina dura dentes (radiographic term; Fig. 2-12) or the bundle bone (histologic term; Fig. 2-2b). The bundle bone is the tissue in which the extrinsic collagen fiber bundles of the periodontal ligament are embedded.

The cortical plates (the outer walls) of the alveolar process meet the alveolar bone proper at the crest of the interdental septum (Fig. 2-10); at sites with a normal periodontium this is located about 1–2 mm apical of the cemento-enamel junction of adjacent teeth. In some portions of the anterior dentition, the spongy bone of the alveolar process may be absent.

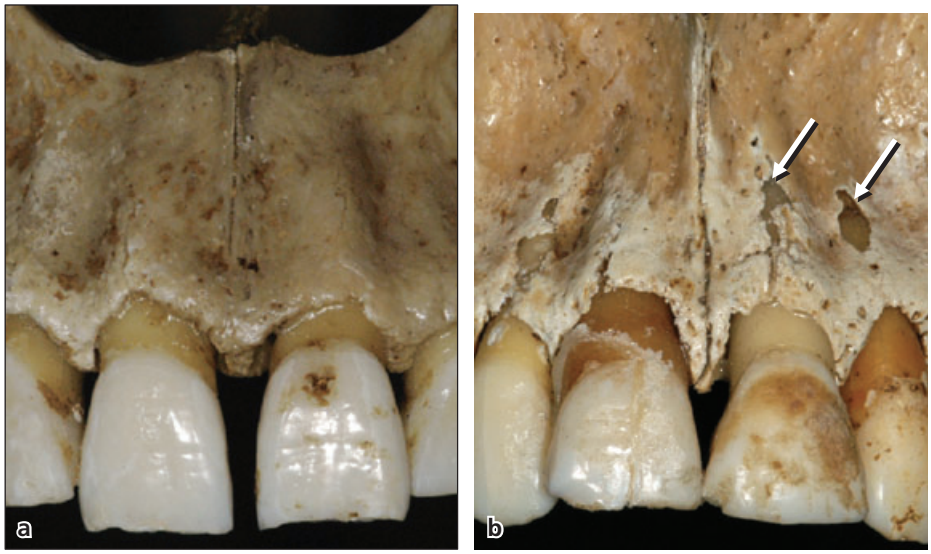

Fig. 2-8 Buccal aspect of the maxillary incisor region of a skull preparation illustrating one subject with a thick (a) and another subject with a thin (b) periodontal biotype. Arrows indicate the presence of fenestrations in the buccal bone.

Fig. 2-9 A buccal–lingual section from a human skull preparation illustrating the outer buccal and lingual cortical plates of the alveolar process, as well as the spongy bone in the center of the ridge.

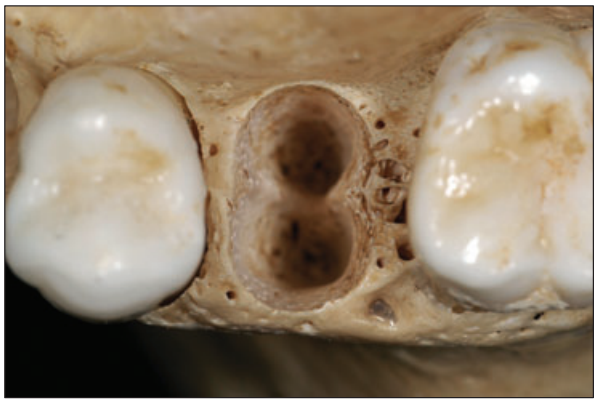

Fig. 2-10 The empty alveolus of a second maxillary premolar is illustrated in the skull preparation. The buccal and palatal cortical plates are continuous with the alveolar bone proper and the bone tissue of the interdental septum. The perforations in the crest region represent the Volkman's canals.

The cortical plates in such locations are continuous with the alveolar bone proper of the socket.

The cortical plate is made up of lamellar bone. Lamellar bone contains both concentric and interstitial lamellae (see Chapter 1). The spongy bone contains trabeculae of lamellar bone; in the adult these are surrounded by a marrow that is rich in adipocytes and pluripotent, mesenchymal stroma cells (Fig. 2-13). Such cells may be induced to form bone, but also to support the differentiation of hemapoietic cells and thereby the differentiation of osteoclasts.

The trabeculae of the spongy bone are orientated in directions that allow them to take up and distribute stress that occurs during mastication and other tooth contacts.

Alterations of the alveolar process following tooth extraction

The alterations that occur in the alveolar ridge following the extraction of single teeth can, for didactic reasons, be divided in two interrelated series of events, namely *intra-alveolar processes* and *extra-alveolar processes.*

Intra-alveolar processes

The healing of extraction sockets in human volunteers was studied by e.g. Amler (1969) and Evian

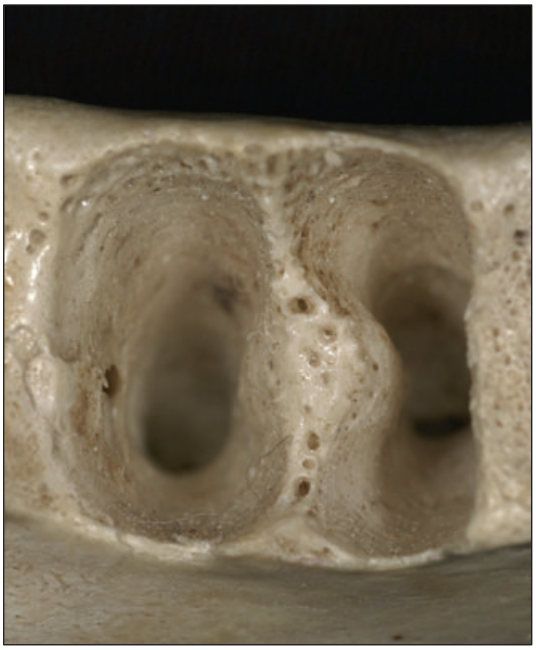

Fig. 2-11 A mandibular molar region of a human skull preparation. The second molar was removed in the skull preparation. In such an anatomic section, the alveolar bone proper (on the inside of the alveolus) is often termed the *cribriform plate*. This is due to the numerous perforations (Volkman's canals) that are present on the bone surface.

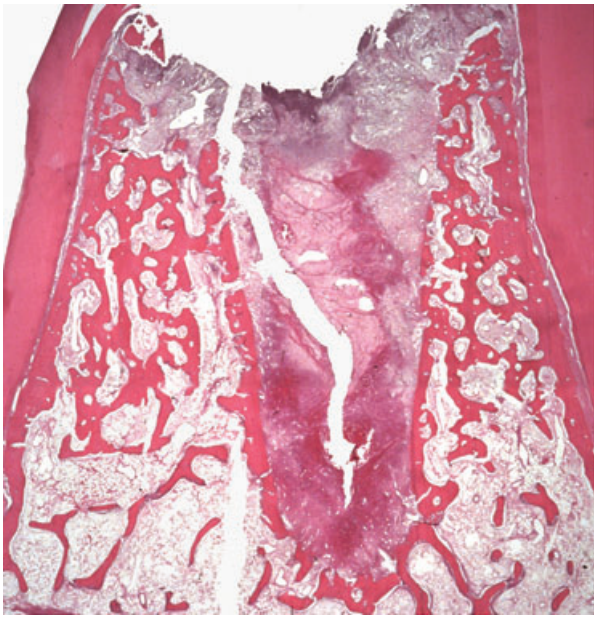

Fig. 2-13 Histologic section presenting the mesio-distal aspect of a fresh extraction socket bordered by two neighboring roots. Note that the alveolar bone from the tooth sites is continuous with the walls of the empty socket. The interdental septum contains cancellous bone including trabeculae of lamellar bone and marrow.

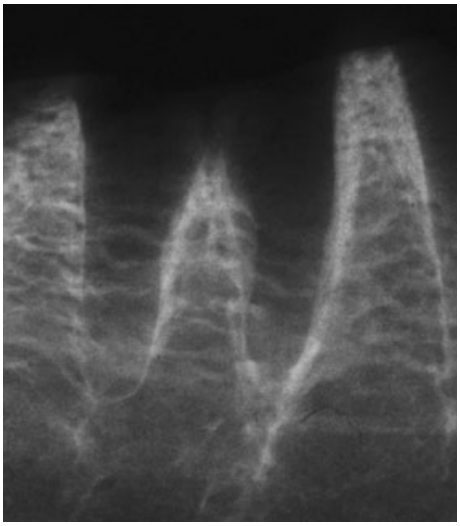

Fig. 2-12 Radiograph obtained from the specimen illustrated in Fig. 2-11. In the radiograph the alveolar bone proper is often identified as lamina dura (dentes).

et al. (1982). Although the biopsy technique used by Amler only allowed the study of healing in the marginal portions of the empty socket, his findings are often referred to. A copy of the drawing included in Amler's publication "The time sequence of tissue regeneration in human extraction wounds" is presented in Fig. 2-14.

Amler stated that following tooth extraction, the first 24 hours are characterized by the formation of a *blood clot* in the socket. Within 2–3 days the blood clot is gradually being replaced with *granulation tissue*. After 4–5 days, the *epithelium* from the margins of the soft tissue starts to proliferate to cover the granulation tissue in the socket. One week after extraction, the socket contains granulation tissue, *young connective tissue*, and *osteoid* formation is ongoing in the apical portion of the socket. After 3 weeks, the socket contains connective tissue and there are signs of mineralization of the osteoid. The *epithelium* covers the wound. After 6 weeks of healing, bone formation in the socket is pronounced and trabeculae of newly formed bone can be seen.

Amler's study was of short duration, so it could only evaluate events that took place in the marginal portion of the healing socket. His experimental data did not include the important later phase of socket healing that involves the processes of modeling and remodeling of the newly formed tissue in various parts of the alveolus. Thus, the tissue composition of the fully healed extraction site was not documented in the study.

The results from a recent, long-term experiment in the dog (Cardaropoli *et al*. 2003) will therefore be used to describe more in detail the various phases of socket healing including processes of both modeling and remodeling. Following the elevation of buccal and lingual full-thickness flaps, the distal roots of mandibular premolars were extracted (Fig. 2-15a). The mucosal flaps were managed to provide soft tissue coverage of the fresh extraction wound (Fig. 2-15b). Healing of the extraction sites was monitored

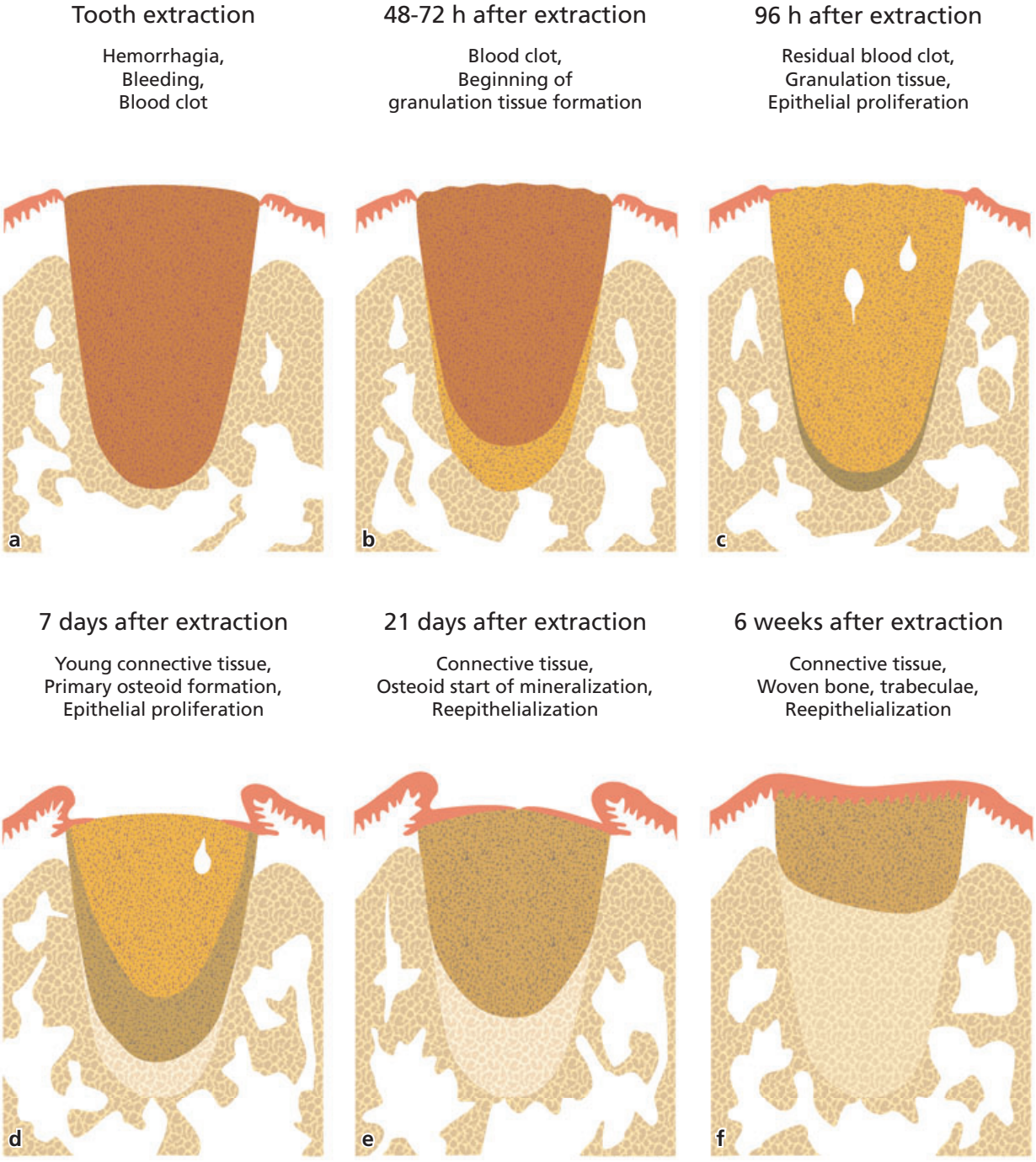

Fig. 2-14 Healing of the alveolar socket after tooth extraction according to Amler (1969). (a) Bleeding and formation of a blood clot immediately after tooth extraction. Blood vessels are closed by trombi and a fibrin network is formed. (b) Already, during the first 48 hours, neutrophilic granulocytes, monocytes and fibroblasts begin to migrate within the fibrin network. (c) The blood clot is slowly replaced by granulation tissue. (d) Granulation tissue forms predominantly in the apical third of the alveolus. There is increased density of fibroblasts. After 4 days, contraction of the clot and proliferation of the oral epithelium is seen. Osteoclasts are visible at the margin of the alveolus. Osteoblasts and osteoids seem to appear in the bottom of the alveolus. (e) Reorganization of the granulation tissue through formation of osteoid trabeculae. Epithelial proliferation from the wound margins on the top of the young connective tissue. Again, the formation of osteoid trabeculae is evident from the wall of the alveolus in a coronal direction. After 3 weeks some of the trabeculae start to mineralize. (f) Radiographically, bone formation may be visible. The soft tissue wound is closed and epithelialized after 6 weeks. However, bone fill in the alveolus takes up to 4 months and does not seem to reach the level of the neighboring teeth.

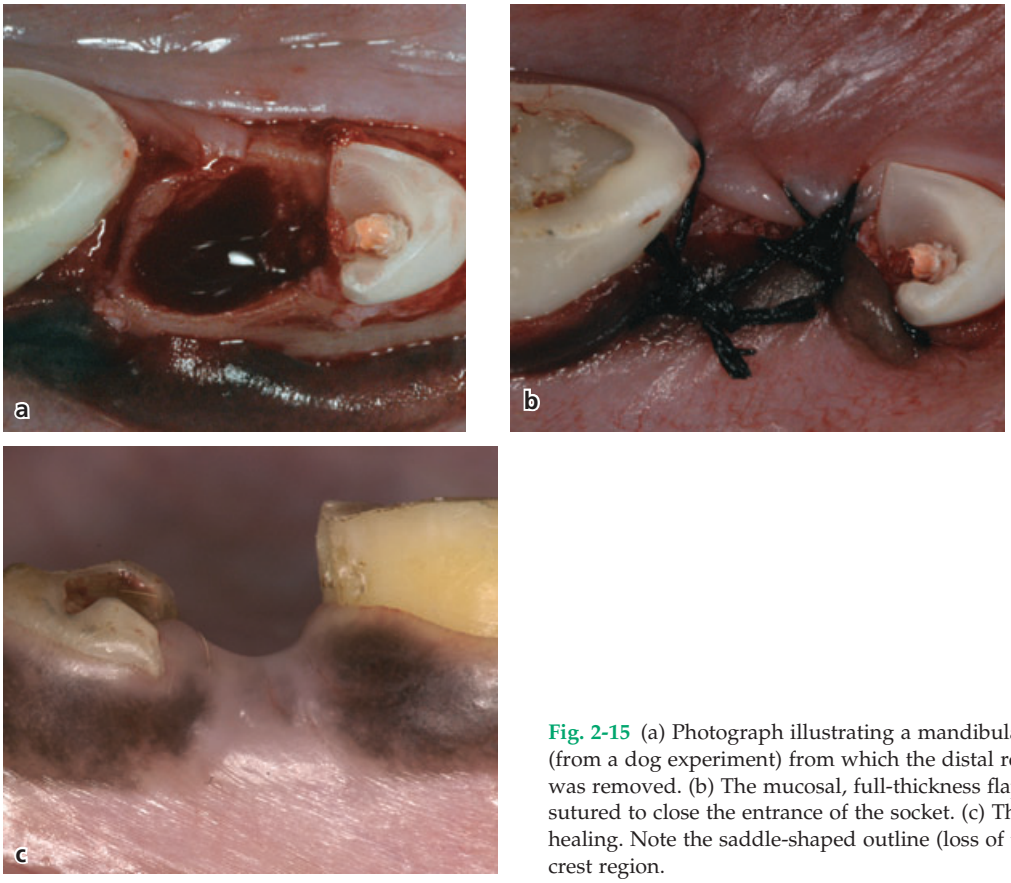

Fig. 2-15 (a) Photograph illustrating a mandibular premolar site (from a dog experiment) from which the distal root of the 4th premolar was removed. (b) The mucosal, full-thickness flaps were replaced and sutured to close the entrance of the socket. (c) The site after 6 months of healing. Note the saddle-shaped outline (loss of tissue) of the alveolar crest region.

in biopsy specimens obtained at time intervals between 1 day and 6 months (Fig. 2-15c).

Overall pattern of socket healing

Figure 2-13 presents a mesio-distal section of a fresh extraction socket bordered by adjacent roots. The socket is filled with a coagulum. The socket walls are continuous with the alveolar bone proper of the neighboring teeth. The tissue inside the interdental (inter-radicular) septa is made up of cancellous bone and includes trabeculae of lamellar bone within bone marrow.

The empty socket is first filled with blood and a *coagulum* (clot) forms (Fig. 2-16a). Inflammatory cells (polymorphonuclear leukocytes and monocytes/macrophages) migrate into the coagulum and start to phagocytose elements of necrotic tissue. The process of wound cleansing is initiated (Fig. 2-16b). Sprouts of newly formed vessels and mesenchymal cells (from the severed periodontal ligament) enter the coagulum and *granulation tissue* is formed. The granulation tissue is gradually replaced with *provisional connective tissue* (Fig. 2-16c) and subsequently immature bone (*woven bone*) is laid down (Fig. 2-16d). The hard tissue walls of the socket – the alveolar bone proper or the bundle bone – are resorbed and the socket wound becomes filled with woven bone (Fig. 2-16e). The initial phases of the healing process are now completed. In subsequent phases the woven bone in the socket is gradually remodeled into lamellar bone and marrow (Fig. 2-16f, g, h).

Important events in socket healing

Blood clotting

Immediately after tooth extraction, blood from the severed blood vessels will fill the cavity. Proteins derived from vessels and damaged cells initiate a series of events that lead to the formation of a fibrin network (Fig. 2-17). *Platelets* form aggregates and interact with the fibrin network to produce a *blood clot* (a coagulum) that effectively plugs the severed vessels and stops bleeding. The blood clot acts as a physical matrix that directs cellular movements and it contains substances that are of importance for the forthcoming healing process. Thus, the clot contains substances that (1) influence mesenchymal cells (i.e. *growth factors*) and (2) enhance the activity of inflammatory cells. Such substances will thus induce and amplify the migration of various types of cells into the socket wound, as well as their proliferation, differentiation and synthetic activity within the coagulum.

Although the blood clot is crucial in the initial phase of wound healing, its removal is mandatory to allow the formation of new tissue. Thus, within a few days after the tooth extraction, the blood clot will start to break down, i.e. the process of "fibrinolysis" is initiated (Fig. 2-18).

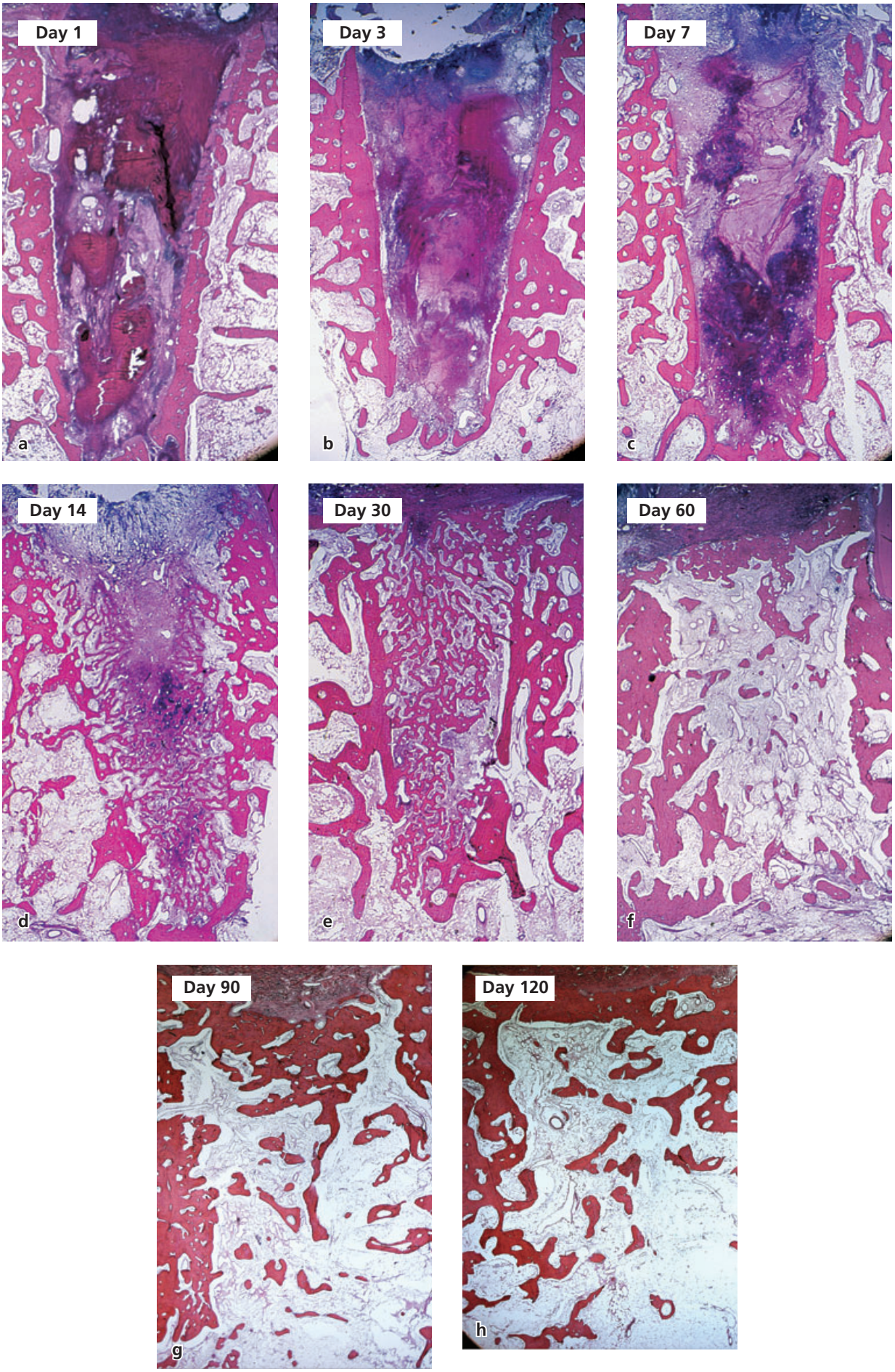

Fig. 2-16 Overall pattern of bone formation in an extraction socket. For details see text.

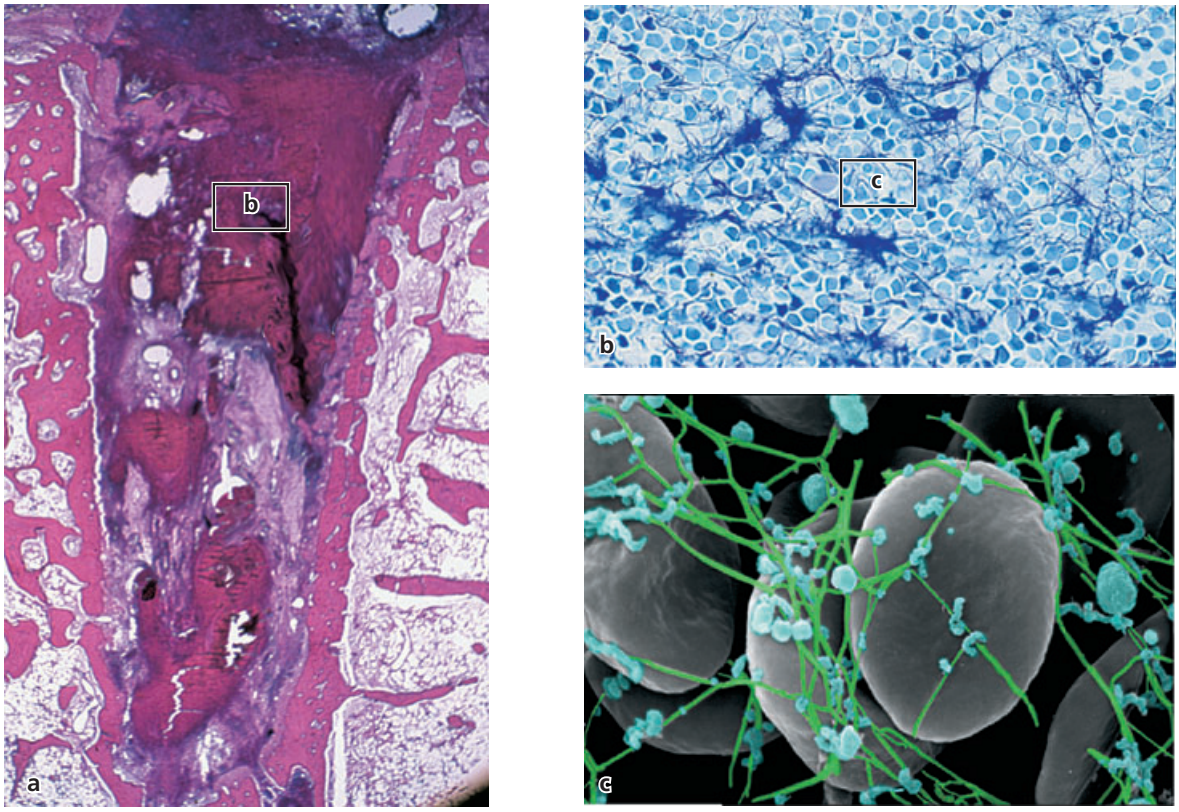

Fig. 2-17 Histologic section (mesio-distal aspect) representing 1 day of healing (a). The socket is occupied with a blood clot that contains large numbers of erythrocytes (b) entrapped in a fibrin network, as well as platelets (blue in (c)).

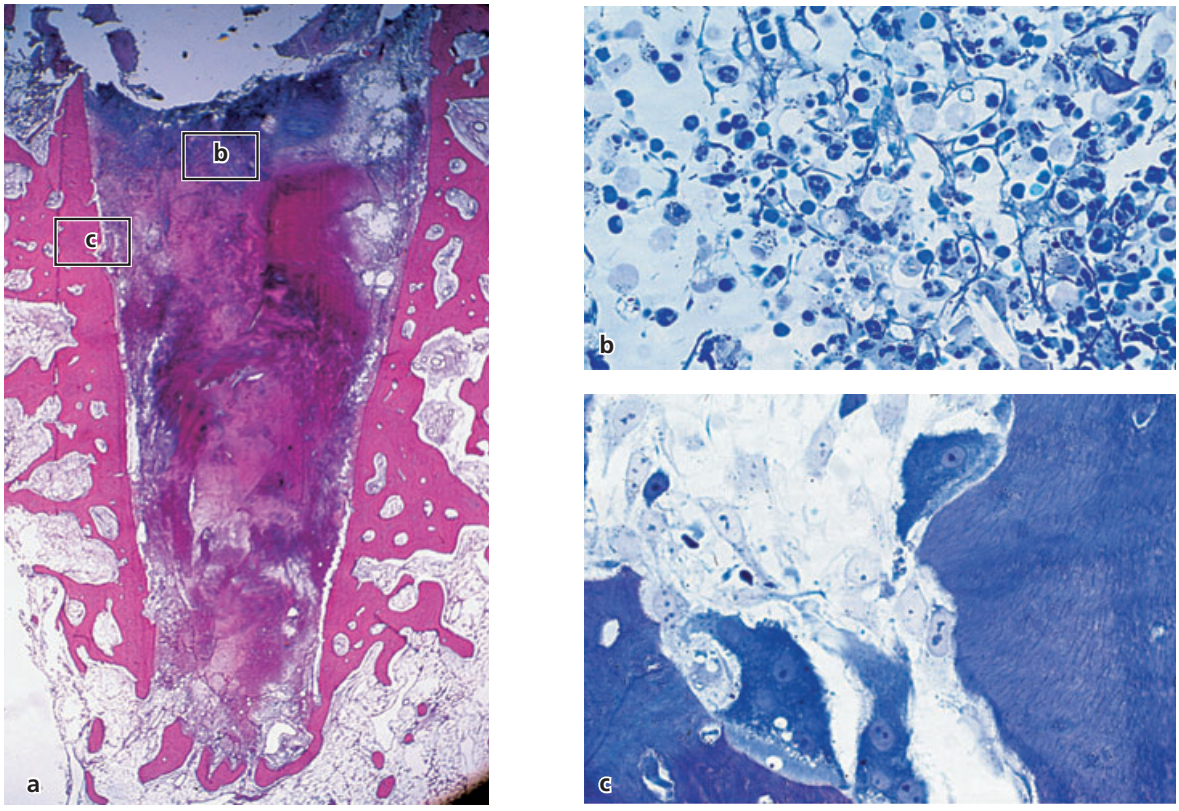

Fig. 2-18 (a) Histologic section (mesio-distal aspect) representing 3 days of healing. (b) Note the presence of neutrophils and macrophages that are engaged in wound cleansing and the break down of the blood clot. (c) Osteoclastic activity occurs on the surface of the old bone in the socket walls.

Wound cleansing

Neutrophils and macrophages migrate into the wound, engulf bacteria and damaged tissue (Fig. 2-18) and clean the site before the formation of new tissue can start. The neutrophils enter the wound early while macrophages appear somewhat later. The macrophages are not only involved in the cleaning of the wound but they also release growth factors and cytokines that further promote the migration, proliferation and differentiation of mesenchymal cells. Once the debris has been removed and the wound has become "sterilized", the neutrophils undergo a programmed cell death (*apoptosis*) and are removed from the site through the action of macrophages. The macrophages subsequently withdraw from the wound.

Tissue formation

Sprouts of vascular structures (from the severed periodontal ligament) as well as mesenchymal, fibroblast-like cells (from the periodontal ligament and from adjacent bone marrow regions) enter the socket. The mesenchymal cells start to proliferate and deposit matrix components in an extracellular location (Fig. 2-19a,b,c); a new tissue, i.e. *granulation tissue*, will gradually replace the blood clot. The granulation tissue eventually contains macrophages, and a large number of fibroblast-like cells as well as numerous newly formed blood vessels. The fibroblast-like cells continue (1) to release growth factors, (2) to proliferate, and (3) to deposit a new extra cellular matrix that guides the ingrowth of additional cells and allows the further differentiation of the tissue. The newly formed vessels provide the oxygen and nutrients that are needed for the increasing number of cells that occur in the new tissue. The intense synthesis of matrix components exhibited by the mesenchymal cells is called *fibroplasia*, while the formation of new vessels is called *angiogenesis*. A *provisional connective tissue* is established through the combination of fibroplasia and angiogenesis (Fig. 2-20).

The transition of the provisional connective tissue into bone tissue occurs along the vascular structures. Thus, osteoprogenitor cells (e.g. pericytes) migrate and gather in the vicinity of the vessels. They differentiate into osteoblasts that produce a matrix of collagen fibers, which takes on a woven pattern. The *osteoid* is formed. The process of mineralization is initiated within the osteoid. The osteoblasts continue to lay down osteoid and occasionally such cells are trapped in the matrix and become osteocytes. This newly formed bone is called *woven bone* (Fig. 2-21).

The woven bone is the first type of bone to be formed and is characterized by (1) its rapid deposition as fingerlike projections along the route of vessels, (2) the poorly organized collagen matrix, (3) the large number of osteoblasts that are trapped in its mineralized matrix, and (4) its low load-bearing capacity. Trabeculae of woven bone are shaped around and encircle the vessel. The trabeculae become

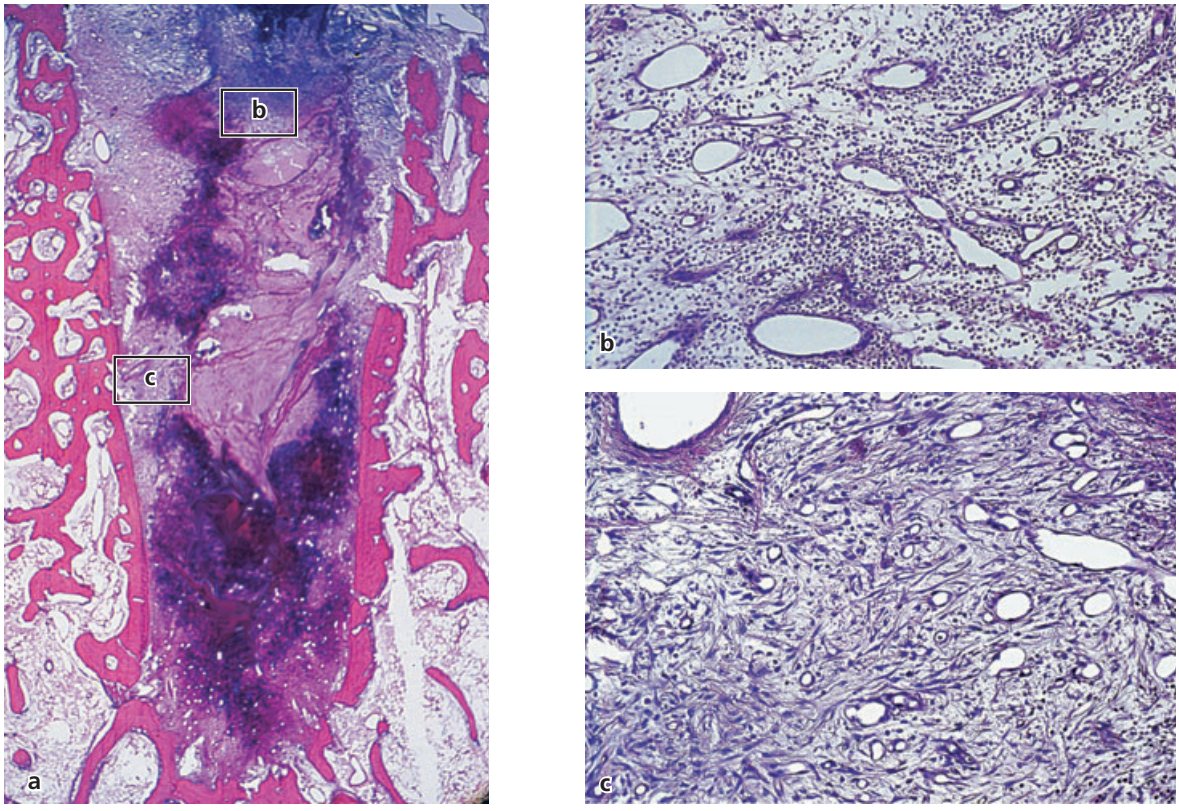

Fig. 2-19 (a) Histologic section (mesio-distal aspect) representing 7 days of healing. (b) Note the presence of a richly vascularized early granulation tissue with large numbers of inflammatory cells in the upper portion of the socket. (c) In more apical areas, a tissue including large numbers of fibroblast-like cells is present, i.e. late granulation tissue.

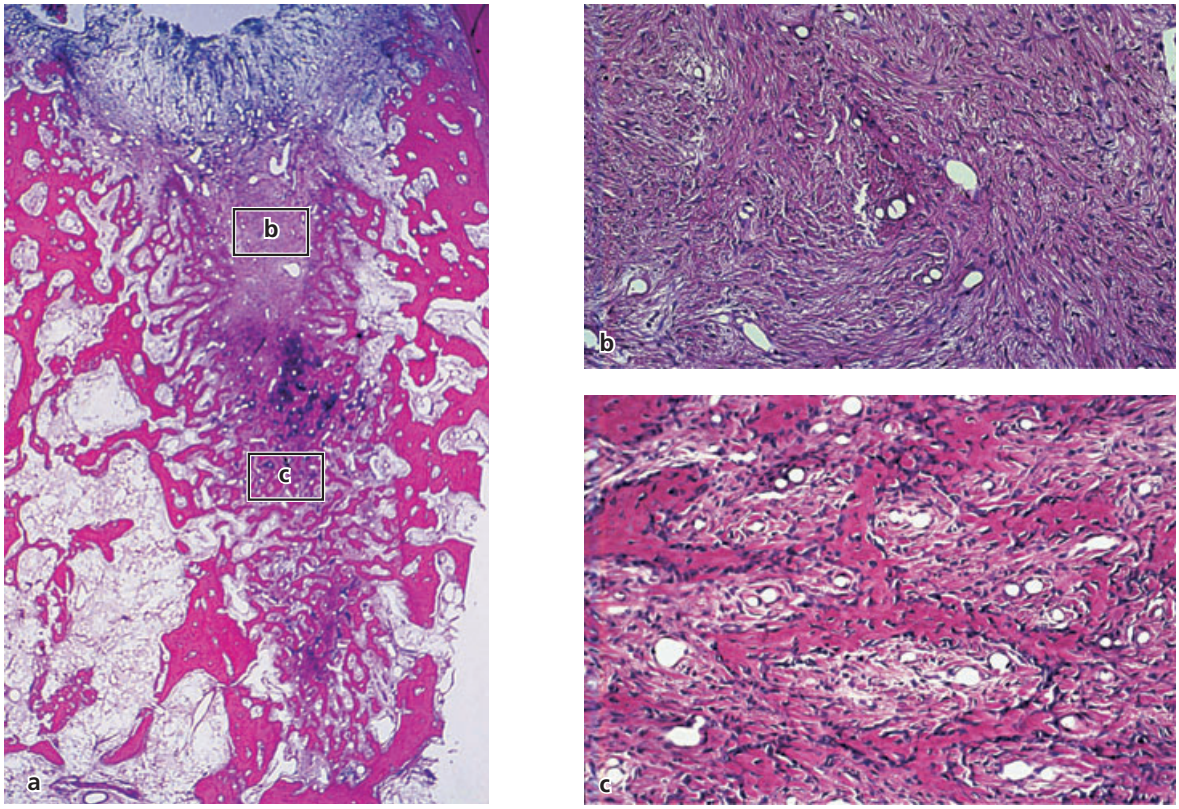

Fig. 2-20 (a) Histologic section (mesio-distal aspect) representing 14 days of healing. (b) In the marginal portion of the wound, a provisional connective tissue rich in fibroblast-like cells is present. (c) The formation of woven bone has at this time interval already begun in apical and lateral regions of the socket.

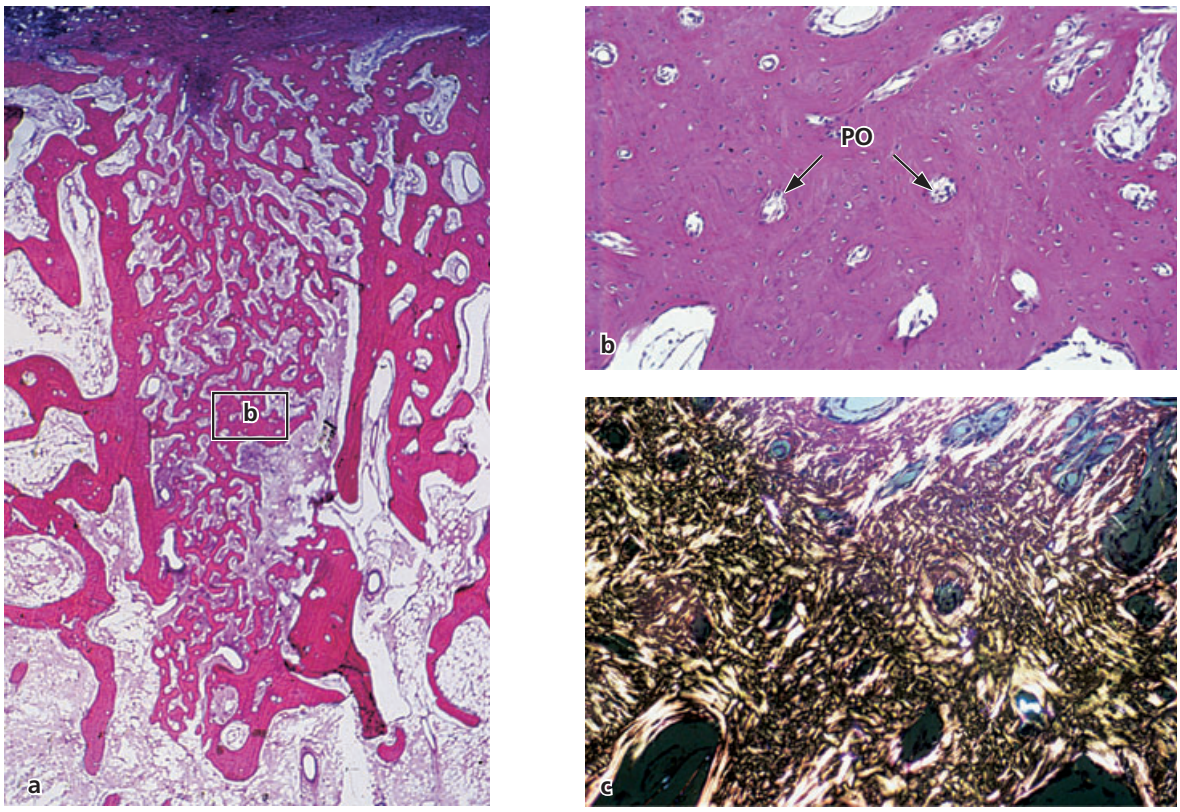

Fig. 2-21 (a) Histologic section (mesio-distal aspect) representing 30 days of healing. The socket is filled with woven bone. (b) This woven bone contains a large number of cells and primary osteons (PO). (c) The woven pattern of the collagen fibers of this type of bone is illustrated (polarized light).

thicker through the deposition of additional woven bone. Cells (osteocytes) become entrapped in the bone tissue and the first set of osteons, the *primary osteons*, are organized. The woven bone is occasionally reinforced by the deposition of so called *parallel-fibered bone*, that has its collagen fibers organized not in a woven but in a concentric pattern.

It is important to realize that during this early phase of healing the bone tissue in the walls of the socket (the bundle bone) is removed and replaced with woven bone.

Tissue modeling and remodeling

The initial bone formation is a fast process. Within a few weeks, the entire extraction socket will become filled with woven bone or, as this tissue is also called, *primary bone spongiosa*. The woven bone offers (1) a stable scaffold, (2) a solid surface, (3) a source of osteoprogenitor cells, and (4) ample blood supply for cell function and matrix mineralization.

The woven bone with its primary osteons is gradually replaced with lamellar bone and bone marrow (Fig. 2-22). In this process, the primary osteons are replaced with *secondary osteons*. The woven bone is first resorbed to a certain level. This level of the resorption front will establish a so-called *reversal line*, which is also the level from which new bone with secondary osteons will form (Fig. 2-23). Although this remodeling may start early during socket healing it will take several months until all woven bone in the extraction socket has been replaced with lamellar bone and marrow.

An important part of socket healing involves the formation of a *hard tissue cap* that will close the marginal entrance to the socket. This cap is initially comprised of woven bone (Fig. 2-24a) but is subsequently remodeled and replaced with lamellar bone that becomes continuous with the cortical plate at the periphery of the edentulous site (Fig. 2-24b). This process is called corticalization.

The wound is now healed, but the tissues in the site will continue to adapt to functional demands. Since there is no stress from forces elicited during mastication and other occlusal contacts there is no demand on mineralized bone in the areas previously occupied by the tooth. Thus, the socket apical of the hard tissue cap will remodel mainly into marrow. Indeed, in many edentulous patients the entire alveolar ridge will regress as a result of continuous adaptation to lack of function.

Extra-alveolar processes

In an experiment in the dog (Araújo & Lindhe 2005) alterations in the profile of the edentulous ridge that occurred following tooth extraction were carefully examined. In this study the 3rd and 4th mandibular

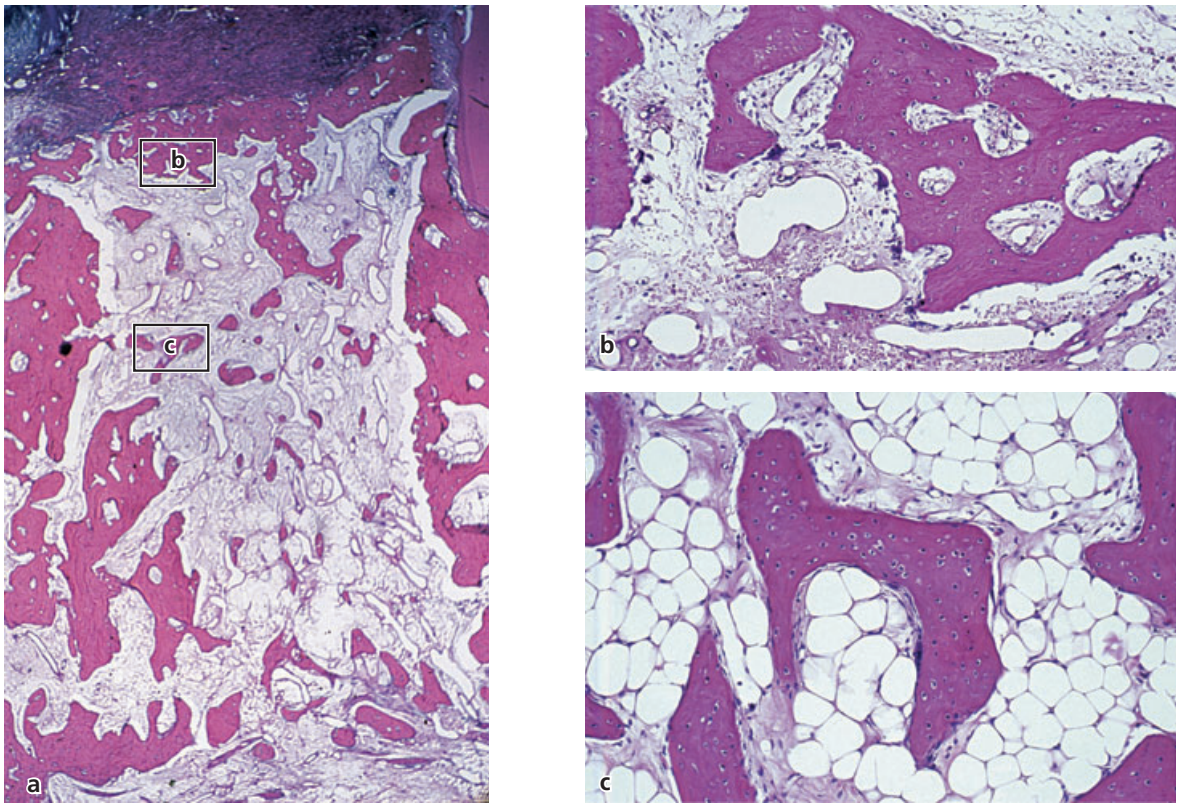

Fig. 2-22 (a) Histologic section (mesio-distal aspect) representing 60 days of healing. (b) A large portion of the woven bone has been replaced with bone marrow. (c) Note the presence of a large number of adipocytes residing in a tissue that still contains woven bone.

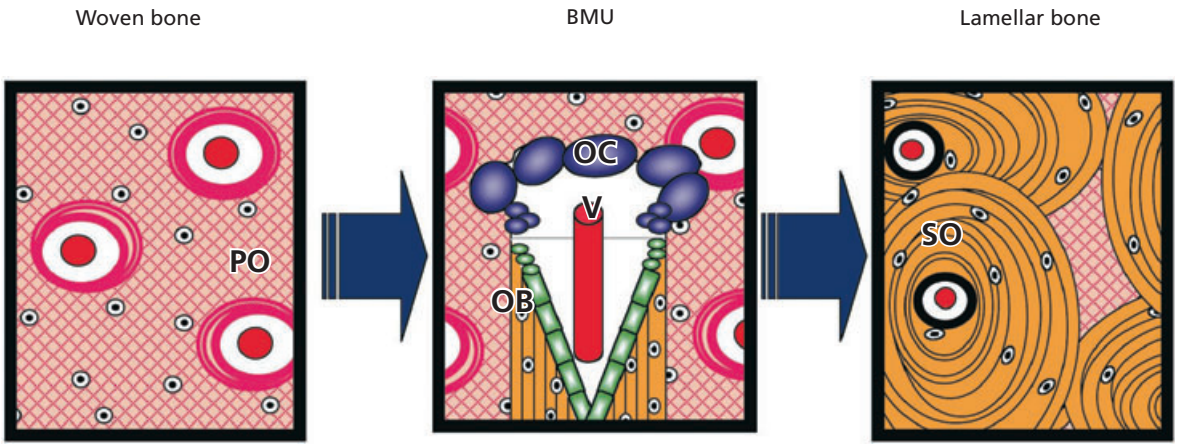

Fig. 2-23 Schematic drawing that describes how woven bone is replaced by lamellar bone. Woven bone with primary osteons is substituted by lamellar bone in a process that involves the presence of bone multicellular units (BMUs). The BMU contains osteoclasts (OC), as well as vascular structures (V) and osteoblasts (OB). Thus, the osteoblasts in the BMU produce bone tissue in a concentric fashion around the vessel, and lamellar bone with secondary osteons is formed.

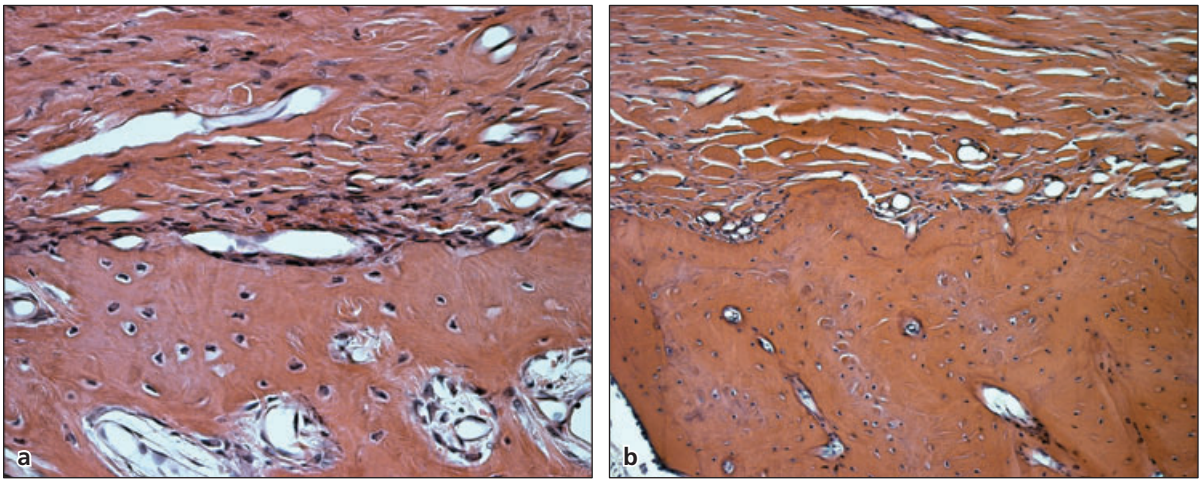

Fig. 2-24 Histologic sections (mesio-distal aspect) describing the hard tissue that has formed at the entrance of a healing extraction socket and the process of corticalization. (a) Woven bone with primary osteons occupies the socket entrance after 60 days of healing. (b) After 180 days the woven bone has been replaced with mainly lamellar bone.

premolars were hemi-sected. Buccal and lingual full-thickness flaps were raised; the distal roots were carefully removed. The flaps were replaced and sutured to cover the fresh extraction socket (Fig. 2-25). Biopsy specimens, including an individual extraction socket and adjacent roots, were obtained after 1, 2, 4, and 8 weeks of healing. The blocks were sectioned in the *buccal–lingual* plane.

Figure 2-26 illustrates a buccal–lingual section of the distal root of an intact 3rd premolar with surrounding soft and hard tissues. The lingual hard tissue wall is substantially wider than its buccal counterpart. The marginal portion of the lingual wall is presented in a higher magnification in Fig. 2-26a. A layer of bundle bone occupies the inner portion of the lingual bone wall. A thin layer of bundle bone is also present at the top of the ridge. Figure 2-26b illustrates the corresponding portion of the buccal bone wall. Note that all the mineralized tissue in the marginal 1–2 mm of the buccal ridge is comprised of bundle bone. In this context, it must be remembered that bundle bone is part of the attachment tissues for the tooth; this tissue has no obvious function following the removal of the tooth and will thus eventually be resorbed and disappear.

- *1 week after tooth extraction* (Fig. 2-27). At this interval the socket is occupied by a coagulum. Furthermore, a large number of osteoclasts can be seen on the outside as well as on the inside of the buccal and lingual bone walls. The presence of osteoclasts on the inner surface of the socket walls indicates that the bundle bone is being resorbed.
- *2 weeks after tooth extraction* (Fig. 2-28). Newly formed immature bone (woven bone) resides in the apical and lateral parts of the socket, while more central and marginal portions are occupied by a provisional connective tissue. In the marginal

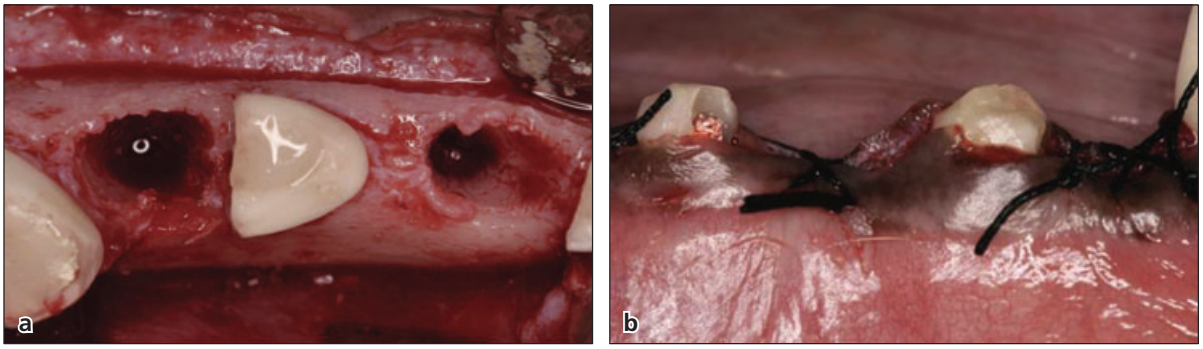

Fig. 2-25 (a) Photograph illustrating mandibular premolar sites (from a dog experiment) from which the distal roots of the 4th and 3rd premolars were extracted. (b) The mucosal, full-thickness flaps were replaced and sutured to close the entrance of the socket.

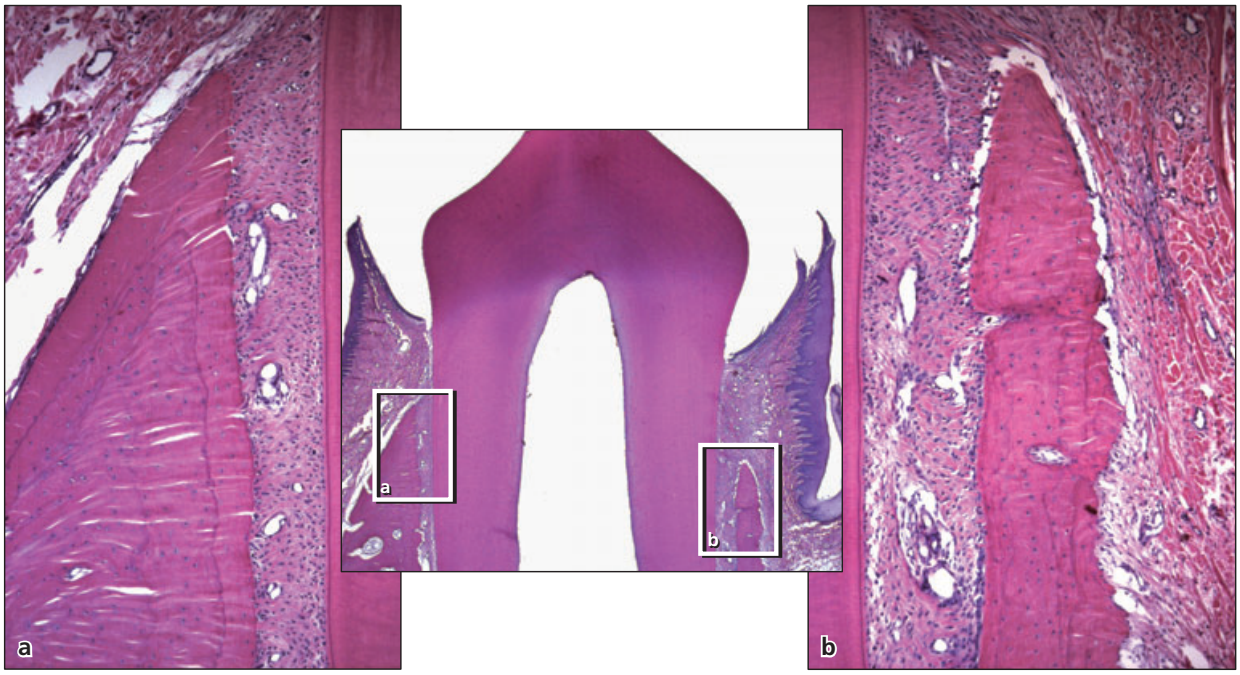

Fig. 2-26 Histologic section (buccal–lingual aspect) of the distal root of an intact 3rd premolar in the dog. Note the wide lingual and thinner buccal bone wall. Higher magnification of the crestal bone of the lingual wall (a) and buccal wall (b). B = buccal bone; L = lingual bone.

and outer portions of the socket walls numerous osteoclasts can be seen. In several parts of the socket walls the bundle bone has been replaced with woven bone.

- *4 weeks after tooth extraction* (Fig. 2-29). The entire socket is occupied with woven bone at this stage of healing. Large numbers of osteoclasts are present in the outer and marginal portions of the hard tissue walls. Osteoclasts also line the trabeculae of woven bone present in the central and lateral aspects of the socket. In other words the newly formed woven bone is being replaced with a more mature type of bone.
- *8 weeks after tooth extraction* (Fig. 2-30). A layer of cortical bone covers the entrance to the extraction site. Corticalization has occurred. The woven bone that was present in the socket at the 4-week interval is replaced with bone marrow and some trabeculae of lamellar bone in the 8-week specimens. On the outside and on the top of the buccal and lingual bone wall there are signs of ongoing hard tissue resorption. The crest of the buccal bone wall is located apical of its lingual counterpart.

The relative change in the location of the crest of the buccal and lingual bone walls that took place during the 8 weeks of healing is illustrated in Fig. 2-31. While the level of the margin of the lingual wall remained reasonably unchanged, the margin of the buccal wall shifted several millimeters in an apical direction.

There are at least two reasons why, in this animal model, more bone loss occurred in the buccal than in the lingual wall during socket healing. First, prior to tooth extraction, the marginal 1–2 mm

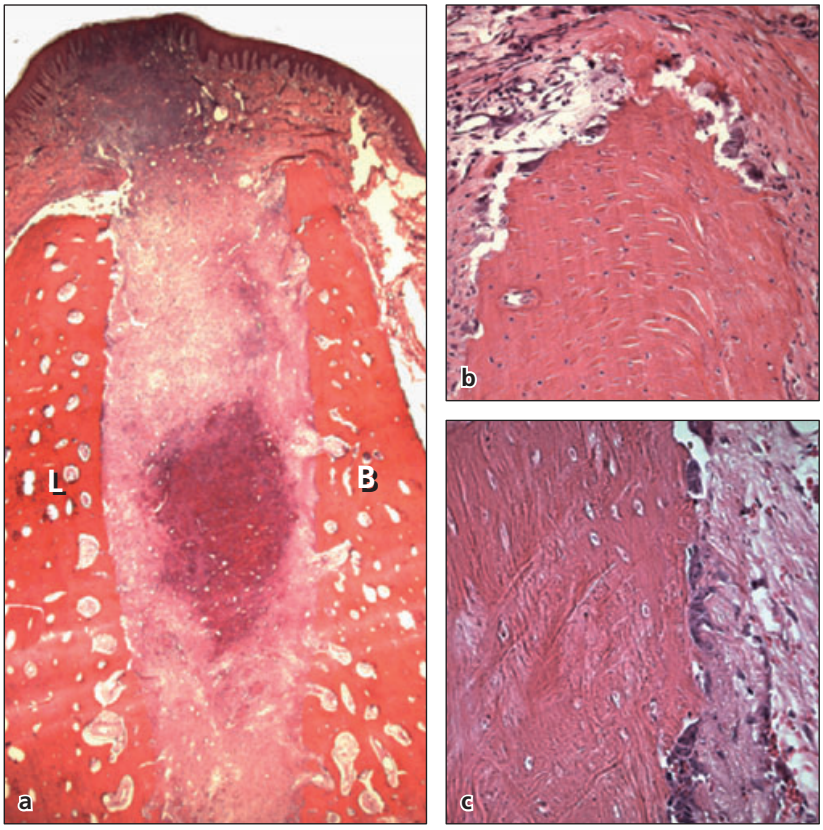

Fig. 2-27 (a) Histologic section (buccal–lingual aspect) of the socket after 1 week of healing. Note the presence of a large number of osteoclasts on the crestal portion (b) and inner portion (c) of the buccal wall. B = buccal bone; L = lingual bone.

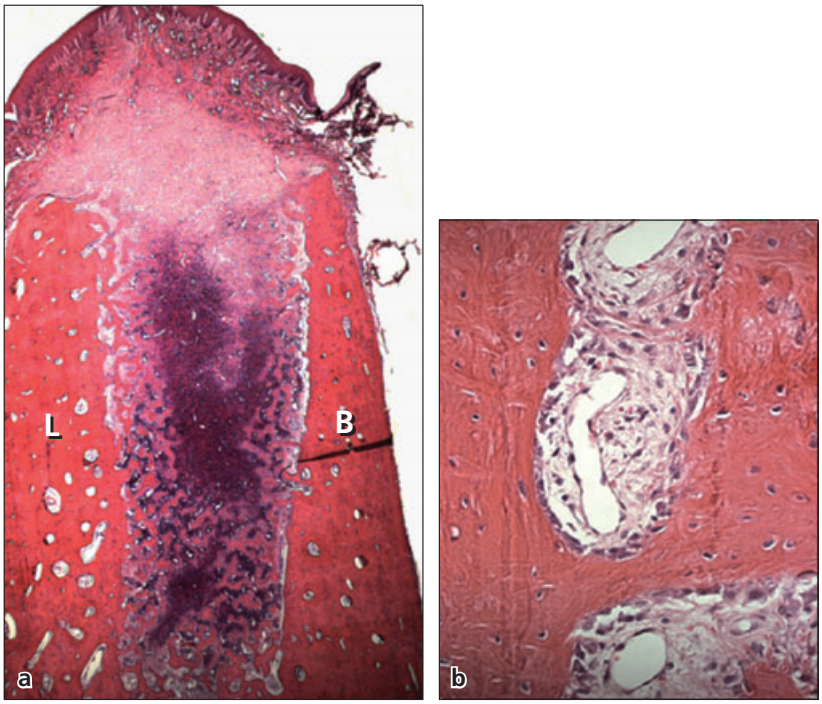

Fig. 2-28 (a) Histologic section (buccal–lingual aspect) of the socket after 2 weeks of healing. (b) Note that the bundle bone in the lingual aspect of the socket is being replaced with woven bone. B = buccal bone; L = lingual bone.

of the crest of the buccal bone wall was occupied by bundle bone. Only a minor fraction of the crest of the lingual wall contained bundle bone. Bundle bone, as stated above, is a tooth-dependent tissue and will gradually disappear after tooth extraction. Thus, since there is relatively more bundle bone in the crest region of the buccal than of the lingual wall, hard tissue loss will become most pronounced in the buccal wall. Secondly, the lingual bone wall of the socket is markedly wider than that of the buccal wall. It is well known from the periodontal literature (e.g. Wilderman *et al*. 1960; Wilderman 1963; Tavtigian 1970; Wood *et al*. 1972; Araújo *et al*. 2005) that flap elevation and the separation of the perios-

teum from the bone tissue will result in surface resorption; this will result in more vertical height reduction of the thin buccal than of the wider lingual bone wall.

Topography of the edentulous ridge

As described previously in this chapter, the processes of modeling and remodeling that occur following tooth extraction (loss) result in pronounced resorption of the various components of the alveolar ridge. The resorption of the buccal bone wall is more pronounced than the resorption of the lingual/palatal wall and hence the center of the ridge will move in lingual/palatal direction. In the extreme case, the entire alveolar process may be lost following tooth loss and in such situations only the bone of the base of the mandible and the base of the maxilla remains.

Figure 2-32 presents a buccal–lingual section of an edentulous site prepared from a biopsy of a dog obtained 2–3 years after tooth extraction. The ridge

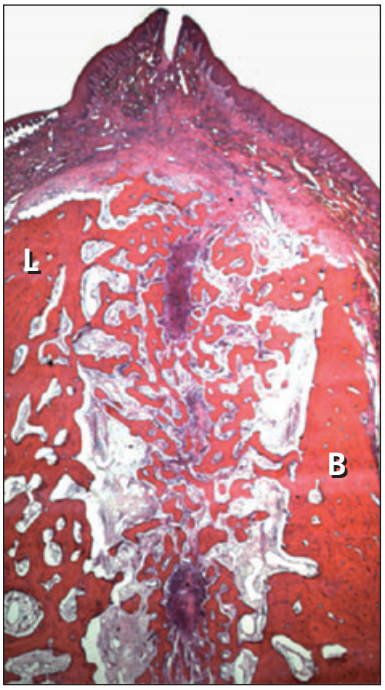

Fig. 2-29 Histologic section (buccal–lingual aspect) of the socket after 4 weeks of healing. The extraction socket is filled with woven bone. On the top of the buccal wall the old bone in the crest region is being resorbed and replaced with either connective tissue or woven bone. B = buccal bone; L = lingual bone.

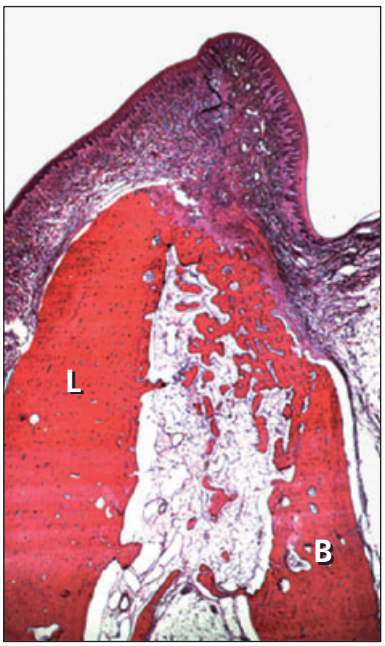

Fig. 2-30 Histologic section (buccal–lingual aspect) of the socket after 8 weeks of healing. The entrance of the socket is sealed with a cap of newly formed mineralized bone. Note that the crest of the buccal wall is located apical of the crest of the lingual wall. B = buccal bone; L = lingual bone.

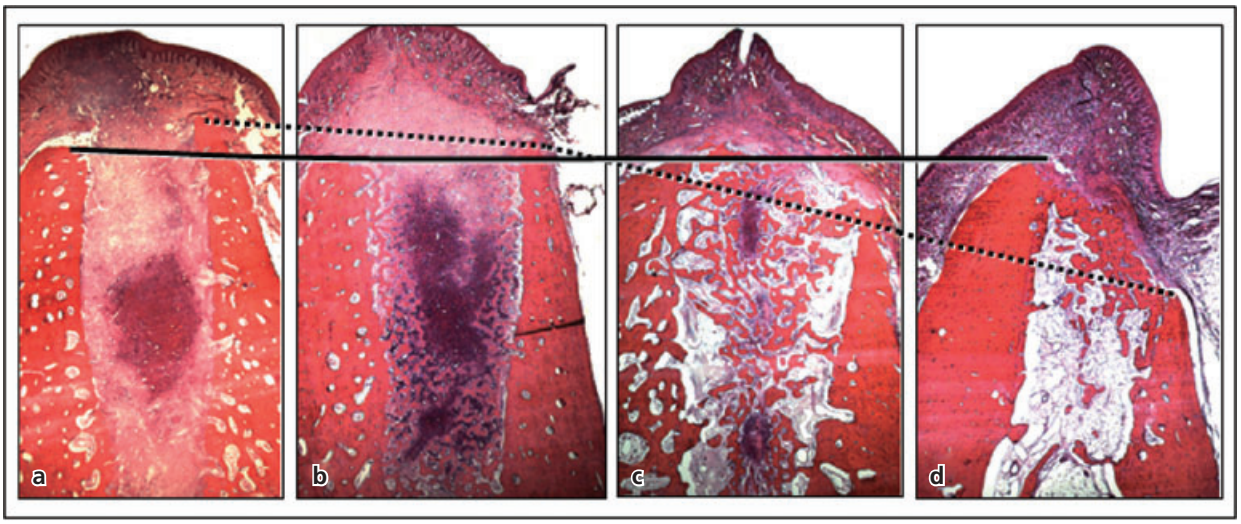

Fig. 2-31 Histologic sections (buccal–lingual aspects) describing the profile of the edentulous region in the dog after (a) 1, (b) 2, (c) 4, and (d) 8 weeks of healing following tooth extraction. While the marginal level of the lingual wall was maintained during the process of healing (solid line), the crest of the buccal wall was replaced >2 mm in the apical direction (dotted line).

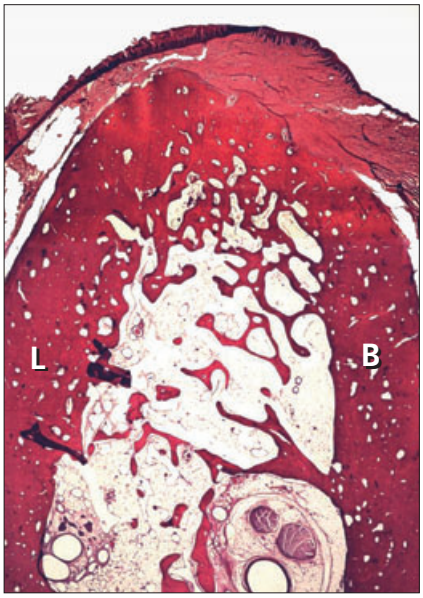

Fig. 2-32 Histologic section (buccal–lingual aspect) describing an edentulous mandibular site (from a dog experiment) 2 years after the extraction of the tooth. Note that the crest is higher at the lingual than at the buccal aspect of the site. B = buccal bone; L = lingual bone.

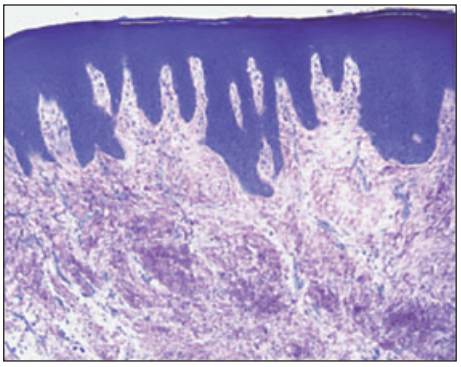

Fig. 2-33 Histologic section illustrating the mucosa residing over the bone crest. The mucosa has a well keratinized epithelium and a connective tissue densely packed with collagen fibers.

is covered by a mucosa (Fig. 2-33) that in this particular case is about 2–3 mm high and is comprised of keratinized epithelium and dense connective tissue that is attached via the periosteum to the cortical bone. Depending on factors such as the biotype, the jaw (maxilla or mandible), the location (anterior, posterior) in the jaw, location of the muco-gingival junction, depth of the buccal and lingual vestibule, and the amount of hard tissue resorption, the edentulous site may be lined with either masticatory, keratinized mucosa or lining, non-keratinized mucosa.

The outer walls of the remaining portion of the alveolar process are comprised of lamellar bone. The buccal bone plate is comparatively thin and the lingual/palatal plate comparatively thick. The cortical plates enclose the cancellous bone that harbors trabeculae of lamellar bone and marrow. The bone marrow contains numerous vascular structures as well as adipocytes and pluripotent mesenchymal cells. As a rule the ridge of the edentulous site in the maxilla contains comparatively more cancellous bone than a site in the mandible.

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Chapter 3

The Mucosa at Teeth and Implants

Jan Lindhe, Jan L. Wennström, and Tord Berglundh

The gingiva

Biologic width

A term frequently used to describe the dimensions of the soft tissues that face the teeth is *the biologic width of the soft tissue attachment*. The development of the *biologic width concept* was based on studies and analyses by, among others, Gottlieb (1921), Orban and Köhler (1924), and Sicher (1959), who documented that the soft tissue attached to the teeth was comprised of two parts, one fibrous tissue and one attachment of epithelium. In a publication by Gargiulo *et al.* (1961) called "Dimensions and relations of the dentogingival junction in humans", sections from autopsy block specimens that exhibited different degree of "passive tooth eruption" (i.e. periodontal tissue breakdown) were examined. Histometric assessments were made to describe the length of the sulcus (not part of the attachment), the epithelial attachment (today called junctional epithelium), and of the connective tissue attachment (Fig. 3-1). It was observed that the length of the connective tissue attachment varied within narrow limits (1.06–1.08 mm) while the length of the attached epithelium was about 1.4 mm at sites with normal periodontium, 0.8 mm at sites with moderate and 0.7 mm at sites with advanced periodontal tissue breakdown. In other words, (1) the biologic width of the attachment varied between about 2.5 mm in the normal case and 1.8 mm in the advanced disease case, and (2) the most variable part of the attachment was the length of the epithelial attachment (junctional epithelium).

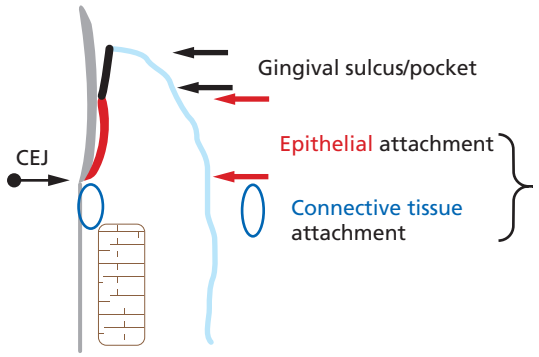


Fig. 3-1 Drawing describing the "biologic width" of the soft tissue attachment at the buccal surface of a tooth with healthy periodontium. The combined length of the junctional epithelium (epithelial attachment) and the connective tissue attachment is considered to represent the "biologic width" of the soft tissue attachment. Note the gingival sulcus is NOT part of the attachment.

Dimensions of the buccal tissue

The morphologic characteristics of the gingiva are related to the dimension of the alveolar process, the form (anatomy) of the teeth, events that occur during tooth eruption, and the eventual inclination and position of the fully erupted teeth (Wheeler 1961; O'Connor & Biggs 1964; Weisgold 1977). Ochenbein

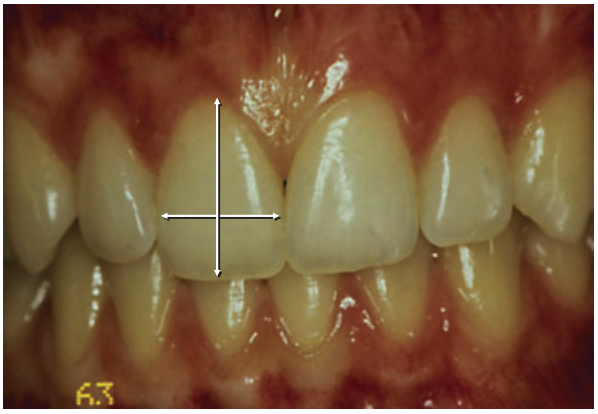


Fig. 3-2 Clinical photograph of a subject that belongs to the "pronounced scalloped" gingival biotype. The crowns of the teeth are comparatively long and slender. The papillae are comparatively long, the gingival margin is thin and the zone of attached gingiva is short.

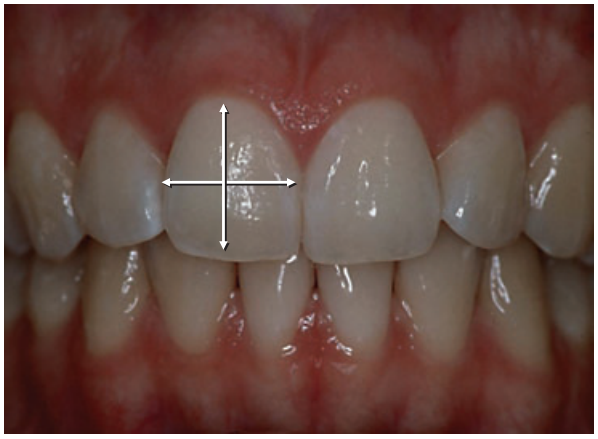


Fig. 3-3 Clinical photograph of a subject that belongs to the "flat" gingival biotype. The crowns of the teeth are comparatively short but wide. The papillae are comparatively short but voluminous and the zone of attached gingiva is wide.

and Ross (1969) and Becker *et al*. (1997) proposed (1) that the anatomy of the gingiva is related to the contour of the osseous crest, and (2) that two basic types of gingival architecture may exist, namely the "*pronounced scalloped*" and the "*flat*" biotype.

Subjects who belong to the "*pronounced scalloped*" biotype have long and slender teeth with tapered crown form, delicate cervical convexity and minute interdental contact areas that are located close to the incisal edge (Fig. 3-2). The maxillary front teeth of such individuals are surrounded with a thin free gingiva, the buccal margin of which is located at or apical of the cemento-enamel junction. The zone of gingiva is narrow, and the outline of the gingival margin is highly scalloped (Olsson *et al*. 1993). On the other hand, subjects who belong to the "*flat*" gingival biotype have incisors with squared crown form with pronounced cervical convexity (Fig. 3-3). The gingiva of such individuals is wider and more voluminous, the contact areas between the teeth are large and more apically located, and the interdental papillae are short. It was reported that subjects with pronounced scalloped gingiva often exhibited more advanced soft tissue recession in the anterior maxilla than subjects with a flat gingiva (Olsson & Lindhe 1991).

Kan *et al*. (2003) measured the dimension of the gingiva – as determined by bone sounding – at the buccal-mesial and buccal-distal aspects of maxillary anterior teeth. Bone sounding determines the distance between the soft tissue margin and the crest of the bone and, hence, provides an estimate that is about 1 mm greater than that obtained in a regular probing pocket depth measurement. The authors reported that the thickness of the gingiva varied between subjects of different gingival biotypes. Thus, the height of the gingiva at the buccal-approximal surfaces in subjects who belonged to the flat biotype was, on average, 4.5 mm, while in subjects belonging to the pronounced scalloped biotype the corresponding dimension (3.8 mm) was significantly smaller. This indicates that subjects who belong to the flat biotype have more voluminous soft buccal/approximal tissues than subjects who belong to the pronounced scalloped biotype.

Pontoriero and Carnevale (2001) performed evaluations of the reformation of the gingival unit at the buccal aspect of teeth exposed to crown lengthening procedures using a denudation technique. At the 1-year follow-up examination after surgery the regain of soft tissue – measured from the level of the denuded osseous crest – was greater in patients with a thick (flat) biotype than in those with a thin (pronounced scalloped) biotype (3.1 mm versus 2.5 mm). No assessment was made of the bone level change that had occurred between the baseline and the follow-up examination. It must, however, be anticipated that some bone resorption had taken place during healing and that the biologic width of the new connective tissue attachment had been re-established coronal to the level of the resected osseous crest.

The dimensions of the buccal gingiva may also be affected by the buccal–lingual position of the tooth within the alveolar process. A change of the tooth position in buccal direction results in reduced dimensions of the buccal gingiva, while an increase is observed following a lingual tooth movement (Coatoam *et al*. 1981; Andlin-Sobocki & Brodin 1993). In fact, Müller and Könönen (2005) demonstrated in a study of the variability of the thickness of the buccal gingiva of young adults that most of the variation in gingival thickness was due to the tooth position and that the contribution of subject variability (i.e. flat and pronounced scalloped) was minimal.

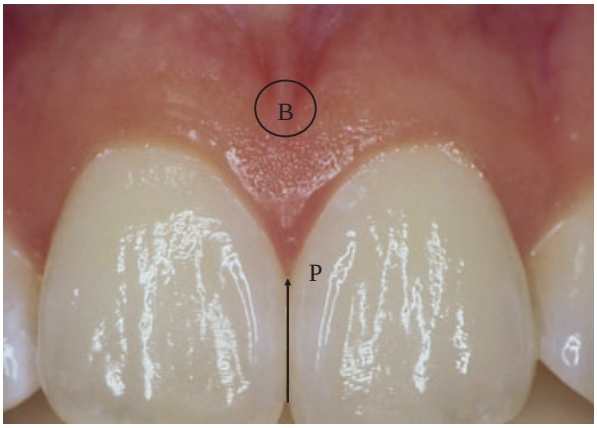


Fig. 3-4 Tarnow *et al.* (1992) measured the distance between the contact point (P) between the crowns of the teeth and the bone crest (B) using sounding (transgingival probing).

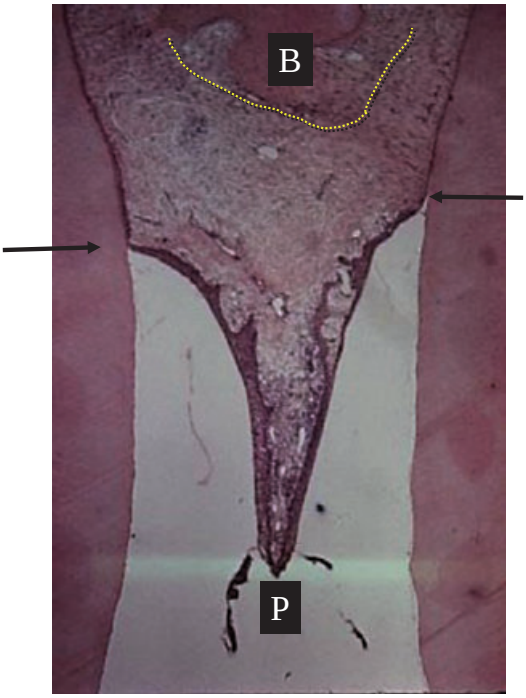


Fig. 3-5 Mesio-distal section of the interproximal area between the two central incisors. Arrows indicate the location of the cemento-enamel junction. Dotted line indicates the outline of the marginal bone crest. The distance between the contact point (P) between the crowns of the teeth and the bone crest (B) indicates the height of the papilla.

Dimensions of the interdental papilla

The interdental papilla in a normal, healthy dentition has one buccal and one lingual/palatal component that are joined in the col region (Chapter 1; Figs. 1-1–1-9). Experiments performed in the 1960s (Kohl & Zander 1961; Matherson & Zander 1963) revealed that the shape of the papilla in the col region was not determined by the outline of the bone crest but by the shape of the contact relationship that existed between adjacent teeth.

Tarnow *et al*. (1992) studied whether the distance between the contact point (area) between teeth and the crest of the corresponding inter-proximal bone could influence the degree of papilla fill that occurred at the site. Presence or absence of a papilla was determined visually in periodontally healthy subjects. If there was no space visible apical of the contact point, the papilla was considered complete. If a "black space" was visible at the site, the papilla was considered incomplete. The distance between the facial level of the contact point and the bone crest (Fig. 3-4) was measured by sounding. The measurement thus included not only the epithelium and connective tissue of the papilla but in addition the entire supra-alveolar connective tissue in the inter-proximal area (Fig. 3-5). The authors reported that the papilla was always complete when the distance from the contact point to the crest of the bone was ≤5 mm. When this distance was 6 mm, papilla fill occurred in about 50% of cases and at sites where the distance was ≥7 mm, the papilla fill was incomplete in about 75% of cases. Considering that the supracrestal connective tissue attachment is about 1 mm high, the above data indicate that the papilla height may be limited to about 4 mm in most cases. Interestingly, papillae of similar height (3.2–4.3 mm) were found to reform following surgical denudation procedures (van der Velden 1982; Pontoriero & Carnevale 2001), but to a greater height in patients with a thick (flat) than in those with a thin (pronounced scalloped) biotype.

Summary

- *Flat gingival (periodontal) biotype*: the buccal marginal gingiva is comparatively thick, the papillae are often short, the bone of the buccal cortical wall is thick, and the vertical distance between the interdental bone crest and the buccal bone is short (about 2 mm).
- *Pronounced scalloped gingival (periodontal) biotype*: the buccal marginal gingiva is delicate and may often be located apical of the cemento-enamel junction (receded), the papillae are high and slender, the buccal bone wall is often thin and the vertical distance between the interdental bone crest and the buccal bone is long (>4 mm).

The peri-implant mucosa

The soft tissue that surrounds dental implants is termed *peri-implant mucosa*. Features of the peri-implant mucosa are established during the process of wound healing that occurs subsequent to the closure of mucoperiosteal flaps following implant installation (one-stage procedure) or following abutment connection (two-stage procedure) surgery. Healing of the mucosa results in the establishment of a soft tissue attachment (transmucosal attachment) to the

implant. This attachment serves as a seal that prevents products from the oral cavity reaching the bone tissue, and thus ensures osseointegration and the rigid fixation of the implant.

The peri-implant mucosa and the gingiva have several clinical and histological characteristics in common. Some important differences, however, also exist between the gingiva and the peri-implant mucosa.

Biologic width

The structure of the mucosa that surrounds implants made of titanium has been examined in man and several animal models (for review see Berglundh 1999). In an early study in the dog, Berglundh *et al.* (1991) compared some anatomic features of the gingiva (at teeth) and the mucosa at implants. Since the research protocol from this study was used in subsequent experiments that will be described in this chapter, details regarding the protocol are briefly outlined here.

The mandibular premolars in one side of the mandible were extracted, leaving the corresponding teeth in the contralateral jaw quadrant. After 3 months of healing following tooth extraction (Fig. 3-6) the fixture part of implants (Brånemark system®, Nobel Biocare, Gothenburg, Sweden) were installed (Fig. 3-7) and submerged according to the guidelines given in the manual for the system. Another 3 months later, abutment connection was performed (Fig. 3-8) in a second-stage procedure, and the animals were placed in a carefully monitored plaque-control program. Four months subsequent to abutment connection, the dogs were exposed to a clinical examination following which biopsy specimens of several tooth and all implant sites were harvested.

The clinically healthy gingiva and peri-implant mucosa had a pink color and a firm consistency (Fig. 3-9). In radiographs obtained from the tooth sites it

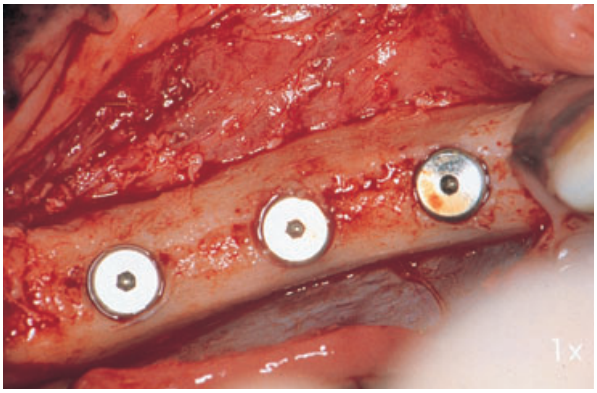


Fig. 3-7 Three titanium implants (i.e. the fixture part and cover screw; Brånemark System®) are installed.

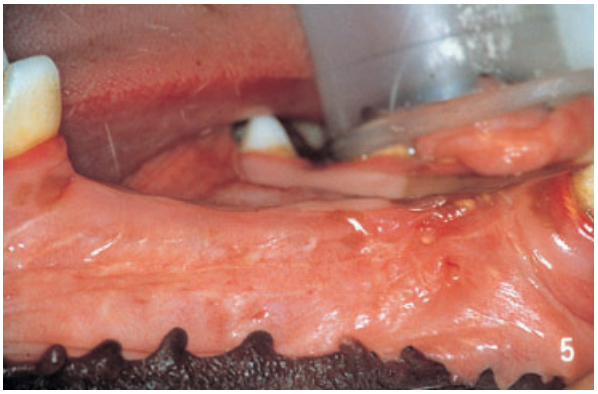


Fig. 3-6 The edentulous mandibular right premolar region 3 months following tooth extraction (from Berglundh *et al.* 1991).

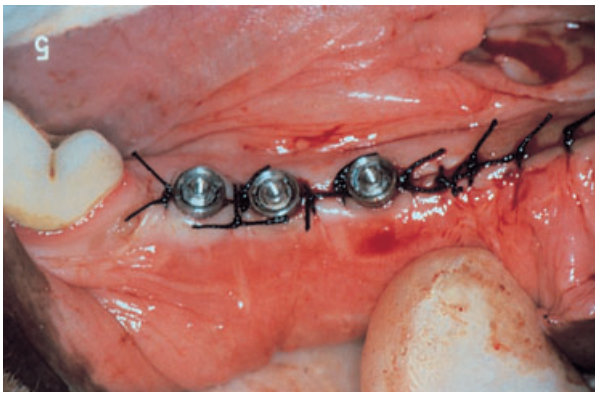
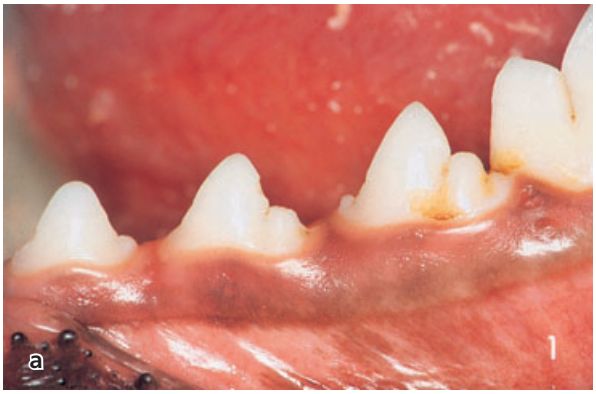


Fig. 3-8 Abutment connection is performed and the mucosa sutured with interrupted sutures.



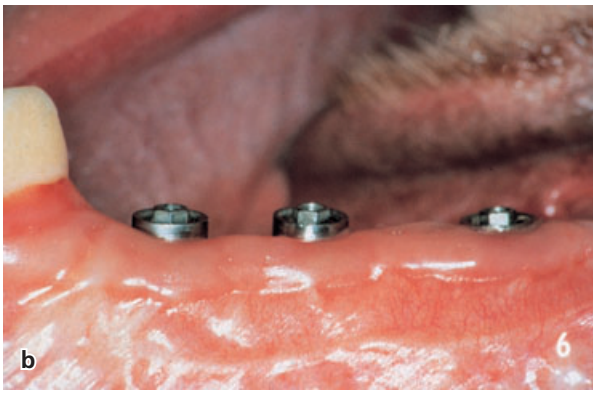


Fig. 3-9 After 4 months of careful plaque control the gingiva (a) and the peri-implant mucosa (b) are clinically healthy.

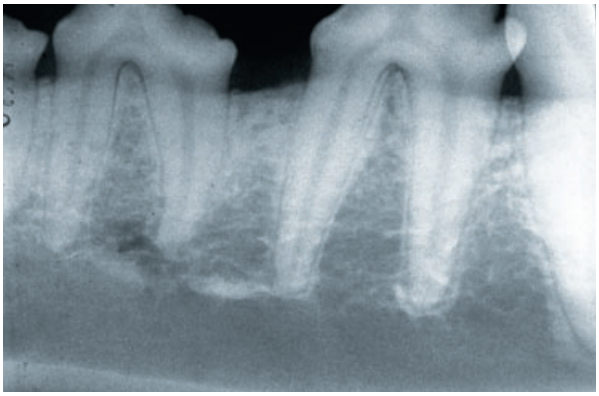


Fig. 3-10 Radiograph obtained from the premolars in the left side of the mandible.

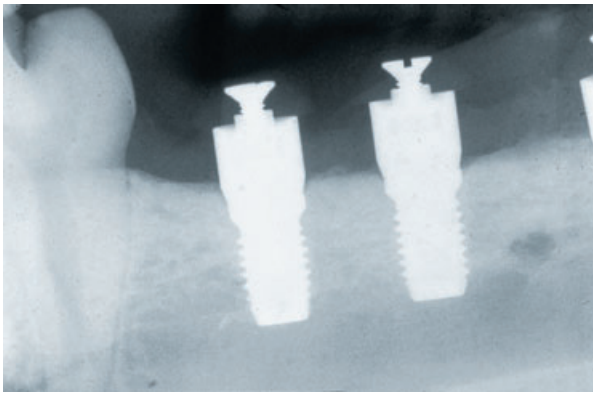


Fig. 3-11 Radiograph obtained from the implants in the right side of the mandible.

was observed that the alveolar bone crest was located about 1 mm apical of a line connecting the cemento-enamel junction of neighboring premolars (Fig. 3-10). The radiographs from the implant sites disclosed that the bone crest was close to the junction between the abutment and the fixture part of the implant (Fig. 3-11).

Histological examination of the sections revealed that the two soft tissue units, the gingiva and the peri-implant mucosa, had several features in common. The oral epithelium of the gingiva was well keratinized and continuous with the thin junctional epithelium that faced the enamel and that ended at the cemento-enamel junction (Fig. 3-12). The supra-alveolar connective tissue was about 1 mm high and the periodontal ligament about 0.2–0.3 mm wide. The principal fibers were observed to extend from the root cementum in a fan-shaped pattern into the soft and hard tissues of the marginal periodontium (Fig. 3-13).

The outer surface of the peri-implant mucosa was also covered by a keratinized oral epithelium, which in the marginal border connected with a thin barrier epithelium (similar to the junctional epithelium at the teeth) that faced the abutment part of the implant (Fig. 3-14). It was observed that the barrier epithelium was only a few cell layers thick (Fig. 3-15) and

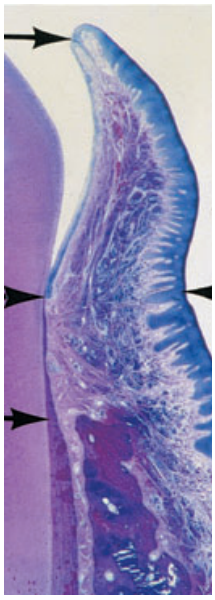


Fig. 3-12 Microphotograph of a cross section of the buccal and coronal part of the periodontium of a mandibular premolar. Note the position of the soft tissue margin (top arrow), the apical cells of the junctional epithelium (center arrow) and the crest of the alveolar bone (bottom arrow). The junctional epithelium is about 2 mm long and the supracrestal connective tissue portion about 1 mm high.

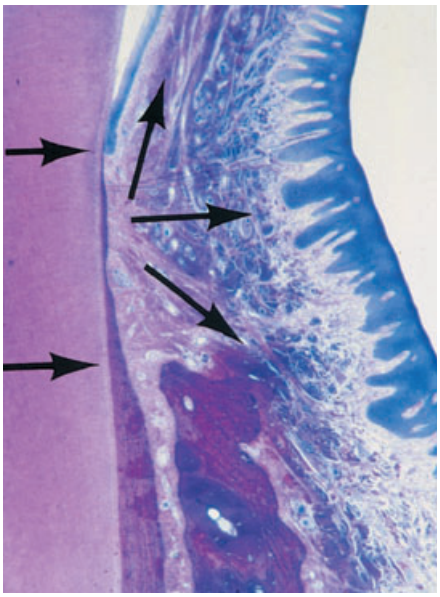


Fig. 3-13 Higher magnification of the supracrestal connective tissue portion seen in Fig. 3-12. Note the direction of the principal fibers (arrows).

that the epithelial structure terminated about 2 mm apical of the soft tissue margin (Fig. 3-14) and 1–1.5 mm from the bone crest. The connective tissue in the compartment above the bone appeared to be in direct contact with the surface (TiO_2) of the implant (Figs. 3-14, 3-15, 3-16). The collagen fibers in this connective tissue apparently originated from the periosteum of the bone crest and extend towards the margin of the soft tissue in directions parallel to the surface of the abutment.

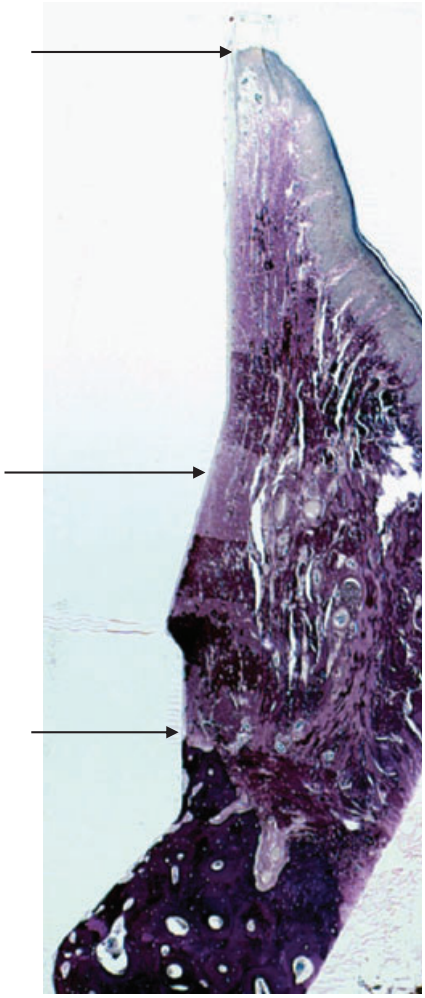


Fig. 3-14 Microphotograph of a buccal–lingual section of the peri-implant mucosa. Note the position of the soft tissue margin (top arrow), the apical cells of the junctional epithelium (center arrow), and the crest of the marginal bone (bottom arrow). The junctional epithelium is about 2 mm long and the implant–connective tissue interface about 1.5 mm high.

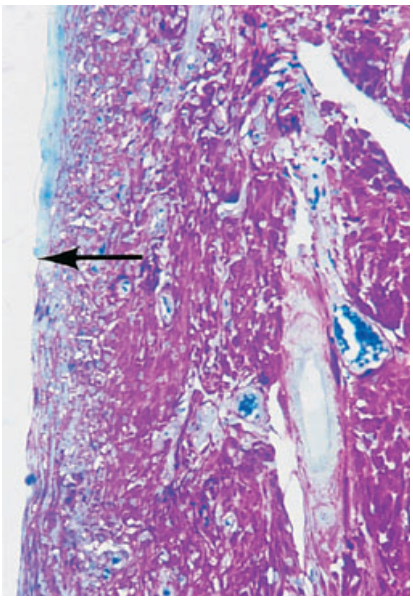


Fig. 3-15 Higher magnification of the apical portion of the barrier epithelium (arrow) in Fig. 3-14.

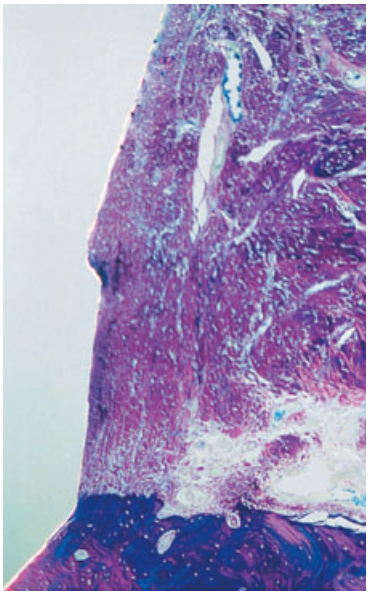


Fig. 3-16 Microphotograph of a section (buccal–lingual) of the implant–connective tissue interface of the peri-implant mucosa. The collagen fibers invest in the periosteum of the bone and project in directions parallel to the implant surface towards the margin of the soft tissue.

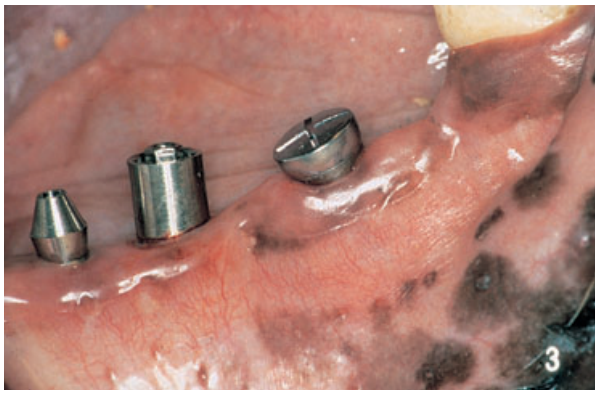


Fig. 3-17 Implants of three systems installed in the mandible of a beagle dog. Astra Tech Implants® Dental System (left), Brånemark System® (center) and ITI® Dental Implant System (right).

The observation that the barrier epithelium of the healthy mucosa consistently ended at a certain distance (1–1.5 mm) from the bone is important. During healing following implant installation surgery, fibroblasts of the connective tissue of the mucosa apparently formed a biological attachment to the TiO_2 layer of the "apical" portion of the abutment portion of the implant. This attachment zone was evidently not recognized as a wound and was therefore not covered with an epithelial lining.

In further dog experiments (Abrahamsson *et al.* 1996, 2002) it was observed that a similar mucosal attachment formed when different types of implant systems were used (e.g. Astra Tech Implant System, Astra Tech Dental, Mölndal, Sweden; Brånemark System®, Nobel Biocare, Göteborg, Sweden; Strau-

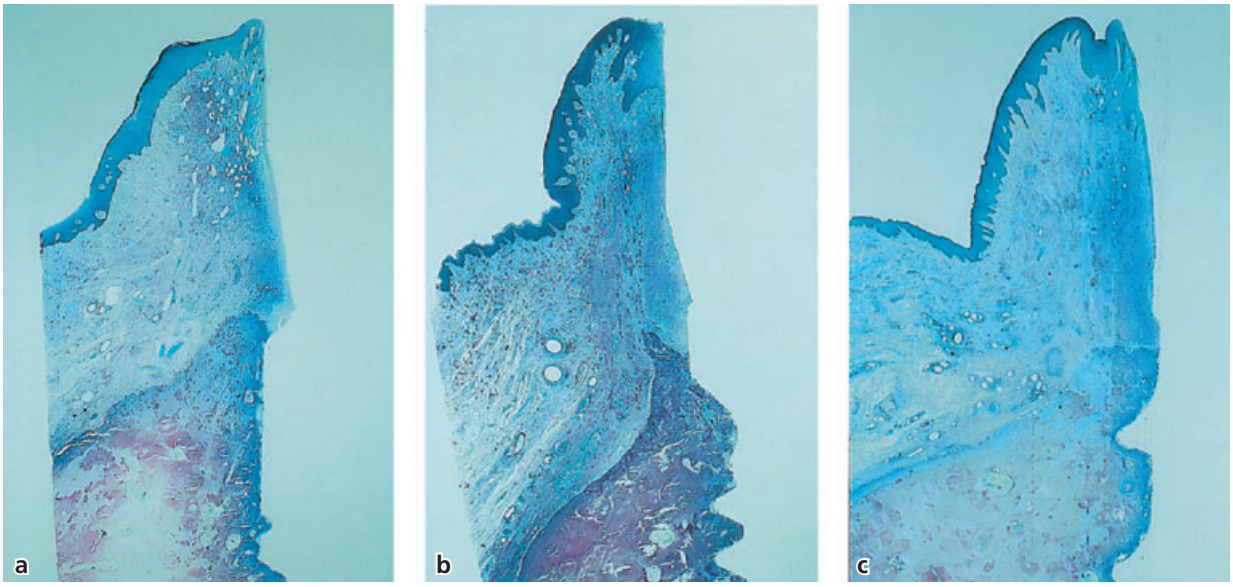


Fig. 3-18 Microphotographs illustrating the mucosa (buccal–lingual view) facing the three implant systems. (a) Astra. (b) Brånemark. (c) ITI.

mann® Dental Implant System, Straumann AG, Basel, Switzerland; 3i® Implant System, Implant Innovation Inc., West Palm Beach, FL, USA). In addition, the formation of the attachment appeared to be independent of whether the implants were initially submerged or not (Figs. 3-17, 3-18).

In another study (Abrahamsson *et al*. 1998), it was demonstrated that the material used in the abutment part of the implant was of decisive importance for the location of the connective tissue portion of the transmucosal attachment. Abutments made of aluminum-based sintered ceramic (Al_2O_3) allowed for the establishment of a mucosal attachment similar to that which occurred at titanium abutments. Abutments made of a gold alloy or dental porcelain, however, provided conditions for inferior mucosal healing. When such materials were used, the connective tissue attachment failed to develop at the abutment level. Instead, the connective tissue attachment occurred in a more apical location. Thus, during healing following the abutment connection surgery, some resorption of the marginal peri-implant bone took place to expose the titanium portion of the fixture (Brånemark System®) to which the connective tissue attachment was eventually formed.

The location and dimensions of the transmucosal attachment were examined in a dog experiment by Berglundh and Lindhe (1996). Implants (fixtures) of the Brånemark System® were installed in edentulous premolar sites and submerged. After 3 months of healing, abutment connection was performed. In the left side of the mandible the volume of the ridge mucosa was maintained while in the right side the vertical dimension of the mucosa was reduced to ≤2 mm (Fig. 3.19) before the flaps were replaced and sutured. In biopsy specimens obtained after another 6 months, it was observed that the transmucosal

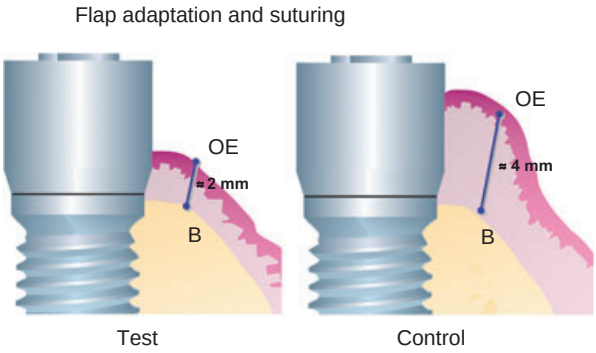


Fig. 3-19 Schematic drawing illustrating that the mucosa at the test site was reduced to about 2 mm. From Berglundh & Lindhe (1996).

attachment at all implants included one barrier epithelium that was about 2 mm long and one zone of connective tissue attachment that was about 1.3–1.8 mm high.

A further examination disclosed that at sites with a thin mucosa, wound healing consistently had included marginal bone resorption to establish space for a mucosa that eventually could harbor both the epithelial and the connective tissue components of the transmucosal attachment (Figs. 3-20, 3-21).

The dimensions of the epithelial and connective tissue components of the transmucosal attachment at implants are established during wound healing following implant surgery. As is the case for bone healing after implant placement (see Chapter 5), the wound healing in the mucosa around implants is a delicate process that requires several weeks of tissue remodeling.

In a recent animal experiment, Berglundh *et al*. (2007) described the morphogenesis of the mucosa attachment to implants made of c.p. titanium. A non-submerged implant installation technique was used and the mucosal tissues were secured to the conical marginal portion of the implants (Straumann® Dental Implant System) with interrupted sutures. The sutures were removed after 2 weeks and a plaque-control program was initiated. Biopsies were performed at various intervals to provide healing periods extending from day 0 (2 hours) to 12 weeks. It was reported that large numbers of neutrophils infiltrated and degraded the coagulum that occupied the compartment between the mucosa and the implant during the initial phase of healing. The first signs of epithelial proliferation were observed in specimens representing 1–2 weeks of healing and a mature barrier epithelium was seen after 6–8 weeks. It was also demonstrated that the collagen fibers of the mucosa were organized after 4–6 weeks of healing. Thus, prior to this time interval, the connective tissue is not properly arranged.

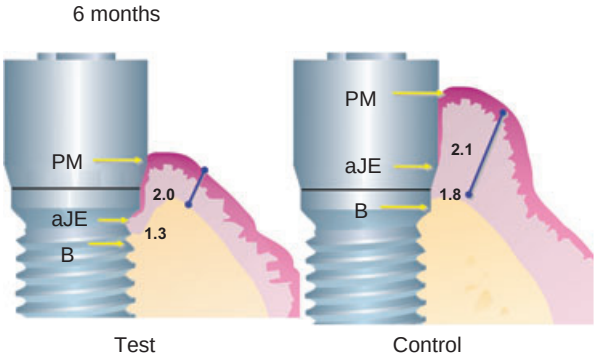


Fig. 3-20 Schematic drawing illustrating that the peri-implant mucosa at both control and test sites contained a 2 mm long barrier epithelium and a zone of connective tissue that was about 1.3–1.8 mm high. Bone resorption occurred in order to accommodate the soft tissue attachment at sites with a thin mucosa. From Berglundh & Lindhe (1996).

Conclusion

The junctional and barrier epithelia are about 2 mm long and the zones of supra-alveolar connective tissue are between 1 and 1.5 mm high. Both epithelia are attached via hemi-desmosomes to the tooth/implant surface (Gould *et al*. 1984). The main attachment fibers (the principal fibers) invest in the root cementum of the tooth, but at the implant site the equivalent fibers run in a direction parallel with the implant and fail to attach to the metal body. The soft tissue attachment to implants is properly established several weeks following surgery.

Quality

The quality of the connective tissue in the supra-alveolar compartments at teeth and implants was examined by Berglundh *et al*. (1991). The authors observed that the main difference between the mesenchymal tissue present at a tooth and at an implant site was the occurrence of a cementum on the root surface. From this cementum (Fig. 3-22), coarse dento-gingival and dento-alveolar collagen fiber bundles projected in lateral, coronal, and apical

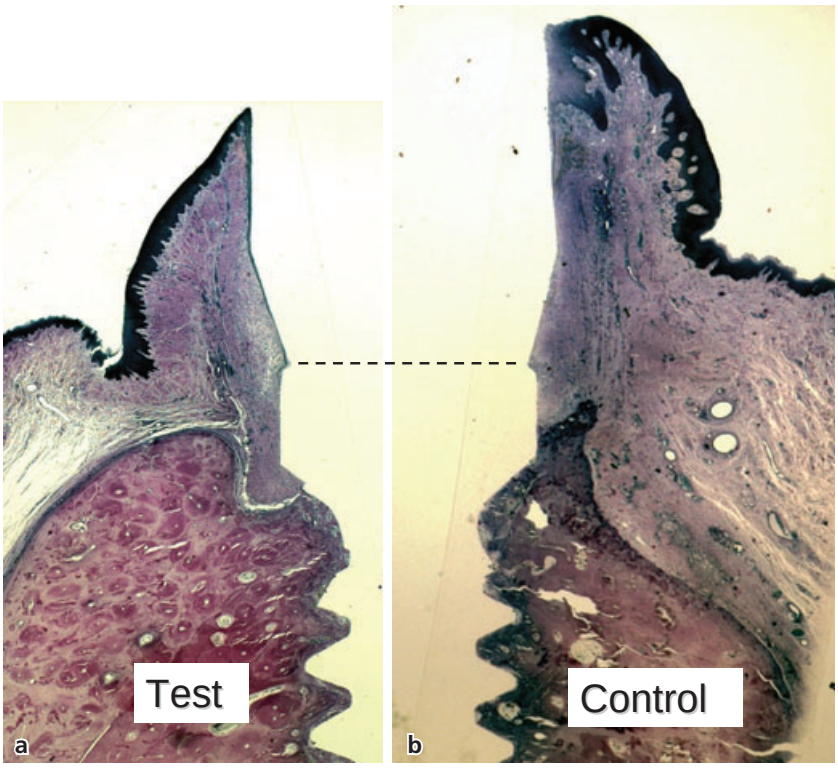


Fig. 3-21 Microphotograph illustrating the peri-implant mucosa of a normal dimension (left) and reduced dimension (right). Note the angular bone loss that had occurred at the site with the thin mucosa.

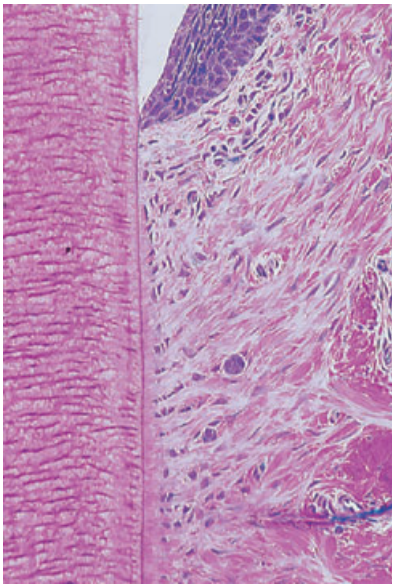


Fig. 3-22 Microphotograph of a tooth with marginal periodontal tissues (buccal–lingual section). Note on the tooth side the presence of an acellular root cementum with inserting collagen fibers. The fibers are orientated more or less perpendicular to the root surface.

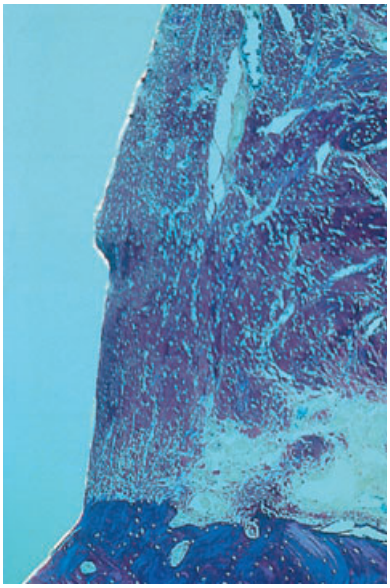


Fig. 3-23 Microphotograph of the peri-implant mucosa and the bone at the tissue/titanium interface. Note that the orientation of the collagen fibers is more or less parallel (not perpendicular) to the titanium surface.

directions (Fig. 3-13). At the implant site, the collagen fiber bundles were orientated in an entirely different manner. Thus, the fibers invested in the periosteum at the bone crest and projected in directions parallel with the implant surface (Fig. 3-23). Some of the fibers became aligned as coarse bundles in areas distant from the implant (Buser *et al*. 1992).

The connective tissue in the supra-crestal area at implants was found to contain more collagen fibers, but fewer fibroblasts and vascular structures, than the tissue in the corresponding location at teeth. Moon *et al*. (1999), in a dog experiment, reported that the attachment tissue close to the implant (Fig. 3-24) contained only few blood vessels but a large number of fibroblasts that were orientated with their long axes parallel with the implant surface (Fig. 3-25). In more lateral compartments, there were fewer fibroblasts but more collagen fibers and more vascular structures. From these and other similar findings it may be concluded that the connective tissue attachment between the titanium surface and the connective tissue is established and maintained by fibroblasts.

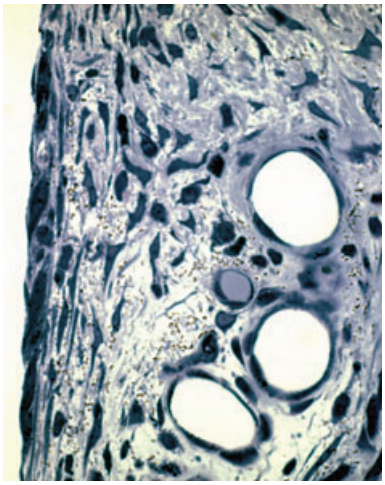


Fig. 3-24 Microphotograph of the implant/connective tissue interface of the peri-implant mucosa. A large number of fibroblasts reside in the tissue next to the implant.

Fig. 3-25 Electron micrograph of the implant–connective tissue interface. Elongated fibroblasts are interposed between thin collagen fibrils (magnification ×24 000).

Vascular supply

The vascular supply to the gingiva comes from two different sources (Fig. 3-26). The first source is represented by the large *supraperiosteal blood vessels*, that put forth branches to form (1) the capillaries of the connective tissue papillae under the oral epithelium and (2) the vascular plexus lateral to the junctional epithelium. The second source is the *vascular plexus of the periodontal ligament*, from which branches run in a coronal direction and terminate in the supra-

alveolar portion of the free gingiva. Thus, the blood supply to the zone of supra-alveolar connective tissue attachment in the periodontium is derived from two apparently independent sources (see also Chapter 1).

Berglundh *et al.* (1994) observed that the vascular system of the peri-implant mucosa of dogs (Fig. 3-27) originated *solely* from the large *supra-periosteal blood vessel* on the outside of the alveolar ridge. This vessel that gave off branches to the supra-alveolar mucosa and formed (1) the capillaries beneath the oral epithelium and (2) the vascular plexus located immediately lateral to the barrier epithelium. The connective tissue part of the transmucosal attachment to titanium implants contained only few vessels, all of which could be identified as terminal branches of the *supra-periosteal blood vessels.*

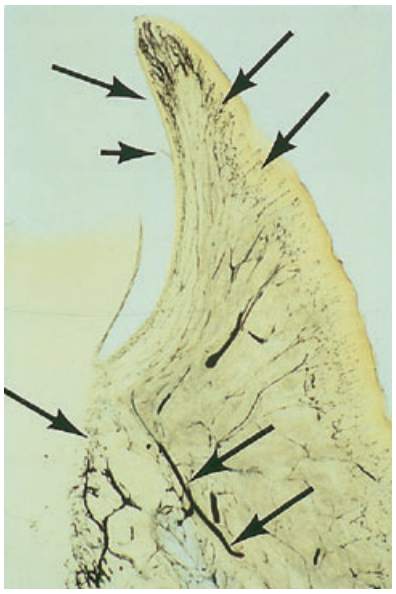


Fig. 3-26 A buccal–lingual section of a beagle dog gingiva. Cleared section. The vessels have been filled with carbon. Note the presence of a supraperiosteal vessel on the outside of the alveolar bone, the presence of a plexus of vessels within the periodontal ligament, as well as vascular structures in the very marginal portion of the gingiva.

Summary

The gingiva at teeth and the mucosa at dental implants have some characteristics in common, but differ in the composition of the connective tissue, the alignment of the collagen fiber bundles, and the distribution of vascular structures in the compartment apical of the barrier epithelium.

Probing gingiva and peri-implant mucosa

It was assumed for many years that the tip of the probe in a pocket depth measurement identified the most apical cells of the junctional (pocket) epithelium or the marginal level of the connective tissue attachment. This assumption was based on findings by, for example, Waerhaug (1952), who reported that the "epithelial attachment" (e.g. Gottlieb 1921; Orban & Köhler 1924) offered no resistance to probing. Waerhaug (1952) inserted, "with the greatest caution", thin blades of steel or acrylic in the gingival pocket of various teeth of >100 young subjects without signs of periodontal pathology. In several sites the blades were placed in approximal pockets, "in which position radiograms were taken of them". It was concluded that the insertion of the blades could be performed without a resulting bleeding and that the device consistently reached to the cemento-enamel junction (Fig. 3.28). Thus, the epithelium or the epithelial attachment offered no resistance to the insertion of the device.

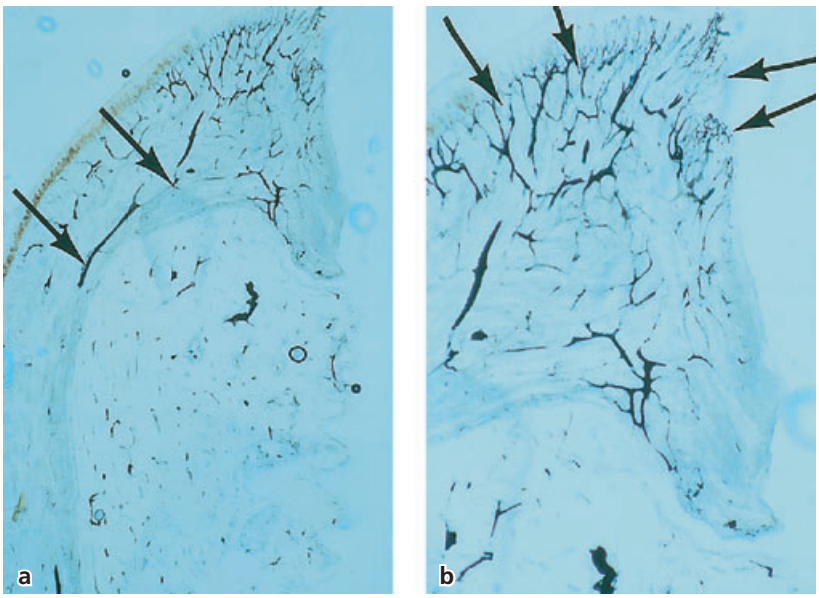


Fig. 3-27 (a) A buccal–lingual cleared section of a beagle dog mucosa facing an implant (the implant was positioned to the right). Note the presence of a supraperiosteal vessel on the outside of the alveolar bone, but also that there is no vasculature that corresponds to the periodontal ligament plexus. (b) Higher magnification (of a) of the peri-implant soft tissue and the bone implant interface. Note the presence of a vascular plexus lateral to the junctional epithelium, but the absence of vessels in the more apical portions of the soft tissue facing the implant and the bone.

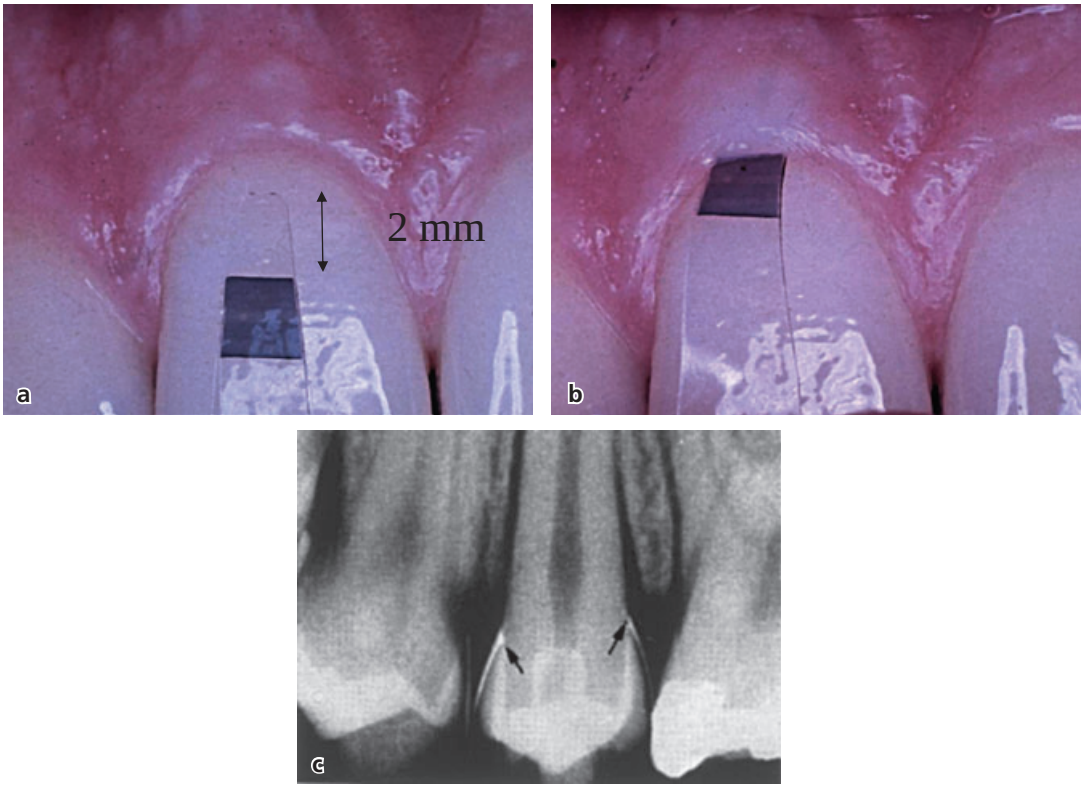


Fig. 3-28 An acrylic strip with a blue zone located 2 mm from the strip margin (a) prior to and (b) after its insertion into a buccal "pocket". The strip could with a light force be inserted 2 mm into the "pocket". (c) Thin blades of steel were inserted in pockets at approximal sites of teeth with healthy periodontal conditions. In radiographs, Waerhaug (1952) could observe that the blades consistently reached the cemento-enamel junction.

In subsequent studies it was observed, however, that the tip of a periodontal probe in a pocket depth measurement only identified the base of the dento-gingival epithelium by chance. In the absence of an inflammatory lesion the probe frequently failed to reach the apical part of the junctional epithelium (e.g. Armitage *et al*. 1977; Magnusson & Listgarten 1980). If an inflammatory lesion, rich in leukocytes and poor in collagen, was present in the gingival connective tissue, however, the probe penetrated beyond the epithelium to reach the apical–lateral border of the infiltrate.

The outcome of probing depth measurements at *implant sites* was examined in various animal models. Ericsson and Lindhe (1993) used the model by Berglundh *et al*. (1991) referred to above and, hence, had both teeth and implants available for examination. The gingiva at mandibular premolars and the mucosa at correspondingly positioned implants (Brånemark System®) were, after extended periods of plaque control, considered clinically healthy. A probe with a tip diameter of 0.5 mm was inserted into the buccal "pocket" using a standardized force of 0.5 N. The probe was anchored to the tooth or to the implant and biopsies from the various sites were performed. The histologic examination of the biopsy material revealed that probing the dento-gingival interface had resulted in a slight compression of the gingival tissue. The tip of the probe was located coronal to the apical cells of the junctional epithelium. At the implant sites, probing caused both compression and a lateral dislocation of the peri-implant mucosa, and the average "histologic" probing depth was markedly deeper than at the tooth site: 2.0 mm versus 0.7 mm. The tip of the probe was consistently positioned deep in the connective tissue/abutment interface and apical of the barrier epithelium. The distance between the probe tip and the bone crest at the tooth sites was about 1.2 mm. The corresponding distance at the implant site was 0.2 mm. The findings presented by Ericsson and Lindhe (1993) regarding the difference in probe penetration in healthy gingiva and peri-implant mucosa are not in agreement with data reported in subsequent animal experiments.

Lang *et al*. (1994) used beagle dogs and prepared the implant (Straumann® Dental Implant System) sites in such a way that at probing some regions were healthy, a few sites exhibited signs of mucositis, and some sites exhibited peri-implantitis. Probes with different geometry were inserted into the pockets using a standardized probing procedure and a force of only 0.2 N. The probes were anchored and block biopsy specimens were harvested. The probe locations were studied in histologic ground sections. The authors reported that the mean "histologic" probing depth at

healthy sites was about 1.8 mm, i.e. similar to the depth (about 2 mm) recorded by Ericsson and Lindhe (1993). The corresponding depth at sites with mucositis and peri-implantitis was about 1.6 mm and 3.8 mm respectively. Lang *et al*. (1994) further stated that at healthy and mucositis sites, the probe tip identified "the connective tissue adhesion level" (i.e. the base of the barrier epithelium) while at peri-implantitis sites, the probe exceeded the base of the ulcerated pocket epithelium by a mean distance of 0.5 mm. At such peri-implantitis sites the probe reached the base of the inflammatory cell infiltrate.

Schou *et al*. (2002) compared probing measurements at implants and teeth in eight cynomolgus monkeys. Ground sections were produced from tooth and implant sites that were (1) clinically healthy, (2) slightly inflamed (mucositis/gingivitis), and (3) severely inflamed (peri-implantitis/periodontitis) and in which probes had been inserted. An electronic probe (Peri-Probe®) with a tip diameter 0.5 mm and a standardized probing force of 0.3–0.4 N was used. It was demonstrated that the probe tip was located at a similar distance from the bone in healthy tooth sites and implant sites. On the other hand, at implants exhibiting mucositis and peri-implantitis, the probe tip was consistently identified at a more apical position than at corresponding sites at teeth (gingivitis and periodontitis). The authors concluded that (1) probing depth measurements at implant and teeth yielded different information, and (2) small alterations in probing depth at implants may reflect changes in soft tissue inflammation rather than loss of supporting tissues.

Recently, Abrahamsson and Soldini (2006) evaluated the location of the probe tip in healthy periodontal and peri-implant tissues in dogs. It was reported that probing with a force of 0.2 N resulted in a probe penetration that was similar at implants and teeth. Furthermore, the tip of the probe was often at or close to the apical cells of the junctional/barrier epithelium. The distance between the tip of the probe and the bone crest was about 1 mm at both teeth and implants (Figs. 3-29, 3-30). Similar observations were reported from clinical studies in which different implant systems were used (Buser *et al*. 1990; Quirynen *et al*. 1991; Mombelli *et al*. 1997). In these studies the distance between the probe tip and the bone was assessed in radiographs and was found to vary between 0.75 and 1.4 mm when a probing force of 0.25–0.45 N was used.

By comparing the findings from the studies reported above, it becomes apparent that probing depth and probing attachment level measurements are also meaningful at implant sites. When a "normal" probing force is applied in healthy tissues the probe seems to reach similar levels at implant and tooth sites. Probing inflamed tissues both at tooth and implant sites will, however, result in a more advanced probe penetration and the tip of the probe may come closer to the bone crest.

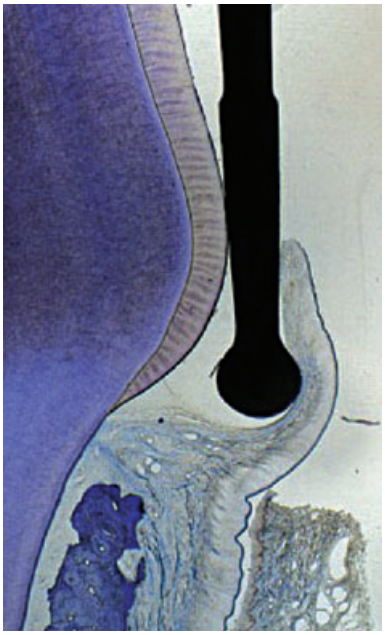


Fig. 3-29 Buccal–lingual ground section from a tooth site illustrating the probe tip position in relation to the bone crest (from Abrahamsson & Soldini 2006).

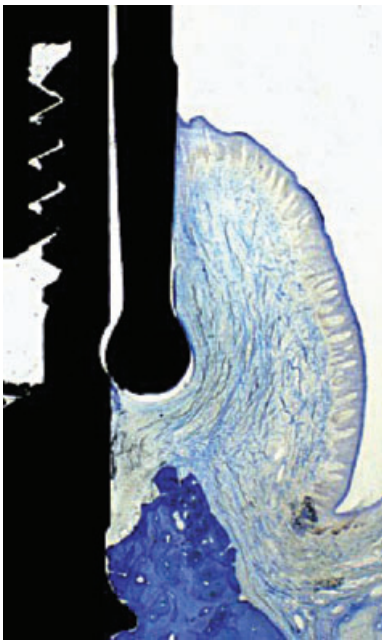


Fig. 3-30 Buccal–lingual ground section from an implant site illustrating the probe tip position in relation to the bone crest (from Abrahamsson & Soldini 2006).

Dimensions of the buccal soft tissue at implants

Chang *et al*. (1999) compared the dimensions of the periodontal and peri-implant soft tissues of 20 subjects who had been treated with an implant-supported single-tooth restoration in the esthetic zone of the maxilla and had a non-restored natural tooth in the contralateral position (Fig. 3-31). In

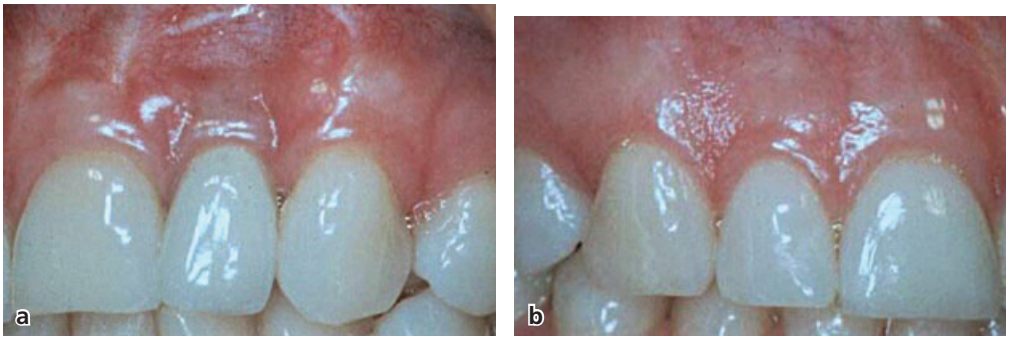


Fig. 3-31 Clinical photographs of (a) an implant-supported single tooth replacement in position 12 and (b) the natural tooth in the contralateral position (from Chang *et al*. 1999).

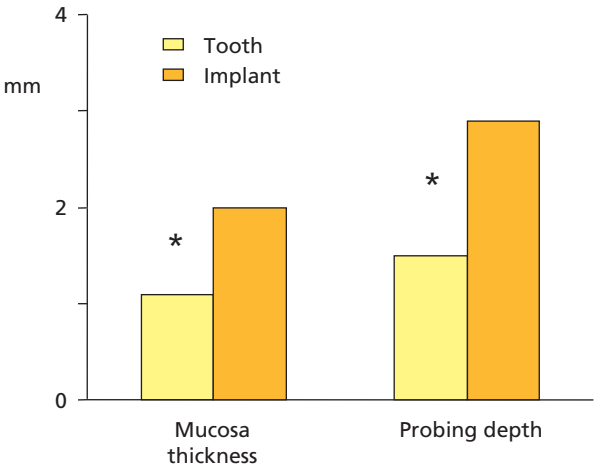


Fig. 3-32 Comparison of mucosa thickness and probing depth at the facial aspect of single-implant restorations and the natural tooth in the contralateral position (from Chang *et al*. 1999).

comparison to the natural tooth, the implant-supported crown was bordered by a thicker buccal mucosa (2.0 mm versus 1.1 mm), as assessed at a level corresponding to the bottom of the probeable pocket, and had a greater probing pocket depth (2.9 mm versus 2.5 mm) (Fig. 3-32). It was further observed that the soft tissue margin at the implant was more apically located (about 1 mm) than the gingival margin at the contralateral tooth.

Kan *et al*. (2003) studied the dimensions of the peri-implant mucosa at 45 single implants placed in the anterior maxilla that had been in function for an average of 33 months. Bone sounding measurements performed at the buccal aspect of the implants showed that the height of the mucosa was 3–4 mm in the majority of the cases. Less than 3 mm of mucosa height was found at only 9% of the implants. It was suggested that implants in this category were (1) found in subjects that belonged to a *thin periodontal biotype*, (2) had been placed too labially, and/or (3) had an overcontoured facial prosthetic emergence. A peri-implant soft tissue dimension of >4 mm was usually associated with a *thick periodontal biotype.*

Dimensions of the papilla between teeth and implants

In a study by Schropp *et al*. (2003) it was demonstrated that following single tooth extraction the height of the papilla at the adjacent teeth was reduced about 1 mm. Concomitant with this reduction (recession) of the papilla height the pocket depth was reduced and some loss of clinical attachment occurred.

Following single tooth extraction and subsequent implant installation, the height of the papilla in the tooth–implant site will be dependent on the attachment level of the tooth. Choquet *et al*. (2001) studied the papilla level adjacent to single-tooth dental implants in 26 patients and in total 27 implant sites. The distance between the apical extension of the contact point between the crowns and the bone crest, as well as the distance between the soft tissue level and the bone crest, was measured in radiographs. The examinations were made 6–75 months after the insertion of the crown restoration. The authors observed that the papilla height consistently was about 4 mm, and, depending on the location of the contact point between adjacent crowns papilla, fill was either complete or incomplete (Fig. 3-33). The closer the contact point was located to the incisal edge of the crowns (restorations) the less complete was the papilla fill.

Chang *et al*. (1999) studied the dimensions of the papillae at implant-supported single-tooth restorations in the anterior region of the maxilla and at non-restored contralateral natural teeth. They found that the papilla height at the implant-supported crown was significantly shorter and showed less fill of the embrasure space than the papillae at the natural tooth (Fig. 3-34). This was particularly evident for the distal papilla of implant-supported restorations in the central incisor position, both in comparison to the distal papilla at the contralateral tooth and to the papilla at the mesial aspect of the implant crown. This indicates that the anatomy of the adjacent natural teeth (e.g. the diameter of the root, the proximal outline/curvature of the cemento-enamel junction/connective tissue attachment

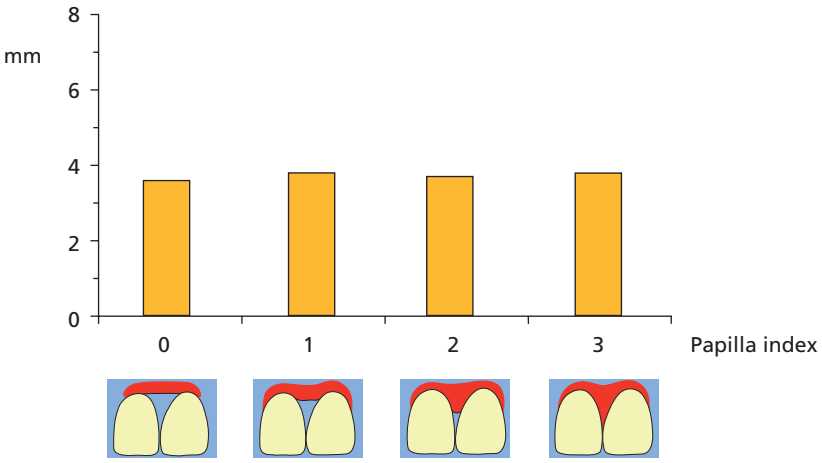


Fig. 3-33 Soft tissue height adjacent to single-tooth dental implants in relation to the degree of papilla fill (from Choquet *et al*. 2001).

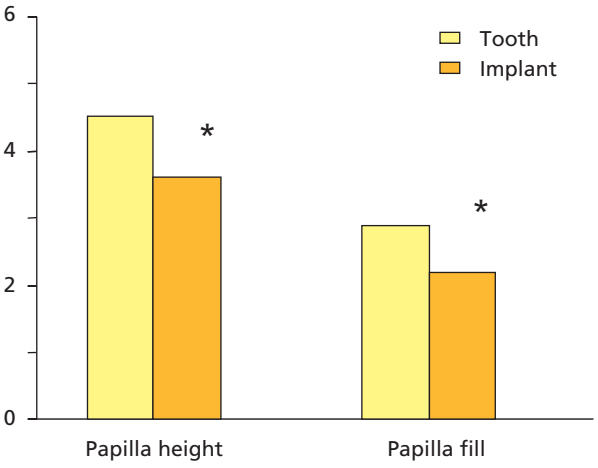


Fig. 3-34 Comparison of papilla height and papilla fill adjacent to single-implant restorations and the natural tooth in the contralateral position (from Chang *et al*. 1999).

level) may have a profound influence on the dimension of the papilla lateral to an implant. Hence, the wider facial–lingual root diameter and the higher proximal curvature of the cemento-enamel junction of the maxillary central incisor – in comparison to corresponding dimensions of the lateral incisor (Wheeler 1966) – may favor the maintenance of the height of the mesial papilla at the single-implant supported restoration.

Kan *et al*. (2003) assessed the dimensions of the peri-implant mucosa lateral to 45 single implants placed in the anterior maxilla and the 90 adjacent teeth using bone sounding measurements. The bone sounding measurements were performed at the mesial and distal aspects of the implants and at the mesial and distal aspects of the teeth. The authors reported that the thickness of the mucosa at the mesial/distal surfaces of the implant sites was on the average 6 mm while the corresponding dimension at the adjacent tooth sites was about 4 mm. It was further observed that the dimensions of the peri-implant mucosa of subjects who belonged to the *thick periodontal biotype* were significantly greater than that of subjects of a *thin biotype*.

The level of the connective tissue attachment on the adjacent tooth surface and the position of the contact point between the crowns are obviously key factors that determine whether or not a complete papilla fill will be obtained at the single-tooth implant-supported restoration (Fig. 3.35). Although there are indications that the dimensions of the approximal soft tissue may vary between individuals having thin and thick periodontal biotypes, the height of the papilla at the single-implant restoration seems to have a biological limit of about 4 mm (compare the dimension of the interdental papilla). Hence, to achieve a complete papilla fill of the embrasure space, a proper location of the contact area between the implant crown and the tooth crown is mandatory. In this respect it must also be recognized that the papilla fill at single-tooth implant restorations is unrelated to whether the implant is inserted according to a one- or two-stage protocol and whether a crown restoration is inserted immediately following surgery or delayed until the soft tissues have healed (Jemt 1999; Ryser *et al*. 2005).

Dimensions of the "papilla" between adjacent implants

When two neighboring teeth are extracted, the papilla at the site will be lost (Fig. 3-36). Hence, at replacement of the extracted teeth with implant-supported restorations the topography of the bone crest and the thickness of the supracrestal soft tissue portion are the factors that determine the position of the soft tissue margin in the inter-implant area ("implant papilla"). Tarnow *et al*. (2003) assessed the height above the bone crest of the inter-implant soft tissue ("implant papilla") by transmucosal probing at 136 anterior and posterior sites in 33 patients who had maintained implant-supported prostheses for at least

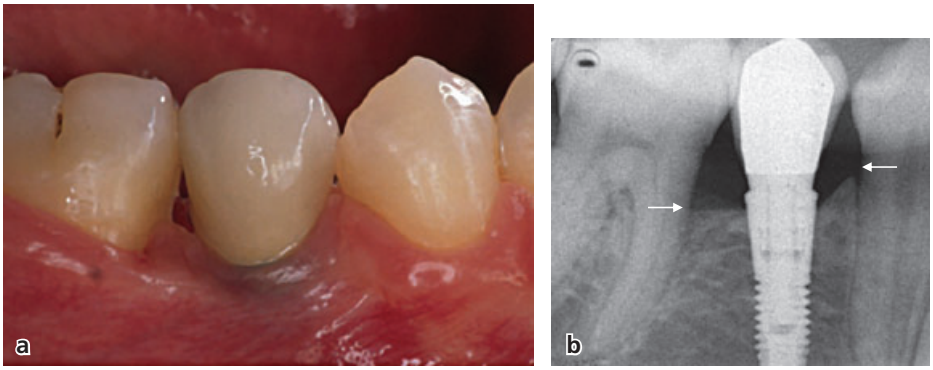


Fig. 3-35 See text for details.

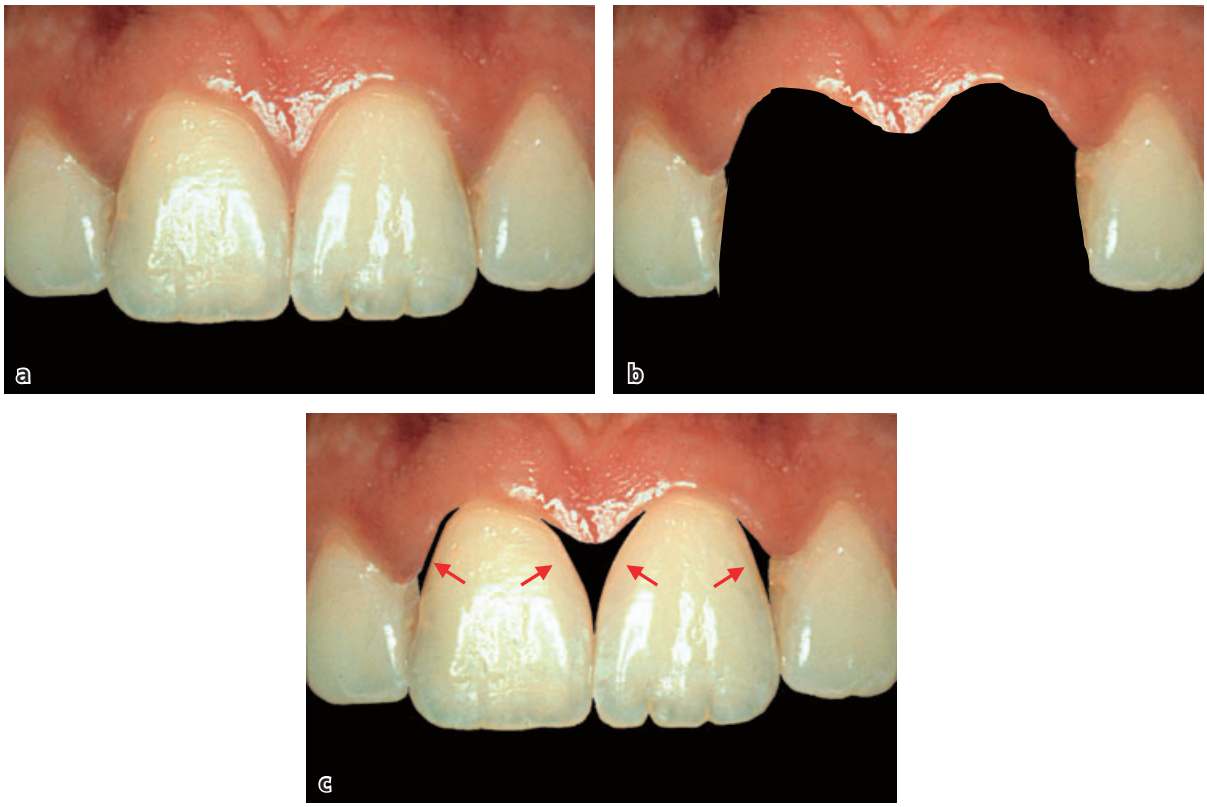


Fig. 3-36 See text for details.

2 months. It was found that the mean height of the "papillae" was 3.4 mm, with 90% of the measurements in the range of 2–4 mm.

The dimension of the soft tissues between adjacent implants seems to be independent of the implant design. Lee *et al.* (2006) examined the soft tissue height between implants of two different systems (Brånemark Implant® and Astra Tech Implant® systems) as well as the potential influence of the horizontal distance between implants. The height of the inter-implant "papilla", i.e. the height of soft tissue coronal to the bone crest measured in radiographs, was about 3.1 mm for both implant systems. No difference was found regarding the "papilla" height for any of the implant systems with regard to sites with <3 mm and ≥3 mm in horizontal distance between the implants. Gastaldo *et al.* (2004) evaluated the presence or absence of "papilla" at 96 inter-implant sites in 58 patients. It was reported that the "papilla" filled the entire space between the implants only when the distance from the bone crest to the base of the contact point between the crown restorations, assessed by sounding, was <4 mm. Thus, taken together these observations indicate that the soft tissue between two implants will have a maximum height of 3–4 mm, and that the location of the contact point between the crown restorations in relation to the bone crest level determines whether a complete soft tissue fill will be obtained in the embrasure space between two implants (Fig. 3-37).

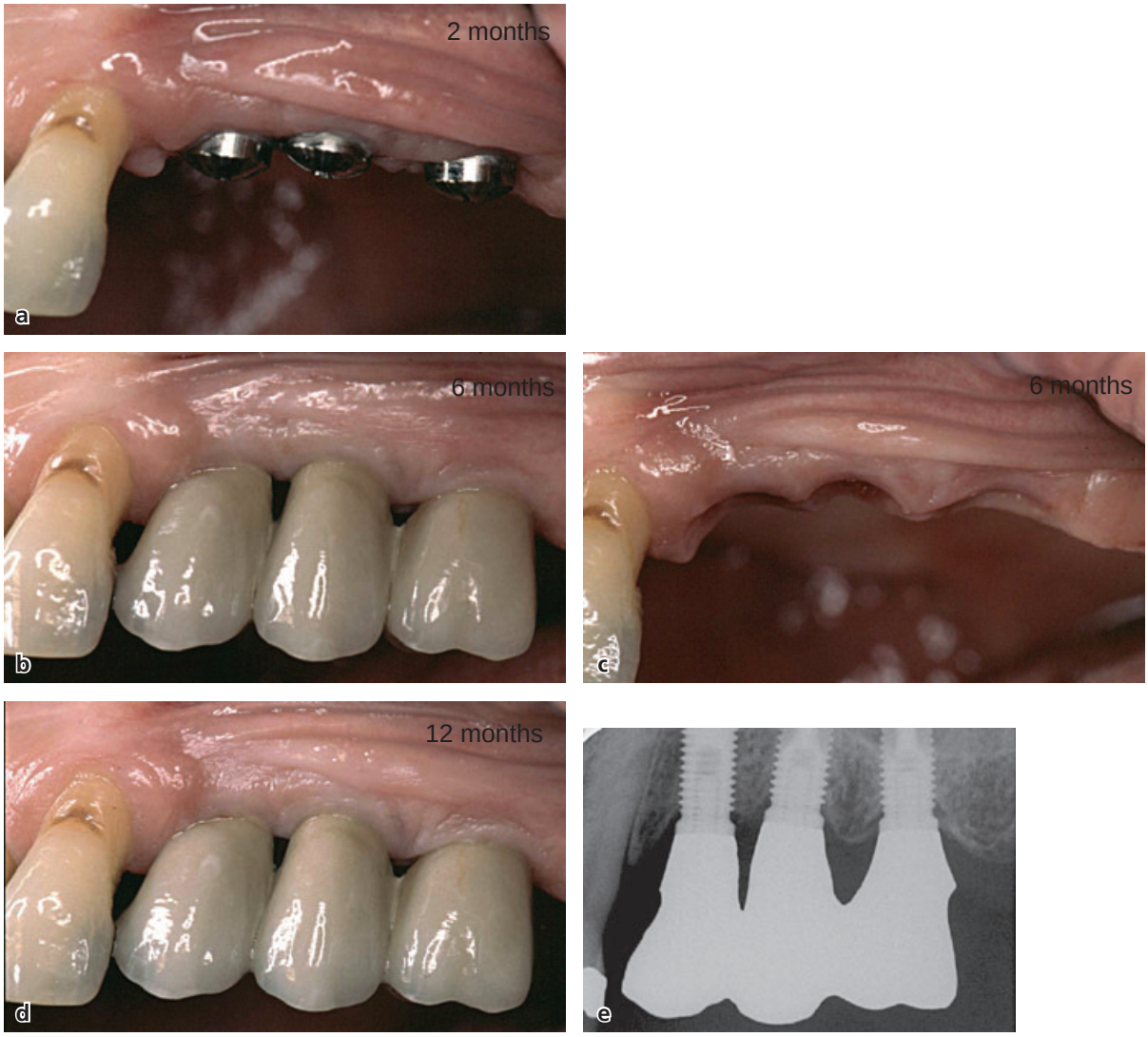


Fig. 3-37 See text for details.

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Chapter 4

Bone as a Tissue

William V. Giannobile, Hector F. Rios, and Niklaus P. Lang

During embryogenesis, in the alveolar process of the maxilla and the mandible, bone is formed within a primary connective tissue. This process is termed *intramembranous* bone formation and also occurs at the cranial vault and in the midshaft or diaphysis of the long bones. In contrast, bone formation in the remaining parts of the skeleton occurs via an initial deposition of a cartilage template that is subsequently replaced by bone. This process is called *endochondral* bone formation.

Alveolar bone lost as a result of disease, trauma or extensive post-extraction bone modeling may pose therapeutic problems in periodontal reconstructive and/or implant dentistry. Thus, implant placement both in the maxilla and in the mandible may be hampered by the lack of sufficient volume of alveolar bone at the recipient sites. *De novo* formation of alveolar bone in such compromised sites may be necessary and different regenerative therapies need to be considered to promote new bone. They all, however, have one aspect in common: the compliance with the principles of bone biology. There are several reconstructive modalities for restoration of the alveolar process, such as bone graft replacements and guided bone regeneration (GBR).

Basic bone biology

Bone is a specialized connective tissue that is mainly characterized by its mineralized organic matrix. The bone organic matrix is comprised of collagenous and non-collagenous proteins. Within this matrix, ions of calcium and phosphate are laid down in the ultimate form of hydroxyapatite. This composition allows the bone tissue to: (1) resist load, (2) protect highly sensitive organs (e.g. the central nervous system) from external forces, and (3) participate as a reservoir of minerals that contribute to systemic homeostasis of the body.

Bone cells

Osteoblasts are the primary cells responsible for the formation of bone; they synthesize the organic extracellular matrix (ECM) components and control the mineralization of the matrix. Osteoblasts are located on bone surfaces exhibiting active matrix deposition and may eventually differentiate into two different types of cells: *bone lining cells* and *osteocytes*. Bone lining cells are elongated cells that cover a surface of bone tissue and exhibit no synthetic activity. Osteocytes are stellate-shaped cells that are trapped within the mineralized bone matrix but remain in contact with other bone cells by thin cellular processes. The osteocytes are organized as a syncytium that provides a very large contact area between the cells (and their processes) and the non-cellular part of the bone tissue. This arrangement allows osteocytes to: (1) participate in the regulation of the blood-calcium homeostasis, and (2) sense mechanical loading and to signal this information to other cells within the bone.

The osteoblasts are fully differentiated cells and lack the capacity for migration and proliferation. Thus, in order to allow bone formation to occur at a given site, undifferentiated mesenchymal progenitor cells (*osteoprogenitor cells*) must migrate to the site and proliferate to become osteoblasts. Friedenstein (1973) divided osteoprogenitor cells into *determined* and *inducible osteogenic precursor cells*. The determined osteoprogenitor cells are present in the bone marrow, in the endosteum and in the periosteum that covers the bone surface. Such cells possess an intrinsic capacity to proliferate and differentiate into osteoblasts. Inducible osteogenic precursor cells, on the other hand, represent mesenchymal cells present in other organs and tissues (e.g. myoblasts or adipocytes) that may differentiate into bone-forming cells when exposed to specific stimuli. As osteogenesis is generally closely related to the ingrowth of vascular tissue,

Table 4-1 Effects of growth factors in bone wound healing

Wound healing phase	Growth factor	Cell of origin	Functions
Inflammatory	PDGF	Platelets	Increases chemotaxis of neutrophils and monocytes
	TGF-β	Platelets, leukocytes, fibroblasts	Increases chemotaxis of neutrophils and monocytes Autocrine expression – generation of additional cytokines (TNFα, IL-1β, PDGF, and chemokines)
	VEGF	Platelets, leukocytes, fibroblasts	Increases vascular permeability
Proliferative	EGF	Macrophages, mesenchymal cells, platelets	Stimulates epithelial proliferation and migration
	FGF-2	Macrophages, endothelial cells	Stimulates fibroblast proliferation and ECM synthesis Increases chemotaxis, proliferation, and differentiation of endothelial cells
	KGF (FGF-7)	Keratinocytes, fibroblasts	Stimulates epithelial proliferation and migration
	PDGF	Macrophages, endothelial cells	Stimulates fibroblast proliferation and ECM synthesis Increases chemotaxis, proliferation, and differentiation of endothelial cells
	TGF-β	Macrophages, leukocytes, fibroblast	Stimulates epithelial proliferation and migration Stimulates fibroblasts proliferation and ECM synthesis Inhibits proteases and enhances inhibitor production
	VEGF	Macrophages	Increases chemotaxis of endothelial progenitor cells Stimulates endothelial cell proliferation
Bone remodeling, matrix synthesis	BMPs 2–4	Osteoblasts	Stimulates mesenchymal progenitor cell migration
	BMP-7	Osteoblasts	Stimulates osteoblast and chondroblast differentiation
	FGF-2	Macrophages, endothelial cells	Stimulates mesenchymal progenitor cell migration
	IGF-II	Macrophages, fibroblasts	Stimulates osteoblast proliferation and bone matrix synthesis
	PDGF	Macrophages, osteoblasts	Stimulates differentiation of fibroblasts into myofibroblasts Stimulates proliferation of mesenchymal progenitor cells
	TGF-β	Fibroblasts, osteoblasts	Induces endothelial cell and fibroblast apoptosis Induces differentiation of fibroblasts into myofibroblasts Stimulates chemotaxis and survival of osteoblasts
	VEGF	Macrophages	Chemotaxis of mesenchymal stem cells, antiapoptotic effect on the bone forming cells, angiogenesis promotion

Adapted from: Kaigler, D., Cirelli, J.A. & Giannobile, W.V. (2006). Growth factor delivery for oral and periodontal tissue engineering. *Expert Opinion on Drug Delivery* **3**, 647–662, with permission.
PDGF = platelet-derived growth factor; TGF = transforming growth factor; VEGF = vascular endothelial growth factor; EGF = epidermal growth factor; FGF = fibroblast growth factor; KGF = keratinocyte growth factor; BMP = bone morphogenetic protein; IGF = insulin-like growth factor; TNFα = tumor necrosis factor alpha.

the stellate-shaped perivascular cell (the *pericyte*) is considered to be the main osteoprogenitor cell. The differentiation and development of osteoblasts from osteoprogenitor cells are dependent on the release of osteoinductive or osteopromotive growth factors (GFs) such as bone morphogenetic proteins (BMP) and other growth factors such as insulin-like growth factor (IGF), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) (Table 4-1).

The bone formation activity is consistently coupled to bone resorption that is initiated and maintained by *osteoclasts*. Osteoclasts are multinucleated cells that originate from hematopoietic precursor cells.

Modeling and remodeling

Once bone has formed, the new mineralized tissue starts to be reshaped and renewed by processes of resorption and apposition, i.e. through *modeling* and *remodeling*. Modeling represents a process that allows a change in the initial bone architecture. It has been suggested that external demands (such as load) on bone tissue may initiate modeling. Remodeling, on the other hand, represents a change that occurs within the mineralized bone without a concomitant alteration of the architecture of the tissue. The process of remodeling is important (1) during bone formation, and (2) when old bone is replaced with new bone. During bone formation, remodeling enables the substitution of the primary bone (woven bone), which has low load-bearing capacity, with lamellar bone that is more resistant to load.

The bone remodeling that occurs in order to allow replacement of old bone with new bone involves two processes: bone resorption and bone apposition (formation). These processes are coupled in time and are

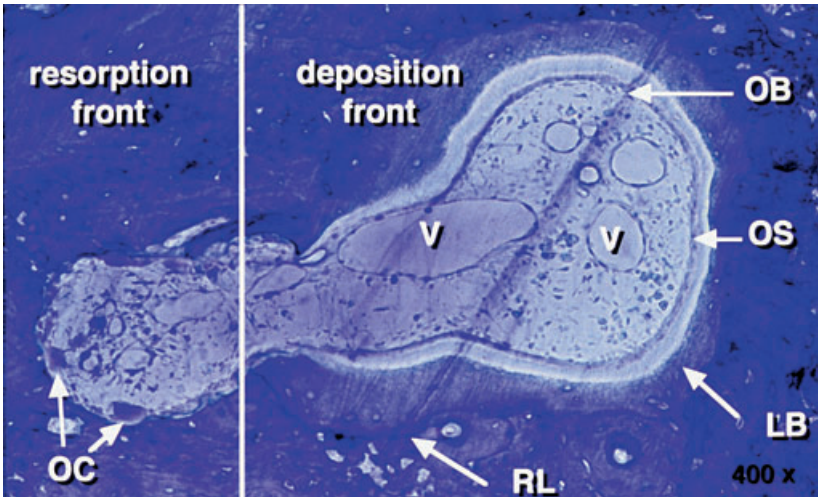

Fig. 4-1 Histological section illustrating a bone multicellular unit (BMU). Note the presence of a resorption front with osteoclast (OC) and a deposition front that contains osteoblasts (OB), and osteoid (OS). Vascular structures (V) occupy the central area of the BMU. RL = reversal line; LB = lamellar bone.

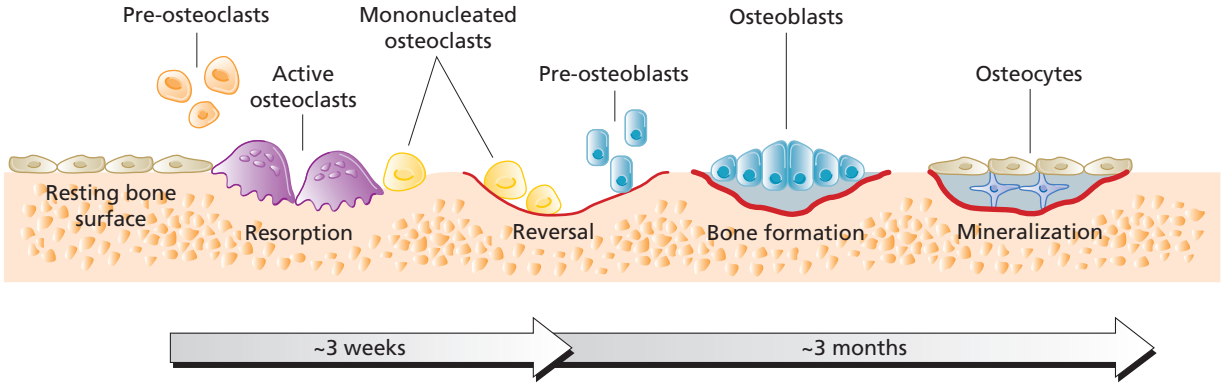

Fig. 4-2 The bone remodeling cycle. Preosteoblasts are recruited to sites of resorption, induced to differentiate into active osteoclasts, and form resoption pits. After their period of active resorption, transient mononuclear cells replace them. Through the process of coupling, preosteoblasts are recruited, differentiate into active matrix-secreting cells, and form bone. Some osteoblasts become entrapped in the matrix and become osteocytes. Adapted from McCauley, L.K. & Nohutcu, R.M. (2002) Mediators of periodontal osseous destruction and remodeling: principles and implications for diagnosis and therapy. *Journal of Periodontology* **73**, 1377–1391, with permission.

characterized by the presence of so called *bone multicellular units* (BMUs). A BMU (Fig. 4-1) is comprised of (1) a front osteoclast residing on a surface of newly resorbed bone (the resorption front), (2) a compartment containing vessels and pericytes, and (3) a layer of osteoblasts present on a newly formed organic matrix (the deposition front). The process of the bone remodeling cycle is shown in Figs. 4-2 and 4-3. Local stimuli and release of hormones, such as parathyroid hormone (PTH), growth hormone, leptin, and calcitonin, are involved in the control of bone remodeling. Modeling and remodeling occur throughout life to allow bone to adapt to external and internal demands.

Growth factors and alveolar bone healing

Understanding the complex processes of wound healing has been a challenge for researchers for many years. Recently, advances in the areas of cellular and molecular biology have allowed the elucidation of functions of GFs and their participation in the different phases of wound healing. Restoration of normal form and function is the ultimate goal of regenerative approaches of alveolar bone disrupted by trauma, surgical resection or infectious disease. However, if the functional integrity of the tissue is not achieved, the process of repair will take place and a fibrous tissue will replace the original tissue (Le *et al.* 2005). Recent studies have confirmed that GFs can improve the capacity of alveolar bone to regenerate, improving cellular chemoattraction, differentiation, and proliferation. GFs are natural biological mediators that regulate important cellular events involved in tissue repair by binding to specific cell surface receptors (Giannobile 1996). After reaching specific target cells, GFs induce intracellular signaling pathways, which result in the activation of genes that change cellular activity and phenotype (Anusaksathien & Giannobile 2002). However, the effect of each GF is regulated through a complex system of feedback loops, which involve other GFs, enzymes, and binding proteins (Schilephake 2002; Ripamonti *et al.* 2005). Recent studies have taken place with the target of defining the proper application for therapeutic purposes of many different growth factors and other cytokines,

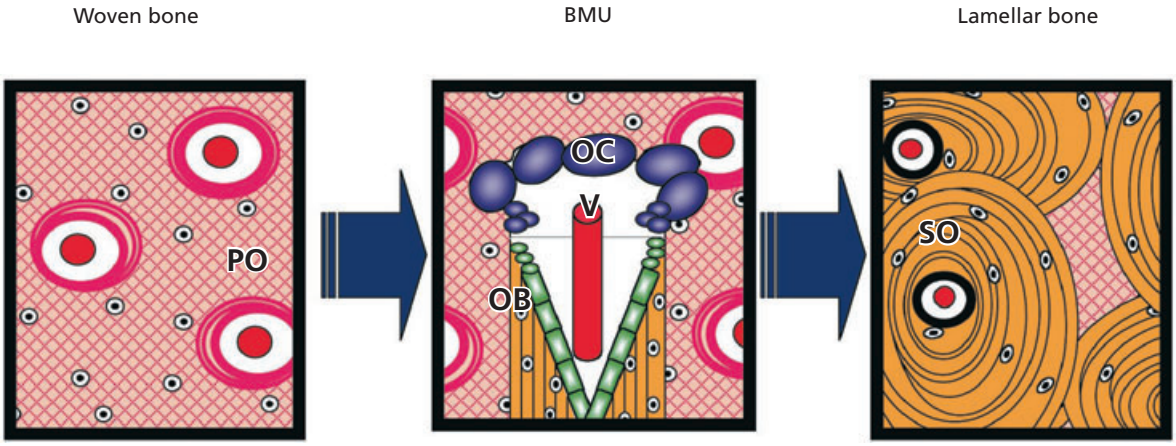

Fig. 4-3 Schematic drawing describing the transition between woven bone and lamellar bone, i.e. remodeling. Woven bone with primary osteons (PO) is transformed into lamellar bone in a process that involves the presence of BMUs. The BMU contains osteoclasts (OC), as well as vascular structures (V) and osteoblasts (OB). Thus, the osteoblasts in the BMU produce bone tissue that has a concentric orientation around the vessel, and secondary osteons (SO) are formed within lamellar bone.

each of which has several functions during the different phases of wound healing (Schilephake 2002; Ripamonti *et al.* 2005).

Healing of osseous tissue is regulated by GFs and other cytokines in a sequence of overlapping events similar to cutaneous wound repair. In ideal circumstances, this process mimics embryonic bone development allowing replacement of damaged bone with new bone, rather than with fibrous scar tissue. This process is driven by cellular and molecular mechanisms controlled by the TGF-β superfamily of genes, which encode a large number of extracellular signaling molecules (Blair *et al.* 2002). Bone morphogenetic proteins (BMPs) are a well studied group of these GFs involved in the processes of bone healing; the human genome encodes at least 20 of these multifunctional polypeptides (Blumenthal *et al.* 2002). Among several functions, BMPs induce the formation of both bone and cartilage by stimulating the cellular events of mesenchymal progenitor cells. However, only a subset of BMPs, most notably BMP-2, -4, -6, -7, and -9, has osteoinductive activity, a property of inducing *de novo* bone formation by themselves (Cheng *et al.* 2003). Studies involving mutations of BMP ligands, receptors, and signaling proteins have shown important roles of BMPs in embryonic and postnatal development. Severe skeletal deformation, development of osteoporosis, reduction in bone mineral density and bone volume are all aberrations associated with disrupted and dysregulated BMP signaling (Chen *et al.* 2004).

Several other GFs produced by osteogenic cells, platelets and inflammatory cells participate in bone healing, including IGF-I and -II, TGFβ-1, PDGF, and FGF-2 (Sykaras & Opperman, 2003). The bone matrix serves as a reservoir for these GFs and BMPs and they are activated during matrix resorption by matrix metalloproteinases (Baylink *et al.* 1993; Janssens *et al.* 2005). Additionally, the acidic environment that develops during the inflammatory process leads to activation of latent GFs (Linkhart *et al.* 1996), which assist in the chemoattraction, migration, proliferation, and differentiation of mesenchymal cells into osteoblasts (Linkhart *et al.* 1996). All of these functions are driven by a complex mechanism of interaction among GFs and other cytokines, which is influenced by several regulatory factors (King & Cochran, 2002).

Local and systemic factors affecting bone volume and healing

Metabolic disorders affecting bone metabolism

A variety of systemic situations can affect local bone density, ultimately influencing tooth support or available bone volume for dental implant installation. Such diseases affecting bone mass include osteopenia, osteoporosis, and diabetes mellitus. The later two will be discussed in detail given their overall prevalence and implications to alveolar bone reconstruction.

Osteoporosis

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of the bone scaffold that result in increased bone fragility and susceptibility to fracture. In osteoporosis, the *bone mineral density* (BMD) is reduced, bone microarchitecture is disrupted, and the amount and variety of non-collagenous proteins in bone is altered. *Dual energy X-ray absorptiometry* (DXA, formerly DEXA) is considered the gold standard for diagnosis of osteoporosis. Diagnosis is made when the BMD is less than or equal to 2.5 standard deviations below that of a young adult reference population. This is translated as a T-score. The World Health Organization has established diagnostic guidelines as T-score –1.0 or greater is "normal", T-score between –1.0 and –2.5 is osteopenia, and –2.5 or below as osteoporosis (WHO Study Group 1994).

Oral bone loss has been shown to be associated with osteoporosis and low skeletal BMD. In their search for oral radiographic changes associated with osteoporosis, most investigators have focused on measures of jaw bone mass or morphology. The commonly used assessment of oral bone status include radiographic measures of loss of alveolar crestal height (ACH), measures of resorption of the residual ridge after tooth loss (RRR), and assessment of oral BMD. Tools used to measure bone mass include single and dual photon absorptiometry, DXA, quantitative computed tomography (QCT), and film densitometry.

Periodontitis results from pathogenic bacterial infection, which produces factors that destroy collagenous support of the tooth, as well as loss of alveolar bone. Systemic factors can lead to loss of BMD throughout the body, including bone loss in the maxilla and mandible. The resulting local reduction of BMD in the jaw bones could set the stage for more rapid ACH loss because a comparable challenge of bacterial bone-resorbing factors could be expected to result in greater alveolar crestal bone loss than in an individual with good bone mass. In addition to this, there are systemic risk factors such as smoking, diabetes, diet, and hormone levels that affect systemic bone level and may also affect periodontitis (discussed in Chapters 12 and 13). Although periodontal disease has historically been thought to be the result of a local infectious process, others have suggested that periodontal disease may be an early manifestation of generalized osteopenia (Whalen & Krook 1996), which would classify osteoporosis as a risk indicator, rather than a risk factor, for periodontal disease.

Mandibular mineral content is reduced in subjects with osteoporotic fractures (von Wowern *et al.* 1994). Further, the BMD of buccal mandibular bone correlates with osteoporosis (low skeletal BMD) (Klemetti *et al*. 1993; Taguchi *et al*. 1996). Mandibular density also correlates with skeletal BMD (Horner *et al*. 1996). Using film densitometry, the optical density of the mandible has been found to be increased in subjects with osteoporosis compared with controls. Further, mandibular radiographic optical density correlates with vertebral BMD in osteoporotic women (Kribbs 1990), control women (Kribbs 1990), and in women with a history of vertebral fracture (Kribbs *et al*. 1990; Law *et al.* 1996). Reduction in cortical and subcortical alveolar bone density has also been reported to correlate with osteoporosis in longitudinal studies (Payne *et al*. 1997, 1999; Civitelli *et al*. 2002). As concluded by Hildebolt (1997), the preponderance of the evidence indicates that the jaws of subjects with osteoporosis show reduced bone mass with potential implications on dental implant installation.

Several potential mechanisms by which osteoporosis or systemic bone loss may be associated with periodontal attachment loss, loss of alveolar bone height or density, and tooth loss have been proposed. One of these mechanisms states that low BMD or loss of BMD may lead to more rapid resorption of alveolar bone after insult by periodontal bacteria. With less dense oral bone to start with, loss of bone surrounding the teeth may occur more rapidly. Another mechanism proposes that systemic factors affecting bone remodeling may also modify local tissue response to periodontal infection. Persons with systemic bone loss are known to have increased production of cytokines (i.e. interleukin-1, interleukin-6) that may have effects on bone throughout the body, including the bones of the oral cavity. Periodontal infection has been shown to increase local cytokine production that, in turn, increases local osteoclast activity resulting in increased bone resorption. A third mechanism would be related to genetic factors that predispose an individual to systemic bone loss and also influence or predispose an individual to periodontal destruction. Also, certain lifestyle factors such as cigarette smoking and suboptimal calcium intake, among others, may put individuals at risk for development of both systemic osteopenia and oral bone loss (Oh *et al.* 2007).

Recently, long-term use of bone anti-resorptive agents, specifically bisphosphonates, has been associated with osteonecrosis of the jaw (ONJ) (Marx 2003; Ruggiero *et al*. 2004). According to a web-based survey conducted by the International Myeloma Foundation (Durie *et al.* 2005), an increased incidence of ONJ has been observed after 36 months from the start of therapy in patients receiving zoledronic acid or pamidronate for the treatment of myeloma or breast cancer. This data also indicated that patients with prior dental problems might have a higher risk of ONJ. As the bisphosphonates are potent osteoclast inhibitors, their long-term use may suppress bone turnover and compromise healing of even physiological micro-injuries within bone (Odvina *et al*. 2005). Despite the encouraging therapeutic results, further long-term studies are warranted to determine the relative risk : benefit ratio of bisphosphonate therapy. See Fig. 4-4 for therapies used to treat bone loss.

With regard to osseointegration, preclinical animal studies note the influence of osteoporosis on bone–implant contact as suggesting a negative effect (Mori *et al*. 1997; Duarte *et al*. 2003; Cho *et al*. 2004). For instance, Cho *et al*. (2004), using an osteoporotic animal model, found a bone contact reduction of 50%. Lugero *et al*. (2000), using an induced osteoporosis rabbit model, also found that integration was impaired, although they pointed out that cortical thickness was decreased as well.

Some early clinical reports have difficulties demonstrating an increased loss of implants during early stages of implant therapy (Becker *et al*. 2000; Friberg *et al*. 2001), mostly because osteopenia is treated at the time of placement. Yet early implant failure is often correlated with local lack of bone density or volume (van Steenberghe *et al*. 2002). For instance, Esposito *et al*. (2005) in a recent systematic review,

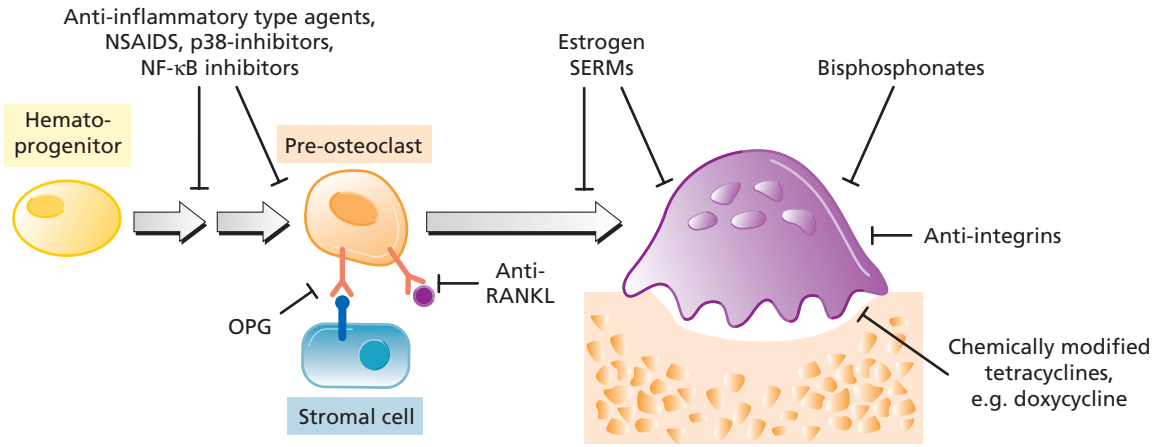

Fig. 4-4 Potential therapeutic strategies to treat bone resorption: agents that block the differentiation or activity of osteoclasts are potential therapeutic agents. Osteoprotegrin (OPG) inhibits the differentiation of osteoclasts through its action as a decoy receptor that blocks RANK (receptor activator of nuclear factor-kappa beta) and RANKL (RANK ligand) juxtacrine interaction. Non-steroidal anti-inflammatory drugs (NSAIDs) and other anti-inflammatory type molecules can inhibit the formation of hematoprogenitor cells to pre-osteoclasts. Antibodies to RANKL can also block this interaction. Estrogen and selective estrogen receptor modulators (SERMs) may inhibit the activity of osteoclasts but also promote apoptosis of osteoclasts, thus reducing their active lifespan. Bisphosphonates also promote osteoclast apoptosis. Chemically modified tetracylines reduce the protease degradation of the organic matrix, and anti-integrins block the initial osteoclast adhesion to the matrix. Adapted with permission from Kirkwood, K.L., Taba, M. Jr., Rossa, C., Preshaw, P. & Giannobile, W.V. (2006). Molecular biology concepts in host-microbe interaction in periodontal diseases. In: Newman M.G. *et al*. (eds). *Carranza's Clinical Periodontology*, 10th Edn. Elsevier Publishing, St. Louis, MO, pp. 259–274.

reported that implant failure is three times greater in the posterior maxilla, where bone density is less, than in the mandible. On the other hand, clinical evaluation or resistance during surgical osteotomy creation for implant installation may be indicative of osteopenia or osteoporosis (Friberg *et al*. 2001). It has also been reported that dental radiography and clinical evaluation at the time of surgery can suggest the presence of osteopenia, but early implant survival is not affected (Becker *et al*. 2000). Although the influence of bone density on early failure is unclear, mostly because bone volume is often a confounding factor, this suggests that it is more critical to study long-term consequences. There is, however, little information available on long-term maintenance of implants in the presence of osteoporosis. Thus, based on the available data, there is evidence to interpret an association between osteoporosis and bone density that exists around teeth and dental implant fixtures. There is also some information to suggest that decreased bone mass may place dental implants at a greater risk to failure or to decreased ability to handle load over the long term.

Diabetes mellitus

Diabetes mellitus is associated with a variety of metabolic sequlae including effects on bone maintenance and healing. There are three main types of diabetes mellitus. Type 1 is caused by damage or destruction of the beta cells of the pancreas which leads to production of insufficient amounts of insulin. Type 2 is caused by resistance to insulin with failure to produce enough additional insulin to compensate for the insulin resistance (see also Chapter 12). Type 2 diabetes constitutes 90–95% of the individuals suffering from diabetes mellitus in the US (Kahn & Flier 2000). There is a third type of diabetes that is gestational and occurs when there is a glucose intolerance of variable severity that starts or is first recognized during pregnancy (Novak *et al*. 2006).

The liver, the skeletal muscles, and the adipose tissue are the main insulin-responsive tissues, yet insulin also influences the physiology of other tissues, including bone and cartilage. In conditions of hypoinsulinemia (e.g. type 1 diabetes) or hyperinsulinemia with or without glucose intolerance or fasting hyperglycemia (type 2 diabetes), endochondral bone growth and bone remodeling show significant alterations.

Type 1 diabetes

Although bone histomorphometry data are lacking, results from biochemical markers of bone formation studies reveal unequivocal evidence that bone formation is decreased in diabetes mellitus. Serum osteocalcin concentrations are about 25% lower in diabetic children, adolescents and adults (Bouillon *et al*. 1995). Several relatively small studies that have investigated the effect of type 1 diabetes on axial bone density have found that the BMD Z score (age-matched BMD) from the lumbar spine or the femoral neck of diabetic patients is either not significantly different from that of the control groups or that there is a small decrease in cortical bone density but no difference in trabecular bone density (Roe *et al*. 1991; Ponder *et al*. 1992;

Gallacher *et al*. 1993; Olmos *et al*. 1994). The conclusion from these studies is that type 1 diabetic subjects have a mean Z score below, but generally within 1 SD of, reference values (Lunt *et al*. 1998; Miazgowski & Czekalski 1998; Rix *et al.* 1999). This effect can be seen within a few years after diagnosis and is not progressive.

Type 2 diabetes

Bone formation and bone mineralization are also decreased in type 2 diabetes. Histomorphometry results showed a significant decrease in the osteoid thickness and in the dynamic bone formation rate of a human bone biopsy specimen of a type 2 diabetic patient with a low BMD Z score at the radius. However, low bone turnover in type 2 diabetes does not cause bone loss (Krakauer *et al*. 1995).

In support of these data, hyperinsulinemia, which is a marker of insulin resistance and the central mechanism in the pathogenesis of type 2 diabetes, has been found to be linked with higher cortical thickness and a small but significant increase in BMD (Wakasugi *et al*. 1993; Rishaug *et al*. 1995; Bauer *et al.* 2002).

Insulin stimulates endochondral bone growth and osteoblast proliferation and function *in vitro* and *in vivo* at physiological concentrations. Severe diabetes in animal models typically induces reduction in bone blood flow, bone growth, periosteal bone apposition, and bone remodeling (both resorption and formation). Consequently, bone size and bone mass are reduced. However, no effect on bone mineral density has been identified when adjusted for bone size. Less apparent changes are observed in (insulin-treated) human type 1 diabetes, although many studies report a mild reduction in growth velocity in pubertal children with this condition, a mild deficit in BMD area (maximum 10%) which does not deteriorate with longer diabetes duration, and significantly reduced bone remodeling parameters. On the other hand, individuals with hyperinsulinemia and/or type 2 diabetes have a mild increase (3–5%) in BMD area.

Apart from insulin deficiency, there are likely to be other causative factors in the development of diabetes bone disease such as alterations in the IGF-IGFBP system and hypercorticolism. The cellular and molecular mechanisms by which diabetes affects chondrocyte, (pre)osteoblast, and (pre)-osteoclast proliferation and function still need to be elucidated.

In conclusion, diabetes is associated with an increased risk of periodontitis and progressive bone loss of the alveolus; however, this risk may vary depending on differences in susceptibility to periodontitis among populations (Kinane *et al.* 2006).

Diabetes as a risk factor for alveolar bone loss around implants

Studies investigating dental implants in the presence of diabetes mellitus are limited, but there is evidence that this disease is not a contra-indication for placement (Shernoff *et al.* 1994). In fact, there is evidence that early implant survival in well controlled patients is similar to that in non-diabetic patients. It is also noticeable that this may be true for all indications (Abdulwassie & Dhanrajani 2002), as well as for more advanced surgical techniques, such as bone grafting (Farzad *et al.* 2002). However, animal experiments have shown that bone–implant contact is affected (Nevins *et al*. 1998), suggesting that clinical consequences in long-term maintenance may arise. In a large prospective 5-year clinical study, Olson *et al*. (2000) found that duration of diabetes was an important factor in implant survival. Other retrospective or observational studies have also concluded that diabetes contributes to an increase in failure rates (Moy *et al*. 2005). In a 4-year retrospective clinical analysis of 215 implants of controlled diabetes mellitus patients, Fiorellini *et al*. (2000) reported an overall success rate of 85.6%, with some variation with regard to implant location and cumulative time in function. They concluded that the implant failure rate was significantly greater than in non-diabetic patients. However, there is controversy as to whether this is due to initial failure (Fiorellini *et al*. 2000).

In contrast to the previous studies where early implant loss was greater in diagnosed patients, Peled *et al*. (2003), in a clinical evaluation of well controlled edentulous patients who had received two implants, found that there was no difference in initial osseointegration. Van Steenberghe *et al*. (2002), in a large clinical evaluation exploring various systemic parameters, found that diabetes was not a detrimental factor during initial phases of integration and prosthesis fabrication, again supporting the importance of long-term studies. The influence of underlying elevated glucose levels on osseointegration is also supported by animal studies (Ottoni & Chopard 2004). For instance, using a diabetic rat model, Siqueira *et al*. (2003) reported a 50% decrease of osseointegration when animals did not receive insulin therapy, suggesting that an association exists. Kopman *et al*. (2005), using a similar model, also reported that bone–implant contact was significantly reduced. Interestingly, these previous studies also found that treatment of the condition did not improve osseointegration, when compared to uncontrolled diabetic animals, suggesting that treated individuals may have impaired implant healing regardless of their disease stability. Furthermore, there are suggestions that poorly controlled conditions could lead to loss of bone–implant contact, resulting in a weaker bone–implant interface (Kwon *et al*. 1997). Therefore, it is likely that long-term risks for complications are greater in the presence of diabetes mellitus. This hypothesis can only be reinforced when diabetes is poorly controlled or undiagnosed.

Diabetes has been reported to adversely affect bone repair by decreasing expression of genes that induce osteoblast differentiation, and diminishing

growth factor and ECM production (Bouillon 1991; Kawaguchi *et al*. 1994; Lu *et al*. 2003). One proposed mechanism for these adverse effects is through the contribution of advanced glycation end-products (AGEs) to decreased extracellular matrix production and inhibition of osteoblast differentiation (McCarthy *et al*. 2001; Cortizo *et al*. 2003; Santana *et al*. 2003). AGEs may also delay wound healing by inducing apoptosis of ECM-producing cells. This enhanced apoptosis would reduce the number of osteoblastic and fibroblastic cells available for the repair of resorbed alveolar bone (Graves *et al*. 2006). In addition to promoting apoptosis, AGEs could affect oral tissue healing by reducing expression of collagen and promoting inflammation. The mechanisms suggested for AGE-enhanced apoptosis include the direct activation of caspase activity, and indirect pathways that increase oxidative stress or the expression of pro-apoptotic genes that regulate apoptosis (Graves *et al*. 2006).

Bone healing

Healing of an injured tissue usually leads to the formation of a tissue that differs in morphology or function from the original tissue. This type of healing is termed *repair*. Tissue *regeneration*, on the other hand, is a term used to describe a healing that leads to complete restoration of morphology and function.

The healing of bone tissue includes both regeneration and repair phenomena depending on the nature of the injury. For example, a properly stabililized, narrow bone fracture (e.g. greenstick fracture) will heal by regeneration, while a larger defect (e.g. segmental bone defect) will often heal with repair. There are certain factors that may interfere with the bone tissue formation following injury, such as:

1. Failure of vessels to proliferate into the wound
2. Improper stabilization of the coagulum and granulation tissue in the defect
3. Ingrowth of "non-osseous" or fibrous tissues with a high proliferative activity
4. Bacterial contamination.

The healing of a wound includes four phases:

1. Blood clotting
2. Wound cleansing
3. Tissue formation
4. Tissue modeling and remodeling.

These phases occur in an orderly sequence but, in a given site, may overlap in such a way that in some areas of the wound, tissue formation may be in progress, while in other areas tissue modeling is the dominating event. Examples of bone remodeling can be also seen in Chapter 2 on the edentulous ridge and Chapter 49 on ridge augmentation procedures.

Bone grafting

Although bone tissue exhibits a large regeneration potential and may restore its original structure and function completely, bony defects may often fail to heal with bone tissue. In order to facilitate and/or promote healing, bone grafting materials have been placed into bony defects. It is generally accepted that the biologic mechanisms forming the basis for bone grafting include three basic processes: *osteogenesis*, *osteoconduction*, and *osteoinduction*.

Osteogenesis occurs when viable osteoblasts and precursor osteoblasts are transplanted with the grafting material into the defects, where they may establish centers of bone formation. Autogenous iliac bone and marrow grafts are examples of transplants with osteogenic properties (see Chapter 49).

Osteoconduction occurs when non-vital implant material serves as a scaffold for the ingrowth of precursor osteoblasts into the defect. This process is usually followed by a gradual resorption of the implant material. Autogenous cortical bone or banked bone allografts may be examples of grafting materials with osteoconductive properties (Fig. 4-5). Such grafting materials, as well as bone-derived or synthetic bone substitutes, have similar osteoconductive properties. However, degradation and substitution by viable bone is often poor. If the implanted material is not resorbable, which is the case for most porous hydroxylapatite implants, the incorporation is restricted to bone apposition to the material surface, but no substitution occurs during the remodeling phase.

Osteoinduction involves new bone formation by the differentiation of local uncommitted connective tissue cells into bone-forming cells under the influence of one or more inducing agents. *Demineralized bone matrix* (DMB) or *bone morphogenetic proteins* (BMP) are examples of such grafting materials (Giannobile & Somerman 2003; Reynolds *et al*. 2003).

It often occurs that all three basic bone-forming mechanisms are involved in bone regeneration. In fact, osteogenesis without osteoconduction and osteoinduction is unlikely to occur, since almost none of the transmitted cells of autogenous cancellous bone grafts survive the transplantation. Thus, the grafting material predominantly functions as a scaffold for invading cells of the host. In addition, the osteoblasts and osteocytes of the surrounding bone lack the ability to migrate and divide which, in turn, means that the transplant is invaded by uncommitted mesenchymal cells that later differentiate into osteoblasts.

On that basis, it is appropriate to define three basic conditions as prerequisites for bone regeneration:

1. The *supply of bone-forming cells* or cells with the capacity to differentiate into bone-forming cells

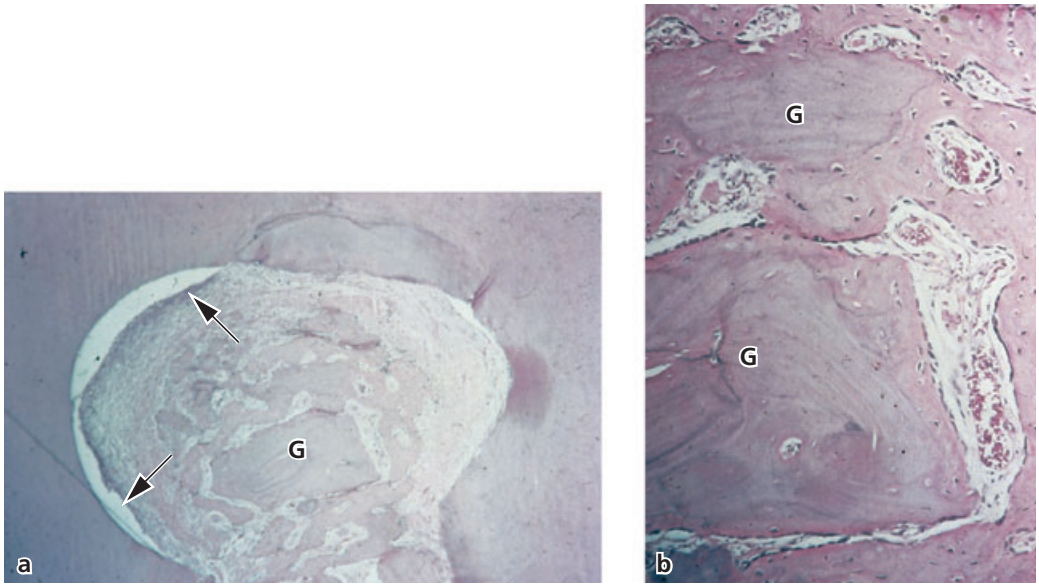

Fig. 4-5 (a) Microphotograph demonstrating bifurcation defect 3 weeks after grafting with autogenous cancellous jaw bone (G). New bone has invaded the defect, and the bone grafts have exerted an osteoconductive function. Epithelium (arrows) has migrated into one side of the defect. (b) Higher magnification of (a) showing that new bone has formed around the bone grafts (G), which have lost their vitality, indicated by the empty osteocyte lacunae.

2. The presence of *osteoinductive stimuli* to initiate the differentiation of mesenchymal cells into osteoblasts
3. The presence of an *osteoconductive environment* forming a scaffold upon which invading tissue can proliferate and in which the stimulated osteoprogenitor cells can differentiate into osteoblasts and form bone.

The placement of bone-grafting materials to favor healing in osseous defects or to augment atrophic alveolar ridges has been evaluated in a number of experimental and clinical studies (Boyne 1970; Thompson & Casson 1970; Steinhauser & Hardt 1977; Fazili *et al*. 1978; Baker *et al*. 1979; Mulliken & Glowacki 1980; Swart & Allard 1985; Block *et al*. 1987; Cullum *et al*. 1988; Hupp & McKenna 1988) (also see Chapter 49). However, there are several reports indicating that this type of treatment fails predictably to produce bone fill and augment alveolar ridges (Korlof *et al.* 1973; Curtis & Ware 1977; Steinhauser & Hardt 1977; Taylor 1983; Davis *et al.* 1984; Jackson *et al.* 1986; Hupp & McKenna 1988). Often the bone grafts do not attach to the graft site through bony attachment and there is bone resorption and bone loss associated with grafting procedures. As a consequence, much of the intended volume is lost, and frequently the defects heal with a fibrous connective tissue instead of bone.

Human experimental studies on alveolar bone repair

At present, most of the information regarding the biologic events which lead to new bone formation is derived from animal studies. Results regarding bone formation collected in animal studies have to be applied with proper caution in humans. In particular, the time sequence of the various steps ultimately leading to the formation of mineralized mature bone in man is different from that in all experimental animal systems known. A few human specimens, often harvested under poorly controlled conditions, contribute relatively little to the understanding of the biologic events of bone regeneration in humans.

A model system was designed to obtain human specimens of regenerated and also newly generated alveolar bone for the study of the biologic events under a variety of conditions (Hämmerle *et al*. 1996). A mucoperiosteal flap was raised in the retromolar area of the mandible of nine healthy volunteers. Following flap reflection, a standardized hole was drilled through the cortical bone into the bone marrow. Congruent test cylinders were firmly placed into the prepared bony bed, yielding primary stability; 1.5–2 mm of the test device were submerged below the level of the surrounding bone, leaving 2–3 mm above the bone surface. The bone-facing end of the cylinder was left open, while the coronal soft tissue-facing end was closed by an expanded polytetrafluoroethylene (ePTFE) membrane. The flap was sutured to obtain primary wound closure. In order to prevent infection, penicillin was prescribed systemically and oral rinses of chlorhexidine were administered. After 2, 7, and 12 weeks, one test device, including the regenerated tissue, was surgically harvested, while after 16, 24, and 36 weeks, respectively, two devices were harvested and processed for soft or hard tissue histology or immunohistochemistry. The tissue generated after 2 and 7 weeks (Fig. 4-6) presented with a cylindrical shape, whereas the specimens harvested at 12 weeks and thereafter resembled the form of an hourglass.

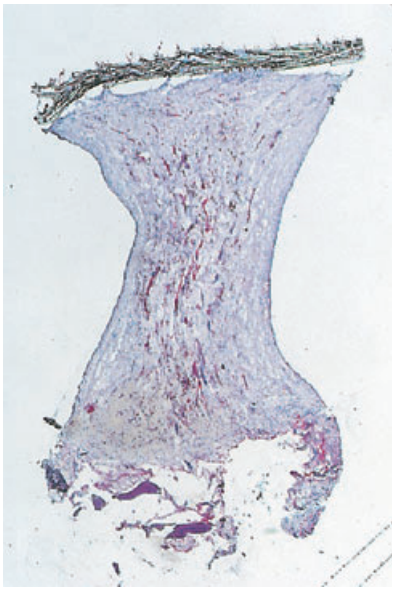

Fig. 4-6 Histological section of a 7-week specimen, comprising non-mineralized connective tissue in the shape of an hourglass. Note the covering e-PTFE membrane.

Fig. 4-7 Histological section of a 9-month specimen. The height of the mineralized tissue has reached the top 20% of the cylinder space area.

Specimens of 12 weeks and less regeneration time were almost entirely composed of soft tissue, while specimens with a regeneration time of 4 months and more were composed of both soft and increasing amounts of mineralized tissue (Fig. 4-7). It was concluded that the model system is suitable for studying temporal dynamics and tissue physiology of bone regeneration in humans with minimal risk of complications or adverse effects for the volunteers.

In a retrospective re-entry study (Lang *et al.* 1994), the bone volume regenerated using non-bioresorbable membrane barriers was assessed. Nineteen patients with jaw bone defects of various sizes and configurations were included. Combined split-thickness/full-thickness mucosal flaps were elevated in the area of missing bone. The size of the defects was assessed geometrically. Following the placement of Gore-Tex® augmentation material as a barrier, the maximum possible volume for bone regeneration was calculated. At the time of membrane removal (3–8 months later), the same measurements were performed and the percentages of regenerated bone in relation to the possible volume for regeneration determined. In six patients in whom the membranes had to be removed early, between 3 and 5 months, due to an increased risk of infection, bone regeneration varied between 0 and 60%. In 13 patients in whom the membranes were left for 6–8 months, regenerated bone filled 90–100% of the possible volume. It was concluded that successful bone regeneration consistently occurred with an undisturbed healing period of at least 6 months.

Conclusion: In summary, the bone of the alveolar process is of critical importance to maintain the structure and function of the jaws and subsequently the housing of teeth or tooth replacements. The physiological and biomechanical influences on bone by local and systemic mediators of bone homeostasis are important in the maintenance of alveolus. Reconstructive modalities aimed at the repair of bone tissues as a result of disease or injury utilize fundamental principles of bone biology. These regenerative biology approaches have been exploited in implant dentistry and periodontology with the use of bone grafting biomaterials, guided bone regeneration approaches, and more recently with polypeptide growth factors. Future work in this area will focus on the implications of systemic disease on bone maintenance during function as well as more predictable modalities for alveolar bone reconstruction.

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Chapter 5

Osseointegration

Jan Lindhe, Tord Berglundh, and Niklaus P. Lang

The edentulous site

The fully healed, edentulous site of the alveolar ridge (see Fig. 2-23 and Chapter 2) is most often covered by a masticatory mucosa that is about 2–3 mm thick. This type of mucosa is covered by a keratinized epithelium and includes a connective tissue, rich in collagen fibers and fibroblasts, that is firmly attached to the bone via the periosteum. The outer walls of the alveolar process, the cortical plates, are comprised of lamellar bone and enclose the spongy or cancellous bone that contains bone trabeculae (lamellar bone) embedded in marrow. The bone marrow contains numerous vascular structures as well as adipocytes and pluripotent mesenchymal cells.

Osseointegration

Different types of implant systems have been used to replace missing teeth, including subperiosteal implants, endosseous implants with fibrous encapsulation, and endosseous implants with direct bone contact (*osseointegrated*). One definition of *osseointegration* (a term originally proposed by Brånemark *et al*. 1969) was provided by Albrektsson *et al*. (1981) who suggested that this was "a direct functional and structural connection between living bone and the surface of a load carrying implant". Another, clinical definition was provided by Zarb and Albrektsson (1991) who proposed that *osseointegration* was "a process whereby clinically asymptomatic rigid fixation of alloplastic materials is achieved and maintained in bone during functional loading".

Schroeder *et al*. (1976, 1981, 1995) used the term *"functional ankylosis"* to describe the rigid fixation of the implant to the jaw bone, and stated that "new bone is laid down directly upon the implant surface, provided that the rules for atraumatic implant placement are followed (rotation of the cutting instrument and less than 800 rpm, cooling with sterile physiologic saline solution) and the implant exhibits primary stability".

Thus, in order to acquire proper conditions for osseointegration (or functional ankylosis), the implant must exhibit proper initial fixation (stability) following installation in the recipient site. This initial (primary) stability is the result of the contact relationship or friction that is established following insertion of the implant, between mineralized bone (often the cortical bone) at the recipient site and the metal device.

Implant installation

Tissue injury

Basic rule: the less traumatic the surgical procedure is and the smaller the tissue injury (the damage) becomes in the recipient site during implant installation, the more expeditious is the process through which new bone is formed and laid down on the implant surface.

The various steps used in the implant installation procedure, such as (1) *incision* of the mucosa, often but not always followed by (2) the elevation of *mucosal flaps* and the separation of the periosteum from the cortical plates, (3) the preparation of the *canal* in the cortical and spongy bone of the recipient site, and (4) the insertion of the titanium device (the implant) in this canal, bring to bear a series of mechanical insults and injury to both the mucosa and the bone tissue. The host responds to this injury with an inflammatory reaction, the main objective of which is to eliminate the damaged portions of the tissues and prepare the site for regeneration or repair. To the above described hard tissue injury must be added the effect of the so-called "press fit", i.e. when the inserted implant is slightly wider than the canal prepared in the host bone at the recipient site. In such situations, (1) the mineralized bone tissue in the periphery of the

implant is compressed, (2) the blood vessels particularly in the cortical portion of the canal are collapsed, (3) the nutrition to this portion of the bone compromised, and (4) the affected tissues most often become non-vital.

The damage or injury to the soft and hard tissues of the recipient site initiates the process of wound healing that ultimately ensures that (1) the implant becomes "ankylotic" with the bone, i.e. osseointegrated, and (2) a delicate mucosal attachment (see Chapter 3) is established and a soft tissue seal formed that protects the bone tissue from substances in the oral cavity.

Wound healing

The healing of the severed bone following implant installation is a complex process that apparently involves different events in the cortical and in the spongy (cancellous) compartments of the surgical site.

In the *cortical bone compartment*, the non-vital mineralized tissue must first be removed (resorbed) before new bone can form. In the *spongy compartment* of the recipient site, on the other hand, the surgically inflicted damage (preparation of the canal and the installation of the implant) results mainly in soft tissue (marrow) injury that initially is characterized by localized bleeding and clot (coagulum) formation. The coagulum is gradually resorbed and the compartment thus becomes occupied by proliferating blood vessels and mesenchymal cells; granulation tissue. As result of the continuous migration of mesenchymal cells from the surrounding marrow, the young granulation tissue becomes replaced with provisional connective tissue and eventually with osteoid. In the osteoid, deposition of hydroxyapatite will occur around the newly formed vascular structures. Hereby, immature bone, most often woven bone, is formed (for detail see Chapter 2) and sequentially osseointegration, a direct connection between the newly formed bone and the metal device, takes place.

In summary: in the initial phase of the process that results in osseointegration, the non-vital lamellar bone in the cortical compartment is of importance for the initial fixation of the implant. Osseointegration, however, is often first established in areas occupied by cancellous bone.

Cutting and non-cutting implants

In this chapter only screw-shaped implants made of c.p. titanium will be discussed. The design of the metal device and the installation protocol followed may influence the speed of the process that leads to osseointegration.

"*Non-cutting*" implants (Fig. 5-1) require meticulous handling of the recipient site including the preparation of a standardized track (thread) on the inside

Fig. 5-1 A "non-cutting" implant (solid screw: Straumann® Implant System).

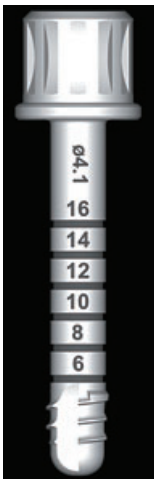

Fig. 5-2 A thread-tap (Straumann® Implant System) that is used to cut a track in the walls of the hard tissue canal. Following this preparation the cavity in the host tissue and the implant are congruent.

of the hard tissue canal. This preparation (precutting) of the track (thread) is made by the use of a thread-tap that is fitted with cutting edges (Fig. 5-2).

Figure 5.1 illustrates a "non-cutting" implant (solid screw, 4.1 mm: Straumann® implant system) that is designed as a cylinder with a rounded "apical" base. The diameter of the cylinder is 3.5 mm. Pilot and twist drills of gradually increasing dimension are used to prepare the hard tissue canal of the recipient site to a final diameter of 3.5 mm. On the surface of the cylinder the implant is designed with a helix-shaped pitch that is 0.3 mm high. The diameter of the entire screw shaped device therefore becomes 4.1 mm.

In sites with a high bone density a thread-tap (Fig. 5-2) is used to cut a 4.1 mm wide helix-shaped track in the walls of the hard tissue canal. The implant and the cavity prepared in the hard tissues of the recipient site are now congruent. When the implant is installed, the pitch on the device will capture and follow the helix-shaped track on the walls of the hard tissue canal and hereby guide the implant with a minimum of force into the pre-prepared position (Fig. 5-3).

Fig. 5-3 Ground section with a "non-cutting" implant and surrounding tissues obtained from a biopsy performed 24 hours after implant installation.

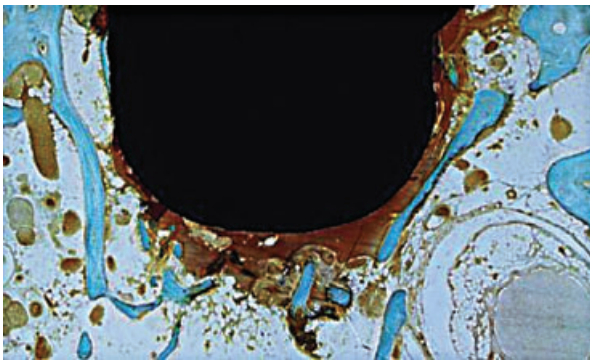

Fig. 5-4 Detail from the apical region of the implant described in Fig. 5-3. Note the presence of a coagulum in the bone marrow.

Figure 5-3 illustrates a "non-cutting" Straumann® solid screw with surrounding tissues in a biopsy sampled 24 hours after implant installation. The implant had proper initial fixation (stability) obtained by the large contact area that was achieved between the metal screw and the buccal and lingual bone walls in the cortical compartment of the recipient site. During site preparation and placement of the implant, bone trabeculae in the spongy compartment of the site were obviously dislocated into the bone marrow. Blood vessels in the marrow compartment were severed, bleeding provoked and a coagulum formed (Fig. 5-4).

After 16 weeks of healing (Fig. 5-5) the marginal portions of the "non-cutting" implant are surrounded by dense lamellar bone that is in direct contact with the rough surface of the metal device. Also in the apical portion of the implant, a thin coat of mature bone can be seen to contact the implant surface and

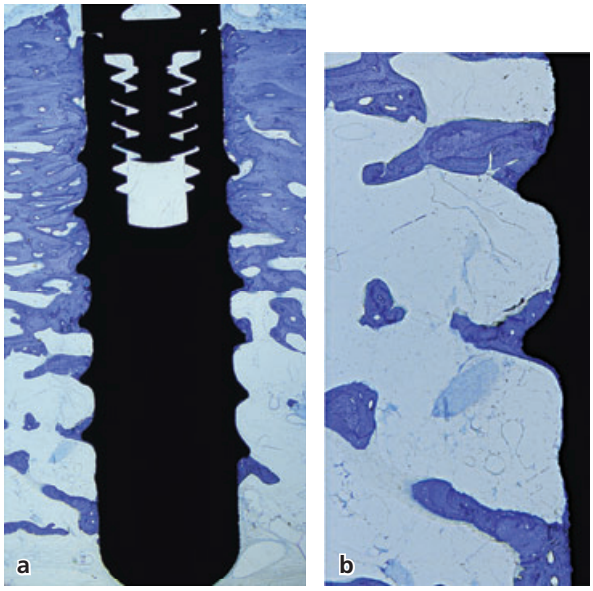

Fig. 5-5 (a) Ground section illustrating a "non-cutting" implant and surrounding bone after 16 weeks of healing. In the cortical portion of the recipient site, the bone density is high. (b) Detail of (a). In more apical areas a thin coat of bone is present on the implant surface. Note also the presence of trabeculae of lamellar bone that extend from the implant into the bone marrow.

Fig. 5-6 A "cutting" implant (Astra Tech® Implant System). Note the presence of cutting edges in the "apical" portion of the implant. During insertion this implant will cut a 0.3 mm wide chip from the lateral border of the canal prepared in the recipient site.

to separate the titanium screw from the bone marrow.

Cutting or self-tapping implants (e.g. Astra Tech® implants, diameter 4.0 mm) (Fig. 5-6) are designed with cutting edges placed in the "apical" portion of the screw-shaped device. The threads of the screw are prepared during manufacturing by cutting a continuous groove into the body of the titanium

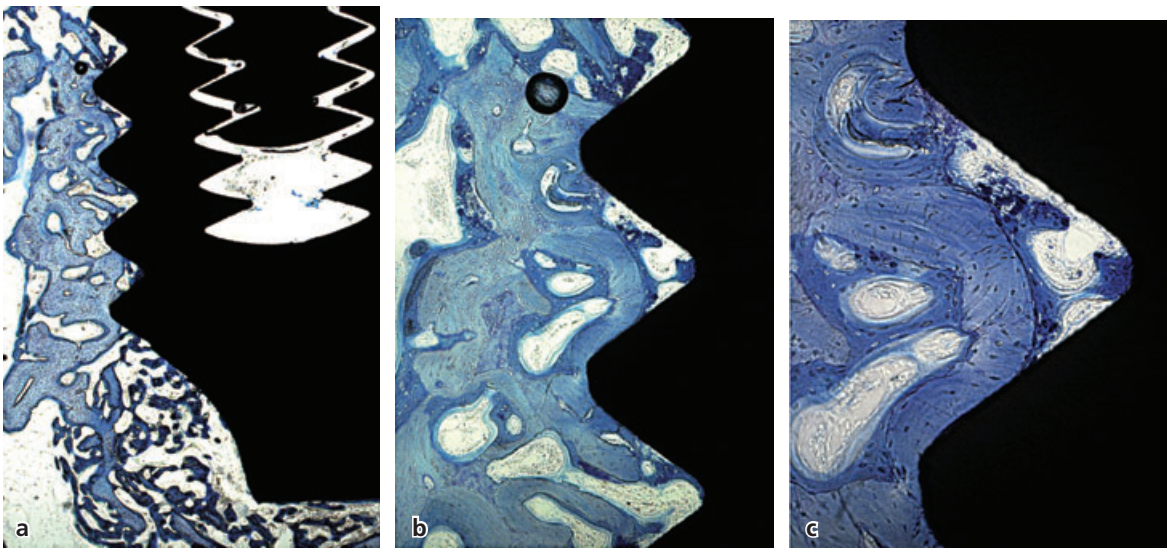

Fig. 5-7 (a) Ground section of an implant (Astra Tech®) site from a biopsy sampled after 2 weeks of healing. In the apical area large amounts of woven bone has formed. (b) Detail of (a). In the threaded region, newly formed bone can be seen to reach contact with the implant surface. (c) Higher magnification of (b). Newly formed bone extends from the old bone and reaches the titanium surface in the invagination between two consecutive "threads".

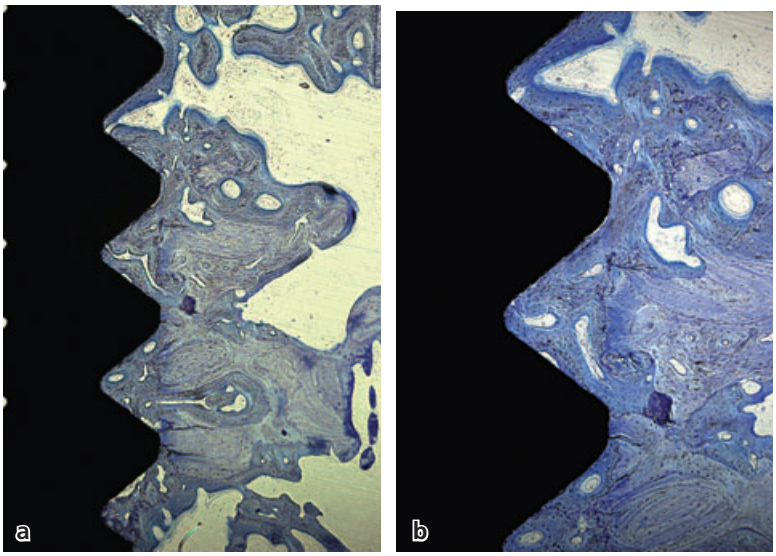

Fig. 5-8 Ground section of an implant site (Astra Tech® self-tapping implant) from a biopsy specimen obtained after 6 weeks of healing. (a) In the marginal area a continuous layer of bone covers most of the TiOblast® surface. (b) Higher magnification. Note the zone of newly formed (darker stained) bone that is in direct contact with the implant surface.

cylinder. When a self-tapping 4.0 mm wide implant is to be placed, the recipient site is first prepared with pilot and twist drills to establish a hard tissue canal that most often has a final diameter of 3.7 mm. During the insertion the cutting edges in the "apical" portion of the implant create a 0.15 mm wide track in the walls of the canal and thereby establish the final 4.0 mm dimension. When the implant has reached its insertion depth, contact has been established between the outer portions of the threads and the mineralized bone in the cortical compartment (initial or primary fixation is hereby secured) and with the severed bone marrow tissue in the spongy compartment.

Figure 5-7 illustrates a recipient site with a self-tapping implant (Astra Tech® implant). This implant is designed with a TiOblast® surface modification. The biopsy was harvested 2 weeks after installation surgery. The outer portion of the thread is in contact with the parent "old" bone, while bone formation is the dominant feature in the invaginations between the threads and in areas lateral to the "apical" portions of the implant. Thus, discrete areas of newly formed bone can be seen also in direct contact with the implant surface. In sections representing 6 weeks of healing (Fig. 5-8), it was observed that a continuous layer of newly formed bone covers most of the TiOblast® surface. This newly formed bone is also in contact with the old, mature bone that is present in the periphery of the recipient site. After 16 months of healing (Fig. 5-9), the bone tissue in the zone of osseointegration has remodeled and the entire hard tissue bed for the implant is comprised of lamellar bone including both concentric and interstitial lamella.

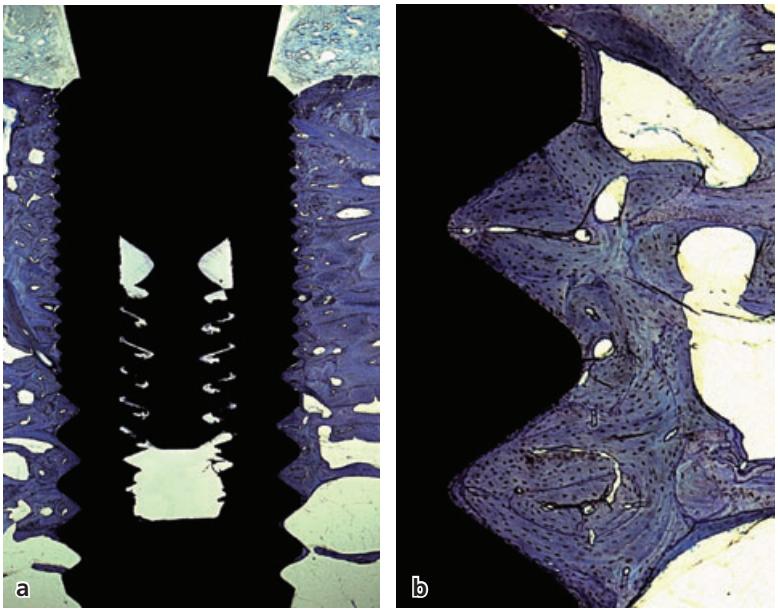

Fig. 5-9 Ground section of an implant site representing 16 months of healing. (a) The implant is surrounded by dense lamellar bone. (b) Higher magnification.

Fig. 5-10 The device used in the dog experiment. The implant is a modification of a solid screw (Straumann® Implant System). The distance between two consecutive threads is 1.25 mm. The depth of the trough is 0.4 mm.

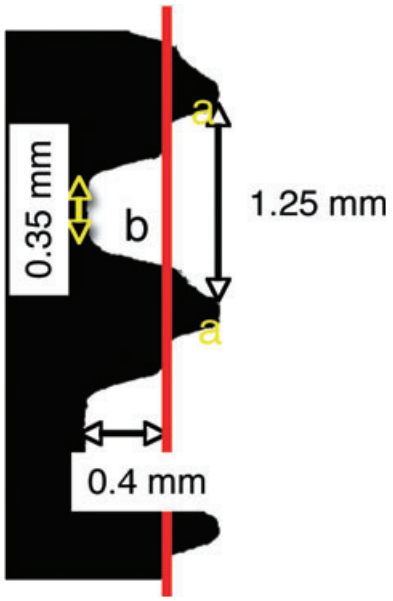

Fig. 5-11 The device. Schematic drawing illustrating the dimensions of the "wound chamber".

The process of osseointegration

De novo bone formation in the severed alveolar ridge following implant placement was studied in experiments in various experimental animal models (for review see Schroeder *et al*. 1995).

Recently Berglundh *et al*. (2003) and Abrahamsson *et al*. (2004) described various steps involved in bone formation and osseointegration to implants placed in the mandible of dogs.

The device: Custom-made implants that had the shape of a solid screw (Straumann® implant), that were made of c.p. titanium and configured with a rough surface topography (SLA®; Straumann) were utilized (Fig. 5-10). In the implant device the distance between two consecutive profiles of the pitch (i.e. the threads in a vertical cross section) was 1.25 mm. A 0.4 mm deep U-shaped circumferential trough had been prepared within the thread region during manufacturing (Fig. 5-11). The tip of the pitch was left untouched. Following the installation of the non-cutting device (Fig. 5-12) the pitch was engaged in the hard tissue walls prepared by the cutting tapping device. This provided intitial or primary fixation of the device. The void between the pitch and the body of the implant established a geometrically well defined wound chamber (Fig. 5-13). Biopsies were performed to provide healing periods extending from 2 hours following implant insertion to 12 weeks of healing. The biopsy specimens were prepared for ground sectioning as well as for decalcification and embedding in epon.

The wound chamber: Figure 5.13 illustrates a cross section (ground section) of an implant with surrounding soft and hard tissues from a biopsy specimen sampled 2 hours after installation of the metal device. The peripheral portions of the pitch were in

contact with the invaginations of the track prepared by the tap in the cortical bone. The wound chambers (Fig. 5-14a) were occupied with a blood clot in which erythrocytes, neutrophils, and monocytes/macrophages occurred in a network of fibrin (Fig. 5-14b). The leukocytes were apparently engaged in the wound cleansing process.

Fibroplasia: Figure 5-15a illustrates a device with surrounding tissues after 4 days of healing. The coagulum had in part been replaced with granulation tissue that contained numerous mesenchymal cells, matrix components, and newly formed vascular structures (angiogenesis) (Fig. 5-15b). A *provisional connective tissue* had been established.

Bone modeling: After 1 week of healing the wound chambers were occupied by a provisional connective tissue that was rich in vascular structures and contained numerous mesenchymal cells (Fig 5-16a). The number of remaining inflammatory cells was relatively small. In large compartments of the chamber, a cell-rich immature bone (woven bone) was seen in the mesenchymal tissues that surrounded the blood vessels. Such areas of woven bone formation occurred in the center of the chamber as well as in discrete locations that apparently were in direct contact with the surface of the titanium device (Fig. 5-16b). This

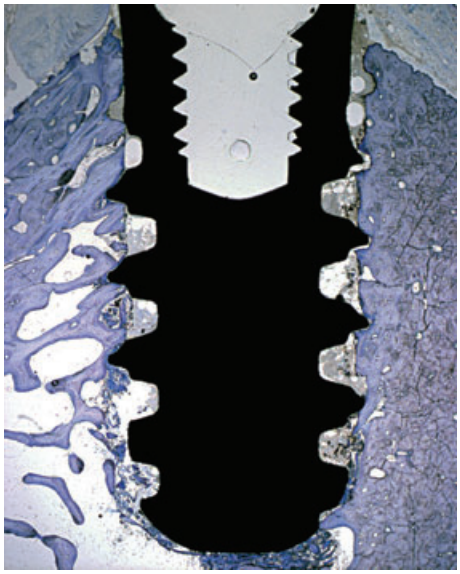

Fig. 5-12 Ground section showing the implant and adjacent tissues immediately after implant installation. The pitch region is engaged in the hard tissue walls. The void between two consecutive pitch profiles includes the wound chamber.

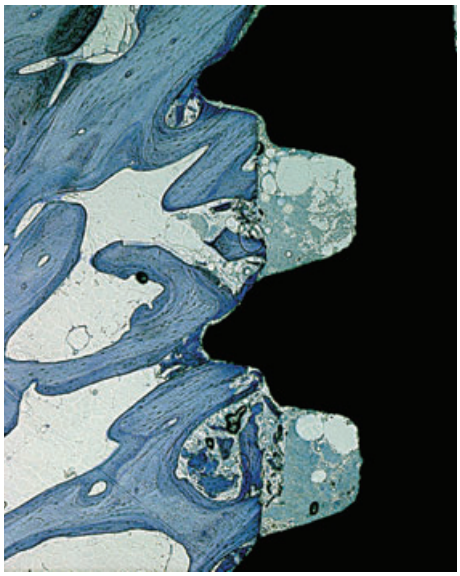

Fig. 5-13 Detail of Fig. 5-12. The wound chamber was filled with blood and a coagulum has formed.

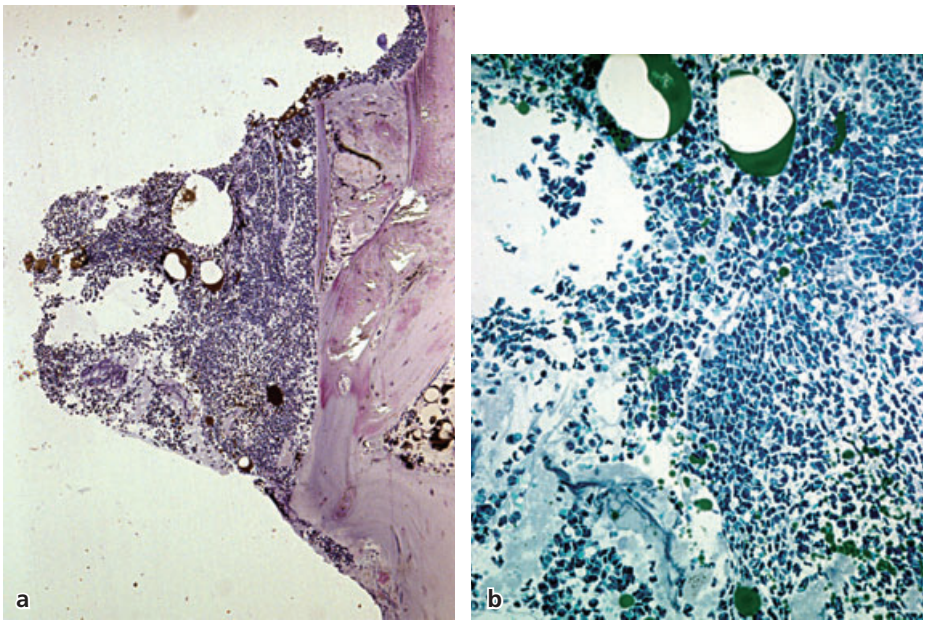

Fig. 5-14 The wound chamber 2 hours after implant installation. Decalcified sections. (a) The wound chamber is filled with blood. (b) Erythrocytes, neutrophils, and macrophages are trapped in a fibrin network.

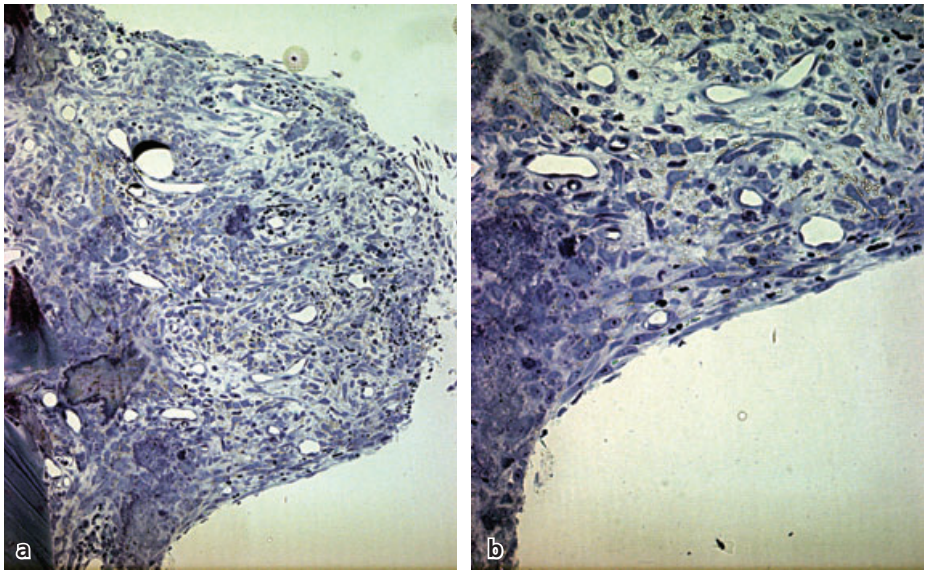

Fig. 5-15 The wound chamber after 4 days of healing (decalcified sctions). (a) Most portions of the wound chamber are occupied by granulation tissue (fibroplasia). (b) In some areas of the chamber provisional connective tissue (matrix) is present. This tissue includes large numbers of mesenchymal cells.

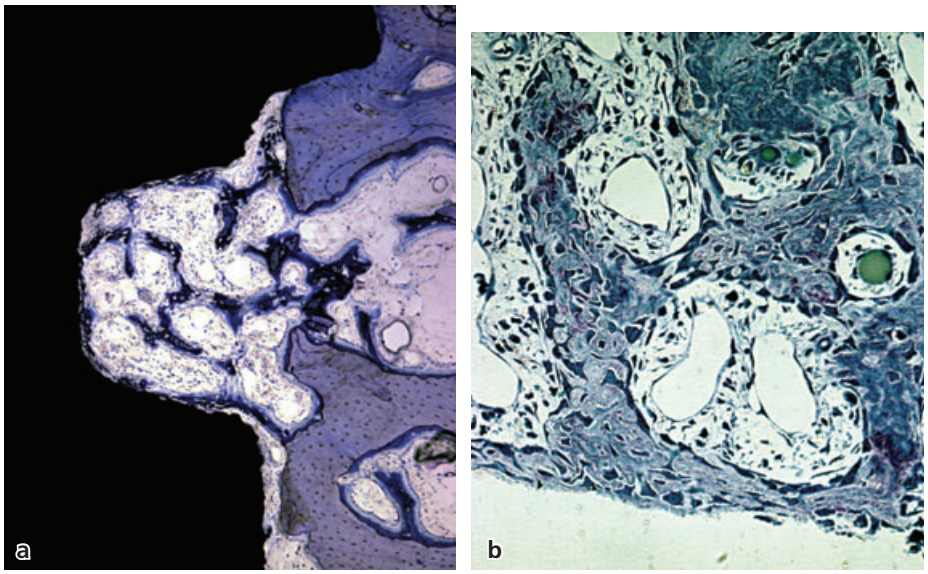

Fig. 5-16 (a) Ground section representing 1 week of healing. Note the presence of newly formed woven bone in the wound chamber. (b) Decalcified section. The woven bone is in direct contact with the implant surface.

was considered to represent the very first phase of osseointegration; contact between the implant surface and newly formed woven bone.

After 2 weeks of healing, woven bone formation appeared to be pronounced in all compartments, apical as well as lateral, surrounding the implant (Fig. 5-17a). Large areas of woven bone were found in the bone marrow regions "apical" of the implant. In the wound chamber, portions of the newly formed woven bone apparently extended from the parent bone into the provisional connective tissue (Fig. 5-17b) and had in many regions reached the surface of the titanium device. At this interval most of the implant surface was occupied by newly formed bone and a more comprehensive and mature osseointegration had been established (Fig. 5-17c). In the pitch regions there were signs of ongoing new bone formation (Fig. 5-17d). Thus, areas of the recipient site located lateral to the device, that were in direct contact with the host bone immediately following installation surgery and provided initial fixation for the implant, had undergone tissue resorption and were also involved in new bone formation after 2 weeks of healing.

At 4 weeks (Fig. 5-18a), the newly formed mineralized bone extended from the cut bone surface into the chamber and a continuous layer of cell-rich, woven bone covered most of the titanium wall of the

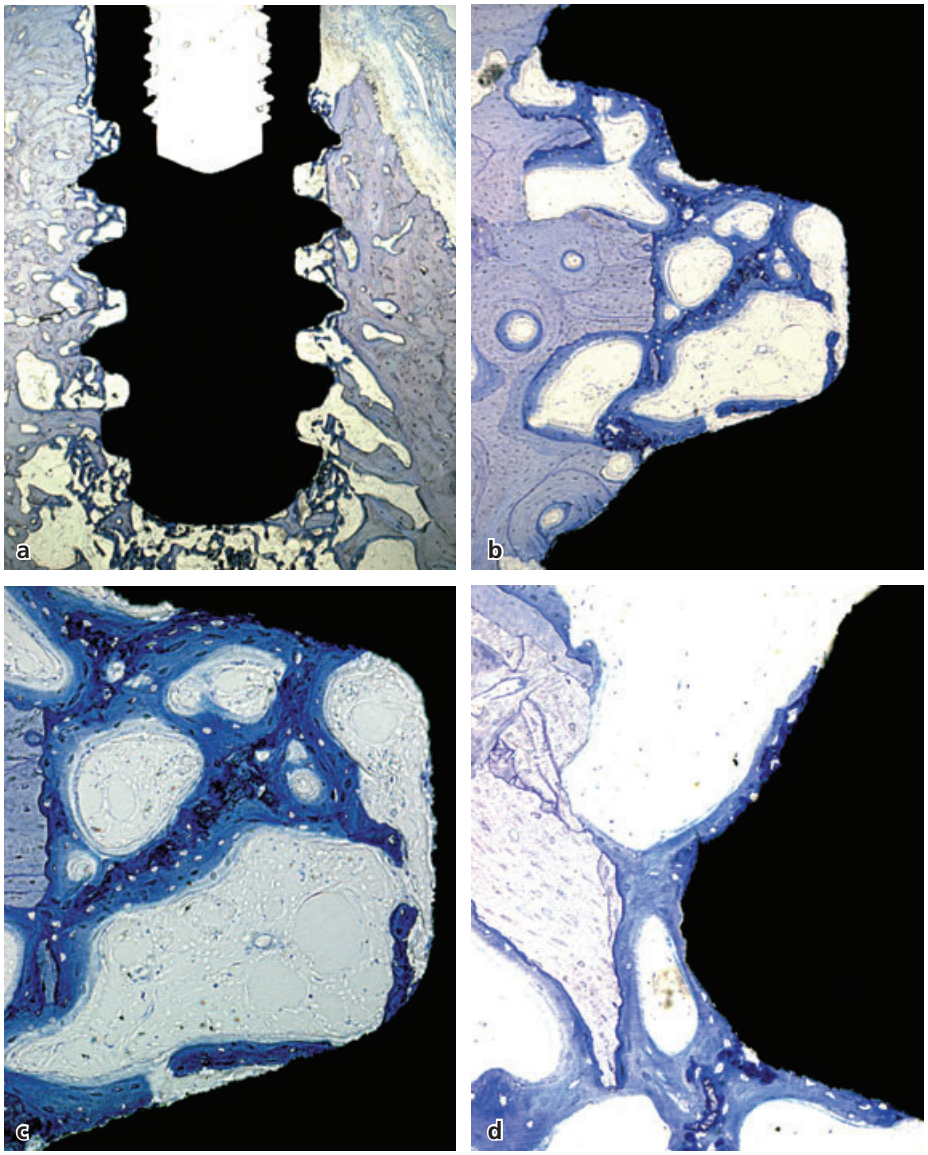

Fig. 5-17 Ground sections illustrating, in various magnifications, the tissues in the wound chamber after 2 weeks of healing. (a) Darker stained woven bone is observed in the apical area of the metal device. (b, c, d) Most portions of the implant surface are coated with bone.

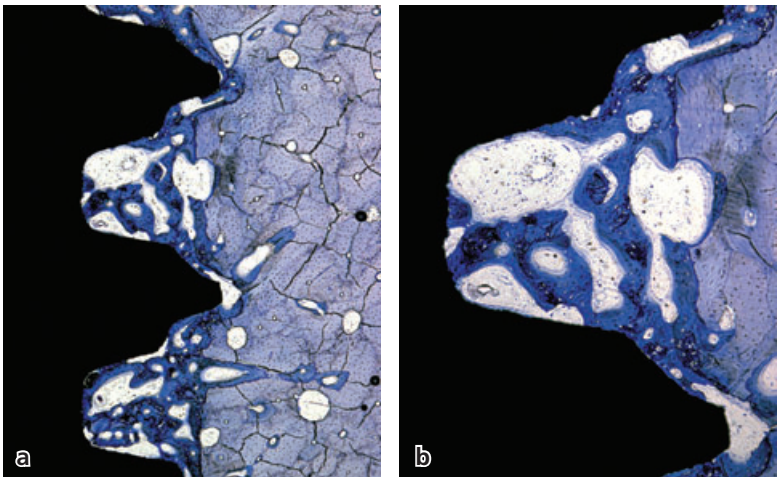

Fig. 5-18 Ground sections representing 4 weeks of healing. (a) The newly formed bone (dark blue) extends from the "old" bone into the wound chamber. (b) Appositional growth. Note the presence of primary osteons.

chamber. The central portion of the chamber was filled with a primary spongiosa (Fig. 5-18b), rich in vascular structures and a multitude of mesenchymal cells.

Remodeling: After 6–12 weeks of healing most of the wound chambers were filled with mineralized bone (Fig. 5-19). Bone tissue, including primary and secondary osteons, could be seen in the newly formed tissue and in the mineralized bone that made contact with the implant surface. Bone marrow that contained blood vessels, adipocytes, and mesenchymal cells was observed to surround the trabeculae of mineralized bone.

Summary: The wound chambers were first occupied with a coagulum. With the ingrowth of vessels and migration of leukocytes and mesenchymal cells, the coagulum was replaced with granulation tissue. The migration of mesenchymal cells continued and the granulation tissue was replaced with a provisional matrix, rich in vessels, mesenchymal cells, and fibers. The process of *fibroplasia* and angiogenesis had started. Formations of newly formed bone could be recognized already during the first week of healing; the newly formed woven bone projected from the lateral wall of the cut bony bed (appositional bone formation; distance osteogenesis) (Davies 1998) but *de novo* formation of new bone could also be seen on the implant surface, i.e. at a distance from the parent bone (contact osteogenesis) (Davies 1998). During subsequent weeks the trabeculae of woven bone were replaced with mature bone, i.e. lamellar bone and marrow (bone remodeling).

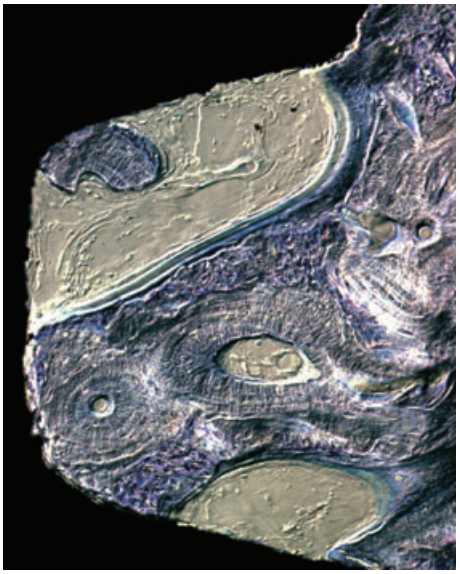

Fig. 5-19 Ground section representing 12 weeks of healing. The woven bone is being replaced with lamellar bone and marrow. Note the formation of secondary osteons.

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Chapter 6

Periodontal Tactile Perception and Peri-implant Osseoperception

Reinhilde Jacobs

Introduction

Perception is the ability to detect external stimuli. In man, several kinds of sensory systems enable perception (vision, audition, balance, somatic function, taste, and smell) (Martin 1991). In all sensory systems, the initial contact with the external world is made through special neural structures called sensory receptors, endings or organs. A distinction is needed between nociceptors, chemo-, photo-, thermo-, and mechanoreceptors, each responding to a particular stimulus. In the oral cavity, taste and somatic sensory systems predominate. The former are sensitive to chemical stimuli while the latter respond to mechanical, thermal, and nociceptive stimuli. In this chapter, only the somatic sensory system is explored. The preponderance of the oral somatosensory system is illustrated by its major representation, besides that of the hand, on the sensory homunculus proposed by Penfield (Penfield and Rasmussen 1950). In general, the somatosensory function is essential for fine-tuning of limb movements. In analogy with the rest of the skeleton, the tactile function of teeth plays a crucial role in refinement of jaw motor control. Periodontal mechanoreceptors, especially those located in the periodontal ligament, are extremely sensitive to external mechanical stimuli. The periodontal ligament can thus be considered as a keystone for masticatory and other oral motor behaviours. Any condition that may influence periodontal mechanoreceptors, may alter the sensory feedback pathway and thus affect tactile function and fine-tuning of jaw motor control (e.g. periodontal breakdown, bruxism, re-implantation, anesthesia).

The most dramatic change may occur after extraction of teeth, as this eliminates all periodontal ligament receptors. This condition may persist after implant placement as functional re-innervation has

not yet been proven in humans. Surprisingly enough, patients with implant-supported prostheses often seem to function quite well. The underlying mechanism of this so-called "osseoperception" phenomenon remains a matter of debate, but the response of assumed peri-implant receptors might help to restore the proper peripheral feedback pathway. This hypothesized physiological integration might thus lead to better acceptance, improved psychological integration, and more natural functioning.

This chapter will unravel periodontal tactile function and guide the reader through the mysteries of peri-implant osseoperception in order to find neuroanatomical, histological, physiological, and psychophysical evidence to confirm the hypothesis.

Neurophysiological background

Afferent nerve fibres and receptors

When considering the human somatic sensory system, four types of afferent nerve fibers can be distinguished in association with sensation: Aα, Aβ, Aδ and C. Some types of afferent nerve fibers exist in specific tissues only, while others are widely distributed throughout the body. Based on the structure or signalling properties, receptors may be divided into several classes or categories (Birder & Perl 1994). Three different groups of receptors are associated with thermal and (vibro)tactile sensation: thermoreceptors, nociceptors and mechanoreceptors.

Thermoreceptors and nociceptors

Thermal sensations are divided into warm and cold and are perceived by specific receptors. There are indeed separate spots on skin and mucosal surface where thermal stimulation elicits either warm or cold sensation. Cold-sensitive spots are more numerous than warm-sensitive with the highest density of both cold and warm spots on the face (Bradley 1995). Unmyelinated neurite complexes are responsible for cold sensation and some free nerve endings for warm sensation (Bradley 1995). Receptors which can induce pain feeling are referred to as nociceptors and mostly supplied by Aδ and C fibers. In the periodontal ligament, one can identify free nerve endings which may be responsive to pain, but not thermal receptors. The majority of the receptors located within the periodontal ligament are of the mechanoreceptive type.

Mechanoreceptors

Mechanoreceptors are responsive to mechanical stimuli. These can be classified on the basis of their morphology, receptive field, and adaptation characteristics. In man, four receptor structures have been associated with mechanoperception: Meissner corpuscles, Pacinian corpuscles, Merkel cells, and Ruffini endings (Martin & Jessell 1991). These structural elements do determine, to some extent, the physiological characteristics of the peripheral receptors. On the basis of their receptive field, two subgroups of mechanoreceptors have been identified: receptors with small and distinct receptive fields (type I) and receptors with large and diffuse receptive fields (type II). Mechanoreceptors can also be subdivided based on their adaptation properties: rapidly adapting (RA) and slowly adapting (SA) receptors. The RA receptors, also called fast adapting receptors, only respond during the dynamic phase of stimulus application. In contrast, the SA receptors respond to both dynamic and static force applications (Iggo 1985). A relationship has been established between the aforementioned receptor morphologies and their adaptation characteristics. Rapidly adapting receptors include Meissner corpuscles (RA I) and Pacinian corpuscles (RA II) while SA receptors include Merkel cells (SA I) and Ruffini endings (SA II).

Trigeminal neurophysiology

Trigeminal neurosensory pathway

The trigeminal nerve is the largest cranial nerve, including a motor root supplying the masticatory muscles, and a predominant sensory root supplying the oral cavity, head, and face. The trigeminal nerve has three divisions (ophthalmic, maxillary, mandibular). The ophthalmic nerve is a sensory nerve and the smallest division. The maxillary nerve is a sensory nerve and intermediate, both in position and size, between ophthalmic and mandibular divisions. The mandibular nerve is the largest and made up of two roots: a large, sensory root and a small motor root.

The sensory inputs of the oral region are carried by the mandibular and maxillary divisions of the trigeminal nerve via the trigeminal ganglion to the brainstem. This is part of an important sensory feedback pathway, involved in refinement of jaw movements. The afferent signals are transmitted either to the main sensory nucleus of the trigeminal nerve (responsive to discriminate tactile senses, light touch and pressure) or to the descending spinal tract nuclei, including: (1) nucleus oralis, responsive to cutaneous sensation of oral mucosa; (2) nucleus interpolaris, responsive to tooth pulp pain; and (3) nucleus caudalis, responsive to pain, temperature, and crude touch.

From there, signals are transferred across the midline and sent to the thalamus and, via thalamocortical projections, to the respective cortical areas involved in orofacial sensation where they can result in conscious perception.

Neurovascularization of the jaw bones

The jaws are richly supplied by neurovascular structures, and it is thus of utmost important to identify vital anatomic structures before carrying out a

Fig. 6-1 These human dry mandibular bone sections illustrate the presence and dimensional importance of the mandibular incisive nerve, even in edentulism. The middle section is actually visualizing the mandibular midline, confirming that there is no true connection between the left and right sections.

surgical procedure. During a radiographic preoperative planning procedure, neurovascular structures need to be precisely localized to attempt avoiding interference. Particular attention should be paid to the anterior jaw bones, which are often considered as relatively safe surgical areas. The increasing rate of surgical interventions in the anterior jaw bone, such as oral implant placement and bone grafting, has indeed highlighted potential risks and raised the number of reported complications. Recent studies reveal that edentulous and dentate anterior jaws present significant variation in the occurrence of the mandibular incisive canal and genial spinal foramina as well as the maxillary nasopalatine canal (for review see Jacobs *et al*. 2007). All these canal structures contain a neurovascular bundle, whose diameter may be large enough to cause clinically significant trauma. While surgeons need to avoid the nervous structures, these critical structures may afterwards become essential to potentially reinnervate peri-implant bone. Indeed, the existence of remaining neurovascular bundles in the edentulous jaw bone may support the idea that nerves may regenerate after tooth extraction and implant placement. This particular assumption is the basis of the so-called osseoperception phenomenon and will be further outlined below.

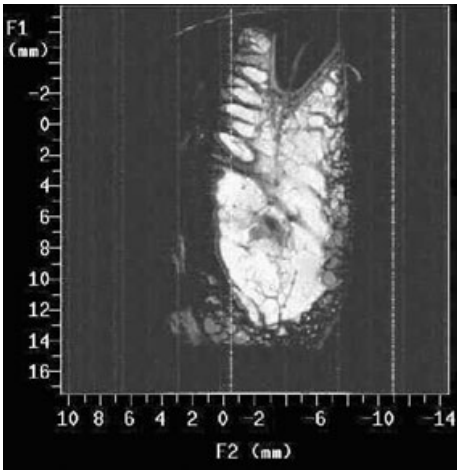

Fig. 6-2 Single cross-sectional slice of an high resolution MRI dataset localized at the incisor region of a dentate anterior human mandible, with the fatty marrow colored white. A black root-form structure corresponds to the root of an incisor tooth. It is surrounded by a small band of intermediate signal intensity, representing the periodontal ligament. The dental neurovascular supply is seen as a line of intermediate signal intensity in the middle of the root. The latter descends to the level of a larger structure of intermediate signal intensity (incisive nerve) with a black oval area on top (vascular structure). (Reprinted from Jacobs *et al*. 2007, Copyright 2006, with permission from Elsevier.)

Mandibular neuroanatomy

The mandibular nerve is the largest of the three divisions of the fifth cranial nerve and gives off the inferior alveolar nerve. The latter enters the mandible through the mandibular foramen and continues to run forward through the mandibular canal. At the mental foramen it gives off an important branch, called the mental nerve. It should not be considered as the only terminal branch of the inferior alveolar nerve. The mandibular incisive nerve is often detected as a second terminal branch with an intraosseous course in a so-called mandibular incisive canal, located anterior to the mental foramen (Mraiwa *et al*. 2003a,b) (Fig. 6-1). Conventional intraoral and panoramic radiographs often fail to show this canal (Jacobs *et al*. 2004). Cross-sectional imaging may however be used to locate the canal and as such avoid any risk for neurovascular damage (Jacobs *et al*. 2002a) The mandibular incisive canal contains a true neurovascular bundle with nervous sensory structures (Fig. 6-2). Its existence in edentulous patients is underlined by reported surgical complications. Indeed, sensory disturbances, caused by direct trauma to the mandibular incisive canal bundle have been reported after implant placement in the interforaminal region (Jacobs & van Steenberghe 2006; Jacobs *et al*. 2007) (Fig. 6-3).

A sensory disorder might also be related to indirect trauma caused by a hematoma in the canal, which acts as a closed chamber; this will affect the mandibular incisive canal bundle and spread to the main mental branch (Mraiwa *et al.* 2003b).

Other anatomic landmarks to be noted are superior and inferior genial spinal foramina and their bony canals, situated in the midline of the mandible in 85–99% of people (Liang *et al*. 2005a,b; Jacobs *et al*. 2007). The superior one is at the level of, or superior to, the genial spine; the inferior one is below the genial spine (Fig. 6-4). The superior genial spinal foramen has been found to contain a branch of the lingual artery, vein and nerve. Furthermore, a branch of the mylohyoid nerve together with branches or anastomoses of sublingual and/or submental arteries and veins have been identified upon entering the inferior genial spinal foramen. This artery could be of sufficient size to provoke hemorrhage intraosseously or in the connective soft tissue, which might be difficult to control (Darriba & Mendonca-Cardad 1997; Liang *et al*. 2005a,b) (Fig. 6-5).

The observation that immediate loading of implants in the anterior mandible results in a significant reduction of tactile function using the Brånemark Novum® concept rather than a conventional implant-supported overdenture might be explained by contact with the aforementioned neurovascular bundles in the anterior mandible (Abarca *et al*. 2006).

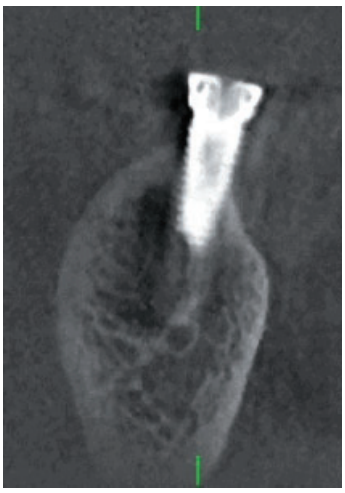

Fig. 6-3 Cross-sectional slice of a cone beam dataset showing an osseointegrated implant placed in an edentulous lateral incisor region, on top of a prominent incisive canal lumen. Chronic pressure on the incisive nerve resulted in a neuropathic pain problem. (Reprinted from Jacobs & van Steenberghe 2006, Copyright 2006, with permission from Blackwell Publishing.)

Maxillary neuroanatomy

The maxillary nerve is a sensory nerve, with its superior nasal and alveolar branches supplying the maxilla, including the palate, nasal and maxillary sinus mucosa, upper teeth and their periodontium. One of the superior nasal branches is named the nasopalatine nerve. It descends to the roof of the mouth through the nasopalatine canal and communicates with the corresponding nerve of the opposite side and with the anterior palatine nerve. The nasopalatine foramen and canals are situated at the maxillary midline, posterior to the central incisor teeth (Mraiwa *et al*. 2004). Typically, it has been described as having a Y-shape with the orifices of two lateral canals, terminating at the nasal floor level in the foramina of Stenson (Fig. 6-6). The nasopalatine nerve and the terminal branch of the descending palatine artery pass through these canals. Occasionally, two additional minor canals are seen (foramina of Scarpa), which may carry the nasopalatine nerves (Fig. 6-7). Mraiwa *et al*. (2004) point out a significant variability both regarding dimensions and morphological appearance of the nasopalatine canal.

To avoid disturbing neurovascular bundles and further complications, this important variability should be taken into account when dealing with surgical procedures such as implant placement in the maxillary incisor region.

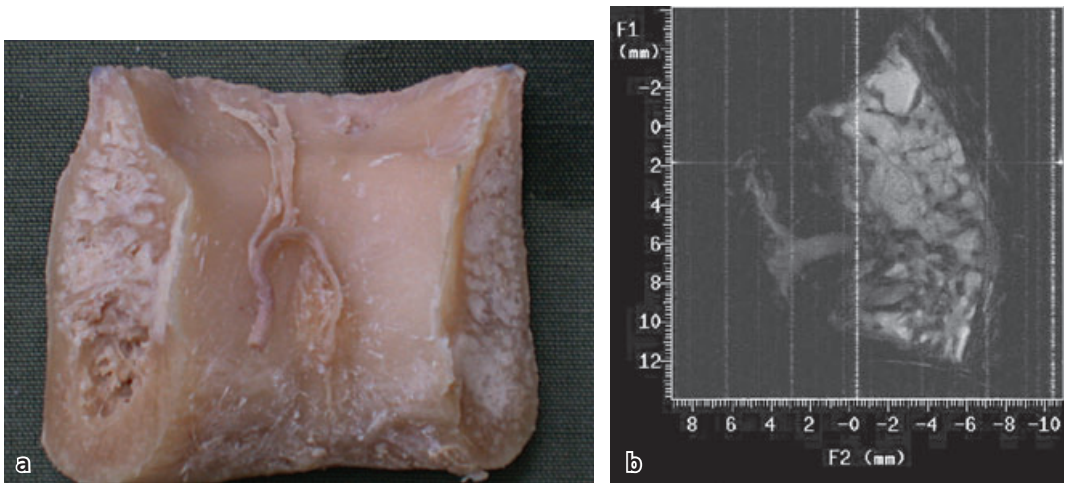

Fig. 6-4 (a) A macroanatomical view of a human anterior mandible showing a clear neurovascular bundle entering the superior genial spinal foramen. (b) A matching horizontal slice acquired through high-resolution MRI confirms the entry of a neurovascular bundle into the superior genial spinal foramen. (Courtesy of Professor I. Lambrichts, University of Hasselt.)

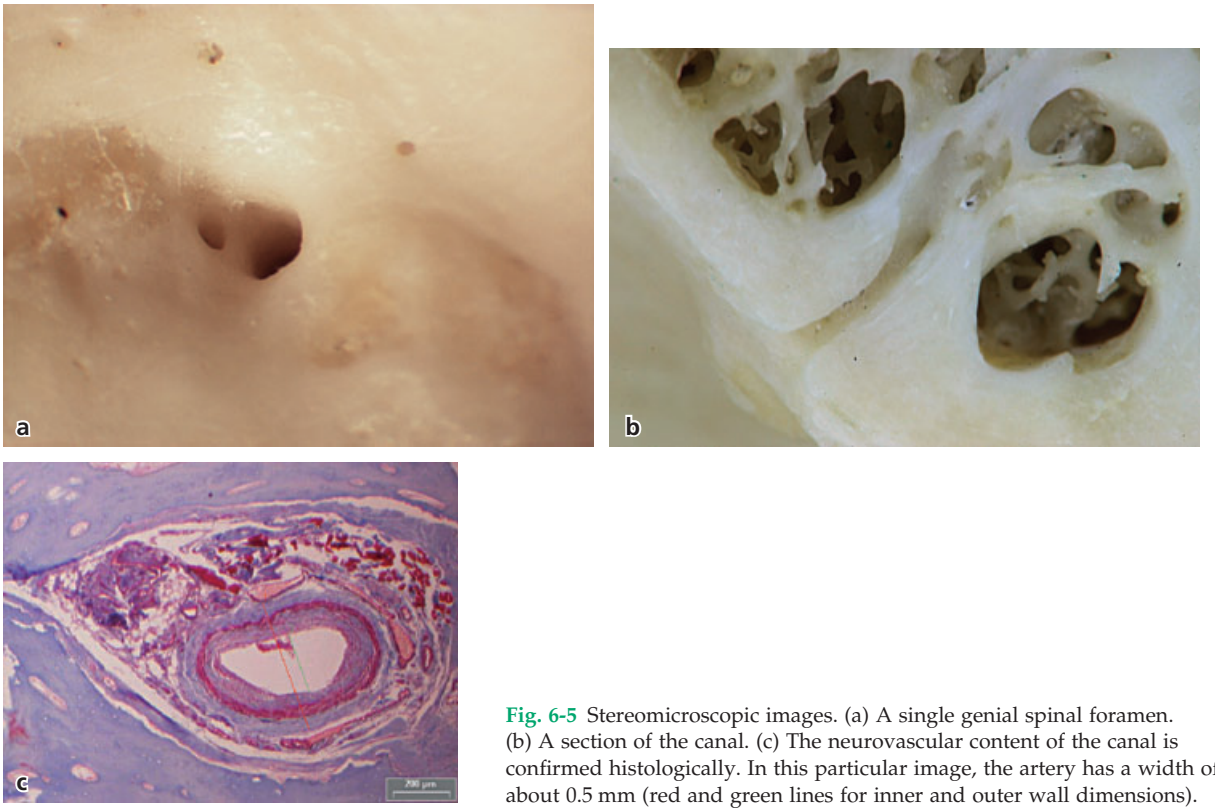

Fig. 6-5 Stereomicroscopic images. (a) A single genial spinal foramen. (b) A section of the canal. (c) The neurovascular content of the canal is confirmed histologically. In this particular image, the artery has a width of about 0.5 mm (red and green lines for inner and outer wall dimensions).

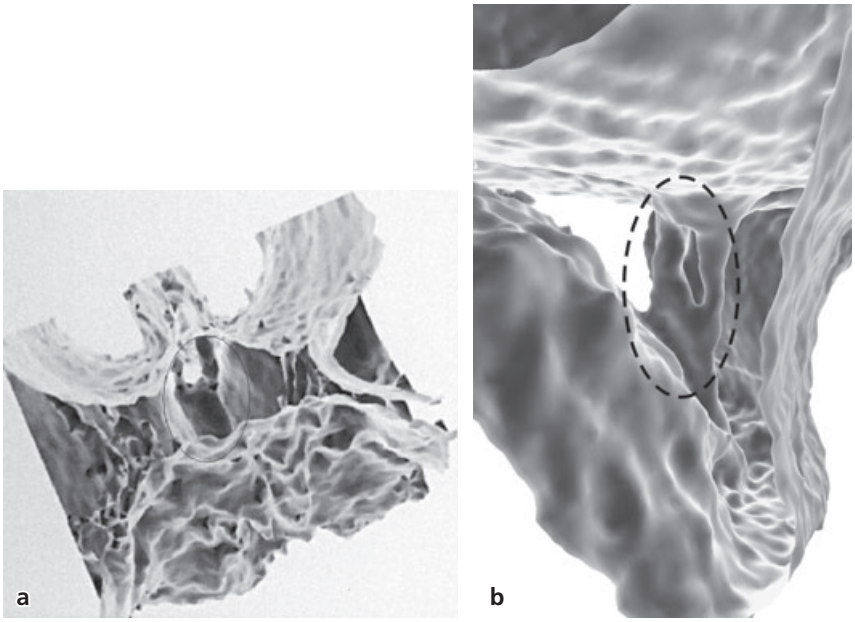

Fig. 6-6 Outline of the common Y-morphology of the nasopalatine canal (seen in black oval) on a three-dimensional reconstruction of the palate and the floor of the nose, seen from a posterior viewing angle (a) and a side view (b).

Periodontal innervation

Periodontal receptors are located within the gingiva, jaw bone, periosteum, and periodontal ligament. Most receptors seem to have mechanoreceptive characteristics, contributing to a sophisticated exteroceptive tactile function. This tactile information is not primarily used for protective purposes, but rather applied by the human brain to improve oral motor behavior and fine-tuning of biting and chewing (Trulsson 2006).

It is clear that the periodontal ligament plays a predominant role in this dedicated mechanoreceptive function. It has an extremely rich sensory nerve supply, especially in those locations that are more prone to displacement (peri-apical, buccal, and lingual periodontal ligament). It contains three types of nerve endings: free nerve endings, Ruffini-like endings, and lamellated corpuscles (Lambrichts *et al*. 1992). Free nerve endings stem from both unmyelinated and myelinated nerve fibers. Lamellated corpuscules are found in close contact to each other. Most

Fig. 6-7 View from the palate of an edentulous dry skull, showing the nasopalatine foramen, formed at the articulation of both maxillae, behind the incisor teeth. In the depth of the canal, the orifices of two lateral canals are seen. As an anatomic variant, two minor canals can be observed on the midline, one anterior and one posterior to the major nasopalatine canals.

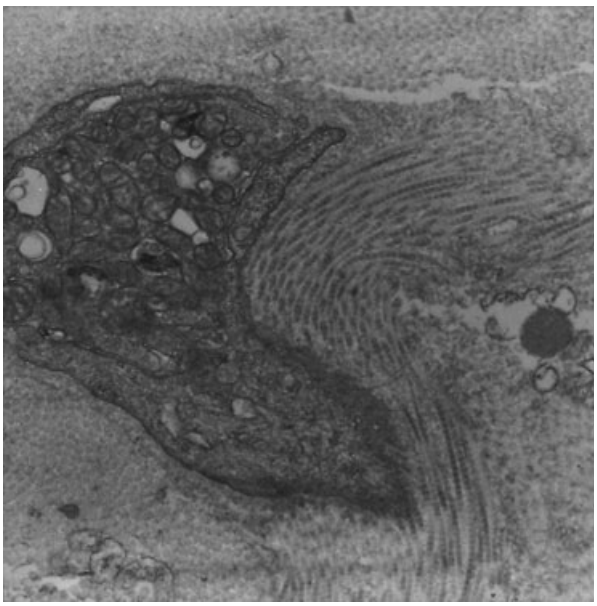

Fig. 6-8 Electron microscope image at the level of the human periodontal ligament, showing collagen fibrils inserted into the basal lamina of an ensheating cell in a Ruffini-like receptor. (Reprinted from Lambrichts *et al.* 1992, Copyright 2006, with permission from Ivo Lambrichts, University of Hasselt and Blackwell Publishing.)

mechanoreceptive endings are, however, Ruffini-like, and are predominantly present in the apical part of the periodontal ligament. Morphologic studies indicate that these endings are in close contact with collagen fibres of the surrounding tissues (Lambrichts *et al.* 1992) (Fig. 6-8). This particular association may explain their extremely high sensitivity upon loading a tooth. This results in low threshold levels for periodontal tactile function, and is considered as the basis of an elaborate sensory apparatus that may be linked to a number of clinical phenomena.

Recordings from the inferior alveolar nerve reveal that human periodontal mechanoreceptors discharge continuously during sustained loading of teeth (Trulsson *et al.*, 1992). Like the slowly adapting type II receptors in the human skin, most periodontal ligament mechanoreceptors are spontaneously active with a regular discharge in response to forces applied to teeth.

The mechanoreceptive function of the periodontal ligament allows it to signal differential information about the mechanical events that occur when manipulating and biting food with anterior teeth and chewing food with the posterior teeth (Trulsson 2006). The detailed differential signalling allows the brain to analyze and characterize the specific mechanical events enabling further processing for fine-tuning, resulting in an optimized masticatory sequence (Trulsson 2006). Considering this crucial role, it is clear that some sensory–motor interactions are impaired or even lost when altering or damaging the periodontal ligament. When teeth are extracted and thus ligament receptors eliminated, tactile functioning may be hampered. Indeed, Haraldson (1983) describes a similar muscle activity during the entire masticatory sequence in patients with implant-supported fixed prosthesis. This finding contrasts to subjects with natural teeth, having a chewing pattern that gradually changes with altering food bolus properties. Jacobs and van Steenberghe (1994) identify a silent period in muscle activity (reflex response) when tapping teeth or implanting neighboring teeth. A reflex response remains absent, however, when tapping implants in a fully edentulous jaw bone. Both findings may illustrate the modulatory role of periodontal ligament input in jaw muscle activity.

Testing tactile function

Neurophysiological assessment

Information on the exteroceptive function can be examined by neurophysiological as well as psychophysical methods. Neurophysiological investigations on the sensory function of the human trigeminal system are scarce. Afferent nerve recordings of the human trigeminal nerve require skilful performance. Only few studies have been performed so far (Johansson *et al.* 1988a,b; Trulsson *et al.* 1992). Alternatively, non-invasive approaches may be considered to evaluate oral tactile function. The first approach is the recording of the so-called trigeminal somatosensory evoked potentials (TSEP) after stimulation of receptors in the oral cavity (Van Loven *et al.* 2000, 2001). This set-up has the advantage of obtaining information on the cortical response of the trigeminal afferent system upon non-invasive stimulation of oral receptors. Unfortunately, SEPs from the trigeminal branches are, in contrast to those recorded from limbs, weak and difficult to discriminate from

the background noise; advanced signal analysis is required to gain reliable information (Swinnen *et al*. 2000; van Loven *et al*. 2000, 2001). Another non-invasive method to assess sensory function is to visualize brain activity by functional magnetic resonance imaging (fMRI) (Borsook *et al*. 2004, 2006). This is a complex but most promising method, which has received hardly any attention in relation to tactile function of teeth and implants (Lundborg *et al*. 2006; Miyamoto *et al*. 2006).

The main drawbacks of fMRI include complexity of the signal, relatively long imaging time, potential hazard imposed by the presence of ferromagnetic material in the vicinity of the imaging magnet, potential risk for claustrophobia, and costs. The technique is most promising, however. When combined with other techniques, such as psychophysics and TSEPs, it may offer a new non-invasive approach to evaluate how the human oral somatosensory system functions (Ducreux *et al*. 2006; Lundborg *et al*. 2006).

Psychophysical assessment

Sensory function can also be evaluated by psychophysical testing, relying on the patient's response. This technique has often been applied for testing oral tactile function (Jacobs & van Steenberghe 1994; Jacobs *et al*. 2002b,c,d). When carried out in a strictly standardized condition, the psychophysical response can be directly linked to the neural receptor activation (Vallbo & Johansson 1984).

Psychophysical studies on the oral sensory function are numerous. A major advantage of this type of study is that they are simple non-invasive techniques that can be performed in a clinical environment. Psychophysics include a series of well defined methodologies to help determine the threshold level of sensory receptors in man. Psychophysical methods allow connection between the psychological response of the patient to the physiological functions of the receptors involved. The methods should be carried out in a standardized and accurate manner, to enable one to draw conclusions about their outcome with regard to sensory function (Jacobs *et al*. 2002b,c,d).

Regardless of the tests used, one must keep in mind that many variables contribute to the subjective nature of psychophysical sensory testing. Some variables are manageable, others are more difficult to deal with. Influencing factors exist in various components of the experiment set-up (environmental influence, psychophysical approach, patient-related factors) (Jacobs *et al.* 2002b).

Environmental factors should be well controlled, as background noise is distracting to patient and examiner. To minimize the effect of noise, testing should be done in a quiet room with stable background illumination.

Patient-related variables may contribute greatly to the outcome of the testing. Psychological and/or physical factors may lead to an inter- and intra-subject variability, making the expression of a threshold level more obvious than assessment of an absolute value. Psychological factors include motivation, level of concentration, and anxiety level. The psychophysical approach may attempt to control such variability.

Different psychophysical procedures have been described in order to assess tactile function reliably (Falmagne 1985). Adaptive methods are generally recommended for threshold level determination, as these seem very effective and consistent. Such approaches are termed adaptive, as the subsequent stimulus value depends on the subject's response in preceding trials. In the staircase method, the stimulus value is changed by a constant amount. When the response shifts from one answer to another, the stimulus direction is reversed. Afterwards, the threshold is determined by averaging peaks and valleys throughout all runs. Some patients may imagine a stimulus when there is none. Others admit feeling a sensation, only if they are absolutely positive that it was felt. The inclusion of false alarms (implying that no stimulus is presented in the specified time interval) may exclude response bias and a guessing strategy of the subject. A thorough and standardized instruction to all subjects is important in this respect.

Other patient-related factors that should be considered are of physical origin and include age, gender, dental status and dexterity. Age is an important variable with respect to implant physiology, considering the fact that edentulous patients are usually found amongst the elderly. Age-related impairment is seen, both of motor function and most sensory modalities in the extremities (Masoro 1986). A decline in oral sensory function is also established. After the age of 80, the ability to differentiate tactile and vibratory stimuli on the lip decreases and two-point discrimination deteriorates on the upper lip, on the cheeks, and on the lower lip, but not on the tongue and the palate (Calhoun *et al*. 1992). Stereognostic ability also declines with age (Müller *et al*. 1995). It is clear that this age effect should be considered in experimental studies.

In contrast to age, the influence of gender on tactile function remains a matter of debate. Taking into account the important inter-individual variability, clear-cut gender differences are not easily discerned with regard to oral sensory function. There is no marked gender effect on stereognostic ability or vibrotactile function (Jacobs *et al*. 1992, 2002b). The tactile sensory systems of men and women seem to operate similarly at both threshold and suprathreshold levels of stimulation (Chen *et al*. 1995). However, females seem to have greater ability to discern subtle changes in lip, cheek, and chin position than males (Chen *et al*. 1995). Dexterity is another patient-related variable. Although there is some relation between masticatory performance and dexterity (Hoogmartens & Caubergh 1987), this is not the case

for either tactile function or stereognosis (Jacobs *et al*. 1992, 2002b).

Periodontal tactile function

A variety of psychophysical tests has been used to evaluate oral exteroceptive function by assessment of threshold levels. Although some of the methods designed for functional psychophysical testing are unable to identify the specific receptor groups involved in the mechanisms of oral sensation, the tests may clearly reflect periodontal tactile function. Assessing light touch or the tactile function of teeth is performed by determination of the threshold levels for active and passive detection and discrimination tasks (Jacobs *et al*. 1992, 2002b,d). The distinction between detection and discrimination is based on the fact that, in a detection task, the subject has to indicate the presence or absence of a stimulus ("yes" or "no" strategy) while in a discrimination task, the subject has to compare two stimuli ("smaller" or "larger" strategy). A further division is made between active and passive tasks. In the passive task, forces are applied to a tooth in the upper jaw. The active tactile function of teeth is evaluated by inserting an object, mostly a foil of a certain thickness, in between two antagonistic teeth. The latter rather reflects daily functioning and automatically involves other than periodontal receptors (e.g. joint, muscle and inner ear receptors), while the passive test involves solely activation of periodontal ligament mechanoreceptors.

Active threshold determination

The active absolute threshold level is determined by the interocclusal detection of small objects such as foils of varying thicknesses (Fig. 6-9). This may involve the activation of mechanoreceptors, mainly originating from the periodontium but also from the muscles, inner ear, and temporomandibular joints (TMJs). It should, however, be realized that the foil materials used may have different thermal and mechanical properties, resulting in conflicting results (Jacobs *et al*. 1992). Foil materials with high thermal conductivity (e.g. steel, aluminium) may lower the threshold level by activation of thermal receptors.

Fig. 6-9 Active threshold determination by interocclusal thickness perception yields superior results for teeth than for implant-supported prostheses, with fixed prostheses being more sensitive than removable ones.

Another factor that may affect the active tactile function is chewing activity, because this involves progressive intrusion of the tooth after each chewing cycle. The latter leads to adaptation of the periodontal mechanoreceptive inputs. Chewing or bruxism may thus lead to an increase in threshold levels up to 60 times the normal values (Kiliaridis *et al*. 1990). An interocclusal discrimination task of small objects determines the differential threshold level. The active threshold level varies according to the experiment set-up, but the most important variable is test stick dimension (Jacobs & van Steenberghe 1994). For size discrimination with a mouth opening of less than 5 mm, periodontal mechanoreceptive input plays the primary role. For increased mouth opening, the response of muscle spindles predominates.

Passive threshold determination

The most common device used in clinical neurology to measure light touch sensation is a set of Semmes-Weinstein monofilaments (Semmes-Weinstein Aesthesiometer®, Stoelting, Illinois, USA). The original idea dates back from the nineteenth century when von Frey suggested testing cutaneous light touch by using calibrated hairs of different stiffness by changing their length and hardness. Later on, the so-called von Frey hairs were replaced by nylon monofilaments mounted into a plastic handle (Fig. 6-10). This technique has also been applied intraorally for assessment of light touch thresholds for teeth, implants or oral mucosa (Jacobs & van Steenberghe 1994; Jacobs *et al*. 2002d). The drawback remains the variation caused by the hand-held and thus variable nature of stimulation application. Other stimulators have therefore been developed, enabling a controlled force level under more standardized stimulation conditions for measuring both manual and oral light touch (Jacobs *et al*. 2002b,d).

The passive discrimination task allows testing of the ability to differentiate between intensities of forces applied to a tooth. It depends on the force characteristics such as the rate of force application and the range of forces presented. When comparing teeth and implants, passive threshold levels are much lower for teeth but at suprathreshold force levels, implants and teeth become equally sensitive. For the passive detection of forces applied to a tooth, different stimulating devices have been developed. In order to avoid tapping and subsequent transmission of the waves through the jaw bone with activation of other receptors, such as in the inner ear, pushing forces are recommended (Fig. 6-11). This is done by placement of the stimulating rod in contact with the tissue under investigation (Jacobs & van Steenberghe 1993).

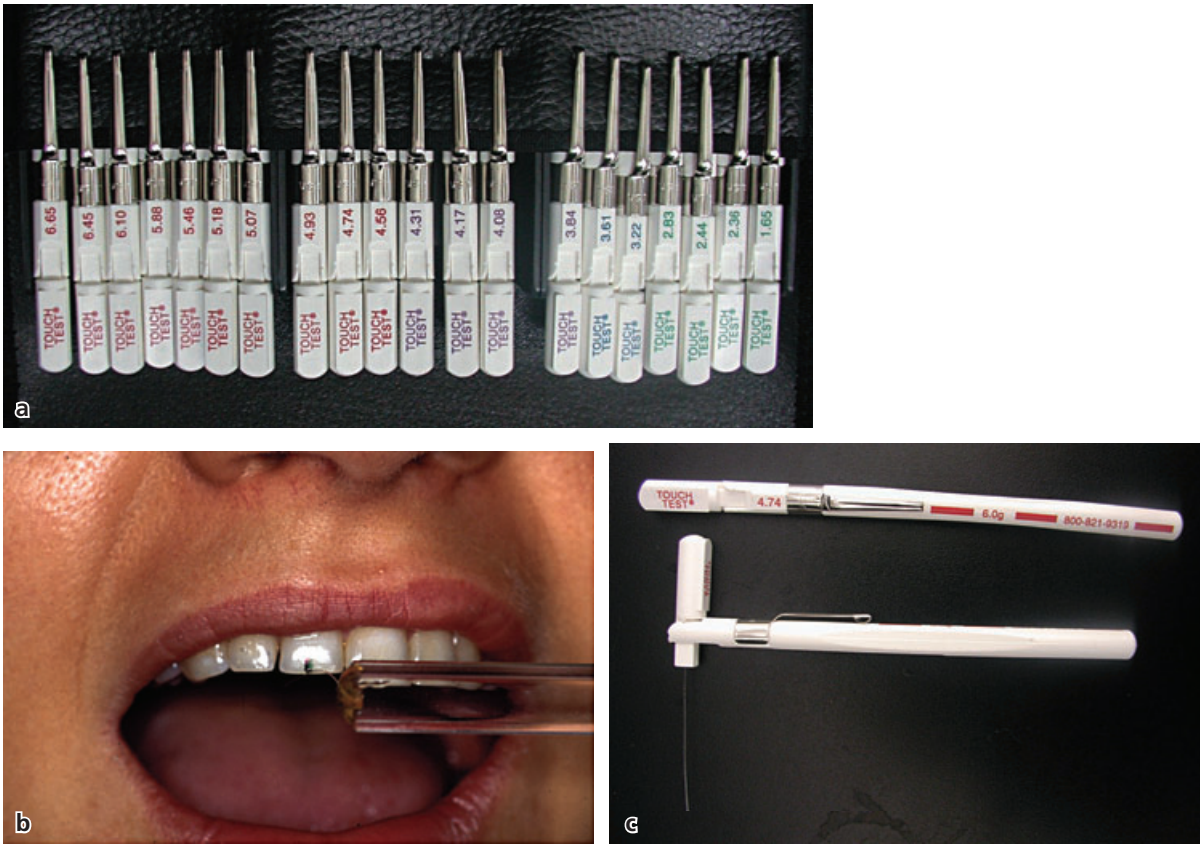

Fig. 6-10 Passive threshold determination. (a) Using a kit of pressure esthesiometers of increasing loads. (b) From determination of the absolute detection threshold upon tooth loading. (c) Using the individual hand-held stimulation rod.

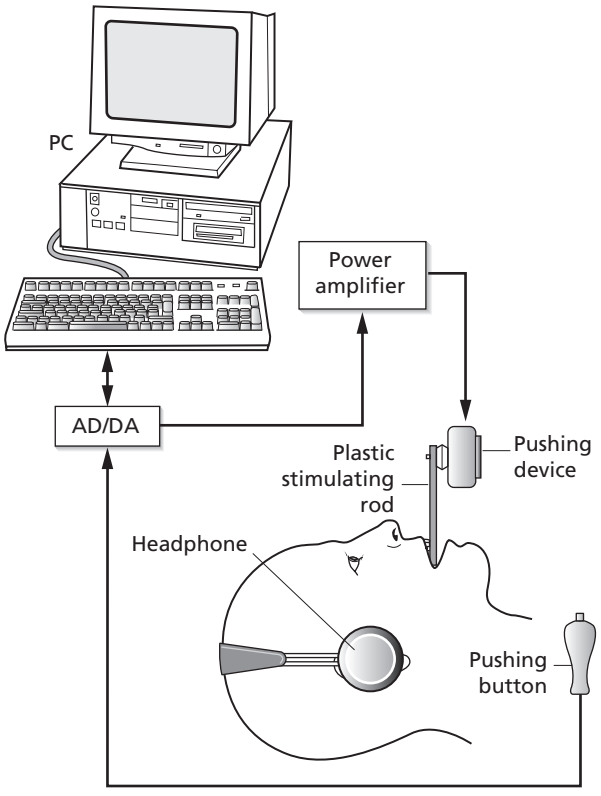

Fig. 6-11 Set-up of passive threshold determination of a maxillary front tooth by applying axial pushing forces against the tooth.

Influence of dental status on tactile function

From several psychophysical studies, it has been established that the oral tactile function is influenced by tooth position and dental status (Jacobs *et al.* 2002b). The tactile function of teeth is primarily determined by the presence of periodontal ligament receptors. Vital or non-vital teeth may show a comparable tactile function. However, when periodontal ligament receptors are reduced or eliminated (e.g. periodontitis, bruxism, chewing, extraction, anesthesia, etc.), tactile function is impaired (Table 6-1). This clinically implies that a patient's ability to detect occlusal inaccuracies (e.g. induced by restorative treatment) is decreased in these situations. Indeed, exteroceptors inform the nervous system on the characteristics of the stimulus, which then allows modulation of the motoneuron pool to optimize jaw motor activity and avoid overloading. Elimination of these exteroceptors by tooth extraction may reduce the tactile function to an important extent (Jacobs *et al.* 2001; Jacobs & van Steenberghe 1991, 1994, 2006; Mericske-Stern 1994; Mericske-Stern *et al.* 1995; Jacobs 1998). Even after rehabilitation with a prosthesis, tactile function remains impaired and inappropriate exteroceptive feedback may thus present a risk for overloading the prosthesis (Jacobs & van Steenberghe 2006). In comparison to the tactile function of a natural dentition, the active threshold is seven to

Table 6-1 Factors influencing the tactile function of teeth (for review see Jacobs *et al*. 2002b; Jacobs & van Steenberghe 2006)

Influencing factors	Active threshold (thickness detection)	Passive threshold (force detection)
Vital tooth	20 µm	2 g
Non-vital tooth	20 µm	2 g
Anesthesia	↑	↑
Periodontitis	↑	↑ (> 5 g)
Chewing	↑	↑
Bruxism	↑	↑
Extraction	↑	↑
Reimplantation	↑	↑
Denture	150 µm	150 g
Implant-supported prosthesis	50 µm	100 g
Ageing	↑	↑
Polyneuropathy	↑	↑

↑: increase in threshold level implying a decrease in tactile function and hampered feedback.

eight times higher for dentures but only three to five times higher for implants (see Table 6-1). For the passive detection of forces applied to upper teeth, thresholds are increased 75 times for dentures and 50 times for implants (see Table 6-1). The large discrepancies between active and passive thresholds can be explained by the fact that several receptor groups may respond to active testing, while the passive method selectively activates periodontal ligament receptors. The latter are eliminated after extraction, which may explain the reduced tactile function in edentulous patients.

After rehabilitation with a bone-anchored prosthesis, however, edentulous patients seem to function quite well. These patients perceive mechanical stimuli exerted on osseointegrated implants in the jaw bone. Some of them even note a special sensory awareness with the bone-anchored prosthesis, coined "osseoperception". It can be defined as a perception of external stimuli transmitted via the implant through the bone by activation of receptors located in peri-implant environment, periosteum, skin, muscles, and/or joints (Jacobs 1998). The existence of this phenomenon could imply that the feedback pathway to the sensory cortex is partly restored with a hypothetical representation of the prosthesis in the sensory cortex; this may allow an adjusted modulation of the motoneuron pool leading to more natural functioning and avoiding overload.

Activation of oral mechanoreceptors during oral tactile function

When performing psychophysical testing, various types of oral mechanoreceptors may be activated. Mechanoreceptors in the oral region may be located in the periodontal ligament, oral mucosa, gingiva, bone, periosteum, and tongue. Mechanoreceptors in the periodontal ligament contribute to the very high sensitivity of teeth to mechanical stimuli (Jacobs & van Steenberghe 1994). The periodontal ligament is richly supplied with mechanoreceptors, with the majority being identified histologically as Ruffini-like endings (Lambrichts *et al*. 1992). During passive threshold determination, these receptors will be activated. The assessment of the active tactile threshold level is, however, not solely based on activation of periodontal mechanoreceptors. Temporomandibular joint receptors are found to only play a minor role, but muscular receptors are important in the discriminatory ability for mouth openings of 5 mm and more (Broekhuijsen & Van Willigen 1983).

Considering that mechanoreceptors in the periodontal ligament largely contribute to tactile function, one can question what happens after tooth extraction. It can be assumed that remaining receptors in the peri-implant environment (gingiva, alveolar mucosa, periosteum, and bone) may take over part of the normal exteroceptive function.

In the oral mucosa, different types of mechanoreceptors can be identified including lamellar organs, Ruffini-like endings, and free nerve endings (Lambrichts *et al*. 1992). The number of nerve fibers per unit area is greater in the anterior areas of the oral cavity, making this region the most sensitive part of the oral mucosa (Mason 1967).

The gingiva contains round and oval lamellar corpuscles. These receptors respond to mechanical stimuli for coordination of the lip and buccal muscles during mastication (Johansson *et al*. 1988a,b). Cutaneous mechanoreceptors in the facial skin are activated by skin stretching or contraction of facial muscles and may operate as proprioceptors involved in facial kinesthesia and motor control (Nordin & Hagbarth 1989).

The periosteum contains free nerve endings, complex unencapsulated, and encapsulated endings. The free nerve endings are activated by pressure or stretching of the periosteum through the action of masticatory muscles and the skin (Sakada 1974). Periosteal innervation has been suggested to play a role in peri-implant tactile function (Jacobs 1998). Indeed, when applying forces to osseointegrated implants in the jaw bone, pressure build-up in the bone is sometimes large enough to allow deformation of the bone and its surrounding periosteum (Jacobs 1998). The involvement of bone innervation in mechanoreception and peri-implant osseoperception remains a matter of debate, however (Jacobs & van Steenberghe 2006).

Functional testing of the oral somatosensory system

Functional testing of the oral somatosensory system may include two-point and size discrimination as

well as stereognosis. Two-point discrimination is the ability to differentiate between two points of simultaneous contact. A traditional disk for two-point discrimination is divided into equal triangles containing two points placed at standard distances, usually between 2 and 25 mm (Fig. 6-12). This kind of test can be applied on different areas of the skin or the oral mucosa (Jacobs *et al*. 2002b,c,d). Size discrimination consists in holding a stick between two antagonistic teeth or fingers. This discriminatory ability is better for antagonistic teeth than for fingers (Morimoto 1990). The most documented and relevant test for the oral cavity is, however, stereognosis, which is considered as a complex functional test, evaluating the ability to recognize and discriminate different forms (Jacobs *et al*. 1997).

Oral stereognosis

While touch may obtain information on the mechanoreceptors activated by simple detection or discrimination of mechanical stimuli, stereognosis is a more complex process. It is a function of both peripheral receptors (touch and kinesthetic) and central integrating processes (Jacobs *et al*. 1998). It may give an idea on daily functioning and may be applied to measure sensory impairment due to the presence of general or local pathology (speech pathology, blindness, deafness, cleft lip and palate, temporary sensory ablations, etc.).

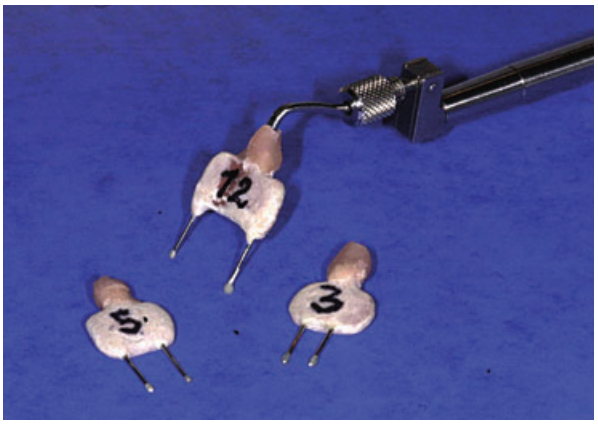

Fig. 6-12 Intraoral two-point discrimination testing device based on a constant pressure probe to compensate for the variability induced by hand-held equipment.

Influence of dental status on stereognostic ability

A change in the oral cavity by means of partial or complete loss of the dentition certainly creates certain changes to the oral sensory function. The roles of periodontal neural receptors and of the tongue seem essential in dentate subjects. After bilateral mandibular block, the stereognostic ability decreases by about 20% (Mason 1967). When comparing teeth with full dentures, a far better stereognostic ability is noted for natural teeth when freely manipulating the test pieces (Litvak *et al*. 1971). When removing the denture(s) in complete denture wearers, a considerable reduction in stereognostic ability is noted (Jacobs *et al*. 1998).

Lundqvist (1993) demonstrated that stereognostic ability improved after rehabilitation with oral implants. Jacobs *et al*. (1997) compared different prosthetic superstructures and noted no significantly different stereognostic ability with implant-supported fixed or removable prostheses, even when eliminating the involvement of tongue and lip receptors (Fig. 6-13).

Other compromising factors for oral stereognosis

Stutterers and speakers with articulation problems have an impaired stereognostic ability in comparison to normal speakers (Moser *et al*. 1967). They require more time to identify objects than normal speakers. Speakers with cerebral palsy also have an impaired stereognostic ability (Moser *et al*. 1967). Hemiplegic

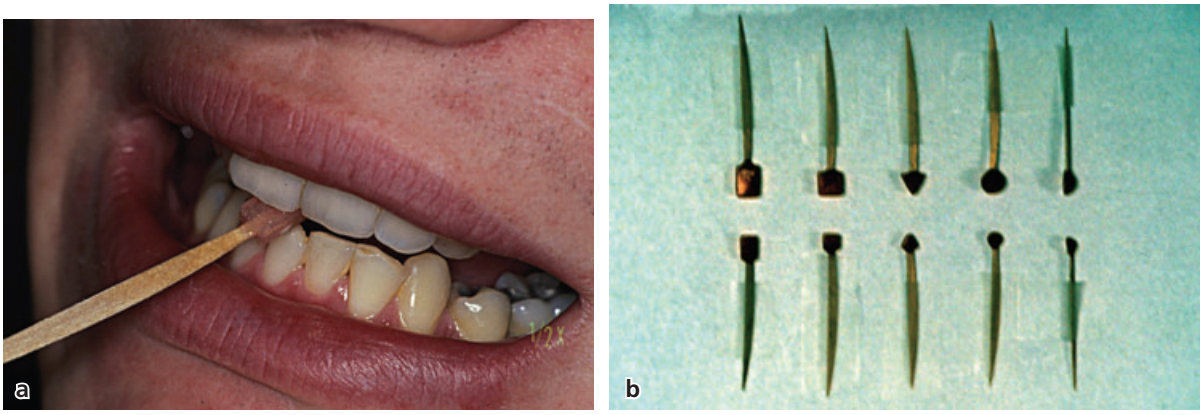

Fig. 6-13 (a) Stereognostic detection of objects in between teeth is better than for implant-supported prostheses. (b) The use of toothpicks to which the forms are attached and manipulated may avoid direct lip and tongue contact.

subjects make approximately three times as many errors as normal subjects in oral stereognosis tests. A surgical reduction of the tongue in case of macroglossia has a minor influence on the subject's performance in the test for oral stereognosis (Ingervall & Schmoker 1990). Other pathological conditions in the perioral area have no direct influence on the stereognostic ability (Jacobs *et al*. 1998). Cleft lip and palate is not accompanied by a sensory deficit of the oral area. There is also no overall sensory impairment following tissue manipulation in cleft lip and palate surgery. Furthermore, the stereognostic ability and oral size perception of patients with burning mouth syndrome is not significantly different from normal subjects (Jacobs *et al*. 1998).

Receptor activation during oral stereognosis

To assess the stereognostic ability, test pieces are inserted in the oral cavity and in most experimental set-ups, free manipulation of the test pieces is allowed. The latter implies activation of a large number of receptor groups (periodontal, mucosal, muscular, articular, etc.). Since the tip of the tongue is one of the most densely innervated areas of the human body, it plays an important role in stereognosis of objects inserted in the mouth (Jacobs *et al*. 1998). Based on studies involving anesthesia of the tongue, the palate or the absence of teeth, it could be stated that oral stereognostic ability is determined mostly by receptors in the tongue mucosa, the palate, and to a lesser extent the periodontal ligament (Jacobs *et al*. 1998). A major modification to the experimental set-up is the insertion of a toothpick in each test piece to eliminate the involvement of lip and tongue receptors, to allow easy handling and standardized placement in between two antagonistic teeth (Jacobs *et al*. 1997) (see Fig. 6-13).

The role of the TMJ receptors is less clear. In fact, in studies on tactile function, an interocclusal thickness of 5 mm and more seems able to activate receptors in the TMJ and the jaw muscles (Jacobs *et al*. 1998, 2002b). In the stereognostic ability tests, pieces are mostly manipulated inside the mouth and seldom kept between two antagonistic teeth, which frequently excludes the need for a mouth opening of 5 mm or even more.

Stereognostic ability testing is not designed to detect specific receptor groups, it rather reflects an overall sensory ability. A good result in a stereognosis test should indicate that the subject receives full and accurate information about what is going on in the mouth. Even if manipulation is allowed to identify the test piece, identification itself is a sensory rather than a motor accomplishment (Jacobs *et al*. 1998). It is an indicator of functional sensibility including synthesis of numerous sensory inputs in higher brain centers.

From periodontal tactile function to peri-implant osseoperception

Tooth extraction considered as sensory amputation

Sensory feedback plays an essential role in fine tuning of limb motor control. Thus, it is clear that amputation of a limb will not only involve destruction of an important part of the peripheral feedback pathways, but also hamper fine motor control. Conventional socket prostheses do not carry enough sensory information to restore the necessary natural feedback pathways for motor function (Jacobs *et al*. 2000). Comparable observations can be made after extraction of teeth. The periodontal ligament harbors a very rich innervation, carrying refined mechanoreceptive properties by an intimate contact between collagen fibres and Ruffini-like endings (Lambrichts *et al*. 1992) (see Fig. 6-8). The role of periodontal neural feedback is well known (Jacobs & van Steenberghe 1994, 2006). After extraction of teeth, however, the periodontal neural feedback pathway may be damaged as periodontal ligament receptors are eliminated. Dentures can be compared to socket prostheses and are not able to fully compensate for normal tooth loading and force transfer. The peripheral feedback mechanisms are more limited since the mucosal mechanoreceptor function is less efficient than the periodontal ligament function. Consequently, oral function remains impaired (Jacobs & van Steenberghe 1991, 1994, 2006; Jacobs *et al*. 1992; Mericske-Stern 1994; Mericske-Stern *et al*. 1995).

It has been assumed that by anchoring prosthetic limbs directly to the bone via osseointegrated implants, partial sensory substitution can be realized (Jacobs 1998; Jacobs *et al*. 2000). If the feedback pathway can be restored, such concept of bone-anchored limb prostheses would signify an important step towards global integration of a prosthesis in the body. Amputees and edentulous patients, rehabilitated with a bone-anchored prosthesis, report a specific feeling around endosseous implants. Psychophysical threshold determination studies confirm that patients may perceive mechanical stimuli exerted on osseointegrated implants in the bone. This phenomenon introduces discussion of which receptor groups are responsible for this perception phenomenon. New insights and more objective non-invasive approaches may help to clarify this question. It seems attractive to explain the observed tactile sensitivity of endosseous implants, coined osseoperception, by the surrounding endosseous and periosteal neural endings. Neurophysiological evidence can be found in some experiments evoking TSEPs upon implant stimulation. By triggering sweeps in the electroencephalogram by means of an implant-stimulation device and by cumulating and advanced analysis of the sweeps, one can observe significant waves (Fig. 6-14). The experiments indicate that endosseous

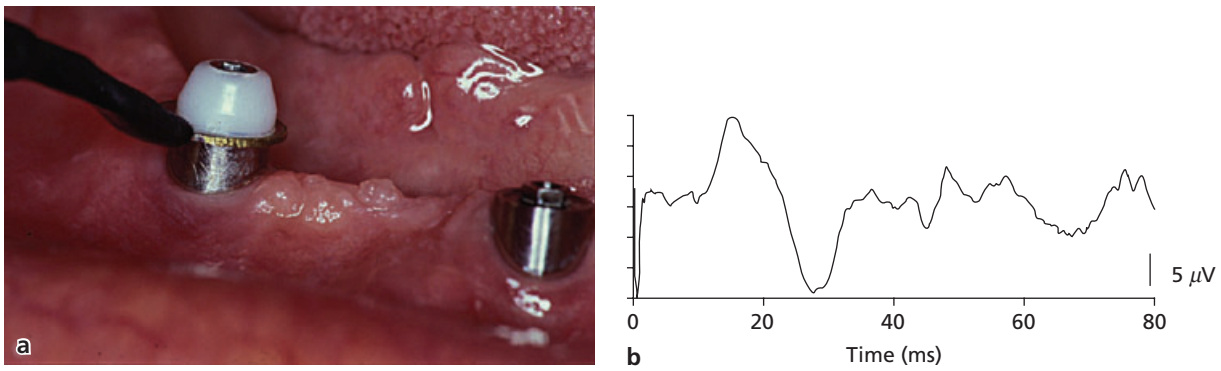

Fig. 6-14 (a) Electrical stimulation of an osseointegrated implant using a ring-shaped stimulation electrode fixed by a coverscrew. (b) Trigeminal evoked potential elicited by electrical stimulation of an osseointegrated implant in the mandible. A similar potential could be maintained after topical anesthesia of the peri-implant soft tissues indicating that the trigeminal potentials originated from other peri-implant structures such as bone and periosteal receptors.

and/or periosteal receptors around the implants convey the sensation (Van Loven *et al*. 2000). These mechanisms could be the basis of implant-mediated sensory–motor control, which may have important clinical implications, because more natural functioning with implant-supported prostheses can be attempted. It may thus open the gate for global integration of implants in the human body.

Histological background of peri-implant osseoperception

Tooth extraction results in damage to a large number of sensory nerve fibres and corresponds to an amputation, where the target organ and peripheral nervous structures have been destroyed (Mason & Holland 1993). After extraction of teeth, the myelinated fibre content of the inferior alveolar nerve is reduced by 20% (Heasman 1984). This finding indicates that fibers originally innervating the tooth and periodontal ligament are still present in the inferior alveolar nerve. Linden and Scott (1989) succeeded in stimulating nerves of periodontal origin in healed extraction sockets, which implies that some nerve endings remain functional. Nevertheless, most of the surviving mechanoreceptive neurons represented in the mesencephalic nucleus may lose some functionality (Linden & Scott 1989). These experiments have been the basis for a further and long-lasting debate on the presence and potential function of sensory nerve fibers in the bone and peri-implant environment. Histologic evidence indicates that there may be some re-innervation around osseointegrated implants (Wang *et al*. 1998; Lambrichts 1998) (Figs. 6-15, 6-16). Indeed, it has been shown that endosseous implants may lead to degeneration of surrounding neural fibers by surgical trauma. Soon however, sprouting of new fibers is observed and the number of free nerve endings close to the bone–implant interface gradually increases during the first weeks of healing (Wada *et al*. 2001). A more recent study in the dog has succeeded in partially regenerating the

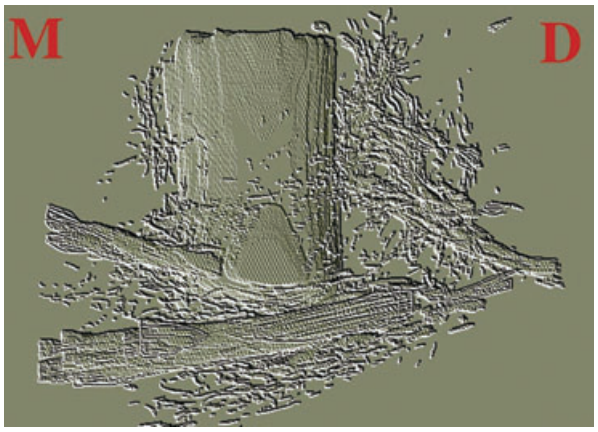

Fig. 6-15 A reconstruction of histologic slices indicating the regeneration of nerve tissue 3 months after implantation of a cylindrical oral implant in a dog's jaw bone. M = mesial; D = distal. (Reprinted from Wang *et al*. 1998, Copyright 2006, with permission from R. Jacobs, editor-publisher of *Osseoperception*, Dept of Periodontology, KU Leuven.)

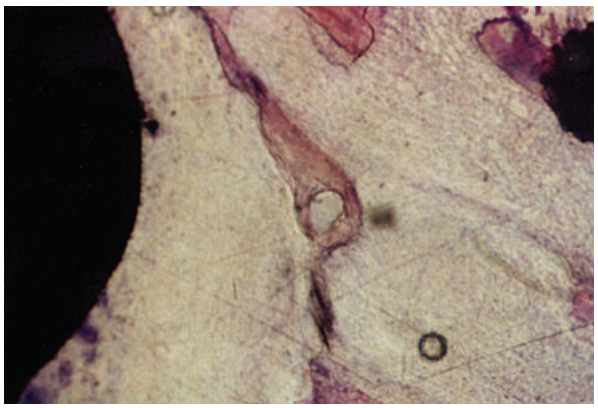

Fig. 6-16 Bone–implant specimen, obtained from a cat model, subjected to a light microscopic and immunohistochemical detection of neural structures. Elaborate neural structures in the bone trabeculae are seen surrounding the titanium implant. This histologic slice visualizes the titanium implant–bone tissue, with a bundle of myelinated nerve fibers in the bone trabeculum. (Reprinted from Lambrichts *et al*. 1998, Copyright 2006, with permission from Ivo Lambrichts, University of Hasselt and R. Jacobs, editor-publisher of *Osseoperception*, Dept of Periodontology, KU Leuven.)

periodontal ligament on an implant surface (Jahangiri *et al*. 2005). Whether such regeneration might also induce restoration of the peripheral feedback pathway needs further verification.

On the other hand, existing mechanoreceptors in the periosteum may also play a role in tactile function upon implant stimulation. It is evident that oral implants offer another type of loading and force transfer than teeth, considering an intimate bone–implant contact with elastic bone properties instead of the characteristic viscoelasticity of the periodontal ligament. Thus, forces applied to osseointegrated implants are directly transferred to the bone and bone deformation may lead to receptor activation in the peri-implant bone and the neighboring periosteum.

Cortical plasticity after tooth extraction

The cortex of the brain reveals a somatotopically ordered representational map with the teeth, gingiva, and jaws (Penfield & Rasmussen 1950). In this so-called sensory homunculus by Penfield, the representation of teeth in the postcentral gyrus of the primary somatosensory cortex is located superior to that of the tongue and inferior to that of the lip. This could be confirmed in a recent fMRI study, although this clear distinction between representation of tongue, lip, and teeth disappeared in the more caudal portions of the postcentral gyrus (Miyamoto *et al*. 2006). This established overlap of sensory representations might assume converging input from various oral structures including teeth. This finding could be relevant to the dedicated but intricate sensory information processing for modulation and coordination of oral motor function.

Recent findings on neuroplasticity of somatosensory and motor processes are also applicable in the orofacial region (Sessle 2006). After limb amputation or extraction, the regions of the cortex deprived of a target acquire new targets. Remodeling takes place at a (sub)cortical level. The potential cortical adaptation and/or plasticity that might occur after tooth extraction and implant placement has not yet been fully explored. A most interesting study was recently carried out on mole-rats, in which lower incisors were extracted (Henry *et al.* 2005). Five to eight months afterwards, functional MRI analysis yielded that the orofacial representation in S1 was considerably reorganized. Neurons in the cortical lower tooth representation were responsive to tactile inputs from surrounding orofacial structures. This study may indicate that cortical representation of teeth may significantly restructure after tooth loss. Unfortunately, until now, similar evidence in humans has not yet been produced. However, a very recent fMRI study by Lundborg *et al*. (2006) demonstrates that upon tactile stimulation of an osseointegrated prosthetic thumb, the primary somatosensory cortex is bilaterally activated in an area corresponding to that of the hand. As one would only expect activation of the contralateral cortex for healthy thumb stimulation, the presence of bilateral cortical activation may be explained by some compensatory mechanism, recruiting additional sensory areas after amputation (Lundborg *et al*. 2006). This recent finding confirms once more that osseoperception and cortical plasticity may truly exist. At present, the central neural pathways and neural characteristics contributing to implant-mediated sensory motor control remain unclear. Future research should therefore try to visualize cortical plasticity after tooth extraction and further functional rehabilitation with implants in man. It should be considered that an immediate extraction and implant rehabilitation protocol might induce different cortical remodeling than a traditional two-stage implant rehabilitation protocol. An interesting phenomenon with respect to sensory–motor integration of osseointegrated implants, may be the so-called phantom tooth (after extraction) or phantom limb (after amputation), allowing perception of lost body parts (Jacobs *et al*. 2002c). In fact, it could be assumed that such a phantom feeling of the lost limb may overlap with or enforce the feeling of a bone-anchored prosthetic limb (Jacobs 1998). In this way, phantom sensations might contribute to physiological integration of a bone-anchored prosthesis in the human body.

If neuroplasticity after amputation and osseointegration could be fully unravelled, it might be considered during treatment to optimize adaptation to oral rehabilitation and implant placement (Feine *et al.* 2006).

From osseoperception to implant-mediated sensory motor interactions

During the last few decades, millions of patients have been rehabilitated by means of osseointegrated implants. Even though part of the peripheral feedback mechanism is lost after tooth extraction, edentulous patients seem to function quite well, especially when rehabilitated with a prosthesis retained by or anchored to osseointegrated implants (Jacobs 1998). These findings correspond well to the observation in amputees rehabilitated with a bone-anchored prosthesis rather than a socket prosthesis. During skeletal reconstruction, psychophysical testing reveals an improved tactile and vibrotactile capacity with an osseointegrated implant and a bone-anchored prosthetic limb (Fig. 6-17). Furthermore, both edentulous patients and amputees seem to report an improved awareness and special feeling with the implant-supported prosthesis, allowing a partial restoration of the peripheral feedback pathway with a hypothesized potential representation of the artifical limb feeling in the sensory cortex (Lundborg *et al*. 2006). If that could be confirmed, osseointegrated implants in the jaw or other skeletal bones might contribute to implant-mediated sensory–motor control allowing

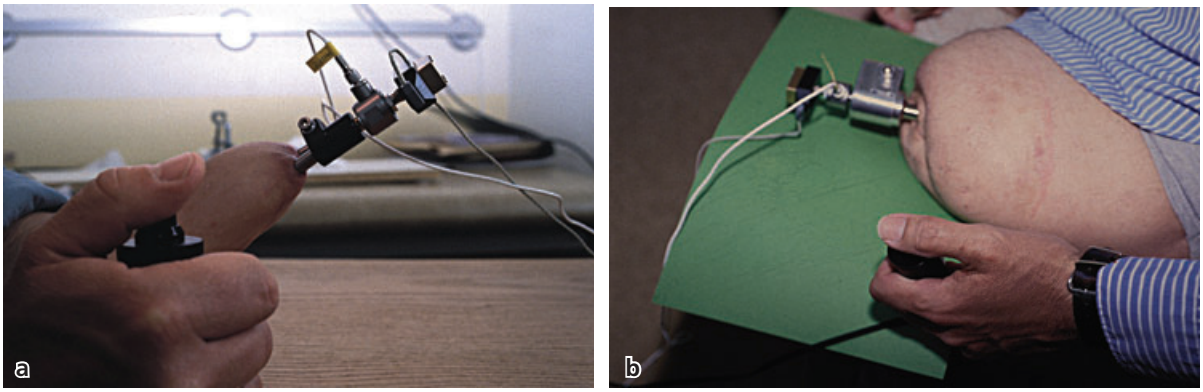

Fig. 6-17 Psychophysical test set-up using a patient-controlled remote control for a vibrotactile stimulator fixed to a radial (a) and femoral (b) osseointegrated implant. This particular test set-up yields superior perception for implants and bone-anchored prosthetic limbs compared to socket prostheses (Jacobs *et al*. 2000).

physiological integration of the implant in the human body, resulting in more natural functioning (Jacobs & van Steenberghe 2006).

Clinical implications of implant-deviated sensory motor interaction

Psychophysical testing on various bone-anchored prostheses confirms an improved tactile function leading to a better physiological integration of the limb. If perception upon implant stimulation is working well, peripheral feedback mechanisms may be restored and help fine tuning of motor control. This implant-mediated sensory–motor interaction may thus help to achieve a more natural function with the bone-anchored prosthesis (Jacobs 1998; Jacobs *et al*. 2000). Osseointegrated thumb prostheses even allow patients to perform the activities of daily life without any problem, which can be attributed to bone anchorage and bilateral cortical representation after prosthesis stimulation (Lundborg *et al*. 1996, 2006).

Considering the increased tactile threshold level for oral implant stimulation, one should, however, consider a few clinical implications. During rehabilitation by means of implant-supported prostheses, dentists should not rely on the patient's perception of occlusion. In this respect, one should also be aware of gradually increasing tactile function during the healing period after implant placement. This may be of particular importance when dealing with immediate loading protocols. To avoid any overloading related to suboptimal feedback mechanisms, patients should be encouraged to limit chewing forces by soft food intake during the healing period. Furthermore, parafunctional habits, such as grinding or clenching, might have a negative impact during the implant healing phase, but more research is needed to confirm this assumption (Lobbezoo *et al*. 2006). Until further evidence is collected, bruxism may be considered as a relative contraindication for immediate loading protocols (Glauser *et al*. 2001).

Conclusions

Sensory feedback plays an essential role in fine tuning of jaw and limb motor control. Periodontal mechanoreceptors, and more specifically those located in the periodontal ligament, are extremely sensitive to external mechanical stimuli. These receptors play the key role in tactile function of teeth, yielding detection thresholds of about 20 µm of thickness in between antagonistic teeth and 1–2 g upon tooth loading. Their sensory characteristics and the related peripheral feedback make the periodontal ligament receptors dedicated for fine tuning of masticatory and other oral motor behaviors.

It is clear that any condition that influences periodontal mechanoreceptors may also alter the sensory feedback pathway, and thus influence tactile function and modulation of jaw motor control (e.g. periodontal breakdown, bruxism, re-implantation, anesthesia). After extraction of teeth, the periodontal ligament has disappeared and so have its mechanoreceptors. After placement of oral implants, detection thresholds are increased to at least 50–100 µm of thickness and 50–100 g upon tooth loading.

Surprisingly enough, patients rehabilitated by means of osseointegrated implants seem to function quite well and/or sense better. In accordance with this, amputees rehabilitated with a lower limb prosthesis anchored to the bone by means of an osseointegrated implant, have reported that they could recognize the type of soil they were walking on, while patients with a bone-anchored thumb prosthesis have a cortical representation and thus conscious perception of their digit.

The underlying mechanism of this so-called "osseoperception" phenomenon remains a matter of debate, but is assumed that mechanoreceptors in the peri-implant bone and neighboring periosteum may be activated upon implant loading. Histological, neurophysiological and psychophysical evidence of osseoperception has been collected, making the assumption more likely that a proper peripheral

feedback pathway can be restored when using osseointegrated implants. This implant-mediated sensory–motor control may have important clinical implications, because a more natural functioning with implant-supported prostheses can be attempted. It may open doors for physiological and psychophysical integration of implants in the human body.

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Part 2: Epidemiology

Chapter 7

Epidemiology of Periodontal Diseases

Panos N. Papapanou and Jan Lindhe

Introduction

The term epidemiology is of Hellenic origin; it consists of the preposition "epi", which means "among" or "against", and the noun "demos" which means "people". As denoted by its etymology, epidemiology is defined as "the study of the distribution of disease or a physiological condition in human populations and of the factors that influence this distribution" (Lilienfeld 1978). A more inclusive description by Frost (1941) emphasizes that "epidemiology is essentially an inductive science, concerned not merely with describing the distribution of disease, but equally or more with fitting it into a consistent philosophy". Thus, the information obtained from an epidemiologic investigation should extend beyond a mere description of the distribution of the disease in different populations (*descriptive* epidemiology). It should be further expanded to (1) elucidate the etiology of a specific disease by combining epidemiologic data with information from other disciplines such as genetics, biochemistry, microbiology, sociology, etc. (*etiologic* epidemiology); (2) evaluate the consistency of epidemiologic data with hypotheses developed clinically or experimentally (*analytical* epidemiology); and (3) provide the basis for developing and evaluating preventive procedures and public health practices (*experimental/intervention* epidemiology).

Based on the above, epidemiological research in periodontology must (1) fulfill the task of providing data on the *prevalence* of periodontal diseases in different populations, i.e. the frequency of their occurrence, as well as on the *severity* of such conditions, i.e. the level of occurring pathologic changes; (2) elucidate aspects related to the *etiology* and the *determinants of development* of these diseases (*causative* and *risk* factors); and (3) provide documentation concerning the effectiveness of preventive and therapeutic measures aimed against these diseases on a population basis.

Methodological issues

Examination methods – index systems

Examination of the periodontal status of a given individual includes clinical assessments of inflammation in the periodontal tissues, recording of probing depths and clinical attachment levels and radiographic assessments of supporting alveolar bone. A variety of index systems for the scoring of these parameters has been developed over the years. Some of these systems were designed exclusively for examination of patients in a dental practice set-up, while others were developed in order to be utilized in epidemiologic research. The design of the index systems and the definition of the various scores inevitably reflects the knowledge of the etiology and pathogenesis of periodontal disease at the time these systems were introduced, as well as concepts related to the current therapeutic approaches and strategies. This section will not provide a complete list of all available scoring systems, but rather give a brief description of a limited number of indices that are either currently

used or are likely to be encountered in the recent literature. For description of earlier scoring systems and a historical perspective of their development, the reader is referred to Ainamo (1989).

Assessment of inflammation of the periodontal tissues

Presence of inflammation in the marginal portion of the gingiva is usually recorded by means of probing assessments, according to the principles of the Gingival Index outlined in the publication by Löe (1967). According to this system, entire absence of visual signs of inflammation in the gingival unit is scored as 0, while a slight change in color and texture is scored as 1. Visual inflammation and bleeding tendency from the gingival margin right after a periodontal probe is briefly run along the gingival margin is scored as 2, while overt inflammation with tendency for spontaneous bleeding is scored as 3. A parallel index for scoring plaque deposits (Plaque Index) in a scale from 0 to 3 (Silness & Löe 1964) was introduced, according to which absence of plaque deposits is scored as 0, plaque disclosed after running the periodontal probe along the gingival margin as 1, visible plaque as 2 and abundant plaque as 3. Simplified variants of both the Gingival and the Plaque Index (Ainamo & Bay 1975) have been extensively used, assessing presence/absence of inflammation or plaque, respectively, in a binomial fashion (*dichotomous scoring*). In such systems, bleeding from the gingival margin and visible plaque score 1, while absence of bleeding and no visible plaque score 0.

Bleeding after probing to the base of the probeable pocket (Gingival Sulcus Bleeding Index) has been a common way of assessing presence of subgingival inflammation (Mühlemann & Son 1971). In this dichotomous registration, 1 is scored in cases where bleeding emerges within 15 seconds after probing. Presence/absence of bleeding on probing to the base of the pocket is increasingly tending to substitute the use of the Gingival Index in epidemiologic studies.

Assessment of loss of periodontal tissue support

One of the early indices providing indirect information on the loss of periodontal tissue support was the Periodontal Index (PI) developed in the 1950s by Russell (1956), and until the 1980s it was the most widely used index in epidemiologic studies of periodontal disease. Its criteria are applied to each tooth and the scoring is as follows: a tooth with healthy periodontium scores 0, a tooth with gingivitis around only part of the tooth circumference scores 1, a tooth with gingivitis encircling the tooth scores 2, pocket formation scores 6, and loss of function due to excessive tooth mobility scores 8. Due to the nature of the criteria used, the PI is a reversible scoring system, i.e. after treatment a tooth or an individual can have the score lowered or reduced to 0.

In contrast to the PI system, the Periodontal Disease Index (PDI), developed by Ramfjord (1959), is a system designed to assess *destructive* disease; it measures *loss of attachment* instead of *pocket depth* and is, therefore, an irreversible index. The scores, ranging from 0–6, denote periodontal health or gingivitis (scores 0–3) and various levels of attachment loss (scores 4–6).

In contemporary epidemiologic studies, loss of periodontal tissue support is assessed by measurements of pocket depth and attachment level. Probing pocket depth (PPD) is defined as the distance from the gingival margin to the location of the tip of a periodontal probe inserted in the pocket with moderate probing force. Likewise, probing attachment level (PAL) or clinical attachment level (CAL) is defined as the distance from the cemento-enamel junction (CEJ) to the location of the inserted probe tip. Probing assessments may be carried out at different locations of the tooth circumference (buccal, lingual, mesial or distal sites). The number of probing assessments per tooth has varied in epidemiologic studies from two to six, while the examination may either include all present teeth (*full-mouth*) or a subset of *index* teeth (*partial-mouth* examination).

Carlos *et al*. (1986) proposed an index system which records loss of periodontal tissue support. The index was denoted the Extent and Severity Index (ESI) and consists of two components (*bivariate* index): (1) the *Extent*, describing the proportion of tooth sites of a subject examined showing signs of destructive periodontitis, and (2) the *Severity*, describing the amount of attachment loss at the diseased sites, expressed as a mean value. An attachment loss threshold of >1 mm was set as the criterion for a tooth site to qualify as affected by the disease. Although arbitrary, the introduction of a threshold value serves a dual purpose: (1) it readily distinguishes the fraction of the dentition affected by disease at levels exceeding the error inherent in the clinical measurement of attachment loss, and (2) it prevents unaffected tooth sites from contributing to the individual subject's mean attachment loss value. In order to limit the assessments to be performed, a partial examination comprising the mid-buccal and mesiobuccal aspects of the upper right and lower left quadrants was recommended. It has to be emphasized that the system was designed to assess the cumulative effect of destructive periodontal disease rather than the presence of the disease itself. The bivariate nature of the index facilitates a rather detailed description of attachment loss patterns: for example an ESI of (90, 2.5) suggests a generalized but rather mild form of destructive disease, in which 90% of the tooth sites are affected by an average attachment loss of 2.5 mm. In contrast, an ESI of (20, 7.0) describes a severe, localized form of disease. Validation of

various partial extent and severity scoring systems against the full-mouth estimates has been also performed (Papapanou *et al*. 1993).

Radiographic assessment of alveolar bone loss

The potential and limitations of intraoral radiography to describe loss of supporting periodontal tissues were reviewed by Lang and Hill (1977) and Benn (1990). Radiographs have been commonly employed in cross-sectional epidemiologic studies to evaluate the result of periodontal disease on the supporting tissues rather than the presence of the disease itself and are thought to provide valid estimates of the extent and severity of destructive periodontitis (Pitiphat *et al*. 2004). Radiographic assessments have been particularly common as screening methods for detecting subjects suffering from juvenile periodontitis as well as a means for monitoring periodontal disease progression in longitudinal studies. Assessments of bone loss in intraoral radiographs are usually performed by evaluating a multitude of qualitative and quantitative features of the visualized interproximal bone, e.g. (1) presence of an intact lamina dura, (2) the width of the periodontal ligament space, (3) the morphology of the bone crest ("even" or "angular" appearance), and (4) the distance between the CEJ and the most coronal level at which the periodontal ligament space is considered to retain a normal width. The threshold for bone loss, i.e. the CEJ – bone crest distance considered to indicate that bone loss has occurred, varies between 1 and 3 mm in different studies. Radiographic data are usually presented as (1) mean bone loss scores per subject (or group of subjects), and (2) number or percentage of tooth surfaces per subject (or group of subjects) exhibiting bone loss exceeding certain thresholds. In early studies, bone loss was frequently recorded using "ruler" devices, describing the amount of lost or remaining bone as a percentage of the length of the root or the tooth (Schei *et al*. 1959; Lavstedt *et al*. 1975).

Assessment of periodontal treatment needs

An index system aimed at assessing the need for periodontal treatment in large population groups was developed, at the initiative of the World Health Organization (WHO), by Ainamo *et al*. (1982). The principles of the Community Periodontal Index for Treatment Needs (CPITN) can be summarized as follows:

1. The dentition is divided into six *sextants* (one anterior and two posterior tooth regions in each dental arch). The treatment need in a sextant is recorded when two or more teeth, not intended for extraction, are present. If only one tooth remains in the sextant, the tooth is included in the adjoining sextant.
2. Probing assessments are performed either around all teeth in a sextant or around certain index teeth (the latter approach has been recommended for epidemiologic surveys). However, only the most severe measure in the sextant is chosen to represent the sextant.
3. The periodontal conditions are scored as follows:
   - *Code 1* is given to a sextant with no pockets, calculus or overhangs of fillings but in which bleeding occurs after gentle probing in one or several gingival units.
   - *Code 2* is assigned to a sextant if there are no pockets exceeding 3 mm, but in which dental calculus and plaque-retaining factors are seen or recognized subgingivally.
   - *Code 3* is given to a sextant that harbors 4–5 mm deep pockets.
   - *Code 4* is given to a sextant that harbors pockets 6 mm deep or deeper.
4. The treatment needs are scores based on the most severe code in the dentition as TN 0, in case of gingival health, TN 1 indicating need for improved oral hygiene if code 1 has been recorded, TN 2 indicating need for scaling, removal of overhangs, and improved oral hygiene (codes 2 + 3) and TN 3 indicating complex treatment (code 4).

Although not designed for epidemiological purposes, this index system has been extensively used worldwide, and CPITN-based studies have often been the exclusive source of epidemiologic information on periodontal conditions, particularly from developing countries. A later modification of the index, termed Community Periodontal Index (CPI; WHO 1997), places more emphasis on the assessment of periodontal conditions rather than the assessment of periodontal treatment needs. A substantial amount of data generated by the use of CPITN/CPI have been accumulated in the WHO Global Oral Data Bank (Miyazaki *et al*. 1992; Pilot & Miyazaki 1994 Petersen *et al.* 2005; Petersen & Ogawa 2005) and are accessible electronically through servers maintained at the Niigata University, Japan (WHO Collaborating Centre) and University of Malmö, Sweden (WHO Collaborating Centre).

Critical evaluation

A fundamental prerequisite for any meaningful comparative assessment of prevalence is a valid and accurate definition of the disease under investigation. Unfortunately, no uniform criteria have been established in periodontal research for this purpose. Epidemiologic studies have employed a wide array of symptoms, including gingivitis, probing depth, clinical attachment level, and radiographically assessed alveolar bone loss, in an inconsistent manner. Considerable variation characterizes the threshold values employed for defining periodontal pockets as "deep" or "pathologic", or the clinical attachment level and

alveolar bone scores required for assuming that "true" loss of periodontal tissue support has, in fact, occurred. In addition, the number of "affected" tooth surfaces required for assigning an individual subject as a "case", i.e. as suffering from periodontal disease, has varied. These inconsistencies in the definitions inevitably affect the figures describing the distribution of the disease (Papapanou 1996; Kingman & Albandar 2002) and, consequently, the identification of risk factors (Borrell & Papapanou 2005). A review of the literature charged with the task of comparing disease prevalence or incidence in different populations or at different time periods must first be confronted with the interpretation of the figures reported and literally "decode" the published data in order to extract relevant information that is amenable to inter-study comparisons. These problems have been addressed in the literature and two specific aspects have attracted special attention, namely (1) the ability of partial recording methodologies to reflect full-mouth conditions, and (2) the use of the CPITN system in epidemiological studies of periodontal disease.

There is little doubt that an optimal examination of periodontal conditions should include circumferential probing assessments around all teeth. Nevertheless, the majority of epidemiological studies have, for practical reasons, employed partial recording methodologies. The rationale for the use of partial examinations has been the assumption that (1) the time required for the performance of a partial survey, and consequently its cost, is significantly decreased, and (2) the amount of information lost is kept to a minimum, provided that the examined segments adequately reflect the periodontal condition of the entire dentition. However, attempts to quantify accurately the amount of information lost through the different partial recording systems made by several investigators (Hunt 1987; Kingman *et al*. 1988; Hunt & Fann 1991; Stoltenberg *et al*. 1993a; Diamanti-Kipioti *et al*. 1993; Eaton *et al*. 2001; Susin *et al*. 2005a) have revealed that the discrepancy between the findings obtained by means of partial and full-mouth surveys may be substantial. These studies have typically employed full-mouth data for a series of periodontal parameters and compared them with the values obtained by assessments performed at a subset of teeth or tooth surfaces. Their results suggest that:

1. High correlations between full-mouth and half-mouth attachment loss scores should be expected in adult populations, due to the apparent symmetry of periodontal conditions around the midline.
2. The performance of a partial recording system is directly dependent on the actual prevalence of periodontal disease in the population in question and, consequently, on the age of the subjects examined; the less frequent the disease in the population and the lower the number of sites that are affected in each individual mouth, the more difficult it becomes for the partial examination to detect the periodontal lesions.
3. A full-mouth examination provides the best means of accurately assessing the prevalence and severity of periodontal disease in a population.

The use of the CPITN system in epidemiological studies of periodontal disease was critically evaluated in a number of publications (Grytten & Mubarak 1989; Holmgren & Corbet 1990; Schürch *et al*. 1990; Butterworth & Sheiham 1991; Baelum *et al*. 1993a,b, 1995; Benigeri *et al*. 2000). At the time the system was designed, the conversion of periodontal health to disease was thought to include a continuum of conditions, ranging from an inflammation-free state developing through gingivitis (bleeding), calculus deposition, shallow and deep pocket formation to progressive, destructive disease. The treatment concepts were based on the assumption that probing depths determined the choice between non-surgical and more complicated, surgical periodontal therapy. It should also be remembered that this particular index was clearly intended for screening large population groups in order to determine treatment needs and to facilitate preventive and therapeutic strategies and not for describing prevalence and severity of periodontal disease. In view of the revised, contemporary views on the pathogenesis and treatment of the periodontal diseases, studies have questioned the suitability of the CPITN for such purposes. For example, Butterworth and Sheiham (1991) addressed the suitability of CPITN to record changes in periodontal conditions and examined patients of a general dental practice before and after periodontal therapy. Despite a substantial improvement in the state of health of the periodontal tissues, assessed through gingivitis, calculus, and pocketing scores, the CPITN scores were only marginally improved. In a rural Kenyan subject sample, Baelum *et al*. (1993b) examined and refuted the validity of the hierarchical principle of the CPITN, i.e. the assumptions that a tooth with calculus is assumed to be positive also for bleeding on probing, and that a tooth with moderately deep or deep pockets is assumed to be positive for both calculus and bleeding. In a companion paper, results from a full-mouth examination were compared with those generated by the use of the ten index teeth recommended by the WHO for surveys of adults (Baelum *et al*. 1993a). The study revealed that the partial CPITN methodology seriously underestimates the more severe periodontal conditions both in terms of prevalence and severity, since it fails to detect a substantial proportion of subjects with periodontal pockets. Finally, an examination of the relationship between CPITN findings and the prevalence and severity of clinical attachment loss, demonstrated that the CPITN scores do not consistently correlate with attachment loss measures, but tend to overestimate prevalence and severity among younger

subjects while they underestimate such parameters in elderly populations (Baelum *et al*. 1995). The above data call for caution in the interpretation of epidemiologic studies based on the CPITN/CPI systems.

Prevalence of periodontal diseases

Introduction

The currently used classification of periodontal diseases was introduced by the 1999 International Workshop for a Classification of Periodontal Diseases and Conditions (Anon 1999) and encompasses eight main categories, namely:

I Gingival diseases
II Chronic periodontitis
III Aggressive periodontitis
IV Periodontitis as a manifestation of systemic diseases
V Necrotizing periodontal diseases
VI Abscesses of the periodontium
VII Periodontitis associated with endodontic lesions
VIII Developmental or acquired deformities and conditions.

Since the current nomenclature has been in use for less than a decade, a substantial part of the existing literature on the prevalence and extent of periodontal diseases in various populations is still based on earlier classification systems. Inevitably, the following review of epidemiologic studies uses data stemming from publications employing both the earlier and the current diagnostic systems. Although the current classification no longer employs the individual subject's age as a primary determinant of diagnosis, the descriptive epidemiologic findings have still been grouped in the text below according to age, in order to facilitate data extraction from studies using inconsistent terminologies.

Periodontitis in adults

An epidemiologic survey performed during the 1950s in India used assessments of alveolar bone height to distinguish between gingivitis and destructive periodontal disease in a sample involving 1187 dentate subjects (Marshall-Day *et al*. 1955). The authors reported (1) a decrease in the percentage of subjects with "gingival disease without any bone involvement" with increasing age concomitant with an increase in the percentage of subjects with "chronic, destructive periodontal disease", and (2) a 100% occurrence of destructive periodontitis after the age of 40 years. Findings from other epidemiologic studies from the same period verified a high prevalence of destructive periodontal disease in the adult population in general, and a clear increase in disease prevalence with age. In the 1960s, Scherp (1964) reviewed the available literature on the epidemiology of periodontal disease and concluded that (1) periodontal disease appears to be a major, global public health problem affecting the majority of the adult population after the age of 35–40 years, (2) the disease starts as gingivitis in youth, which, if left untreated, leads to progressive destructive periodontitis, and (3) more than 90% of the variance of the periodontal disease severity in the population can be explained by age and oral hygiene. These notions, based on established concepts on the pathogenesis of periodontal disease of that time, dominated the periodontal literature until the late 1970s.

Studies performed during the 1980s provided a more thorough description of the site-specific features of periodontal disease and the high variation in periodontal conditions between and within different populations. Contrary to what was customary until then, the prevalence issue was no longer addressed through a mere assignment of individuals to a "periodontitis-affected" or a "disease-free" group, based on presence or absence of attachment or alveolar bone loss. Instead, studies began to unravel details concerning the *extent* to which the dentition was affected by destructive disease (i.e. the percentage of tooth sites involved), and the *severity* of the defects (expressed through the magnitude of the tissue support lost due to the disease). The traditional description of pocket depth and attachment loss scores through *subject mean values* was soon complemented by *frequency distributions*, revealing percentages of tooth sites exhibiting probing depth or attachment level of varying severity. Such an additional analysis appeared necessary after it became clear that mean values offer a crude description of periodontal conditions and fail to reflect the variability in the severity of periodontal disease within and between individuals. In an article presenting different methods of evaluating periodontal disease data in epidemiological research, Okamoto *et al*. (1988) proposed the use of *percentile plots* in the graphic illustration of attachment loss data. As exemplified by Fig. 7-1, such plots make it possible to illustrate simultaneously both the proportion of subjects exhibiting attachment loss of different levels and the severity of the loss within the subjects. Similar plots may be produced for other parameters, such as gingivitis, probing depths and gingival recession, and may provide a comprehensive description of both the prevalence and the severity of periodontal disease in a given sample.

Pioneering research by a Danish research group made significant contributions to our current understanding of epidemiologic issues in periodontal research. Baelum *et al*. (1986) described cross-sectional findings on dental plaque, calculus, gingivitis, loss of attachment, periodontal pockets, and tooth loss in a sample of adult Tanzanians aged 30–69 years. Despite the fact that the subjects examined exhibited large amounts of plaque and calculus,

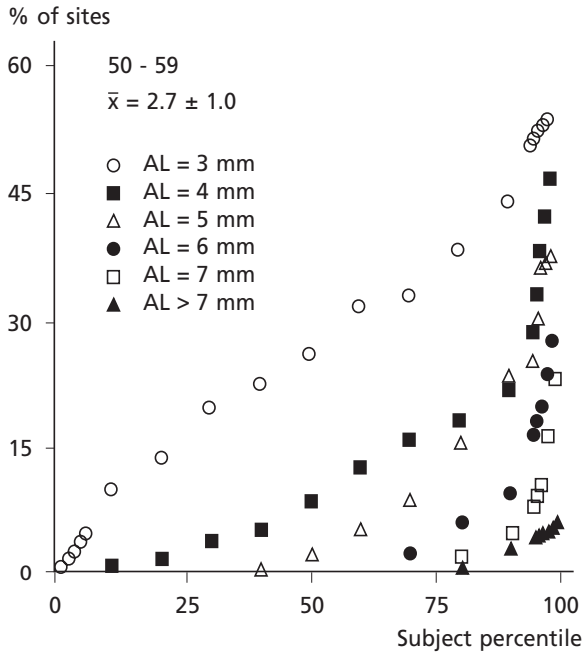

Fig. 7-1 Attachment loss in a group of Japanese subjects 50–59 years of age. The mean value of attachment level and the standard deviation are shown in the top of the figure. The x-axis represents the subject percentile and the y-axis represents the percentage of sites in the subjects showing attachment loss of 3, 4, 5, 6, 7, and >7 mm (represented by 8). Subjects with no or only minor signs of attachment loss are reported to the left and subjects with increasing amounts of periodontal destruction are reported to the right of the graph. For example, the median subject (50th percentile), exhibited 5 mm attachment loss at 2%, 4 mm loss at 8%, and 3 mm attachment loss at 25% of its sites. From Okamoto *et al*. (1988), reproduced with permission.

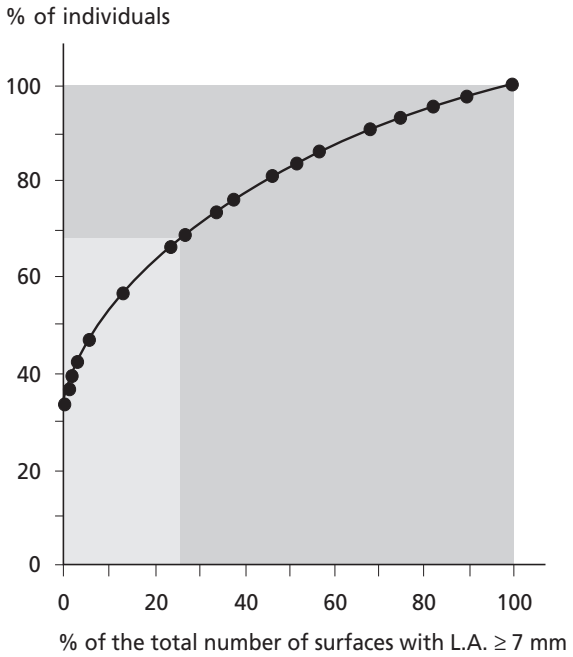

Fig. 7-2 Cumulative distribution of individuals aged ≥50 years according to the cumulated proportion of surfaces with loss of attachment (L.A.) ≥7 mm. All individuals are arranged according to increasing number of surfaces with L.A. ≥7 mm present in each individual. Thus, individuals with few such surfaces are represented by the dots in the left side of the diagram and those with many such surfaces by dots in the right side. It is seen that 31% (100%–69%) of the individuals account for 75% (100%–25%) of the total number of surfaces with L.A. ≥7 mm present (shaded area). From Baelum *et al*. (1986), reproduced with permission.

pockets deeper than 3 mm and attachment loss of >6 mm occurred at less than 10% of the tooth surfaces. Edentulousness was virtually non-existent, and a very small percentage of subjects had experienced major tooth loss. Of particular interest was the analysis of the distribution of sites within subjects (Fig. 7-2). This analysis revealed that 75% of the tooth sites with attachment loss of ≥7 mm were found in 31% of the subjects, indicating that a subfraction of the sample was responsible for the major part of the observed periodontal breakdown. In other words, advanced periodontal disease was not evenly distributed in the population and not readily correlated to supragingival plaque levels; instead, the majority of the subjects examined exhibited negligible periodontal problems while a limited group was affected by advanced disease.

In a study of similar design performed in Kenya, the same investigators analyzed data from 1131 subjects aged 15–65 years and confirmed their earlier observations (Baelum *et al*. 1988a). Poor oral hygiene in the sample was reflected by high plaque, calculus, and gingivitis scores. However, pockets ≥4 mm deep were found in less than 20% of the surfaces and the proportion of sites per individual with deep pockets and advanced loss of attachment revealed a pronounced skewed distribution. The authors suggested that "destructive periodontal disease should not be perceived as an inevitable consequence of gingivitis which ultimately leads to considerable tooth loss" and called for a more specific characterization of the features of periodontal breakdown in those individuals who seem particularly susceptible.

At approximately the same time, Löe *et al*. (1986) published their landmark paper that showed that the *progression* of untreated periodontitis also shared similar features. In a population never exposed to any preventive or therapeutic intervention related to oral diseases in Sri Lanka, an original cohort of 480 male tea-plantation laborers, aged 14–31 years, was initially recruited in 1970, and underwent subsequent follow-up examinations. A total of 161 of subjects were re-examined at the final examination in 1985, essentially generating data on the natural history of periodontal disease between the age of 14 and 46 years. Despite poor plaque control and virtually ubiquitous gingival inflammation in the entire sample, three distinct patterns of progression of periodontitis were observed over the follow-up period, based on interproximal longitudinal attachment loss and tooth mortality rates: one group, comprising approximately 8% of the total, with rapid progression of periodontal disease (RP); another group (approximately 11%) who exhibited no progression

(NP) of periodontal disease beyond gingivitis; and a third group between the two extremes (approximately 81%) with moderate progression (MP). The mean loss of attachment in the RP group was 9 mm and 13 mm, at the age of 35 and 45 years, respectively, as opposed to 1 mm and 1.5 mm in the NP group, and 4 mm and 7 mm in the MP group. As a result, the annual rate of longitudinal attachment loss in the RP group varied between 0.1 and 1.0 mm, in the MP group between 0.05 and 0.5 mm, and in the NP group between 0.05 and 0.09 mm. Thus, what this study clearly demonstrated is the huge variability in progression of periodontitis in a seemingly homogeneous population, and suggested that variables other than age, plaque, and gingival inflammatory status are important determinants of periodontal deterioration over time.

Several epidemiological studies have been published in the last two decades, verifying the above principals. In these studies, periodontal disease has been assessed by means of clinical examination of the periodontal tissues (Brown *et al*. 1989, 1990; McFall *et al*. 1989; Stuck *et al*. 1989; Beck *et al*. 1990; Horning *et al*. 1990; Hunt *et al*. 1990; Matthesen *et al*. 1990; Gilbert & Heft 1992; Löe *et al*. 1992; Bagramian *et al*. 1993; Douglass *et al*. 1993; Kiyak *et al*. 1993; Locker & Leake 1993; Slade *et al*. 1993; Weyant *et al*. 1993; Querna *et al*. 1994; Söder *et al*. 1994; Anagnou Vareltzides *et al*. 1996; Oliver *et al*. 1998; Albandar *et al*. 1999; Albandar & Kingman 1999; Schürch & Lang 2004; Susin *et al*. 2004a; Krustrup & Erik Petersen 2006; Thomson *et al*. 2006); radiographic assessments of alveolar bone loss (Papapanou *et al*. 1988; Jenkins & Kinane 1989; Wouters *et al*. 1989; Salonen *et al*. 1991; Diamanti-Kipioti *et al*. 1995); or a combination of clinical and radiographic means (Hugoson *et al*. 1998a, 1992, 2005; Papapanou *et al*. 1990).

Table 7-1 summarizes the design and main findings from a number of cross-sectional studies in adults from geographically divergent areas that involve samples of a relatively large size. Most of the studies focus on assessments of prevalence of "advanced periodontitis", the definition of which is, however, far from identical among the studies, rendering comparisons difficult. Nevertheless, it appears that severe forms of periodontitis affect a minority of the subjects in the industrialized countries, at proportions usually not exceeding 10–15% of the population. The percentage of such subjects increases considerably with age and appears to reach its peak at the age of 50–60 years. The increased tooth loss occurring after this age appears to account for the subsequent decline in prevalence. It is worth pointing out that, among the studies reviewed in Table 7-1, the study employing probing assessments at six sites per tooth around all teeth (Susin *et al*. 2004a) reported the highest prevalence of advanced disease, suggesting that the impact of the methodology used may have been decisive. The interesting issue of disparities in the severity of periodontitis was brought up by Baelum *et al*. (1996). The authors recalculated their own data from a Kenyan (Baelum *et al*. 1988a) and a Chinese (Baelum *et al*. 1988b) adult population to conform with the methods of examination and data presentation utilized in each of six other surveys (from Japan (Yoneyama *et al*. 1988); Norway (Löe *et al*. 1978); New Mexico (Ismail *et al*. 1987); Sri Lanka (Löe *et al*. 1978); and two South Pacific islands (Cutress *et al*. 1982)). Among the samples included in this analysis, only the Sri Lankan and the South Pacific subjects appeared to suffer a severe periodontal tissue breakdown, while the distribution of advanced disease was strikingly similar in six out of the eight samples, despite marked differences in oral hygiene conditions. Hence, the data failed to corroborate the traditional generalization that the prevalence and severity of periodontitis is markedly increased in African and Asian populations. On the other hand, data from the Third National Health and Nutrition Study (NHANES III; Albandar *et al*. 1999) which examined a large nationally representative, stratified, multistage probability sample in the USA clearly showed that the prevalence of deep pockets and advanced attachment loss was more pronounced in non-Hispanic black people and Hispanics than in non-Hispanic white subjects. This observation was consistent even when several alternative thresholds defining advanced disease were employed. Thus, current evidence suggests that the prevalence of severe periodontitis is not uniformly distributed among various races, ethnicities, or socioeconomic groups (Hobdell 2001).

Table 7-2 summarizes a number of prevalence studies of periodontal disease in elderly subjects. In five studies (Beck *et al*. 1990; Hunt *et al*. 1990; Gilbert & Heft 1992; Locker & Leake 1993; Weyant *et al*. 1993) data on attachment loss have been used to calculate extent and severity index scores (ESI) which appear to be relatively consistent between the surveys. It is evident that attachment loss of moderate magnitude was frequent and widespread in these subject samples; however, severe disease was again found to affect relatively limited proportions of the samples and generally only a limited proportion of teeth per subject. Similar findings were reported in more recent studies carried out in Iowa, USA (Levy *et al*. 2003), Pomerania, Germany (Mack *et al*. 2004), Japan (Hirotomi *et al*. 2002), and Sweden (Holm-Pedersen *et al*. 2006). Interestingly, a significant relationship was reported between advanced periodontitis and other co-morbidities in both institutionalized (Maupome *et al*. 2003) and home-dwelling elderly individuals (Ajwani *et al*. 2003).

The limitations of the findings from studies using the CPITN system were discussed above. However, a substantial part of the available information from the developing countries has been collected by the use of this index. An article providing a summary of almost 100 CPITN surveys from more than 50 countries performed over the period 1981–89 for the age

Table 7-1 Selected prevalence studies of periodontitis in adults

Authors/country	Sample/methodology	Findings
Löe *et al*. (1978) Norway/Sri Lanka	Two samples, one comprising 565 Norwegian students and academicians and the other 480 Sri Lankan tea laborers, of ages 16–30+ yrs; assessments of plaque, gingivitis, calculus, PD and AL at the mesial and facial aspects of all teeth	Norwegian group: excellent oral hygiene, negligible amounts of plaque and gingivitis, virtually no deep pockets and minimal attachment loss; mean AL at the age of 30 < 1 mm. Sri Lankan group: poor oral hygiene, abundant plaque and calculus, attachment loss present at the age of 16, increasing with age; mean AL at the age of 30 ≈ 3 mm, a substantial number of teeth with AL of > 10 mm
Baelum *et al*. (1988a) Kenya	A stratified random sample of 1131 subjects, 15–65 yrs; full-mouth assessments of tooth mobility, plaque, calculus, bleeding on probing (BoP), PD and AL	Plaque in 75–95% and calculus in 10–85% of all surfaces; PD ≥ 4 mm in < 20% of the sites; AL of ≥ 1 mm in 10–85% of the sites; the percentage of sites/subject with PD or AL of ≥ 4 mm or ≥ 7 mm conspicuously skewed
Yoneyama *et al*. (1988) Japan	A random sample of 319 subjects, 20–79 years old; full-mouth probing assessments of PD, AL, and gingival recession	0.2% of the sites in subjects 30–39 years and 1.2% of the sites in subjects 70–79 years had a PD of > 6 mm; AL > 5 mm affected 1% of the sites in the youngest group and 12.4% of the sites in the oldest group; skewed distribution of advanced AL; advanced disease more prevalent and widespread in older ages
Brown *et al*. (1990) USA	A sample of 15 132 subjects, stratified by geographic region, representing 100 million employed adults aged 18–64 years; probing assessments at mesial and buccal sites in one upper and one lower quadrant; mesial assessments performed from the buccal aspect of the teeth; assessments of gingivitis, PD, AL, and gingival recession	44% of all subjects had gingivitis at an average of 2.7 sites/subject and at < 6% of all sites assessed; pockets 4–6 mm were observed in 13.4% of the subjects at an average of 0.6 sites/person and at 1.3% of all sites assessed; corresponding figures for pockets ≥ 7 mm were 0.6%, 0.01 and 0.03%; AL ≥ 3 mm was prevalent in 44% of the subjects (increasing with age from 16% to 80%) affecting an average of 3.4 sites/subject; corresponding figures for AL ≥ 5 mm were 13% (2–35%) and 0.7 sites/subject
Salonen *et al*. (1991) Sweden	A random sample of 732 subjects, 20–80+ yrs, representing 0.8% of the population a southern geographic region; full-mouth radiographic examination; alveolar bone level expressed as a percentage of the root length (B/R ratio); B/R of ≥ 80% represents intact periodontal bone support	Age group of 20–29 yrs: 38% of the subjects had no sites with B/R < 80% and 8% of the subjects had five or more sites below this threshold; corresponding figures for the age group 50–59 years were 5% and 75%; after the age of 40, women displayed more favorable B/R ratios than men
Hugoson *et al*. (1998a) Sweden	Three random samples of 600, 597, and 584 subjects aged 20–70 years, examined in 1973, 1983, and 1993, respectively; full-mouth clinical and radiographic examination; based on clinical and radiographic findings, the subjects were classified according to severity of periodontal disease in five groups, where group 1 included subjects with close to faultless periodontal tissues and group 5 subjects with severe disease	Edentulism decreased over the 20-year period from 11% to 8% to 5%; percentage distribution of the subjects in the five groups in 1973, 1983, and 1993 respectively, was as follows: G1: 8%/23%/22%, G2: 41%/22%/38%, G3: 47%/41%/27%, G4: 2%/11%/10%, G5: 1%/2%/3%; the increase in the prevalence of subjects with severe disease was apparently due to increase of dentate subjects in older ages
Albandar *et al*. (1999) USA	A nationally representative, multi-stage probability sample comprising 9689 subjects, 30–90 years old (NHANES III study); probing assessments at mesial and buccal sites in one upper and one lower quadrant; mesial assessments performed from the buccal aspect of the teeth; assessments of gingivitis, PD, and location of the gingival margin in relation to the CEJ	Pockets ≥ 5 mm were found in 8.9% of all subjects (7.6% in non-Hispanic white subjects, 18.4% in non-Hispanic black subjects, and 14.4% in Mexican Americans); AL ≥ 5 mm occurred in 19.9% of all subjects (19.9% in non-Hispanic white subjects, 27.9% in non-Hispanic black subjects, and 28.34% in Mexican Americans)
Schürch & Lang (2004) Switzerland	A total of 1318 subjects, randomly selected based on community rosters in seven regions, aged 20–89 years; probing assessments of PD and AL at all present teeth; assessments of plaque and gingivitis at index teeth	7.1% of the subjects were edentulous; the mean number of present teeth in dentate subjects was 21.6; mean values of probing depth reached a plateau of 3 mm in the age of 49 years; however, but attachment levels increased dramatically after the age of 50 years and paralleled a marked loss of teeth
Susin *et al*. (2004a) Brazil	A sample of 853 dentate individuals, selected by multi-stage probability sampling, aged 30–103 years; full-mouth examination of AL at six sites per tooth	Moderate AL (≥ 5 mm) and advanced AL (≥ 7 mm) occurred in 70% and 52% of the subjects, affecting an average of 36% and 16% of their teeth, respectively; in comparison to 30–39-year-olds, 40–49-year-olds had three-fold increased risk for moderate and 7.4-fold increased risk for advanced AL; corresponding figures for ≥ 50 year olds were 5.9-fold and 25.4-fold, respectively

PD = probing depth; AL = attachment level; CEJ = cemento-enamel junction.

Table 7-2 Selected prevalence studies of periodontitis in elderly subjects

Authors/country	Sample/methodology	Findings
Baelum *et al*. (1988b) China	544 persons, aged 60+, from two urban and one rural area of Beijing area; assessments of plaque, calculus, gingivitis, loss of attachment, pocket depth, and tooth mobility	0–29% edentulous; mean number of teeth 6.9–23.9, depending on age and sex; ≈ 50% of all surfaces with plaque and calculus; 50% of all sites with AL of ≥ 4 mm, < 15% with PD ≥ 4 mm; conspicuously skewed percentage of sites/person with AL of ≥ 7 mm and PD ≥ 4 mm
Locker & Leake (1993) Canada	907 subjects, aged 50–75+ years, living independently in four communities; probing assessments at mesio-buccal and mid-buccal aspects of all teeth; mid-palatal and mesio-palatal probing assessments in upper molars; 23% of the subjects edentulous; calculation of extent and severity index (ESI) with AL threshold set at ≥ 2 mm; "severe disease": more than four sites with AL ≥ 5 mm and PD ≥ 4 mm at one or more of those sites	59% of the subjects with PD of ≥ 4 mm, 16% with ≥ 6 mm and 3% with ≥ 8 mm; 86% of the subjects with AL of ≥ 4 mm, 42% with ≥ 6 mm and 16% with ≥ 8 mm; 20% of the subjects with a mean AL of ≥ 4 mm; severe disease at 22% of the subjects; mean ESI: 77, 2.44
Beck *et al*. (1990) USA	690 community-dwelling adults, age 65+; probing assessments at mesio- and mid-buccal surfaces, all teeth; "advanced disease": four or more sites with AL of ≥ 5 mm and one or more of these sites with PD of ≥ 4 mm	Mean ESI in black people: 78, 4; in white people: 65, 3.1; advanced disease in 46% of the black people and 16% of the white people
Gilbert & Heft (1992) USA	671 dentate subjects, 65–97 years old, attending senior activity centers; probing assessments at mesial and buccal surfaces of one upper and one lower quadrant; questionnaire data; calculation of ESI	An average of 17.0 teeth/subject; 50.7% of the subjects with most severe mesial pocket of 4–6 mm and 3.4% with pockets ≥ 7 mm; 61.6% with most severe AL of 4.6 mm and 24.2% with AL of ≥ 7 mm; ESI increased with age: 84.8, 3.6 (65–69 years); 88.7, 3.8 (75–79 years); 91.2, 3.9 (85+ years)
Douglass *et al*. (1993) USA	1151 community-dwelling elders, age 70+ yrs; probing assessments at three or more sites/tooth, all teeth; 57% of the sample female, predominantly white (95%); 37.6% edentulous; mean no. of teeth present between 21.5 and 17.9, depending on age	85% of the subjects with BOP; 66% with 4–6 mm deep pockets affecting an average of 5.3 teeth/subject; 21% with pockets of > 6 mm affecting an average of 2.2 teeth; 39% with AL of 4–6 mm at 6.7 sites/subject and 56% AL of > 6 mm at 2.7 teeth/subject
Kiyak *et al*. (1993) USA	1063 residents in 31 nursing homes, 72–98 years old; visual inspection of the oral cavity; periodontal status assessed indirectly through registration of intraoral swelling or suppuration, sore or bleeding gums, increased tooth mobility, and poor oral hygiene	42% of the subjects with remaining natural teeth; 43% of those with sore or bleeding gums, 18% with significant tooth mobility, 6% with intraoral swelling or suppuration and 72% with poor oral hygiene
Weyant *et al*. (1993) USA	650 long-term residents of nursing home care units, mean age 72 years; probing assessments at mesial and buccal surfaces, all teeth; demographic, oral, and general health data recorded; sample predominantly male and white; calculation of ESI scores	42% of the sample edentulous; 60% of the subjects with PD of mm at an average of 5.8 sites/person; 3.7% with PD of ≥ 6 mm at < 1 site/person; overall mean mesial ESI: 74, 2.91
Bourgeois *et al*. (1999) France	603 non-institutionalized elderly, 65–74 years old; stratified sample with respect to gender, place of residence and socioeconomic group; periodontal conditions assessed by means of the CPITN	16.3% of the sample edentulous; 31.5% of the subjects had pockets ≥ 4 mm; 2.3% had pockets ≥ 6 mm
Pajukoski *et al*. (1999) Finland	181 hospitalized patients (mean age 81.9 yrs) and 254 home-living patients (mean age 76.9 yrs); periodontal conditions assessed by means of the CPITN	66.3% of the hospitalized and 42.1% of the non-hospitalized subjects were edentulous; 26% of both the hospitalized and the non-hospitalized subjects had pockets ≥ 6 mm
Levy *et al*. (2003) USA	From a sample of 449 community-dwelling elders, mean age 85 years, 342 (76%) were dentate and 236 were examined with respect to PD and AL at four sites per tooth in all present teeth	91% of the subjects had one or more site with ≥ 4 mm AL, 45% had one or more site with ≥ 6 mm AL, and 15% one or more site with ≥ 8 mm AL
Mack *et al*. (2004) Germany	1446 randomly selected subjects aged 60–79 years; per tooth; plaque calculus and BoP were assessed at half-mouth examination of PD and AL at four sites index teeth	16% of the 60–65 year olds and 30% of the 75–79 year olds were edentulous; among 70–79 year olds, the median BoP was 37.5% in men and 50% in women, the prevalence of PD ≥ 6 mm was 31.8% and 28.5%, and the prevalence of AL ≥ 5 mm 71.9% and 66.9%, respectively

PD = probing depth; AL = attachment level; BoP = bleeding on probing; CEJ = cemento-enamel junction; ESI = Extent and Severity Index; CPITN = Community Periodontal Index of Treatment Needs.

group of 35–44 years was published by Miyazaki *et al*. (1991b). These studies indicate a huge variation in the percentage of subjects with one or several deep (≥6 mm) pockets both between and within different geographic areas. Hence, the percentage of subjects with such pockets ranged between 1 and 74% in Africa (data from 17 surveys), 8 and 22% in North and South America (4 surveys), 2 and 36% in the eastern Mediterranean (6 surveys), 2 and 40% in Europe (38 surveys), 2 and 64% in South-East Asia, and between 1 and 22% in the western Pacific area (17 surveys). The average number of sextants per subject with ≥6 mm deep pockets varied also considerably and ranged between 0 and 2.1 in Africa, 0.1 and 0.4 in America, 0.1 and 0.6 in the eastern Mediterranean, 0.1 and 0.8 in Europe, 0.1 and 2.1 in South-East Asia and between 0 and 0.4 in the western Pacific area. However, it is difficult to assess the extent at which these values reflect true differences in the periodontal conditions given the methodological limitations of the CPITN system.

Periodontal disease in children and adolescents

The form of periodontal disease that affects the *primary* dentition, the condition formerly termed *prepubertal periodontitis*, has been reported to appear in both a generalized and a localized form (Page *et al*. 1983). Information about this disease was mainly provided by clinical case reports and no data related to the prevalence and the distribution of the disease in the general population are available. However, a few studies involving samples of children have provided limited data on the frequency with which deciduous teeth may be affected by loss of periodontal tissue support. The criteria used in these studies are by no means uniform, hence the prevalence data vary significantly. In an early study, Jamison (1963) examined by the use of the Periodontal Disease Index the "prevalence of destructive periodontal disease" (indicated by PDI scores >3) in a sample of 159 children in Michigan, USA and reported figures of 27% for 5–7-year-old children, 25% for 8–10-year-olds and 21% for 11–14-year-olds. Shlossman *et al*. (1986) used an attachment level value of ≥2 mm as a cut-off point and reported a prevalence of 7.7% in 5–9-year-olds and 6.1% in 10–14-year-olds in a sample of Pima Indians. Sweeney *et al*. (1987) examined radiographs obtained from 2264 children, aged 5–11 years, who were referred to a University Clinic for routine dental treatment and reported that a distinct radiographic bone loss was evident at one or more primary molars in 19 children (0.8%), 16 of whom were black, 2 Caucasian and 1 Asian.

In contrast, relatively uniform criteria have been used in epidemiologic studies of *aggressive periodontitis* in young subjects, the condition formerly termed *juvenile periodontitis* (JP), and particularly the *localized* form, formerly termed *localized juvenile periodontitis* (LJP). Typically, a two-stage approach has been adopted in these studies: first, bite-wing radiographs are used to screen for bone lesions adjacent to molars and incisors and then a clinical examination is performed to verify the diagnosis. As illustrated by the data in Table 7-3, the prevalence of localized aggressive periodontitis (LAP) varies in geographically and/or racially different populations. In Caucasians, the disease appears to affect females more frequently than males and the prevalence is low (approximately 0.1%). In other races, and in particular in black subjects, the disease is more prevalent, probably at levels over 1%, and the sex ratio appears to be reversed, since males are affected more frequently than females. Smoking and low socioeconomic status have been confirmed to be associated with aggressive periodontitis in various populations (Lopez *et al*. 2001; Susin & Albandar 2005; Levin *et al*. 2006).

Epidemiological studies of periodontal conditions in adolescents have been also carried out by means of the CPITN system. Miyazaki *et al*. (1991a) presented an overview of 103 CPITN surveys of subjects aged 15–19 years from over 60 countries. The most frequent finding in these groups was the presence of calculus which was much more prevalent in subjects from non-industrialized than industrialized countries. Probing pocket depths of 4–5 mm were present in about two thirds of the populations examined. However, deep pockets (≥6 mm) were relatively infrequent: score 4 quadrants were reported to occur in only ten of the examined populations (in 4 out of 9 examined American samples, 1 out of 16 African, 1 out of 10 eastern Mediterranean, 2 out of 35 European, 2 out of 15 South-East Asian and in none out of 18 western Pacific samples).

The progression pattern of periodontitis in a sample of 167 adolescents in the UK was studied in a 5-year longitudinal study by Clerehugh *et al*. (1990). In this study, 3% of the initially 14-year-olds had loss of attachment of ≥1 mm affecting <1% of their sites. However, at age 19 years, 77% showed a similar level of attachment loss and 31% of their sites were affected. Presence of subgingival calculus at baseline was significantly linked to disease progression. In a study involving a larger sample size in the US, Brown *et al*. (1996) studied a nationally representative sample comprising 14 013 adolescents with respect to the pattern of progression of the disease entity formerly termed *early-onset periodontitis*, i.e. the kind of periodontitis that occurs in individuals of a young age. Subjects were diagnosed at baseline as free from periodontitis, or suffering from localized aggressive periodontitis (LAP), generalized aggressive periodontitis (GAP), or incidental attachment loss (IAL). Of the individuals diagnosed with localized aggressive periodontitis at baseline, 62% continued to display localized periodontitis lesions 6 years later, but 35% developed a generalized disease pattern. Among the group initially diagnosed as suffering

Table 7-3 Selected prevalence studies of localized and generalized aggressive periodontitis (LAP and GAP) in adolescents and young adults

Authors/country	Sample/methodology	Findings
Saxén (1980) Finland	A random sample of 8096 16-year olds; radiographic and clinical criteria (bone loss adjacent to first molars without any obvious iatrogenic factors and presence of pathologic pockets)	Prevalence of LAP 0.1% (eight subjects, five of which were females)
Kronauer *et al*. (1986) Switzerland	A representative sample of 7604 16-year olds; two-step examination (radiographic detection of bone lesion on bite-wing radiographs, clinical verification of presence of pathological pockets)	Prevalence of LAP of 0.1%; 1 : 1 sex ratio
Saxby (1987) UK	A sample of 7266 schoolchildren; initial screening by probing assessments around incisors and first molars; LAP cases diagnosed definitively by full-mouth clinical and radiographic examination	Overall prevalence of LAP of 0.1%, 1 : 1 sex ratio; however, prevalence varied in different ethnic groups (0.02% in Caucasians, 0.2% in Asians and 0.8% in Afro-Caribbeans)
Neely (1992) USA	1038 schoolchildren 10–12 years old, volunteers in a dentifrice trial; three-stage examination including radiographic and clinical assessments; bite-wing radiographs screened for possible cases; bone loss measurements of the CEJ–bone crest distance of ≥ 2 mm used to identify probable cases; LAP diagnosed clinically as PD of ≥ 3 mm at one or more first permanent molars in absence of local irritants	117 possible and 103 probable cases identified in step 1 and 2, respectively; out of 99 probable cases contacted, 43 were examined clinically; two cases of LAP could be confirmed in stage 3, yielding a prevalence rate of 0.46%
Cogen *et al*. (1992) USA	4757 children, age < 15 yrs, from the pool of a children's hospital; retrospective radiographic examination of two sets of bite-wings; LAP diagnosed in case of arc-shaped alveolar bone loss in molars and/or incisors	White people: LAP prevalence 0.3%, female:male ratio 4 : 1; black people: LAP prevalence 1.5%, female : male ratio ≈ 1 : 1; among black LAP cases with available radiographs from earlier examinations, 85.7% showed evidence of bone loss in the mixed dentition and 71.4% in the deciduous dentition
Löe & Brown (1991) USA	National Survey of US children, multi-stage probability sampling representing 45 million schoolchildren; 40 694 subjects, 14–17 years old examined; probing assessments at mesial and buccal sites, all teeth; LAP: ≥ 1 first molar and ≥ 1 incisor or second molar and ≤ 2 cuspids or premolars with ≥ 3 mm AL; GAP: if LAP criteria not met and four or more teeth (of which two or more were second molars, cuspids or premolars) with ≥ 3 mm attachment loss (AL); incidental loss of attachment (ILA): if neither LAP nor GAP criteria met but one or more teeth with ≥ 3 mm AL; bivariate and multi-variate analysis	Population estimates: LAP 0.53%; GAP 0.13%; ILA 1.61%; altogether 2.27% representing almost 300 000 adolescents; black people at much higher risk for all forms of early-onset disease than whites; males more likely (4.3 : 1) to have GAP than females, after adjusting for other variables; black males 2.9 times as likely to have LAP than black females; white females more likely to have LAP than white males by the same odds
Bhat (1991) USA	A sample of 11 111 schoolchildren, 14–17 years old; probing assessments at mesial and buccal surfaces of all teeth; multi-stage cluster sampling stratified by age, sex, seven geographic regions, and rural or urban residence; not stratified by race or ethnicity	22% of the children with one or more site with AL of ≥ 2 mm, 0.72% of ≥ 4 mm and 0.04% of ≥ 6 mm; supra- and subgingival calculus in 34% and 23% of the children, respectively
van der Velden *et al*. (1989) The Netherlands	4565 subjects 14–17 years old examined; randomization among high school students; probing assessments at the mesio- and distofacial surfaces of first molars and incisors; one bacterial sample from the dorsum of the tongue and one subgingival plaque sample from the site with maximal attachment loss obtained from 103 out of the 230 subjects with AL and cultured for identification of *A. actinomycetemcomitans*	Overall, AL occurred in 5% of the sample and was more frequent in males; 16 subjects (0.3%) had one or more site with AL of 5–8 mm; female : male ratio in this group 1.3 : 1; *A. actinomycetemcomitans* was identified in 17% of the sampled subjects with AL
Lopez *et al*. (1991) Chile	2500 schoolchildren in Santiago (1318 male, 1182 female), 15–19 years of age; clinical and radiographic assessments; three stage screening: (1) clinical assessments of probing depth at incisors and molars, (2) children with two or more teeth with PD of ≥ 5.5 mm subjected to a limited radiographic	After screening, 27 subjects had a tentative diagnosis of LAP out of which eight were confirmed (seven female, one male); overall prevalence of LAP 0.32%, 95% confidence limits between 0.22% and 0.42%; LAP significantly more frequent in the low socioeconomic group

(*Continued*)

Table 7-3 *Continued*

Authors/country	Sample/methodology	Findings
	examination, and (3) children with alveolar bone loss of ≥ 2 mm invited for a full-mouth clinical and radiographic examination	
Ben Yehouda *et al*. (1991) Israel	1160 male Israeli army recruits, aged 18–19 years; panoramic radiography; juvenile periodontitis diagnosed on the basis of bone loss involving ≥ 30% of the root length adjacent to first molars or incisors	Ten recruits (0.86%, 95% CI 0.84–0.88%) had a bone loss pattern consistent with localized juvenile periodontitis
Melvin *et al*. (1991) USA	5013 military recruits, 17–26 years old; panoramic radiography followed by full-mouth clinical examination; diagnosis of JP if bone loss and attachment loss was greater at first molars and/or incisors than at other teeth	Overall prevalence of JP 0.76%, female : male ratio 1.1 : 1; prevalence in black subjects 2.1%, female: male ratio 0.52 : 1; prevalence in white subjects 0.09%, female : male ratio 4.3 : 1
Tinoco *et al*. (1997) Brazil	7843 schoolchildren, 12–19 years old; two-stage screening: (1) clinical assessment of PD at first molars, (2) children with one or more tooth with PF ≥ 5 mm examined further; LAP diagnosed if a person with no systemic disease presented with AL > 2 mm at one or more sites with radiographic evidence of bone loss and one or more infrabony defects at molars/incisors	119 subjects identified at initial screening; 25 confirmed cases of LAP; overall prevalence 0.3%; ethnic origins and gender ratios not reported
Lopez *et al*. (2001) Chile	A random sample of 9162 high school students, 12–21 years old; probing assessments of AL at six sites per tooth at all incisors and molars	The prevalence of AL of ≥ 1 mm was 69.2%, of ≥ 2 mm was 16% and of ≥ 3 mm was 4.5%. Al was associated with higher age, female gender, poor oral hygiene, and lower socioeconomic status
Levin *et al*. (2006) Israel	642 army recruits (87.5% men), 18–30 years old (mean 19.6); radiographic and clinical examination of first molars and incisors	AP prevalence was 5.9% (4.3% LAP, 1.6% GAP); current smoking and north African origin were significantly related to AP

Terms used in all but Levin ***et al.*** (2006): "localized juvenile periodontitis" instead of "localized aggressive periodontitis" (LAP), and "generalized juvenile periodontitis" instead of "generalized aggressive periodontitis" (GAP).
PD = probing depth; AL = attachment level; CEJ = cemento-enamel junction; AP = aggressive periodontitis.

from IAL, 28% developed localized or generalized aggressive periodontitis, while 30% were reclassified in the no attachment loss group. Molars and incisors were the teeth most often affected in all three affected groups. Thus, the study indicated that these three forms of periodontitis may progress in a similar fashion, and that certain cases of localized, aggressive disease may develop into generalized aggressive periodontitis.

The possibility that *localized aggressive periodontitis* and *prepubertal periodontitis* are associated conditions, i.e. that the former is a development of the latter, has also attracted attention. In a pilot study, Sjödin *et al*. (1989) retrospectively examined radiographs of the primary dentition of 17 subjects with LAP and reported that 16 of the subjects showed a CEJ–bone crest distance of ≥3 mm in at least one tooth site of their deciduous dentition. The same research group (Sjödin & Matsson 1992) examined the CEJ–bone crest distance in radiographs from 128 periodontally healthy children aged 7–9 years, in order to define a threshold value that, if exceeded, would entail periodontal pathology around the deciduous teeth with high probability. Having set this threshold value to 2 mm, Sjödin *et al*. (1993) examined radiographs of the deciduous dentition retrospectively from 118 patients with aggressive periodontitis and 168 age- and gender-matched periodontally healthy controls. The patients were divided in two groups, one comprising subjects with only one affected site (45 subjects) and another (73 subjects) including subjects with 2–15 sites with bone loss in their permanent dentition. It was found that 52% of the subjects in the latter group, 20% of the subjects in the former group and only 5% of the controls exhibited at least one site with bone loss in their primary dentition. The authors concluded that, at least in some young subjects with aggressive periodontitis, the onset of the disease may be manifested in the primary dentition. Similar results were reported by Cogen *et al*. (1992), from a study in the US. Among systemically healthy young black people with aggressive periodontitis and available radiographs of the primary dentition, 71% showed alveolar bone loss adjacent to one or several primary teeth. Finally, an interesting recent radiographic study of the mixed dentition in Australian children aged 5–12 years was carried out by Darby *et al*. (2005). These authors investigated the prevalence of alveolar bone loss around first permanent molars, and first and second deciduous molars. Based on

radiographs of 542 children, 13.0% were found to display definite bone loss, i.e. bone levels >3.0 mm from the CEJ. Half of all lesions with definite bone loss occurred at the second deciduous molars and, in the vast majority, at distal tooth surfaces. In other words, this study showed that the tooth surface of the deciduous dentition most frequently affected by bone loss was the one in close proximity with the most frequent localization of aggressive periodontitis in young age groups, i.e. the mesial surface of the first permanent molar.

Periodontitis and tooth loss

Tooth loss may be the ultimate consequence of destructive periodontal disease. Teeth lost due to the sequels of the disease are obviously not amenable to registration in epidemiological surveys and may, hence, lead to an underestimation of the prevalence and the severity of the disease. The well established epidemiologic concept of *selection bias* (also referred to as the *healthy survivor effect*, indicating that the comparatively healthier subjects will present for an examination while the more severely affected may refuse participation or fail to present because of the morbidity itself) is in this context applicable on the individual tooth level, since the severely affected teeth may have already been extracted/lost. Aspects related to tooth loss on a population basis have been addressed in numerous publications. Important questions that were analyzed included: (1) the relative contribution of periodontitis as a reason underlying tooth extractions in subjects retaining a natural dentition (Cahen *et al*. 1985; Bailit *et al*. 1987; Brown *et al*. 1989; Corbet & Davies 1991; Heft & Gilbert 1991; Klock & Haugejorden 1991; MacDonald Jankowski 1991; Stephens *et al*. 1991; Reich & Hiller 1993; McCaul *et al*. 2001); (2) its role in cases of full-mouth extractions, the so-called *total tooth clearance* (Eklund & Burt 1994; Takala *et al*. 1994), and (3) risk factors for tooth loss (Burt *et al*. 1990; Phipps *et al*. 1991; Krall *et al*. 1994; Drake *et al*. 1995; Hunt *et al*. 1995; Warren *et al*. 2002; Copeland *et al*. 2004; Neely *et al*. 2005; Susin *et al*. 2005b).

Typically, surveys addressing the first topic have utilized questionnaire data obtained from general practitioners instructed to document the reasons for which teeth were extracted over a certain time period. The results indicate that the reason underlying the vast majority of extractions in ages up to 40–45 years is dental caries. However, in older age cohorts, periodontal disease becomes about equally responsible for tooth loss. Overall, periodontitis is thought to account for 30–35% of all tooth extractions while caries and its sequelae for up to 50%. In addition, caries appears to be the principal reason for extractions in cases of total tooth clearance. Finally, identified risk factors for tooth loss include smoking, perceived poor dental health, sociobehavioral traits, and poor periodontal status.

Obviously, it is not feasible to "translate" tooth loss data into prevalence figures of periodontal disease. An evaluation, however, of the periodontal status on a population level, and in particular in older age cohorts, must weigh in information provided by tooth loss data, otherwise underestimation of the occurrence and the sequels of the disease is inevitable (Gilbert *et al*. 2005).

Risk factors for periodontitis

Introduction – definitions

There is an abundance of both empirical evidence and substantial theoretical justification for accepting the widespread belief that many diseases have more than one cause, i.e. that they are of *multi-factorial etiology* (Kleinbaum *et al.* 1982). Consequently, in any particular instance when a *causal relationship* is investigated, the specificity of the relation between exposure to an etiologic agent and effect, i.e. the *necessity* or the *sufficiency* of the condition, may be challenged. In the case of most infectious diseases for example, it is known that the presence of the microbial agent (which we define as the necessary condition) is not always accompanied by signs or symptoms characteristic of that disorder. Thus, the agent itself is not sufficient to cause any pathologic occurrence; rather, the disease development may be dependent on multiple, diverse additional factors, including specific host responses, toxic exposures, nutritional deficiencies, emotional stress, and the complex impact of social influences. In non-infectious diseases (except for genetic abnormalities), there is usually no factor known to be present in every single case of the disease. For example, smoking is not necessary for the development of lung cancer, and no degree of coronary atherosclerosis is a necessary condition for myocardial infarction.

The *causal inference*, i.e. the procedure of drawing conclusions related to the cause(s) of a disease, is a particularly complex issue in epidemiological research. In the 1970s, Hill (1971) formalized the criteria that have to be fulfilled in order to accept a causal relation. These included:

1. *Strength of the association.* The stronger the association is between the potential (*putative*) risk factor and disease presence, the more likely it is that the anticipated causal relation is valid.
2. *Dose–response effect.* An observation that the frequency of the disease increases with the dose or level of exposure to a certain factor supports a causal interpretation.
3. *Temporal consistency.* It is important to establish that the exposure to the anticipated causative factor occurred prior to the onset of the disease. This may be difficult in case of diseases with long latent periods or factors that change over time.

4. *Consistency of the findings.* If several studies investigating a given relationship generate similar results, the causal interpretation is strengthened.
5. *Biological plausibility.* It is advantageous if the anticipated relationship makes sense in the context of current biological knowledge. However, it must be realized that the less that is known about the etiology of a given disease, the more difficult it becomes to satisfy this particular criterion.
6. *Specificity of the association.* If the factor under investigation is found to be associated with only one disease, or if the disease is found to be associated with only one factor among a multitude of factors tested, the causal relation is strengthened. However, this criterion can by no means be used to reject a causal relation, since many factors have multiple effects and most diseases have multiple causes.

It is important to realize that the criteria described above are meant as guidelines when a causal inference is established. None of them, however, is either necessary or sufficient for a causal interpretation. Strict adherence to any of them without concomitant consideration of the other may result in incorrect conclusions.

A distinction has to be drawn between a *causal* factor, assessed as above, and a *risk* factor. In a broad sense, the term risk factor may indicate an aspect of personal behavior or life-style, an environmental exposure, or an inborn or inherited characteristic which, on the basis of epidemiologic evidence, is known to be associated with disease-related conditions. Such an attribute or exposure may be associated with an increased probability of occurrence of a particular disease without necessarily being a causal factor. A risk factor may be modified by intervention, thereby reducing the likelihood that the particular disease will occur.

The principles of the *risk assessment process* were discussed by Beck (1994) and should consist of the following four steps:

1. The *identification* of one or several individual factors that appear to be associated with the disease.
2. In case of multiple factors, a *multi-variate risk assessment model* must be developed that discloses which combination of factors does most effectively discriminate between health and disease.
3. The *assessment* step, in which new populations are screened for this particular combination of factors, with a subsequent comparison of the level of the disease assessed with the one predicted by the model.
4. The *targeting* step, in which exposure to the identified factors is modified by prevention or intervention and the effectiveness of the approach in suppressing the *incidence* of the disease is evaluated.

Thus, according to this process, *potential* or *putative risk factors* (often also referred to as *risk indicators*) are first identified and thereafter tested until their significance as *true risk factors* is proven.

Finally, distinction must be made between *prognostic* factors (or *disease predictors*), i.e. characteristics related to the progression of *pre-existing* disease and *true risk factors*, i.e. exposures related to the *onset* of the disease. For example, it is established in longitudinal studies of periodontal disease (Papapanou *et al*. 1989), that the amount of alveolar bone loss or the number of teeth present at baseline may be used to predict further progression of the disease. These variables are, in fact, alternative measures of the disease itself and express the level of susceptibility of a given subject to periodontal disease. Although they may be excellent predictors for further disease progression, they clearly cannot be considered as risk factors.

There are several ways to study the relation between exposure to a certain factor and the occurrence of a particular disease, as required under point 1. One of these is described in Fig. 7-3 which illustrates a hypothetical situation where exposure to the potential risk factor Z is studied in a cross-sectional

	Exposed	Non-exposed	
Diseased	155	25	180
Healthy	340	480	820
	495	505	1000

Fig. 7-3 Contingency table describing the distribution of a group of 1000 subjects according to exposure to a particular factor and disease status.

study including a sample of 1000 subjects, 180 of whom are found to suffer from the disease D ("diseased") while 820 are disease-free ("healthy"). In this particular setting, it was observed that 155 out of the 180 diseased subjects had been exposed to factor Z but this was also the case for 340 non-diseased subjects. The association between exposure and disease may, in this example, be expressed by the *odds ratio* (OR), which is the ratio of exposure among the diseased and the healthy. For the data in Fig. 7-3, the odds ratio is calculated as (155/25) over (340/480) = (155×480) / (340×25) = 8.75. This indicates that the diseased were 8.75 times more likely to have been exposed to factor Z than the healthy. Note that the OR is frequently misinterpreted to describe the risk of an exposed subject to develop disease, something that is correctly assessed in a prospective cohort rather than a cross-sectional study and is described by the *relative risk*. In the example of Fig. 7-3, if a sample of 495 subjects exposed to factor Z and 505 subjects not exposed to factor Z are prospectively followed over a given time period, and 155 among the exposed and 25 among the non-exposed develop disease D over this period, then the relative risk is calculated as (155/495) over (25/505) = 6.4. In other words, an individual exposed to factor Z is 6.4 times more likely to develop disease D than a non-exposed subject.

In a study of the association between exposure to a risk factor and the occurrence of disease, *confounding* can occur when an additional factor associated with the disease is unevenly distributed among the groups under investigation. For instance, in a study between radon exposure and a form of cancer, smoking may act as a confounder, if the smoking habits of the subjects exposed to radon are different from those of the subjects not exposed.

There are various ways to assess simultaneously the effect of several putative risk factors identified in step 1 and generate the multi-variate model required for step 2. For example, the association between exposure and disease may, for reasons of simplicity, have the form of the following linear equation:

$$y = a + b_1x_1 + b_2x_2 + b_3x_3 + \ldots b_nx_n$$

where y represents occurrence or severity of the disease, a is the intercept (a constant value), x_1, x_2 , . . . x_n describe the different exposures (putative risk factors), and b_1, b_2, . . . b_n are *estimates* defining the relative importance of each individual exposure as determinant of disease, after taking all other factors into account. Such an approach may identify factors with statistically and biologically significant effect and may eliminate the effect of confounders.

In the third step (assessment step), a new population sample that it is independent of the one used in the construction of the multi-variate model is screened for occurrence of disease and presence of the relevant factors included in the multi-variate model of step 2. Alternatively, in the case of a prospective cohort study, exposure to the relevant factors is assessed among the subjects of the new sample, and disease incidence, i.e. the number of new cases of disease, is determined over a time period after a longitudinal follow-up of the subjects. Subsequently, disease predicted by means of the model is compared to the actually observed disease, and the *external validity* of the model (i.e., the "behavior" or "fitness" of the model in the new population) is evaluated.

Lastly, during the targeting step, aspects of causality or risk are verified if disease occurrence is suppressed when exposure is impeded. Ideally, such studies should be designed as randomized clinical trials, in which treatment is randomly assigned in one of two groups and the effectiveness of the intervention is assessed in direct comparison to outcomes in an untreated, control group. Additionally, an evaluation of the particular preventive/therapeutic strategy from a "cost–benefit" point of view is also facilitated in such studies.

In the context of periodontitis, it should be realized that few of the putative risk factors for disease development have been subjected to the scrutiny of all four steps. In fact, risk assessment studies in dental research in general have been frequently confined to the first two steps. Numerous cross-sectional studies identifying potential factors are available, but a relatively limited number of longitudinal studies has involved a multi-variate approach in the identification of exposures of interest while simultaneously controlling for the effect of possible confounders. Intervention studies in the form of randomized clinical trials are sparse. In the following text, the issue of risk factors is addressed according to the principles described above. Results from cross-sectional studies are considered to provide evidence for putative risk factors that may be further enhanced if corroborated by longitudinal studies involving multi-variate techniques, or prospective intervention studies. As reviewed by Borrell and Papapanou (2005), distinction is also made between putative factors that are not amenable to intervention (non-modifiable background factors) and modifiable factors (environmental, acquired, and behavioral).

Non-modifiable background factors

Age

The relationship between age and periodontitis is complex. Early evidence demonstrates that both the prevalence and severity of periodontitis increase with older age, suggesting that age may be a marker for periodontal tissue support loss (van der Velden 1984, 1991; Johnson 1989; Johnson *et al*. 1989; Burt 1994). However, the concept of periodontitis as an inevitable consequence of ageing has been challenged over the years and the alleged 'age effect' likely represents the cumulative effect of prolonged exposure to true risk factors (Papapanou *et al*. 1991). Notably, the association between age and periodontitis appears to be different for pocket depth and clinical

attachment loss. While there is a pronounced effect of increasing attachment loss with age, the effect on pocket depth appears to be minimal (Albandar 2002a,b). Interestingly, the effect of age on attachment loss is reduced after adjustment for covariates, such as oral hygiene levels or access to dental care services (Albandar 2002a). However, studies have often failed to adjust for important covariates such as presence of systemic diseases, consumption of multiple medications, and co-morbidities related to nutritional disturbances in the older population. It is therefore difficult to rule out the possibility of an age-related, as opposed to an age-dependent, increased susceptibility to periodontitis in older people.

Gender

There is no established, inherent difference between men and women in their susceptibility to periodontitis, although men have been shown to exhibit worse periodontal health than women in multiple studies from different populations (Okamoto *et al*. 1988; Brown *et al*. 1989; Hugoson *et al*. 1992; Albandar 2002a; Susin *et al*. 2004a). This difference has been traditionally considered to be a reflection of better oral hygiene practices (Hugoson *et al*. 1998b; Christensen *et al*. 2003) and/or increased utilization of oral health care services among women (Yu *et al*. 2001; Dunlop *et al*. 2002; Roberts-Thomson & Stewart 2003). On the other hand, periodontitis is a bacterial infection determined to a large extent by the host immunoinflammatory response to the bacterial challenge. Although gender-specific differences in these responses have not been unequivocally demonstrated, it is biologically plausible that such differences may in fact exist.

Race/ethnicity

Differences in the prevalence of periodontitis between countries and across continents have been demonstrated (Baelum *et al*. 1996; Albandar 2002a), but no consistent patterns across racial/ethnic groups have been documented when covariates such as age and oral hygiene are accounted for (Burt & Eklund 1999). National surveys in the USA consistently show a racial/ethnic differential pattern in the prevalence of periodontitis, with African Americans exhibiting the highest prevalence of periodontitis followed by Mexican Americans and non-Hispanic white people, and these findings are fairly consistent regardless of the case-definition used (Albandar *et al*. 1999; Arbes *et al*. 2001; Borrell *et al*. 2002; Hyman & Reid 2003). However, race/ethnicity is usually a social construct that determines an array of opportunities related to access, status and resources (Williams 1997, 1999). As a result, race/ethnicity and socioeconomic status (SES) are strongly intertwined, suggesting that the observed racial/ethnic effect may be partially attributed to confounding by SES due to the unequal meaning of SES indicators across racial/ethnic groups (Williams 1996; Kaufman *et al*. 1997; Krieger *et al*. 1997; Lynch & Kaplan 2000). Corroborating this point, a recent study found that African Americans demonstrated a lower benefit from education and income on periodontal health status than their Mexican American and white peers (Borrell *et al*. 2004). Such findings confirm that socioeconomic indicators across racial/ethnic groups are not commensurable but, probably, reflect the broad implications of historic unequal opportunities among certain racial groups.

Gene polymorphisms

Evidence from classical twin studies (Michalowicz *et al*. 1991) suggests that genetic determinants are significant modifiers of the periodontitis phenotype (Michalowicz 1994; Hart & Kornman 1997; Schenkein 2002) but the role of single nucleotide polymorphisms remains unclear. After the seminal work by Kornman *et al*. (1997) reporting an association of a composite genotype based on specific polymorphisms in the interleukin-1 gene cluster with severe periodontitis in non-smokers, there has been an exponential increase in publications that examined a plethora of gene polymorphisms as severity markers of periodontitis. These include additional investigations of the particular IL-1 gene polymorphism in cross-sectional and case–control settings (Gore *et al*. 1998; Diehl *et al*. 1999; Armitage *et al*. 2000; Mark *et al*. 2000; McDevitt *et al*. 2000; Parkhill *et al*. 2000; Socransky *et al*. 2000; Walker *et al*. 2000; Hodge *et al*. 2001; Laine *et al*. 2001; Papapanou *et al*. 2001; Caffesse *et al*. 2002; Meisel *et al*. 2002, 2003, 2004; Anusaksathien *et al*. 2003; Gonzales *et al*. 2003; Guzman *et al*. 2003; Sakellari *et al*. 2003; Li *et al*. 2004; Quappe *et al*. 2004; Scapoli *et al*. 2005), as well as longitudinal studies (Ehmke *et al*. 1999; De Sanctis & Zucchelli 2000; Lang *et al*. 2000; Cullinan *et al*. 2001; Christgau *et al*. 2003; Jepsen *et al*. 2003). Similar work was quickly expanded to include the study of other gene polymorphisms such as the interleukin-1 receptor antagonist (Tai *et al*. 2002); interleukin-6 (Anusaksathien *et al*. 2003; Trevilatto *et al*. 2003); interleukin-10 (Kinane *et al*. 1999; Yamazaki *et al*. 2001; Gonzales *et al*. 2002; Berglundh *et al*. 2003; Scarel-Caminaga *et al*. 2004); interleukin-4 (Michel *et al*. 2001; Scarel-Caminaga *et al*. 2003; Gonzales *et al*. 2004; Pontes *et al*. 2004); interleukin-2 (Scarel-Caminaga *et al*. 2002); tumor necrosis factor (Galbraith *et al*. 1998; Endo *et al*. 2001; Shapira *et al*. 2001; Craandijk *et al*. 2002; Fassmann *et al*. 2003; Soga *et al*. 2003; Perez *et al*. 2004; Shimada *et al*. 2004); transforming growth factor-beta 1 (TGF-beta 1) (Holla *et al*. 2002b); Fc receptor of immunoglobulin G (Kobayashi *et al*. 1997, 2000a,b, 2001; Sugita *et al*. 1999, 2001; Meisel *et al*. 2001; Chung *et al*. 2003; Loos *et al*. 2003; Yasuda *et al*. 2003; Yamamoto *et al*. 2004; Wolf *et al*. 2006); CD14 receptor (Holla *et al*. 2002a); vitamin D

receptor (Hennig *et a*l. 1999; Tachi *et al*. 2003; de Brito Junior *et al*. 2004; Park *et al*. 2006); N-acetyltransferase 2 (Meisel *et al*. 2000; Kocher *et al.* 2002); and matrix metalloproteinase 1 and 3 (Holla *et al*. 2004; Itagaki *et al*. 2004).

Typically, the majority of the cross-sectional studies above report positive associations between the investigated polymorphisms and the extent or the severity of periodontitis. The results, however, are not unequivocal, as the strength of the reported associations is not uniformly consistent across populations, the frequency of occurrence of these polymorphisms appears to vary extensively between ethnic groups, the subject samples involved are generally of limited size, the definitions of the outcome variable (periodontitis) vary considerably, and adequate adjustments for other important covariates and risk factors have frequently not been carried out. Importantly, there appear to be differences in the impact of these polymorphisms on early-onset versus adult forms of periodontitis. For example, in the case of IL-1 polymorphisms, while it is the rare allele (allele 2) that has been linked with severe disease in adults, it is allele 1 that has been found to be more prevalent in subjects with early-onset periodontitis (Diehl *et al*. 1999; Parkhill *et al*. 2000).

The relatively few longitudinal studies that have studied specific gene polymorphisms as exposures are similarly conflicting. Ehmke *et al*. (1999) reported no bearing of the IL-1 gene polymorphism on the prognosis of periodontal disease progression following non-surgical periodontal therapy. Jepsen *et al*. (2003) failed to provide evidence that the IL-1 risk genotype was associated with higher gingival crevicular fluid (GCF) volume and percentage bleeding on probing (BoP) during the development of experimental gingivitis. In contrast, Lang *et al*. (2000) concluded that IL-1 genotype-positive subjects have a genetically determined hyper-inflammatory response that is expressed clinically in the periodontal tissues as increased prevalence and incidence of bleeding on probing during maintenance. Three treatment studies examined the impact of this particular polymorphism in regenerative therapy: De Sanctis and Zucchelli (2000) reported that the IL-1 positive genotype was associated with inferior long-term outcome of regenerative therapy of intrabony defects. In contrast, Christgau *et al*. (2003) and Weiss *et al*. (2004) failed to document such an association in similar studies of the regenerative potential of such defects. Finally, in a 5-year prospective study of 295 subjects, Cullinan *et al*. (2001) reported an interaction between the positive genotype, age, smoking and colonization by *Porphyromonas gingivalis* and concluded that the positive genotype is a contributory but non-essential factor for the progression of periodontal disease.

In conclusion, there is insufficient epidemiologic evidence that convincingly establishes any of the above polymorphisms as true risk factors for periodontitis.

Environmental, acquired, and behavioral factors

Specific microbiota

The microbial etiology of gingivitis (Löe *et al.* 1965; Theilade *et al*. 1966) and periodontitis (Lindhe *et al*. 1973) has been established for several decades. Yet, epidemiologic studies that systematically investigated the role of specific microbiota as risk factors for periodontitis were undertaken fairly recently. In a classic paper, Haffajee and Socransky (1994) adapted Koch's postulates to be used in the identification of periodontal pathogens and proposed the following criteria: (1) association, i.e. elevated odds ratios in disease; (2) elimination, i.e. conversion of disease to health when bacteria are suppressed; (3) development of a host response; (4) presence of virulence factors; (5) evidence from animal studies corroborating the observations in humans; and (6) support from risk assessment studies. Based on the above criteria, the consensus report of the 1996 World Workshop in Periodontics identified three species, *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Bacteroides forsythus*, as causative factors for periodontitis (since then, two of the three causative species have been renamed: *A. actinomytemcomitans* to *Aggregatibacter actinomycetemcomitans* (Norskov-Lauritsen & Kilian 2006) and *B. forsythus* to *Tanerella forsythia* (Sakamoto *et al*. 2002; Maiden *et al*. 2003)). However, given that only approximately 50% of the bacteria of the oral cavity are currently recognized (Paster *et al*. 2001), it is clear that these three species cannot be considered to be the only causative pathogens, but are rather the ones for which sufficient data have accumulated.

Over the last decade, interesting data have emerged on the prevalence of these causative bacteria in different populations, in states of both periodontal health and disease. Studies performed in children (Tanner *et al*. 2002; Yang *et al*. 2002) that analyzed plaque from the gingival crevice, tooth surface and the dorsum of the tongue revealed that sizeable proportions of subjects harbored *P. gingivalis*, *T. forsythia*, and *A. actinomycetemcomitans* despite absence of overt gingival inflammation. A comparably high carrier state was documented in studies that sampled infants, children, adolescents and adults with good clinical periodontal status (McClellan *et al*. 1996; Könönen 1993; Kamma *et al*. 2000; Lamell *et al*. 2000). Thus, contrary to the conclusions of earlier, culture-based studies that these bacteria occur infrequently in periodontally healthy oral cavities and behave as exogenous pathogens, the above studies that have employed molecular techniques for bacterial identification demonstrate the contrary. However, both the prevalence of and the level of colonization by these pathogens have been shown to vary significantly between populations of different racial or geographic origin (Sanz *et al*. 2000; Ali *et al*. 1994; Haffajee *et al*. 2004; Lopez *et al*. 2004).

Several epidemiologic studies have examined the prevalence of the established periodontal pathogens and its relation to clinical periodontal status in population samples from both developed and developing countries. Griffen *et al*. (1998) examined a convenience sample recruited from a university clinic, and reported that 79% of the diseased and 25% of the healthy subjects were positive for *P. gingivalis*. Interestingly, the prevalence of *P. gingivalis* in the periodontally healthy group varied substantially with race/ethnicity, as it occurred in 22% of white people, 53% of African Americans, and 60% of Asian Americans. In a case–control study of periodontitis patients and age- and gender-matched controls with no or only minimal attachment loss in Sweden, Papapanou *et al*. (2000) reported a high prevalence of *P. gingivalis*, *A. actinomycetemcomitans*, *T. forsythia*, and *Treponema denticola* in periodontitis patients (95%, 83%, 97%, and 93%, respectively), but also similarly high prevalence rates among control subjects (82%, 90%, 82%, and 94%). However, in a quantitative analysis of bacterial load, substantial differences in colonization at high levels (i.e. at an average count $\geq 10^5$ bacterial cells/plaque sample) were observed between patients and controls for three of the four bacteria: 19% versus 3% for *P. gingivalis*, 54% vs. 12% for *T. forsythia*, and 46% vs. 19% for *Tr. denticola*. In contrast, corresponding percentages were similar for *A. actinomycetemcomitans* (1% in both cases and controls). Substantially different prevalence data were reported in a study of blue- and white-collar University employees in Australia (Hamlet *et al*. 2001). These authors detected *A. actinomycetemcomitans* in 23% and *P. gingivalis* in 15% of the subjects.

A number of studies investigated the epidemiology of periodontal pathogens in Asian populations. Timmerman *et al*. (1998) examined a sample of adolescents in rural Indonesia, and detected *P. gingivalis* in 87% and *A. actinomycetemcomitans* in 57% of the subjects. Mombelli *et al*. (1998) examined young factory workers in China and detected *A. actinomycetemcomitans* in 62% and *P. gingivalis* in 55% of the subjects. In contrast, an almost ubiquitous presence of *P. gingivalis* and *T. forsythia* was reported in rural subject samples in China (Papapanou *et al*. 1997) and Thailand (Papapanou *et al*. 2002), while *A. actinomycetemcomitans* was detected in 83% and 93% of the subjects in the Chinese and Thai samples, respectively. Despite this high prevalence, a quantitative analysis of bacterial load correlated well with periodontal status in both studies. For example, a discriminant analysis performed on the data from the Thai study (Papapanou *et al*. 2002) identified threshold levels of average bacterial load which, when exceeded, conferred increased odds for presence of three or more sites with pocket depth ≥5 mm. For three species (*P. gingivalis*, *T. forsythia*, and *Tr. denticola*), colonization above these calculated thresholds resulted in statistically significant, elevated odds for periodontitis. In addition, an analysis of the association between colonization at high levels by the "red complex" bacteria (Socransky *et al*. 1998) and specific periodontal conditions, defined in this particular study by the presence of three or more sites with pocket depth ≥5 mm and by two different levels of extent of periodontal tissue loss (≥10 and ≥30 sites with ≥5 mm attachment loss, respectively), revealed statistically significant odds ratios ranging between 3.7 and 4.3 for the "red complex" bacteria and all three disease definitions. Similar cross-sectional associations of statistically significant odd ratios for severe periodontitis conferred by specific bacteria have been also observed in several other studies involving subject samples from the western world (Grossi *et al*. 1994, 1995; Alpagot *et al*. 1996, Craig *et al*. 2001).

Importantly, the association between high levels of colonization by specific periodontal pathogens and the progression of periodontal disease has been corroborated by longitudinal data in untreated populations. For example, in the study by Papapanou *et al*. (1997), a discriminant analysis based on quantitative assessments of subgingival bacterial load classified correctly the substantial majority of the subjects with progression of periodontitis over a preceding 10-year period. Indeed, bacterial profiles classified correctly 75% of the subjects with ten or more sites with longitudinal attachment loss of ≥3 mm, and 85% of those that remained stable over the observation period. In a 7-year follow-up study of Indonesian adolescents (Timmerman *et al*. 2000, 2001), and in a subsequent 15-year follow-up of the same cohort (Van der Velden *et al*. 2006), it was shown that subgingival presence of *A. actinomycetemcomitans* was associated with disease progression, defined as presence of longitudinal attachment loss of ≥2 mm. In a follow-up of 2–5 years' duration, Machtei *et al*. (1999) reported that subjects colonized by *T. forsythia* at baseline exhibited greater alveolar bone loss, a larger proportion of "loser" sites, and twice as high longitudinal tooth loss than non-colonized subjects. In a 3-year study, Hamlet *et al*. (2004) reported odds ratios of 8.2 for attachment loss in adolescents with persistent colonization with *T. forsythensis*.

Collectively, data generated in the past 15 years have enhanced our knowledge on the role of specific periodontal bacteria as risk factors for periodontitis (Table 7-4), but have also clarified the significance of bacterial load rather than that of mere positive colonization in conferring risk for disease progression. Obviously, the "targeting" criterion of the risk assessment process has been abundantly fulfilled in the case of microbial risk factors. Indeed, a wide body of literature data, recently compiled in systematic reviews, has demonstrated that an antimicrobial approach, including removal of subgingival plaque with or without adjunctive antiseptics or antibiotics followed by adequate maintenance care, is the single most successful and consistent strategy in the treatment of periodontitis (Heitz-Mayfield *et al*. 2002, Herrera *et al*. 2002; Hallmon & Rees 2003).

Table 7-4 Selected studies using bacteria as exposures of significance for periodontitis. **(L)** indicates a longitudinal study

Authors/country	Sample/methodology	Findings
Beck *et al*. (1990) USA	690 community-dwelling adults, age 65+; probing assessments at mesio- and mid-buccal surfaces, all teeth; logistic regression for advanced AL and deep pocketing; "advanced disease": four or more sites with AL of ≥ 5 mm and one or more of these sites with PD of ≥ 4 mm	Black people: 78% of their sites with attachment loss, mean AL on these sites 4 mm; white people: 65%, 3.1 mm; Odds ratios in black people: tobacco use 2.9; *Porphyromonas gingivalis* > 2% 2.4; *Pr. intermedia* > 2% 1.9; last dental visit > 3 years 2.3; bleeding gums 3.9; in white people: tobacco use 6.2; presence of *P. gingivalis* (+) 2.4; no dental visits for > 3 years plus BANA (+) 16.8
Haffajee *et al*. (1991b) USA	38 subjects, 14–71 years old, with prior evidence of attachment loss; 2-month follow-up; probing assessments at six sites/tooth, all teeth; 28 subgingival samples per subject at baseline, DNA-probe analysis with respect to 14 bacterial species; progression threshold: ≥ 3 mm of LAL; the mean percentage of the total cultivable microbiota was averaged across active and inactive sites; odds ratios computed at different thresholds for each species	Significant odds ratios for new disease: *P. gingivalis* 5.6, *Campylobacter rectus* 3.8, *Veillonella parvula* 0.16, and *Capnocytophaga ochracea* 0.08; discriminant analysis using the significantly related species was useful in predicting subjects at risk for new attachment loss
Grossi *et al*. (1994) USA	Random sample of 1426 subjects, aged 25–74 years, in a metropolitan community; full-mouth probing assessments; multi-variate analysis of risk indicators for attachment loss. Exposures: (1) clinical: supragingival plaque, gingival bleeding, subgingival calculus, PD, CAL; (2) microbial: *Aggregatibacter actinomycetemcomitans*, *Tanerella forsythia*, *C. rectus*, *Eubacterium saburreum*, *Fusobacterium nucleatum*, *P. gingivalis*, *Capnocytophaga spp* and *Pr. intermedia*; (3) co-variates: age, gender, race, education, income, smoking and numbers of packs/year, exposure to occupational hazards, systemic diseases	In a multivariable logistic regression model, *P. gingivalis* (OR 1.59, 95% CI 1.11–2.25) and *T. forsythia* (OR 2.45, 95% CI 1.87–3.24) were positively associated with severity of AL, while *Capnocytophaga* spp. (OR 0.60, 95% CI 0.43–0.84) were protective against AL
Grossi *et al*. (1995) USA	Same sample as in Grossi *et al*. (1994); 1361 subjects, aged 25–74 years; assessments of interproximal bone loss from full-mouth radiographs; the degree of association between bone loss and explanatory variables was analyzed by stepwise logistic regression	In a multivariable logistic regression model, *P. gingivalis* (OR 1.73, 95% CI 1.27–2.37) and *T. forsythia* (OR 2.52, 95% CI 1.98–3.17), were significantly associated with increasing severity of BL
Beck *et al*. (1997) USA **(L)**	540 dentate adults, aged 65+ years, examined at baseline, 18, 36, and 60 months; incidence of AL was defined as additional AL ≥ 3 mm; microbial variables included presence of *A. actinomycetemcomitans*, *Pr. intermedia*, and *P. gingivalis* and the BANA test; covariates included age, gender, missing teeth, education, smoking, dental visit	BANA (+), and presence of *P. gingivalis* were significantly associated with incident disease
Papapanou *et al*. (1997) China **(L)**	148 subjects, 30–39 and 50–59 years old in a rural area examined 10 years apart; full-mouth assessments of PD and AL at six sites per tooth; 14 subgingival plaque samples were obtained from each subject at the follow-up examination (1864 in total) and analyzed with respect to 18 bacterial species	Ubiquitous prevalence for the majority of the investigated species on the subject level. Bacterial colonization at high levels by *P. gingivalis*, *Prevotella intermedia*, *Pr. nigrescens*, *T. forsythia*, *F. nucleatum*, *Tr. denticola*, *Micromonas micros*, and *C. rectus* conferred statistically significant odds ratios for being classified as "downhill" (ten or more sites with longitudinal AL loss of ≥ 3 mm)
Machtei *et al*. (1999) USA **(L)**	A sample of 415 subjects, aged 25–75 years, followed for a period of 2–4 years; full-mouth examination at six sites per tooth at all teeth present; full-mouth intraoral radiographs; bacterial samples obtained from 12 index teeth analyzed with respect to: *A. actinomycetemcomitans*, *T. forsythia*, *C. rectus*, *P. intermedia*, *Capnocytophaga* species, *P. gingivalis*, *E. saburreum*, *F. nucleatum*; covariates included age, gender, smoking (current smokers 15.4%), education, income	Subjects harboring *T. forsythia* at baseline showed significantly higher longitudinal bone loss, greater proportion of "loser" sites (sites with additional AL of ≥ 2 mm) and twice as high tooth mortality

(*Continued*)

Table 7-4 *Continued*

Authors/country	Sample/methodology	Findings
Timmerman *et al*. (2000) Indonesia **(L)**	A sample 255 subjects, 15–25 year old, in a rural area, examined 7 years apart; assessments of PD and AL at vestibular surfaces of all teeth; bacterial samples harvested from a variety of intraoral sites and analyzed with respect to *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, spirochetes, and motile microorganisms	Progressive disease (PDS) was defined as one or more site with longitudinal AL ≥ 2 mm; subgingival presence of *A. actinomycetemcomitans* (OR 4.2, 95% CI 1.4–12.7), *P. gingivalis* (OR 2.3, 95% CI 1.0–5.2) and motile microorganisms (OR 2.2, 95% CI 1.0–5.0) were associated with PDS; in a multivariable logistic model, including age and subgingival calculus, subgingival presence of *A. actinomycetemcomitans* (OR 4.61, p = 0.01) was associated with PDS
Papapanou *et al*. (2002) Thailand	Random sample of 356 subjects 30–39 and 50–59 years old, in a rural area; PD and CAL were assessed at six sites/tooth, at all teeth apart from third molars; subjects were grouped according to different levels of pocketing/attachment loss: subjects with three or more sites with PD ≥ 5 mm (59%, G1); ≥ 10 sites with CAL ≥ 5 mm (50%, G2); and ≥ 30 sites with CAL ≥ 5 mm (24%, G3). Subgingival plaque samples were obtained at maximally 14 sites/subject; checkerboard hybridizations were used to analyze a total of 4343 samples with respect to 27 bacterial species	Odds ratios for heavy colonization by "red complex" species (*P. gingivalis*, *T. forsythia*, *Tr. denticola*) were 3.7 (95% CI 2.3–5.9) for G1; 4.0 (95% CI 2.5–6.6) for G2; and 4.3 (95% CI 2.6–7.1) for G3. Odds ratios for heavy colonization by selected "orange complex" species (*F. nucleatum*, *Pr. intermedia*, *Pr. nigrescens*, *Pe. micros*, *E. nodatum*, *Campylobacter rectus*, and *C. showae*) were 1.5 (95% CI 0.8–2.9) for G1; 1.5 (95% CI 0.8–2.9) for G2; and 1.5 (95% CI 0.8–3.1) for G3
Van der Velden *et al*. (2006) **(L)**	15-year follow-up of 128 subjects from the above cohort (Timmerman *et al*. 2000)	In a multi-variable logistic model, subgingival presence of *A. actinomycetemcomitans* (OR 4.3, 95% CI 1.2–15.7) was confirmed as a risk factor for the onset of the disease, i.e. longitudinal AL during the first 7-year period, but not for progression of disease during the subsequent 8-year period

PD = probing depth; AL= attachment level; CEJ = cemento-enamel junction; CPITN = Community Periodontal Index of Treatment Needs; BANA = N-benzoyl-DL-arginine-2-naphthylamide; a substrate hydrolyzed in the presence of *Treponema denticola, Porphyromonas gingivalis,* and *Tannerella forsythia*.

Cigarette smoking

The biological plausibility of an association between tobacco smoking and periodontitis was founded on the broad effects of multiple tobacco-related substances on cellular structure and function. Smoking has been shown to affect the vasculature, the humoral and cellular immune responses, cell signaling processes, and tissue homeostasis (for recent reviews see Kinane & Chestnutt 2000; Palmer *et al*. 2005). A substantial number of studies, a selection of which is summarized in Table 7-5, established the association of smoking to poor periodontal status (Axelsson *et al*. 1998; Bergström 1989; Goultschin *et al*. 1990; Haber & Kent 1992; Locker 1992; Ragnarsson *et al*. 1992; Haber *et al*. 1993; Jette *et al*. 1993; Stoltenberg *et al*. 1993b; Wouters *et al*. 1993; Martinez Canut *et al*. 1995; Albandar *et al*. 2000; Bergström *et al*. 2000b; Tomar & Asma 2000; Paulander *et al*. 2004b; Susin *et al*. 2004b; Kocher *et al*. 2005). Importantly, the inferior periodontal status of smokers cannot be attributed to poorer plaque control or more severe gingivitis (Bergström 1989). While earlier reports suggested a rather similar composition of the subgingival microflora in smokers and non-smokers (Stoltenberg *et al*. 1993b), recent studies demonstrated that shallow sites in smokers are colonized at higher levels by periodontal pathogens, such as *T. forsythia*, *Treponema denticola*, and *P. gingivalis*, and that these differences are obscured in deep, diseased pockets. In an attempt to quantitate the effects of smoking on the periodontal conditions, Haber *et al*. (1993) suggested that the excess prevalence of periodontal disease in the population attributed solely to smoking is much greater than the that owed to other systemic predispositions, such as diabetes mellitus. Data derived from the NHANES III study (Tomar & Asma 2000) suggested that as many as 42% of periodontitis cases in the US can be attributed to current smoking, and another 11% to former smoking. Similarly, in a study from Brazil, Susin *et al*. (2004b) reported that the attributable fraction of clinical attachment loss due to cigarette smoking was 37.7% and 15.6% among heavy and moderate smokers, respectively. In longitudinal studies, smoking has been found to confer a statistically significant increased risk for periodontitis progression after adjustment for other covariates (Beck *et al*. 1995, 1997; Machtei *et al*. 1999; Norderyd *et al*. 1999; Chen *et al*. 2001; Ogawa *et al*. 2002; Paulander *et al*. 2004b).

Figure 7-4 describes a *meta-analysis* of data from studies studying the association between smoking and periodontal conditions. In essence, meta-analysis is a statistical method which combines results from

Table 7-5 Selected studies using smoking as exposure of significance for periodontitis. **(L)** indicates a longitudinal study

Authors/country	Sample/methodology	Findings
Bergström (1989) Sweden	Patients referred for periodontal therapy (155 subjects, 30, 40 and 50 years old); a random sample of the Stockholm population served as controls; full-mouth probing assessments; sites with PD ≥ 4 mm considered diseased; recording of plaque and gingivitis scores	56% of the patients and 34% of the controls were smokers (odds ratio 2.5); significantly higher frequency of periodontally involved teeth in smokers; no notable difference between smokers and non-smokers with respect to plaque and gingivitis
Haber & Kent (1992) USA	196 patients with PD in a periodontal practice and 209 patients from five general practices; probing assessments at six sites/tooth and full-mouth radiographs; questionnaire on smoking habits; patients with negative history of periodontal therapy from the general practices included as controls; comparison of (1) the prevalence of smoking among the two patient groups, and (2) PD disease severity among current and never smokers	Overall smoking history in the periodontal practice 75%; in the general practice 54%; summary odds ratio for positive smoking history in perio versus general practice patients was 2.6; in the perio group, frequency of current smoking increased with increasing severity of PD
Locker (1992) Canada	907 adults, ≥ 50 years old, living independently in four Ontario communities; partial, probing assessments; half of the participants reported a positive history of smoking and 20% were current smokers	Current smokers had fewer teeth, were more likely to have lost all their natural teeth and had higher extent and severity of PD than those who had never smoked
Haber *et al*. (1993) USA	132 diabetics and 95 non-diabetics, 19–40 years old; probing assessments at six sites/tooth, all teeth; questionnaire on smoking habits; calculation of the population attributable risk percent (PAR%), as an estimate of the excess prevalence of periodontitis in the study population that is associated with smoking	The prevalence of periodontitis was markedly higher among smokers than non smokers within both the diabetic and non-diabetic groups; PAR% among non diabetics was 51% in ages 19–30 years and 32% in ages 31–40 years
Stoltenberg *et al*. (1993b) USA	Out of 615 medically healthy adults, 28–73 years old, attending a health maintenance organization, selection of 63 smokers and 126 non-smokers of similar age, sex, plaque, and calculus scores; probing assessments at the proximal surfaces of premolars and molars in a randomly selected posterior sextant; detection of *P. gingivalis*, *Pr. intermedia*, *A. actinomycetemcomitans*, *Eikenella corrodens*, and *F. nucleatum* by a semi-quantitative fluorescence immunoassay, in one buccal and one lingual sample per tooth examined; logistic regression to determine if any of the bacteria or smoking were indicators of mean posterior probing depth of ≥ 3.5 mm	Odds ratio for a smoker having a mean PD of ≥ 3.5 mm was 5.3 (95% CI 2.0–13.8); no statistically significant difference between smokers and non-smokers with respect to prevalence of the bacteria examined; the logistic model revealed that a mean PD of ≥ 3.5 mm was significantly associated with the presence of *A. actinomycetemcomitans*, *Pr. intermedia*, *E. corrodens* and smoking; smoking was a stronger indicator than any of the bacteria examined
Jette *et al*. (1993) USA	1156 community dwellers, age 70+ years; probing assessments at four sites/tooth, all teeth; evaluation if lifelong tobacco use is a modifiable risk factor for poor dental health; multiple regression analysis	18.1% of men and 7.9% of women were tobacco users (overall 12.3%; including 1% smokeless tobacco users); years of exposure to tobacco products was a statistically significant factor for tooth loss, coronal root caries, and periodontal disease, regardless of other social and behavioral factors; periodontal disease (no. of affected teeth) was predicted by longer duration of tobacco use, male sex, and more infrequent practice of oral hygiene
Martinez Canut *et al*. (1995) Spain	889 periodontitis patients, aged 21–76 years; probing assessments at six sites/tooth, all teeth; analysis of variance to examine the role of smoking on the severity of periodontitis	Smoking was statistically related to increased severity of periodontitis in multi-variate analysis; a dose–response effect was demonstrated, with subjects smoking > 20 cigarettes/day showing significantly higher attachment loss
Kaldahl *et al*. (1996) USA **(L)**	74 patients with moderate to advanced periodontitis including 31 heavy smokers (≥ 20 cigarettes/day); the effects of cigarette consumption and smoking history on the response to active periodontal treatment and to up to 7 years of supportive periodontal treatment was evaluated. Full-mouth examinations performed at baseline, 4 weeks after mechanical plaque control, 10 weeks following periodontal surgery, and yearly during 7 years of supportive periodontal treatment	Past and never smokers consistently exhibited a significantly greater reduction in PD and greater gains in AL than heavy and light smokers; all groups experienced a similar decrease in the prevalence of BoP following active therapy

(*Continued*)

Table 7-5 *Continued*

Authors/country	Sample/methodology	Findings
Grossi *et al*. (1997b) USA **(L)**	143 subjects aged 35–65 years with established periodontitis, including 60 current, 55 former, and 28 non-smokers, examined at baseline and 3 months after non-surgical periodontal therapy	Current smokers showed less reduction in PD and less AL gain than former- and non smokers; fewer smokers harbored no *P. gingivalis* or *T. forsythia* after treatment, compared to former and non-smokers
Axelsson *et al*. (1998) Sweden	A random sample of 1093 subjects, aged 35, 50, 65, and 75 years; prevalence of smoking in the four age groups was 35%, 35%, 24%, and 12%, respectively; recordings included AL, CPITN scores, DMF surfaces, plaque, and stimulated salivary secretion rate (SSSR)	In the oldest age group, 41% of the smokers and 35% of the non-smokers were edentulous; in every age group, mean attachment loss was statistically significantly increased in smokers by 0.37, 0.88, 0.85, and 1.33 mm, respectively; smokers had higher CPITN and DMF scores, increased SSSR, but similar plaque levels
Tomar & Asma (2000) USA	12 329 subjects, aged ≥ 18 years, participants in the NHANES III study; probing assessments at mesial and buccal sites in one upper and one lower quadrant; mesial assessments performed from the buccal aspect of the teeth; assessments of gingivitis, PD, and location of the gingival margin in relation to the CEJ; "periodontitis" was defined as one or more site with AL ≥ 4 mm and PD ≥ 4 mm	27.9% of the participants were current smokers and 9.2% met the definition for periodontitis; current smokers were four times as likely to suffer from periodontitis than never smokers, after adjustments for age, gender, race/ethnicity, education, and income: poverty ratio; among current smokers, there was a dose–response relationship between cigarettes/day and periodontitis; 41.9% of periodontitis cases were attributable to current smoking and 10.9% to former smoking
Bergström *et al*. (2000b) Sweden	257 subjects, aged 20–69 years, including 50 current smokers, 61 former smokers, and 133 non-smokers; full mouth clinical and radiographic assessments of the periodontal tissues; smoking exposure defined in terms of consumption (number of cig/day), duration (number of years of smoking) and life-time exposure (product of daily consumption and years of duration-cig/years); threshold levels used: heavy versus light consumption: ≥ 10 cigarettes/day versus < 10 cigarettes/day; duration: ≥ 15 years versus < 15 years; life-time exposure: ≥ 200 cig/years versus < 200 cig/years	Compared to former and non-smokers, current smokers had the highest prevalence of diseased sites (AL ≥ 4 mm); 40–69-year-old current smokers showed a significantly higher prevalence than 20–39-year-old current smokers (27% vs. 4%); the same pattern emerged when comparing heavy versus light smokers according to consumption, duration and life-time exposure; in multiple regression, life-time exposure was highly associated with the frequency of diseased sites and periodontal bone height after adjusting for age, gingival bleeding and plaque index
Albandar *et al*. (2000) USA	705 subjects, aged 21–92 years, 52% males and 87% white; full-mouth examination of PD and AL at six sites; periodontitis was classified as advanced, or mild; cigar, pipe, and cigarette smoking were classified as current, former and never	In multiple linear regression, current and former smoking, regardless of type, was associated with increased percentage of subjects with moderate/advanced periodontitis after adjusting for age, gender, race and numbers of years of being smoking cigarette, cigar and pipe; current smoking was also associated with higher number of missing teeth
Bergström *et al*. (2000a) Sweden **(L)**	10-year follow-up of a sample of 84 dentally aware musicians, including 16 current, 28 former, and 40 non-smokers; full-mouth clinical and radiographic assessments of periodontal status	The prevalence of PD ≥ 4 mm (diseased sites) was 18.7% for current, 11.1% for former, and 8.7% for non-smokers at baseline. At 10 years, these figures were 41.6%, 7.8% and 6.6%; a similar pattern was observed for alveolar bone levels; after adjusting for age, gingival bleeding, plaque index, and frequency of diseased sites at baseline, current smoking was a significant predictor of the increase in diseased sites at 10 years
Susin *et al*. (2004b) Brazil	974 subjects, aged 30–103 years; full mouth examination of PD and AL; severe attachment loss was defined as AL ≥ 5 mm in ≥ 30% of the teeth; exposure to smoking classified as current/former, heavy/moderate/light/none, and quantified as lifetime consumption	Heavy and moderate smokers had significantly higher prevalence of AL ≥ 5 mm than non-smokers; in multivariate analysis heavy (OR 3.6, 95% CI 2.2–6.0) and moderate smoking (OR 2.0, 95% CI 1.4–2.9) conferred higher odds for AL; the attributable fraction of AL due to smoking was 37.7% and 15.6% among heavy and moderate smokers, respectively

PD = probing depth; AL = attachment level; BoP = bleeding on probing; CEJ = cemento-enamel junction; CPITN = Community Periodontal Index of Treatment Needs; DMF = decayed, missing, filled.

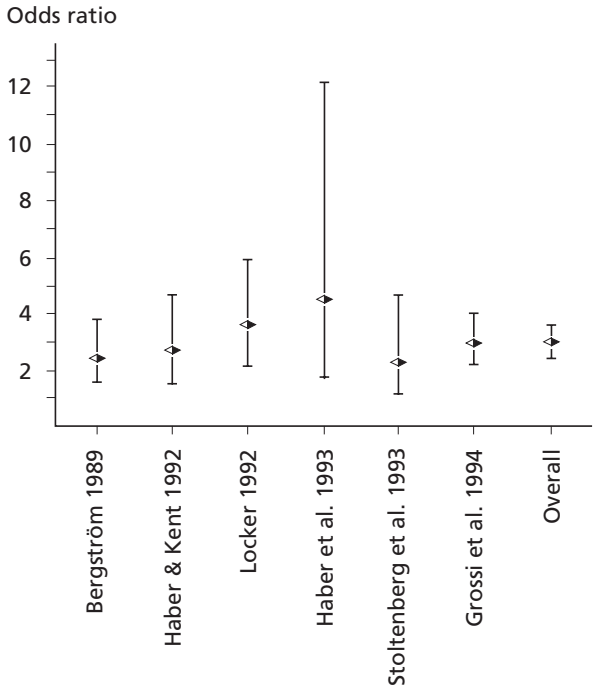

Fig. 7-4 Meta-analysis of smoking as a risk factor for periodontal disease. The studies included are: Bergström (1989), Haber & Kent (1992), Locker (1992), Haber *et al*. (1993), Stoltenberg *et al*. (1993), and Grossi *et al*. (1994). Bars indicate the 95% confidence limits for the depicted odds ratios. From Papapanou (1996), reproduced with permission.

different studies of similar design, in order to gain an overall increased *power*, i.e. an enhanced potential to reveal biological associations which may exist but are difficult to detect (Chalmers 1993; Oakes 1993; Proskin & Volpe 1994). This analysis, initially published as part of the 1996 World Workshop in Periodontics (Papapanou 1996), incorporated data from six studies, including a total of 2361 subjects, with known smoking habits and periodontal status (Bergström & Eliasson 1989; Haber & Kent 1992; Locker 1992; Haber *et al*. 1993; Stoltenberg *et al*. 1993b; Grossi *et al*. 1994). It can be observed that smoking entailed an overall increased, statistically and clinically significant risk for severe disease (estimated overall odds ratio of 2.82; 95% confidence limits 2.36–3.39).

Studies examining the effects of smoking on the outcome of periodontal treatment have demonstrated that treatment responses are modified by cigarette consumption, with current smokers exhibiting poorer responses than former or never smokers (Ah *et al*. 1994; Kaldahl *et al*. 1996; Renvert *et al*. 1996; Grossi *et al*. 1997b; Kinane & Radvar 1997; Boström *et al*. 1998; Machtei *et al*. 1998; Tonetti *et al*. 1998; Scabbia *et al*. 2001; Trombelli *et al*. 2003; Van der Velden *et al*. 2003; Papantonopoulos 2004; Paulander *et al*. 2004a; Rieder *et al*. 2004; Stavropoulos *et al*. 2004; Sculean *et al*. 2005). Notably, these studies have confirmed the negative effect of smoking on the outcome of several periodontal treatment modalities including non-surgical, surgical, and regenerative periodontal therapy. Two recent meta-analyses of the effects of smoking on the outcome of periodontal therapy (Garcia 2005; Labriola *et al*. 2005) support the above conclusions.

In contrast, smoking cessation was shown to be beneficial to the periodontal tissues. In a longitudinal study (Bolin *et al*. 1993), 349 subjects with ≥20 remaining teeth were examined on two occasions 10 years apart (1970 and 1980). Progression of periodontal disease was assessed on radiographs at all approximal tooth surfaces and was shown to be almost twice as rapid in smokers than in non-smokers. It was also observed that subjects who quit smoking at some time point within the observation period had a significantly retarded progression of bone loss than the one occurring in smokers. Similar observations were made by Krall *et al*. (1997) who reported that, over a mean follow-up period of 6 years, subjects who continued to smoke had a 2.4–3.5-fold risk of tooth loss when compared to non-smokers. Finally, in a 10-year follow-up study, Bergström *et al*. (2000a) observed an increase of periodontally diseased sites concomitant with loss of periodontal bone height in current smokers, as compared to non-smokers whose periodontal health condition remained unaltered throughout the period of investigation. The periodontal health condition in former smokers was similarly stable to that of non-smokers, underscoring the beneficial effects of smoking cessation.

In conclusion, cigarette smoking appears to fulfill the majority of the required steps of the risk assessment process stipulated by Beck (1994) and is considered one of the major risk factors for periodontitis.

Diabetes mellitus

Diabetes as a risk factor for periodontitis has been debated for decades (Genco & Löe 1993), but several biologically plausible mechanisms by which the disease may contribute to impaired periodontal conditions have been identified over the past decade (for reviews see Lalla *et al*. 2000; Mealey & Oates 2006). Table 7-6 summarizes epidemiological evidence based on a number of case–control and prospective cohort studies that examine the periodontal status of patients with diabetes (Hugoson *et al*. 1989; Shlossman *et al*. 1990; Emrich *et al*. 1991; de Pommereau *et al*. 1992; Oliver & Tervonen 1993; Thorstensson & Hugoson 1993; Pinson *et al*. 1995). This association is especially pronounced in subjects with poor metabolic control and a long duration of the disease (Taylor *et al*. 1996; Grossi & Genco 1998; Taylor *et al*. 1998a; Lalla *et al*. 2004). The age of onset of diabetes-related manifestations in the periodontal tissues has also been addressed in studies examining children and adolescents with type 1 diabetes (de Pommereau *et al*. 1992; Pinson *et al*. 1995) and both type 1 and type 2 diabetes (Lalla *et al*. 2006). All three studies documented more pronounced gingival inflammation in subjects with diabetes in ages between 6 and 18 years. The case–control study by Lalla *et al*. (2006) further

Table 7-6 Selected studies using diabetes mellitus as exposure of significance for periodontitis. **(L)** indicates a longitudinal study

Authors/country	Sample/methodology	Findings
Hugoson *et al*. (1989) Sweden	82 subjects with long- and 72 with short-duration IDDM; 77 non-diabetics (age 20–70 years); full-mouth, probing assessments at four sites/tooth; radiographs of lower molar–premolar regions; subjects assigned into five groups according to increasing severity of periodontal disease; no multi-variate analysis	No notable difference in plaque, calculus, and no. of teeth between diabetics and non-diabetics; long-duration diabetics were more frequently classified in groups 4 and 5 and had significantly more tooth surfaces with PD of ≥ 6 mm than non-diabetics; significantly more extensive ABL in long-duration diabetics 40–49 years old
Shlossman *et al*. (1990) Arizona, USA	3219 Pima Indians, ≥ 5 years; prevalence of NIDDM 23% (20% in men, 25% in women); probing assessments at six sites/tooth, at six index teeth; alveolar bone loss from panoramic radiographs; 2878 subjects with available radiographic data, probing assessments or both; comparison between diabetics and non-diabetics with respect to AL and ABL	Median attachment loss and alveolar bone loss higher in diabetics for all age groups and in both sexes
Emrich *et al*. (1991) USA	Sample and methodology same as above (Shlossman *et al*. 1990); 1342 Pima Indians, 15 years and older, with natural teeth; 19% (254) with diabetes and 12% (158) with impaired glucose tolerance; linear logistic models to predict prevalence and severity of periodontal disease; prevalence: one or more sites with AL of ≥ 5 mm or ABL ≥ 25% of the root length; severity: square root of average AL or ABL	Diabetes, age, and calculus were significant risk markers for periodontitis; odds ratios for a diabetic to have PD was 2.8 (clinically assessed) and 3.4 (radiographically)
de Pommereau *et al*. (1992) France	85 adolescents with IDDM aged 12–18 years and 38 healthy age-matched controls; probing assessments at six sites/tooth, all teeth; bite-wing radiographs at molars and sites with AL > 2 mm; patients divided according to disease duration (more or less than 6 years); sexual maturation according to Tanner's classification; metabolic control expressed through glycosylated hemoglobin (HbA1c); non-parametric pair-wise analysis	None of the subjects had sites with AL ≥ 3 mm or radiographic signs of periodontitis; despite similar plaque scores, diabetic children had significantly more gingival inflammation; no significant relation between gingival condition and age, Tanner's index, HbA1c level or disease duration
Oliver & Tervonen (1993) USA	114 diabetic patients, 20–64 years old (60% with IDDM and 40% with NIDDM); half-mouth, probing assessments at four sites/tooth; data from the 1985–86 National Survey served as controls	Tooth loss was similar among diabetics and US employed adults; 60% of the diabetics and 16% of the controls had one or more site with PD ≥ 4 mm; attachment level data were comparable in both groups
Thorstensson & Hugoson (1993) Sweden	83 IDDM patients and 99 age- and sex-matched non-diabetics (age 40–70 years); full-mouth, probing assessments at four sites/tooth; radiographs of lower molar-premolar regions; subjects assigned into five groups according to increasing severity of periodontal disease; uni-variate analysis	Diabetics 40–49 years old (mean disease duration 25.6 years) had more periodontal pockets ≥ 6 mm and more extensive alveolar bone loss than non-diabetics, but this was not the case for subjects aged 50–59 or 60–69 years (mean disease duration 20.5 and 18.6 years, respectively). Disease duration appeared to be a significant determinant of periodontitis development
Pinson *et al*. (1995) USA	26 IDDM children, 7–18 years old and 24 controls, 20 of whom were siblings of the diabetic patients; full-mouth, probing assessments at six sites/tooth; metabolic control assessed through glycosylated hemoglobin (GHb); analysis of covariance	Overall, no statistically significant differences between cases and controls; no association between GHb and clinical variables; after correcting for plaque, diabetics showed more severe gingival inflammation in specific tooth regions
Bridges *et al*. (1996) USA	A sample of 233 men, aged 24–78 years, including 118 diabetic (46 type 1 and 72 type 2) and 115 non-diabetic subjects, matched for age and BMI	Plaque and gingivitis, bleeding scores, PD, AL, and missing teeth were significantly higher in diabetic than non-diabetic men
Tervonen & Karjalainen (1997) Finland **(L)**	36 patients with type 1 diabetes and 10 controls, aged 24–36 years, received non-surgical periodontal therapy and were followed at 4 weeks, 6 and 12 months; patient with diabetes were further grouped according to diabetic status as: D1 (n = 13) with no diabetic complications and good long-term metabolic control; D2 (n = 15) moderate metabolic control with/without retinopathy; D3 (n = 8) severe diabetes with poor metabolic control and/or multiple complications; periodontal status was monitored radiographically	The periodontal status of the diabetic patients with good control and no complications (D1) and those with moderate control (D2) was similar to non-diabetic controls. Diabetic subjects with poor metabolic control and/or multiple complications (D3) exhibited higher extent of AL ≥ 2 mm at baseline and higher recurrence of PD ≥ 4 mm during follow-up

(*Continued*)

Table 7-6 *Continued*

Authors/country	Sample/methodology	Findings
Taylor *et al*. (1998a) USA **(L)**	2-year study of 21 patients with type 2 diabetes, including 14 with poor and 7 with better metabolic control, and 338 controls, aged 15–57 years, Native Americans; progression of bone loss was assessed on radiographs; covariates included age, calculus, gingival and plaque indices, time to follow up, alcohol consumption, smoking, obesity (BMI > 27), coronary heart disease, and gender	In multiple logistic regression, poorly controlled diabetic subjects were 11 times more likely (95% CI 2.5–53.3) to have more pronounced bone loss progression than non-diabetic subjects; no such differences were found between better controlled and non-diabetic controls; age, time to follow-up, pronounced bone loss at baseline and calculus index were significant predictors of bone loss progression
Taylor *et al*. (1998b) USA **(L)**	2-year study of 24 subjects with NIDDM and 362 subjects without diabetes, aged 15–57 years; degree of bone loss on panoramic radiographs was assessed in a scale of 0–4	A regression model having progression of bone loss as the dependent variable revealed a cumulative odds ratio for NIDDM of 4.23 (95% CI 1.8–9.9); the association was modified by age, with younger adults exhibiting higher risk for alveolar bone loss progression
Lalla *et al*. (2006) USA	Case–control study of 182 children and adolescents (6–18 years of age) with diabetes (predominantly type 1) and 160 non-diabetic control subjects; half-mouth examination at four sites/tooth in all fully erupted teeth with respect to PD and AL	Children with diabetes had significantly more plaque and gingival inflammation than controls and higher number of teeth with AL; when controlling for age, gender, ethnicity, gingival bleeding, and frequency of dental visits, diabetes remained significantly correlated with attachment loss; body mass index was significantly correlated with AL in children with diabetes

PD = probing depth; AL = attachment level; CEJ = cemento-enamel junction.
IDDM and NIDDM = insulin-dependent and non-insulin-dependent diabetes mellitus, respectively; both terms have been abolished and replaced by type 1 and type 2 diabetes.

reported that attachment loss was more pronounced in young patients with diabetes after adjustment for age, gender, ethnicity, gingival bleeding, and frequency of dental visits. In a subsequent publication, Lalla *et al*. (2007b) reported data on 350 children with either type 1 or type 2 diabetes and found a strong positive association between mean HbA1c levels over the 2 years preceding the dental examination and periodontitis. Finally, in a report including a total of 700 children, 350 with diabetes and 350 non-diabetic controls, Lalla *et al*. (2007a) documented a statistically increased periodontal destruction in children with diabetes across all disease definitions tested and in both age subgroups of 6–11 and 12–18 years.

Several studies suggest a two-way relationship between diabetes and periodontitis, with more severe periodontal tissue destruction in people with diabetes but also a poorer metabolic control of diabetes in subjects with periodontitis (Lalla *et al*. 2000; Soskolne & Klinger 2001; Taylor 2001). Irrespective of the variability in the case definition employed in these studies, subjects with diabetes have higher prevalence, extent, and severity of periodontal disease (Grossi *et al*. 1994; Bridges *et al*. 1996; Firatli 1997; Tervonen & Karjalainen 1997; Taylor *et al*. 1998a,b; Lalla *et al*. 2004). These observations are consistent for both type 1 and type 2 diabetes. In addition, these studies provide evidence of a dose–response relationship between poor metabolic control and the severity as well as the progression of periodontitis (Seppälä *et al*. 1993; Tervonen & Oliver 1993; Tervonen & Karjalainen 1997; Taylor *et al*. 1998a; Guzman *et al*. 2003). Further expanding this observed dose–response relationship into the pre-diabetic state, a recent study also indicated that the level of glucose intolerance in non-diabetic individuals also correlated with the severity of periodontal disease (Saito *et al*. 2004). In line with the above observations, the outcome of periodontal treatment in well controlled diabetic patients is similar to that of non-diabetic subjects, while poorly controlled diabetics display an inferior outcome (Tervonen & Karjalainen 1997).

Collectively, the above data strongly indicate that diabetes mellitus is a major risk factor for periodontitis.

Obesity

The biologic plausibility of a potential link between obesity and periodontitis has been suggested to involve a hyper-inflammatory state and an aberrant lipid metabolism prevalent in obesity, as well as the pathway of insulin resistance (Saito *et al*. 1998; Nishimura & Murayama 2001) all of which may collectively result in an enhanced breakdown of the periodontal tissue support. Indeed, a number of recent studies point to a positive association between obesity, defined as body mass index (BMI) ≥30, and periodontitis (Anon 2000; Saito *et al*. 2001; Al-Zahrani *et al*. 2003; Wood *et al*. 2003).

Three separate publications have documented such an association in the NHANES III database. In the first publication Al-Zahrani *et al.* (2003) reported a significant association between both BMI and waist-to-hip ratio and periodontitis in younger adults, but no association in middle-aged or older adults (Table 7-1). Wood *et al*. (2003), using a subset of the NHANES III sample including Caucasian subjects aged 18 years and above, reported that BMI, waist-to-hip ratio, visceral fat, and fat-free mass were associated with periodontitis after adjusting for age, gender, history of diabetes, current smoking, and socioeconomic status. Finally, Genco *et al*. (2005), reported that overweight subjects in the upper quartile of insulin resistance index were 1.5 times more likely to have periodontitis compared to their counterparts with high BMI but low insulin resistance index.

In an independent subject sample including 643 apparently healthy Japanese adults, Saito *et al*. (2001) reported that waist-to-hip ratio, BMI, and body fat were significant risk indicators for periodontitis after adjustments for known risk factors. In addition, in a separate analysis of the subsample of subjects with high waist-to-hip ratio, higher BMI and increased body fat significantly increased the adjusted risk of periodontitis, when compared to subjects with low waist-to-hip ratios, BMI or body fat.

Given that the above publications are based on only two population samples, and that inferences on temporality or mechanisms are not possible based on cross-sectional studies, additional research on the role of obesity in periodontitis is warranted.

Osteopenia/osteoporosis

Several cross-sectional studies, of limited sample size and largely confined to postmenopausal women, have suggested that women with low bone mineral density are more likely to have CAL, gingival recession and/or pronounced gingival inflammation (von Wowern *et al*. 1994; Mohammad *et al*. 1996, 1997; Tezal *et al*. 2000). In a radiographic study of 1084 subjects aged 60–75 years, Persson *et al*. (2002) reported a positive association between osteoporosis and periodontitis with an odds ratio of 1.8 (95% CI 1.2–2.5) However, studies that failed to report such an association have been published as well (Weyant *et al*. 1999; Lundström *et al*. 2001).

Based on these studies it has been hypothesized that the systemic loss of bone density in osteoporosis may, in combination with hormone action, heredity, and other host factors, provide a host system that is increasingly susceptible to the infectious destruction of periodontal tissue (Wactawski-Wende 2001). However, the data from longitudinal studies are similarly conflicting. Contrary to Payne *et al*. (1999, 2000) who reported an enhanced longitudinal alveolar bone loss in osteoporotic women versus women with normal mineral bone density, Reinhardt and colleagues (1999) reported no significant impact of serum estradiol levels on longitudinal attachment loss over a 2-year period. In contrast, Yoshihara *et al*. (2004) found, after adjustments, a significant association between bone mineral density and 3-year longitudinal attachment loss in Japanese subjects ≥70 years old. It appears therefore that additional research is needed to unequivocally establish or refute the role of osteoporosis as a risk factor for periodontitis.

Human immunodeficiency (HIV) infection

After the early studies published in the late 1980s which seemed to indicate that both the prevalence and the severity of periodontitis were exceptionally high in patients with acquired immunodeficiency syndrome (AIDS) (Winkler & Murray 1987), a more tempered picture emerged in subsequent publications. While it cannot be ruled out that the initial reports actually included biased samples, it is also possible that the successful control of immunosuppression in HIV-positive subjects by means of high activity anti-retroviral therapy (HAART) and other continuously evolving drugs has influenced the incidence of periodontal disease progression in HIV-seropositive subjects and has resulted in less severe periodontal manifestations of HIV infection (Chapple & Hamburger 2000). For example, a cross-sectional study of 326 HIV-infected adults (McKaig *et al*. 1998) revealed that, after adjustments for CD4 counts, persons taking HIV-antiretroviral medication were five times less likely to suffer from periodontitis than those not taking such medication, underscoring the importance of the host's immunologic competency in this context.

Nevertheless, publications of the last decade continue to generate conflicting results. Thus, although studies (Smith *et al.* 1995a; Robinson *et al*. 1996; Ndiaye *et al*. 1997; McKaig *et al*. 1998) indicated higher prevalence and severity of periodontitis in HIV-positive subjects when compared to controls, other studies are either not supportive of this notion or indicate that the differences in periodontal status between HIV-seropositive and -seronegative subjects are limited (Cross & Smith 1995; Lamster *et al*. 1997; Scheutz *et al*. 1997; Lamster *et al*. 1998; Vastardis *et al*. 2003). Studies investigating the pathobiology of periodontitis in HIV infected subjects suggested that specific IgG subclass responses to periodontopathic bacteria were similar in HIV-positive and HIV-negative subjects (Yeung *et al*. 2002), while CD4 count levels were not found to correlate with the severity of periodontitis (Martinez Canut *et al*. 1996; Vastardis *et al*. 2003).

The few available longitudinal studies are equally conflicting. Two companion publications reporting from a short-term follow-up study (Cross & Smith 1995; Smith *et al*. 1995b) involved a group of 29 HIV-seropositive subjects who were examined at baseline and 3 months and reported a low prevalence and incidence of attachment loss. The subgingival

microbial profiles of the seropositive subjects resembled those obtained from non-systemically affected subjects, and were not correlated to their CD4 and CD8 lymphocyte counts. Similarly, in a small follow-up study of 12 months duration, Robinson *et al*. (2000) found no difference in the progression of periodontitis between HIV-positive and HIV-negative subjects. Hofer *et al*. (2002) demonstrated that compliant HIV-positive subjects can be successfully maintained in a manner similar to non-infected controls. However, a 20-month follow-up study of 114 homosexual or bisexual men by Barr *et al*. (1992) revealed a clear relationship between incidence of attachment loss and immunosupression, expressed through CD4 cell counts. The authors suggested that seropositivity in combination with older age confers an increased risk for attachment loss. Similar observations were reported by Lamster *et al*. (1997) who concluded that periodontitis in the presence of HIV infection is dependent upon the immunologic competency of the host as well as the local inflammatory response to both typical and atypical subgingival microbiota.

It appears therefore that there is no consensus in the literature on the association of HIV/AIDS and periodontitis. Variance due to ongoing advancements in therapy will likely further contribute to the diversity of the findings.

Psychosocial factors

The mechanisms by which psychosocial stress may affect the periodontal status are complex. It has been suggested that one of the plausible pathways may involve behavioral changes leading to smoking and poor oral hygiene that, in turn, may affect periodontal health (Genco *et al*. 1998). In the absence of a biological measure of stress, a limited number of studies have used proxy measures of stress to study its association with periodontitis. In a study of 1426 subjects in Erie County, NY, USA, Genco *et al*. (1999) reported that adult subjects who were under financial strain and exhibited poor coping behaviors were at increased risk of severe periodontitis when compared with subjects who demonstrated good coping behavior patterns under similar financial strain, or with controls under no financial strain. In a limited size study that included 23 employed adults, Linden *et al.* (1996) evaluated the association between occupational stress and the progression of periodontitis and reported that longitudinal attachment loss was significantly predicted by increasing age, lower socioeconomic status, lower job satisfaction, and type A personality, characterized by aggressive, impatient, and irritable behavior. In contrast, a study of 681 subjects carried out in Lithuania (Aleksejuniene *et al*. 2002) could not document an association between psychosocial stress and periodontitis, although they reported that the disease did correlate with lifestyle factors.

Clearly, the study of the role of stress in periodontitis is in its infancy and multiple gaps in our knowledge exist. Nevertheless, given the established role of the sympathetic, parasympathetic, and the peptidergic/sensory nervous systems, as well as that of the hypothalamic–pituitary–adrenal axis on brain-to-immune regulatory pathways, such a role is clearly biologically plausible. Recent experimental animal studies have begun to shed light on basic mechanisms that may explain the link between psychosocial factors and periodontitis. For example, a recent study by Breivik *et al*. (2006) demonstrated that experimentally induced depression in rats accelerated tissue breakdown in a ligature periodontitis model and that pharmacologic treatment of depression attenuated this breakdown. Additional basic and epidemiologic research is needed to fully elucidate this relationship.

Remarks

The analytical epidemiologic studies described above are obviously diverse with respect to important elements of design and methodology, such as definitions of disease, sample size, use of full-mouth or partial-mouth recording protocols, length of follow-up in longitudinal studies, comprehensive or not adjustment for potential confounders, etc. Nevertheless, despite these apparent shortcomings, a number of conclusions can be made with reasonable certainty:

1. Specific bacteria, cigarette smoking, and diabetes mellitus are the major established risk factors for periodontitis. A number of biologically plausible, potentially important additional factors are in need of further investigation in future studies.
2. There is a need to introduce a uniform definition of periodontitis to be used in analytical epidemiologic studies, to facilitate valid comparisons and establish whether seemingly conflicting data reflect true biological variation or are exclusively owed to methodological inconsistencies. To address this point, the Consensus Report of 5th European Workshop in Periodontology (Tonetti & Claffey 2005) suggested a two-level definition of periodontitis as follows: (i) presence of proximal attachment loss of ≥3 mm in two or more non-adjacent teeth, and (ii) presence of proximal attachment loss of ≥5 mm in ≥30% of teeth present. Likewise, the following case definition for the progression of periodontitis was proposed: presence of two or more teeth demonstrating a longitudinal loss of proximal attachment of ≥3 mm, or in cases where attachment level measurements are not available, longitudinal radiographic bone loss of ≥2 mm at two or more teeth may be used as a substitute. Obviously, no definition is devoid of shortcomings and the above proposals are no exception. Nevertheless, a consistent "common denominator" definition across studies will greatly facilitate valid comparisons.

3. Studies need to distinguish clearly between risk factors and disease predictors. Although the use of the latter as explanatory variables in multivariate models may increase the coefficient of determination (i.e. the proportion of the variance explained by means of the models), it may obscure the significance of true etiologic factors. For example, as shown by Ismail *et al*. (1990), factors with biologically plausible etiologic potential (such as dental plaque) may not retain their significance in multi-variate models that include alternative expressions of disease such as tooth mobility. It has been demonstrated that baseline levels of disease and morphologic features such as angular bony defects are powerful predictors of future disease progression (Papapanou *et al*. 1989; Papapanou & Wennström 1991). Haffajee *et al*. (1991a) showed that age, plaque, and bleeding on probing are related to both baseline disease levels as well as to incident disease. In the search of true exposures of significance for disease onset or progression, inclusion of a factor in a model may thus erroneously discredit a co-varying, biologically significant other factor.
4. The progression pattern of periodontitis over time appears to follow a skewed distribution similar to the skewed distribution of the prevalence of severe periodontitis in the population. In other words, although a majority of subjects may harbor sites which progress over time, it is a small subfraction of subjects that suffer substantial longitudinal attachment loss or bone loss at multiple sites.

Finally, an interesting observation was brought up in a report by Beck *et al*. (1995). In a longitudinal study, the authors compared characteristics of patients experiencing attachment loss at previously non-diseased sites with those of patients suffering progression of already established disease. While low income and medication with drugs associated with soft tissue reactions were features in common for both groups of patients, new lesions were more frequent in patients who used smokeless tobacco and had a history of oral pain. Risk for progression of established disease was higher in cigarette smokers, subjects with high levels of subgingival *P. gingivalis*, and individuals with worsening financial problems. These data suggest that periodontitis may be like other diseases for which the factors associated with the initiation of the disease may be different from the ones involved in its progression. If this observation is verified in other studies, such a distinction may have implications for future assessment strategies and may improve the accuracy of the risk/prediction models.

Periodontal infections and risk for systemic disease

During the past decade and a half, an entirely new area of periodontal research has emerged, commonly referred to as "periodontal medicine". Following some initial reports suggesting a link between periodontal infections and a number of systemic conditions, researchers are increasingly dwelling into the exploration of additional epidemiological and experimental evidence as well as possible underlying pathogenic mechanisms. The biological plausibility of the proposed associations between periodontitis and atherosclerosis, cardiovascular and cerebrovascular disease, pregnancy complications, and diabetes mellitus, and the relevant epidemiological evidence available today are summarized in the following text.

Atherosclerosis – cardiovascular/cerebrovascular disease

A wealth of data originating from diverse areas of investigation have implicated chronic, low-level inflammation as an important factor in atherosclerotic cardiovascular disease (CVD) (Ross 1999). Supporting studies stemming from a variety of disciplines, such as cell biology, epidemiology, clinical trials, and experimental animal research, have consistently revealed that atherosclerotic lesions involve an inflammatory component. The cellular interactions in atherogenesis are fundamentally similar to those in chronic inflammatory–fibroproliferative diseases, and atherosclerotic lesions represent a series of highly specific cellular and molecular responses that can best be described, in aggregate, as an inflammatory disease (Ross 1993, 1999).

It is well established that the periodontal diseases represent mixed infections of the periodontal tissues caused by primarily anaerobic, Gram-negative bacteria (Haffajee & Socransky 1994). As discussed above, the prevalence of these infections, especially of mild or moderate severity, may be substantial in certain populations. The deepening of the periodontal sulcus which occurs during the course of these infections is concurrent with a marked bacterial proliferation, resulting in bacterial cell levels reaching 10^9 or 10^{10} bacteria within a single pathological periodontal pocket. The ulcerated epithelial lining of the periodontal pocket may constitute a substantial surface area in cases of generalized periodontitis (Hujoel *et al*. 2001) and provides a gate through which lipopolysaccharide (LPS) and other antigenic structures of bacterial origin challenge the immune system and elicit a local and systemic host response (Ebersole & Taubman 1994). Importantly, a number of pathogenic species involved in the periodontal infections display tissue invasion properties (Meyer *et al*. 1991; Sandros *et al*. 1994; Lamont *et al*. 1995). Frequent transient bacteremias occurring as a result of daily activities such as tooth brushing or chewing (Silver *et al*. 1977; Kinane *et al*. 2005; Forner *et al*. 2006) may confer a significant systemic bacterial challenge to the host. Circulating levels of several cytokines (IL-1 beta, IL-2, IL-6, and IL-8) induced during the course of several infections (Endo *et al*. 1992; Humar *et al*. 1999; Otto

et al. 1999), but also locally in the periodontal tissues in conjunction with periodontitis (Salvi *et al*. 1998), have been identified as biomarkers of cardiovascular disease (Hackam & Anand 2003; Hansson 2005). Interestingly, these pro-inflammatory cytokines have also been detected within atheromatous lesions (Barath *et al*. 1990a,b; Galea *et al*. 1996). In line with the observation that chronic infection may contribute to a pro-coagulant state, elevated von Willebrand factor antigen, a measure of endothelial cell damage, has been demonstrated in individuals with multiple dental infections (Mattila *et al*. 1989; Torgano *et al*. 1999).

A number of studies have examined the presence of oral bacteria in atheromatic plaque lesions. Chiu (1999) investigated the relationship between the presence of multiple infectious agents in human carotid endarterectomy specimens and pathoanatomic features of the corresponding carotid plaques, and reported positive immunostainings for *P. gingivalis* and *Streptococcus sanguis* in several carotid plaque specimens. The bacteria were immunolocalized in plaque shoulders and within a lymphohistiocytic infiltrate, associated with ulcer and thrombus formation, and adjacent to areas of strong labeling for apoptotic bodies. A similar study using the polymerase chain reaction (Haraszthy *et al*. 2000) reported that 30% of the carotid endarderectomy specimens examined were positive for *T. forsythia*, 26% for *P. gingivalis*, 18% for *A. actinomycetemcomitans*, and 14% positive for *Pr. intermedia*. The validity of these data has been recently confirmed in similar studies (Stelzel *et al*. 2002; Fiehn *et al*. 2005). Corroborating the above observations, in an experimental animal study, oral infection of with *P. gingivalis* promoted atherogenesis and *P. gingivalis* DNA was localized within the aortic tissue of infected mice (Lalla *et al*. 2003).

Emerging evidence from epidemiologic studies indicates that periodontal infections have an impact on a host of peripheral blood markers that have been linked to CVD. For example, periodontitis patients have been shown to display higher white blood cell counts (Kweider *et al*. 1993; Loos *et al*. 2000) and C-reactive protein (CRP) levels (Ebersole *et al*. 1997; Loos *et al*. 2000; Slade *et al*. 2000) than periodontally healthy controls. Wu *et al*. (2000) examined the relation between periodontal health status and serum total and high-density lipoprotein cholesterol, CRP, and plasma fibrinogen. Based on an analysis of a total of 10 146 subjects from NHANES III with available cholesterol and CRP and 4461 subjects with available fibrinogen, poor periodontal status was significantly associated with increased CRP and fibrinogen levels. Slade *et al*. (2000) explored the same database and reported that (1) people with extensive periodontal disease had an increase of approximately one third in mean CRP and a doubling in prevalence of elevated CRP compared with periodontally healthy people, and (2) similarly raised CRP levels in edentulous subjects. Based on data of 2973 participants ≥40 years old from the second phase of NHANES III, Dye *et al*. (2005) showed that high serum IgG antibody level to *P. gingivalis* was significantly related to elevated serum CRP. In a sample comprising 5552 subjects aged 52–75 years from the Atherosclerosis Risk in Communities study (ARIC) (Slade *et al*. 2003), participants with extensive periodontal disease (≥30% of sites with pocket depth ≥4 mm) had 30% higher CRP levels than participants with extent of periodontal disease between 0 and 30%. In a multi-variate analysis stratified for BMI, extensive periodontal pocketing remained associated with CRP levels when adjusted for age, sex, diabetes mellitus, cigarette use, and use of non-steroidal anti-inflammatory medications. Finally, Schwahn *et al*. (2004) reported on associations between periodontitis, edentulism, and high plasma fibrinogen levels (>3.25 g/l), in 2738 persons aged 20–59 years, participants in the Study of Health in Pomerania (SHIP). In a two-way interaction model adjusted for multiple co-variates (age, gender, BMI, education, alcohol, gastritis, bronchitis, diabetes, use of medications, use of aspirin, LDL, and smoking), presence of ≥15 pockets with probing depth ≥4 mm was significantly associated with high plasma fibrinogen levels with an OR of 1.9 (95% CI 1.2–2.8). Less extensive pocketing or edentulism were not associated with high plasma fibrinogen levels.

Several studies have investigated the association between periodontitis and subclinical atherosclerosis, commonly measured by means of carotid artery intima media thickness (IMT) assessments. Increased IMT has been documented to be directly associated with increased risk or myocardial infarction and stroke (O'Leary *et al*. 1999). Beck *et al*. (2001) provided the first evidence that periodontitis may be linked to subclinical atherosclerosis. These authors analyzed cross-sectional data on 6017 persons, participants in the ARIC study, and demonstrated that severe periodontitis conferred increased odds for higher carotid artery intima media wall thickness (OR 2.09, 95% CI 1.73–2.53 for IMT of ≥1 mm). A couple of years later, the Oral Infection and Vascular Disease Epidemiology Study (INVEST; a prospective population-based cohort study of randomly selected subjects in a triethnic population, comprising a total of 1056 subjects aged ≥55 years, with no baseline history of stroke, myocardial infarction, or chronic inflammatory conditions) investigated the relationship between carotid artery plaque and IMT with tooth loss and measures of periodontitis. In a first report based on data from 711 subjects (Desvarieux *et al*. 2003), tooth loss of 10–19 teeth was associated with increase in prevalence of atherosclerotic plaques in a model adjusted for age, sex, smoking, diabetes, systolic blood pressure, LDL, HDL, ethnicity, education, tooth brushing, social isolation, physical activity, and years of residence (OR 1.9, CI 1.2–3.0). Since in this cohort a higher number of lost teeth paralleled an increased severity of periodontal disease at the remaining teeth, it was assumed that tooth loss reflected, in part, current or cumulative periodontal disease. In a subsequent publication, Engebretson *et al*. (2005) reported

on a sub-sample of 203 subjects from the INVEST cohort with available panoramic radiographs. In a logistic regression model, severe bone loss was defined as a whole mouth average bone loss of ≥50% of the root length and was associated with presence of carotid atherosclerotic plaque after adjustment for age, sex, hypertension, coronary artery disease, diabetes, smoking, HDL, and LDL. In addition, log-transformed mean carotid plaque thickness increased over tertiles of periodontal bone loss, suggesting a dose-dependent association. A third INVEST report (Desvarieux *et al*. 2005) included 657 patients with available dental and medical variables as described above, as well as data on the prevalence and level of ten bacterial species, assessed by checkerboard DNA–DNA hybridization (Socransky *et al*. 1994) in up to eight subgingival plaque samples per subject. In this study, "etiological bacterial burden" was defined as the aggregate colonization per subject by *A. actinomycetemcomitans*, *P. gingivalis*, *T. forsythia*, and *Tr. denticola*. The data revealed that IMT and while blood cell counts increased significantly over tertiles of etiologic periodontal bacterial burden in a fully adjusted model including age, BMI, gender, race/ethnicity, smoking, systolic blood pressure, education, diabetes, HDL, and LDL as co-variates. Importantly, the association was exclusively observed for "etiologic bacteria", as increased colonization by putative pathogens of the "orange complex" or a number of health-associated bacteria was not associated with increased IMT.

In an ARIC-based study including a sample of 4585 participants (Beck *et al*. 2005b), serum IgG titers for periodontal pathogens were associated with carotid IMT of ≥1 mm. The strongest association emerged when the combined titer against *Campylobacter rectus* and *Micromonas micros* was used. Similarly, a research group from Finland reported on the association between serum titers to periodontal pathogens and IMT in a sub-sample of 1023 men aged 46–64 from the Kuopio Ischemic Heart Disease Risk Factor study (Pussinen *et al*. 2005). Incident IMT assessed 10 years post baseline in participants with no prior coronary heart disease increased significantly across tertiles of IgA titer levels to *A. actinomycetemcomitans* and *P. gingivalis*.

Another group of epidemiologic studies has focused on the association of periodontal infections with clinical events, primarily coronary heart disease (CHD), myocardial infacrtion (MI) or stroke. An early study by DeStefano *et al*. (1993) used a prospective cohort of 9760 subjects and found a nearly two-fold higher risk of CHD for individuals with periodontal disease. Beck *et al*. (1996) used data from a cohort of 1147 subjects who were medically healthy at baseline, 207 of which developed CHD over an average follow-up of 18 years. Radiographic evidence of alveolar bone loss was used to stratify the subjects according to minimal and severe periodontitis. The results, presented as incidence odds ratios adjusted for age and race, showed a significant association between severe bone loss and total CHD, fatal CHD, and stroke.

Another ARIC-stemming report based on a sample of 5002 people (Beck *et al*. 2005a) reported no significant association between incipient or severe periodontitis defined by clinical measurements and CHD. However, in regression models adjusted for age, sex, race, diabetes, hypertension, waist-to-hip ratio, HDL and LDL cholesterol, and education, detectable antibody levels to specific periodontal pathogens were associated with prevalent CHD. When stratified for smoking, titers *to Tr. denticola*, *Prevotella intermedia*, *Capnocytophaga ochracea*, and *Veillonella parvula* conferred significant odds for CHD in ever smokers, while titers to *Prevotella nigrescens* and *A. actinomycetemcomitans* conferred significant odds for CHD in never smokers. In a retrospective follow-up study of a Finnish cohort of 63 men who were free of CHD at entry, but who developed fatal or non-fatal MI during a subsequent 10-year period, and of 63 age-matched controls, Pussinen *et al*. (2004) analyzed serum samples with respect to IgG and IgA antibodies to different strains of *A. actinomycetemcomitans* and *P. gingivalis*. In logistic regression models adjusted for traditional CHD risk factors such as smoking, serum cholesterol, blood pressure, BMI, and diabetes, increasing serum IgA titers to *P. gingivalis* resulted in significantly increasing odds for MI.

Among the group of studies focusing on the potential association of periodontitis and stroke, an early case–control study by Syrjanen *et al.* (1989) compared the level of dental disease in 40 patients who had suffered a cerebrovascular accident with 40 randomly selected community controls, matched for gender and age, and reported that severe chronic dental infection was associated with cerebral infarction in males under 50 years of age. In another case–control study (Grau *et al*. 1997), multiple logistic regression adjusted for age, social status, and a number of established vascular risk factors revealed that poor dental status was independently associated with cerebrovascular ischemia (OR 2.6, 95% CI 1.18–5.7).

Obviously, critical information on the role of periodontal infection as risk factor for atherosclerotic vascular disease and its sequels should be derived from intervention trials, ideally from randomized, placebo-controlled clinical trials. Unfortunately the design and conduct of such studies is particularly challenging, primarily due to the long time between exposure and manifestation of CVD, the relatively low incidence of CVD-related clinical events necessitating the inclusion of large subject samples, and ethical considerations related to the follow-up of untreated periodontal disease over prolonged time periods. Therefore, intervention trials conducted to date have been limited to the study of the effects of periodontal therapy on surrogate markers of risk for CVD or on pathways related to the pathobiology of the disease. For example, D'Aiuto *et al*. (2004) reported

on 94 systemically healthy patients with generalized severe periodontitis who received non-surgical therapy and extractions. In logistic regression analysis, the reduction of CRP-levels 6 months after periodontal therapy was significantly associated with the number of extracted teeth (OR 1.4, CI 1.1–1.8) and a greater than the median probing depth reduction in pockets initially ≥5 mm (OR 4.7, CI 1.4–15.8). In subsequent publications (D'Aiuto *et al*. 2005; D'Aiuto & Tonetti 2005), non-surgical periodontal therapy with and without adjunctive local antibiotics, resulted in a reduction of median CRP-levels at 2 months, with a more pronounced effect in non-smokers than in smokers. Circulating IL-6 levels were significantly reduced only in the group that received adjunctive local antibiotics (intensive treatment), but no significant changes were observed in LDL and HDL cholesterol and triglyceride levels. The same group (D'Aiuto *et al*. 2006) recently reported 6-month data on the effect of standard vs. intensive therapy. In comparison to baseline levels, a significant reduction in white blood cell counts, CRP levels, IL-6 levels, total cholesterol, LDL, and systolic blood pressure was observed in the intensive treatment group, whereas an increase in HDL levels was observed in the standard treatment group. Similarly, Taylor *et al*. (2006) reported that patients undergoing full-mouth extractions who had at least 2 teeth with probing depths ≥6 mm, attachment loss and bleeding on probing showed a significant reduction in CRP levels from 2.5 mg/L to 1.8 mg/L, and this effect was more pronounced in non-smokers.

Finally, another set of studies has focused on the effects of periodontal therapy on endothelial dysfunction, a biomarker of vascular disease (Verma *et al*. 2003). Endothelial dysfunction is defined as the reduced vasodilator capability of peripheral blood vessels and is assessed by measuring the difference in the diameter of a peripheral artery prior to and after reactive hyperemia induced through occlusion of blood flow (Celermajer *et al*. 1992). Endothelial dysfunction was more pronounced in periodontitis subjects than periodontally healthy controls in two studies (Amar *et al*. 2003; Mercanoglu *et al*. 2004). Three intervention studies reporting positive effects of periodontal therapy on endothelial dysfunction are available so far: one using non-surgical periodontal therapy (Mercanoglu *et al*. 2004), one using adjunctive systemic antibiotics (Seinost *et al*. 2005), and a third using a comprehensive "full-mouth disinfection" protocol (Elter *et al*. 2006).

Taken together, the studies above strongly suggest a biologically plausible association between periodontal infections and the pathogenesis of atherosclerotic cardiovascular disease. Obviously studies that have failed to document such an association or that point to a possibility of a more complex, conditional relationship exist as well (Hujoel *et al*. 2000, 2002b; Mattila *et al*. 2000). In particular, it has been suggested that the positive associations in epidemiologic studies between periodontal infections and atherosclerotic cardiovascular disease may be attributed to residual confounding due to insufficient accounting for the effects of smoking (Hujoel *et al*. 2002a; Spiekerman *et al*. 2003) or may be entirely spurious (Hujoel *et al*. 2003, 2006). While such a possibility is hard to rule out, it appears unreasonable to dismiss as an artifact the entire body of supportive data stemming from diverse investigational approaches (epidemiological, experimental, mechanistic, and intervention studies).

Pregnancy complications

Preterm infants are born prior to completion of 37 weeks of gestation. An estimated 11% (Goldenberg & Rouse 1998) of pregnancies end in preterm birth (PTB), and this rate appears to be on the rise in several developed countries, despite significant advances in obstetric medicine and improvements in prenatal care utilization. Of particular interest are the very preterm infants, born prior to 32 gestational weeks, the majority of which require neonatal intensive care due to their increased perinatal mortality, primarily due to impaired lung development and function. Still, the overall contribution of PTB to infant mortality and morbidity is substantial and includes a number of acute and chronic disorders including respiratory distress syndrome, cerebral palsy, pathologic heart conditions, epilepsy, blindness, and severe learning disabilities (McCormick 1985; Veen *et al*. 1991).

Preterm infants often weigh lower at birth (<2500 g), and low birth weight has been used as a surrogate for prematurity in cases where the exact gestational age at birth is difficult to assess. Birth weight is further classified as very low (<1500 g) or moderately low (between 1500 g and 2500 g). An additional term used is small for gestational age, defined as birth weight within the 10^{th} percentile of normal weight at a particular gestational age. The condition may, thus, affect even full term infants due to intra-uterine growth retardation (Ashworth 1998).

A number of risk factors for preterm birth has been identified (Goldenberg *et al*. 2000). These include young maternal age (Wessel *et al*. 1996; Lao & Ho 1997; Scholl *et al*. 1988), multiple gestation (Lee *et al*. 2006), small weight gain during pregnancy (Honest *et al*. 2005), cervical incompetence (Althuisius & Dekker 2005), smoking, alcohol and drugs of abuse (Myles *et al*. 1998), black race (Kleinman & Kessel 1987; David & Collins 1997), and a number of maternal infections (uterine track infections, bacterial vaginosis, chorioamnionitis) (Romero *et al*. 2001). Obstetric history of PTB is a robust marker of future PTB (Mutale *et al*. 1991). Importantly, approximately 50% of the variance in the incidence of preterm birth remains unexplained (Holbrook *et al*. 1989).

Despite the established role of genito-urinary tract infections in the pathobiology of preterm birth,

women with preterm labor do not invariably present with positive amniotic fluid cultures (Romero *et al*. 1988), leading to the hypothesis that PTB may be indirectly mediated through *distant* infections resulting in translocation of bacteria, bacterial vesicles or LPS in the systemic circulation. The possibility that periodontal infections may constitute such maternal infections that adversely influence birth outcome was raised for the first time in the late 1980s (McGregor *et al*. 1988). Transient bacteremias occur commonly in subjects with inflamed gingiva (Ness & Perkins 1980; Kinane *et al*. 2005; Forner *et al*. 2006) and may conceivably reach the placental tissues, providing the inflammatory impetus for labor induction (Offenbacher *et al*. 1998). An interesting publication in this context by Hill (1998) reported that amniotic fluid cultures from women with vaginosis rarely contained bacteria common to the vaginal tract but frequently harbored fusobacteria of oral origin, i.e. common constituents of the periodontal microbiota. Thus, these authors proposed that oral bacteria may reach amniotic fluids and influence maternal fetal tissues via hematogenous spread, resulting in a chorioamniotic challenge. In line with these observations, experimental evidence on the role of oral infections on pregnancy outcomes was first provided is a series of pioneering studies by Collins *et al*. (1994a,b), who demonstrated that injection of *P. gingivalis* in the pregnant hamster resulted in intrauterine growth retardation, smaller fetuses, and an increase in pro-inflammatory mediators such as IL-1beta and PGE_2 in the amniotic fluid. Subsequent studies in pregnant mice (Lin *et al*. 2003a,b) and rabbits (Boggess *et al*. 2005) confirmed and expanded these observations to include experimental infections by *Campylobacter rectus*.

The accumulating body of evidence available from human studies investigating a potential link between oral infections and adverse pregnancy outcomes were recently reviewed (Bobetsis *et al*. 2006; Xiong *et al*. 2006). In an early case–control study, Offenbacher *et al*. (1996) examined 124 mothers, of whom 93 ("cases") gave birth to children with birth weight of less than 2500 g, prior to 37 weeks of gestation. "Controls" were 46 mothers who delivered at term infants of normal birth weight. Assessments included a broad range of known obstetric risk factors, such as tobacco use, drug use, alcohol consumption, level of prenatal care, parity, genitourinary infections, and nutrition. The data showed a small, albeit statistically significant difference, in attachment loss between cases and controls (3.1 vs 2.8 mm). Multivariate logistic regression models, controlling for other risk factors and covariates, demonstrated that periodontitis, defined as ≥60% of all sites with attachment loss of ≥3 mm, conferred adjusted ORs of 7.9 for preterm, low birthweight babies. Following this report, several additional case–control studies were published, most of which reported a positive association between periodontitis and adverse pregnancy outcomes (Offenbacher *et al*. 1996; Dasanayake *et al*. 2001; Canakci *et al*. 2004; Goepfert *et al*. 2004; Mokeem *et al*. 2004; Radnai *et al*. 2004), although a number of studies that failed to document an association were published as well (Davenport *et al*. 2002; Buduneli *et al*. 2005; Moore *et al*. 2005).

Non-uniform data were also generated by cohort studies, i.e. studies that evaluated the periodontal status of pregnant women prior to completion of the second trimester and compared prospectively the incidence of adverse pregnancy outcomes in women with and without periodontitis. In the first prospective cohort study reporting a positive relationship between periodontitis and prematurity, Jeffcoat *et al*. (2001) assessed the periodontal conditions of 1313 primarily African American pregnant women at 21–24 weeks of gestation and reported that for women with generalized periodontitis, defined as ≥90% of all sites with attachment loss of 3 mm or more, adjusted odds ratios were 4.45 for delivery prior to 37 weeks' gestational age, 5.28 for delivery before 35 weeks' gestational age, and 7.07 for delivery before 32 weeks' gestational age. Corroborating positive data were reported by additional cohorts in the US (Offenbacher *et al*. 2001), Chile (Lopez *et al*. 2002a), and Switzerland (Dortbudak *et al*. 2005). Similar positive associations were reported for very preterm delivery (Offenbacher *et al*. 2006), small-for gestational-age infant (Boggess *et al*. 2006a), pre-eclampsia (Boggess *et al*. 2003), fetal exposure to oral pathogens, assessed by the presence of IgM antibodies in the fetal cord blood (Madianos *et al*. 2001), and with ante-partum vaginal bleeding and risk for premature delivery prior to 35 gestational weeks (Boggess *et al*. 2006b). In contrast, four cohort studies (Romero *et al*. 2002; Holbrook *et al*. 2004; Moore *et al*. 2004; Rajapakse *et al*. 2005) failed to document such an association. Of particular interest is the study by Moore *et al*. (2004) who reported data on 3738 women recruited on attending an ultrasound scan at approximately 12 weeks of pregnancy. Regression analysis indicated no significant relationships between the severity of periodontal disease and either preterm birth or low birth weight, although a positive correlation was reported between poorer periodontal health and late miscarriage.

Five intervention studies on the effects of periodontal treatment on pregnancy outcomes have been published to date. The first (Mitchell-Lewis *et al*. 2001) examined a cohort of 213 young, minority, pregnant, and post-partum women with respect to clinical periodontal status and analyzed the available birth outcome data for 164 women, 74 of whom received oral prophylaxis during pregnancy, and 90 who received no prenatal periodontal treatment. In this cohort with particularly high incidence of preterm low birth weight (PLMW of 16.5%), no differences in clinical periodontal status were observed between PLBW cases and women with normal birth outcomes. However, PLBW mothers harbored

statistically significantly higher levels of *T. forsythia* and *C. rectus*, and consistently elevated counts for a number of species examined. Interestingly, PLBW occurred in 18.9% of the women who did not receive periodontal intervention, and in 13.5% (ten cases) of those who received such therapy, reflecting a substantial, although statistically non-significant, incidence reduction of approximately 30%. However, the small sample size in combination with the fact that the participants were not randomly assigned into the two treatment groups were important shortcomings of the study design.

In a pilot intervention study, Jeffcoat *et al*. (2003) recruited 366 women with periodontitis between 21 and 25 weeks' gestation and randomized them to one of three treatment groups with stratification on previous spontaneous preterm birth prior to 35 weeks, BMI <19.8, or bacterial vaginosis assessed by Gram stain of vaginal smear samples. The treatment arms included a group that received supragingival dental prophylaxis and a placebo capsule; a group that received scaling and root planing (SRP) plus a placebo capsule; and a group that received SRP and systemic metronidazole 250 mg t.i.d. for 1 week. An additional group of 723 pregnant women who enrolled in a prospective study served as an untreated reference group. The results revealed that the rate of PTB before 35 gestational weeks was 4.9% in the prophylaxis group, 3.3% in the SRP plus metronidazole group, and 0.8% in the SRP plus placebo group. The corresponding PTB rate in the reference group was 6.3%. Although the difference between the prophylaxis and the SRP plus placebo group approached, but did not reach, statistical significance, the study suggested that periodontal therapy has the potential to reduce PTB, but that adjunctive systemic metronidazole did not enhance the pregnancy outcome. The latter observation is in line with the findings of a multicenter trial that suggested that systemic metronidazole used in the treatment of asymptomatic bacterial vaginosis does not reduce the occurrence of preterm delivery (Carey *et al*. 2000).

In contrast, impressive positive findings were reported from two randomized clinical trials conducted in Chile (Lopez *et al*. 2002b, 2005). In the first trial (Lopez *et al*. 2002b), 400 pregnant women with periodontal disease were enrolled and randomly assigned to either a treatment group which received periodontal therapy before 28 weeks of gestation or to a control group which received treatment after delivery. The incidence of PLBW (i.e. gestational age at birth <37 weeks or birth weight <2500 g) among the 351 women who completed the trial was 1.8% in the treatment group and 10.1% in the control group, resulting in an OR of 5.5 (95% CI 1.6–18.2, p = 0.001). In a multi-variate logistic regression model accounting for previous PLBW, frequency of prenatal visits, and maternal low weight gain, periodontitis remained the strongest factor with OR of 4.7 (95% CI 1.3–17.1). Of note in this trial is the relatively high drop-out rate (12.2%), as well as the fact that approximately one fifth of the women in the treatment group received adjunctive systemic antibiotics (amoxicillin and metronidazole) for the control of aggressive periodontitis. The second trial from the same group (Lopez *et al*. 2005) examined the effect of treatment of gingivitis on adverse pregnancy outcomes. Out of 870 pregnant women with gingivitis enrolled, two thirds received plaque control, scaling, and daily rinsing with 0.12% clorhexidine prior to 28 weeks of gestation, followed by maintenance every 2–3 weeks until delivery (treatment group) while a control group received therapy after delivery. With 834 women completing the trial, the incidence of PTLBW was 2.1% in the treatment group and 6.7% in the control group (OR 3.3, 95% CI 1.6–6.8; p = 0.0009).

Finally, a multicentre randomized, blinded, controlled trial examined the effect of non-surgical periodontal treatment on preterm birth (Michalowicz *et al*. 2006). After screening a total of 3504 women for a minimum extent and severity of periodontitis to satisfy the study's enrollment criteria, 823 women were randomly assigned to either receive scaling and root planing before 21 weeks (413 women) or after delivery (410 women). Participants in the treatment group underwent additional recall visits. The findings (Fig. 7-5) showed that preterm birth before 37 gestational weeks occurred in 49 of 407 women (12.0%) in the treatment group and in 52 of 405 women (12.8%) in the control group (hazard ratio for treatment group vs. control group, 0.93; p = 0.70; 95% CI 0.63–1.37). There were no significant differences between the treatment and control groups in birth weight or in the rate of delivery of infants that were small for gestational age. However, almost three times as many spontaneous abortions or stillbirths occurred in the control group than in the treatment group (14 vs 5, p = 0.04). Thus, this study failed to document a positive effect of periodontal treatment on rates of preterm birth, low birth weight, or fetal growth restriction, although it demonstrated that periodontal treatment of pregnant women is safe.

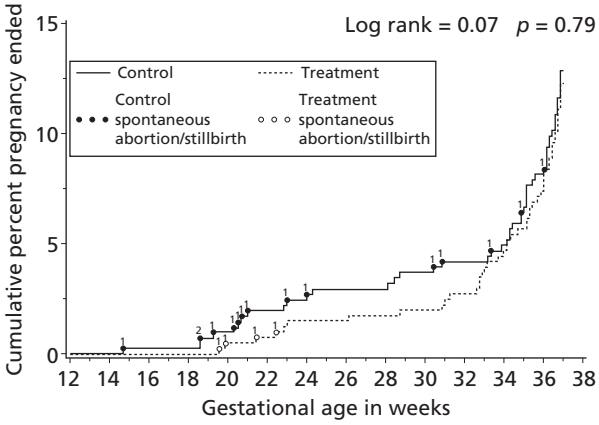

Fig. 7-5 Kaplan–Meier curve for the cumulative incidence of pregnancies ending before 37 weeks in the Obstetrics and Periodontal Therapy study. Adapted from Michalowicz *et al*. 2006, reproduced with permission. Copyright © 2006 Massachusetts Medical Society.

The observed discrepancy in spontaneous abortions and stillbirths between the two groups observed in the above study is clearly intriguing. An effect of periodontal treatment on early adverse outcomes is plausible in light of observational studies that suggest that periodontitis is more strongly associated with late miscarriage (Moore *et al*. 2004), stillbirth, and early spontaneous preterm birth rather than with preterm birth in general. It was suggested therefore (Goldenberg & Culhane 2006) that future studies may preferentially focus on late miscarriage, early stillbirth, and preterm birth prior to 32 weeks, rather than on all preterm births prior to 37 weeks. Additional issues to be addressed in future studies relate to the timing and the intensity of the periodontal intervention, as well as the possibility that such effects may vary with race/ethnicity. Currently, there are at least three randomized controlled trials underway, all of which involve larger subject samples that the study by Michalowicz *et al*. (2006), that will contribute with more definitive answers on whether periodontal treatment has a role in reducing the rate of adverse pregnancy outcomes.

Diabetes mellitus

The role of diabetes as a risk factor for periodontitis has been discussed above; however, limited data seem to suggest that an inverse relationship may also be present. In line with the concept that infections may contribute to impaired metabolic control of diabetes (Rayfield *et al*. 1982; Lang 1992; Ling *et al*. 1994), studies of both type 1 (Thorstensson *et al*. 1996) and type 2 (Taylor *et al*. 1996) diabetic subjects have indicated that periodontal infections may also be detrimental in this context. The former study involved 39 diabetic subjects with severe periodontitis and an equal number of diabetic subjects with gingivitis or mild periodontitis. Both groups had a median duration of diabetes of 25 years. Over a median follow-up period of 6 years, significantly higher prevalence of proteinuria and cardiovascular complications was observed in the severe periodontitis group. A 2-year follow-up study of 90 subjects with type 2 diabetes with good to moderate metabolic control revealed that severe periodontitis at baseline was associated with increased risk for poor glycemic control.

A limited number of studies has examined the effect of treatment of periodontitis on diabetic metabolic control, as reflected by levels of glycated hemoglobin A1c (HbA1c) or plasma glucose. Interestingly, all studies that solely included mechanical periodontal therapy (Seppälä *et al*. 1993; Aldridge *et al*. 1995; Smith *et al*. 1996; Grossi *et al*. 1997a; Christgau *et al*. 1998) but one (Stewart *et al*. 2001) reveal no effect on diabetes metabolic control, regardless of periodontal disease severity, baseline level of metabolic control, type and duration of diabetes. Interestingly, Stewart *et al*. (2001) followed 72 patients with type 2 diabetes for 18 months, half of whom received mechanical periodontal therapy, but reported that both the periodontally treated and the untreated group showed statistically significant decreases in HbA1c levels (17.1% vs. 6.7%, respectively). In contrast, studies including antibiotics as an adjunct to mechanical therapy (Williams & Mahan 1960; Grossi *et al*. 1997a; Miller *et al*. 1992) reported a limited, short-term improvement in metabolic control. For example, Grossi *et al*. (1997a) reported a 10% improvement in glycated hemoglobin (HbA1c) at 3 months after the completion of non-surgical periodontal therapy combined with adjunctive systemic doxycycline, although this effect was not sustainable at later time points. Interestingly, no such effect on HbA1c was observed in subjects that did not receive adjunctive antibiotic therapy. Rodrigues *et al*. (2003) randomly assigned 30 type 2 patients to two treatment groups, one group receiving non-surgical periodontal therapy with amoxicillin/clavulanic acid and the other receiving only mechanical therapy. At 3 months, HbA1c levels were reduced in both groups, but the reduction was statistically significant only in the group that received scaling and root planing alone. Nevertheless, a recent meta-analysis of ten intervention studies aiming at the quantification of the effects of periodontal treatment on HbA1c level among diabetic patients, including a total of 456 patients, revealed a non-statistically significant decrease in actual HbA1c levels (Janket *et al*. 2005). Indeed, the weighted average decrease in actual HbA1c level was found to be 0.38% for all studies, 0.66% when restricted to type 2 diabetic patients, and 0.71% if adjunctive antibiotics were administered. Clearly, further studies are needed to clarify the conditions under which periodontal treatment can contribute to improved metabolic control, especially in type 1 diabetes.

Concluding remarks

One of the issues related to the descriptive epidemiology of periodontal infections that is still under debate is whether their worldwide prevalence has been decreasing over the last decades. Unfortunately, the data do not allow a clear answer for a number of reasons. First, no universal conclusion is possible, since the prevalence of periodontal disease appears to vary with race and geographic region. Second, the quality of the data available from the developing and the developed countries is clearly not comparable. While some well conducted epidemiologic surveys that provide detailed information have been carried out in a number of countries, the majority of the studies in the developing world have used the CPITN system, which produced data of inadequate detail. Moreover, studies using the exact same methodology to evaluate random samples drawn from the same population over time are sparse. Among the few exceptions is a series of studies from Sweden (Hugoson *et al*. 1998b, 1992, 2005) that documented, by clinical and radiographic means, the frequency

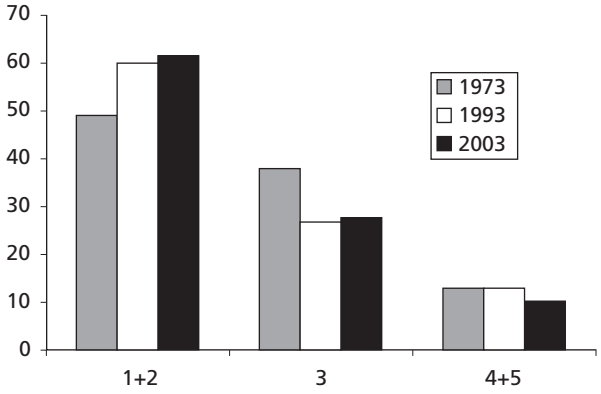

Fig. 7-6 Frequency distribution of subjects with healthy periodontal conditions or gingivitis (groups 1 + 2), moderate periodontitis (group 3), and advanced and severe periodontal disease (groups 4 + 5), in a Swedish cohort in 1973, 1993, and 2003. For definitions see text. Adapted after personal communication with Dr. Anders Hugoson, based on data by Hugoson *et al*. (1992, 1998, 2006).

distribution of various levels of severity of periodontitis in four cross-sectional studies over a 30-year period (in 1973, 1983, 1993, and 2003). In these studies, subjects were grouped according to the severity of their periodontal conditions in five groups: groups 1 and 2 included subjects who were periodontally healthy or only had gingivitis, group 3 included subjects with moderate periodontitis, i.e. whose loss of periodontal tissues support did not extend beyond one third of the root length, while groups 4 and 5 included subjects with more severe destructive disease. As shown in Fig. 7-6, a clear increase in the frequency of subjects in groups 1 and 2 was noted over the 30-year period, from 49% in 1973 to 60% in 1993 to almost 62% in 2003. This increase occurred primarily at the expense of group 3 which declined from 38% in 1973 to 27% in 1993 and apparently reached a plateau at 28% in 2003. Nevertheless, the frequency of subjects in groups 4 and 5 was virtually stable over the 30-year period: 13% in 1973, 13% in 1993 and 10.5% in 2003. Based on these data derived from a population with arguably the best access to and utilization of oral health care in the world, we may conclude that the fraction of the population which is apparently most susceptible to severe periodontitis is apparently not declining in frequency. Instead, the main beneficiaries of the improved oral health awareness, access to care and increased utilization of therapeutic resources that occurred over the last decades appear to be the individuals with moderate levels of periodontitis whose prevalence is clearly lower.

What was also well documented in these and other studies is that the rate of edentulism has decreased substantially over the past 30 years, with elderly groups retaining their natural dentition and higher mean numbers of teeth than their counterparts a generation ago. As a consequence, this fact *per se* should contribute to an increased prevalence of periodontal disease in older age cohorts, since retained teeth in the elderly are more likely to experience substantial cumulative attachment loss which forms the basis of the assessment of prevalence (Douglass & Fox 1993). It has been argued, however, that such a potential increase, may not necessarily result in increased need for periodontal therapy (Oliver *et al*. 1989). Additional research is clearly required to further elucidate these issues, and an adequate and consistent epidemiological methodology is essential for generating valid comparative data. On the other hand, the need for description of prevalence and incidence of periodontal diseases in every conceivable population has been questioned (Baelum & Papapanou 1996), although such information may be of value for local oral health planners. Instead, the principle task of future epidemiological research is arguably the identification of risk factors for disease development, laying the ground for an enhanced understanding of the pathobiology of periodontitis. Although several risk factors have already been established and a wide array of disease markers has been recognized, the impact of the intervention with such factors on the state of periodontal health on a population level has yet to be documented. To assess the magnitude of the clinical benefit achieved by such modulation, prospective, long-term epidemiological surveys have to be conducted.

Somewhat provocatively, it has been stated that modern science has a tendency to re-discover issues brought up a long time back and (then) rejected. One cannot help bringing the "focal infection" theory in mind, when encountering the emerging plethora of publications dealing with the role of periodontal infections as risk factors for systemic disease. Although the proposed associations appear to be biologically plausible, at this stage, we cannot draw any definitive conclusions on whether these associations are in fact causal, and if so, on the magnitude of their biological effects. Nevertheless, these studies underscore that the oral cavity is an integral part of the human body, and that systemic health must encompass oral, and periodontal, health as well. Last but certainly not least, these studies have provided a unique opportunity for us oral health researchers to expand our investigative sphere, interact fruitfully with our colleagues in medicine, and acquire more knowledge. Irrespective of the definitive conclusions of these research efforts, its by-products may prove to be just as important as the elucidation of the research task *per se*.

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Part 3: Microbiology

Chapter 8

Oral Biofilms and Calculus

Niklaus P. Lang, Andrea Mombelli, and Rolf Attström

Microbial considerations

Throughout life, all the interface surfaces of the body are exposed to colonization by a wide range of microorganisms. In general, the establishing microbiota live in harmony with the host. Constant renewal of the surfaces by shedding prevents the accumulation of large masses of microorganisms. In the mouth, however, teeth provide hard, non-shedding surfaces for the development of extensive bacterial deposits. The accumulation and metabolism of bacteria on hard oral surfaces is considered the primary cause of dental caries, gingivitis, periodontitis, peri-implant infections, and stomatitis. Massive deposits are regularly associated with localized disease of the subjacent hard or soft tissues. In 1 mm^3 of dental plaque weighing approximately 1 mg, more than 10^8 bacteria are present. Although over 300 species have been isolated and characterized in these deposits, it is still not possible to identify all the species present. In the context of the oral cavity, the bacterial deposits have been termed *dental plaque* or *bacterial plaque*. Classical experiments have demonstrated that accumulation of bacteria on teeth reproducibly induces an inflammatory response in associated gingival tissues (Fig. 8-1a,b). Removal of plaque leads to the disappearance of the clinical signs of this inflammation (Löe *et al*. 1965; Theilade *et al*. 1966). Similar cause and effect relationships have been demonstrated for plaque and peri-implant mucositis (Pontoriero *et al*. 1994).

Germ-free animals provide an experimental model which has demonstrated that the absence of bacteria is associated with optimal dental and gingival health. Clinical studies have convincingly demonstrated that regular daily removal of dental plaque in most patients prevents further dental disease. Dental professionals and patients, therefore, consider regular mechanical removal of all bacterial deposits from non-shedding oral surfaces the primary prerequisite to prevent disease.

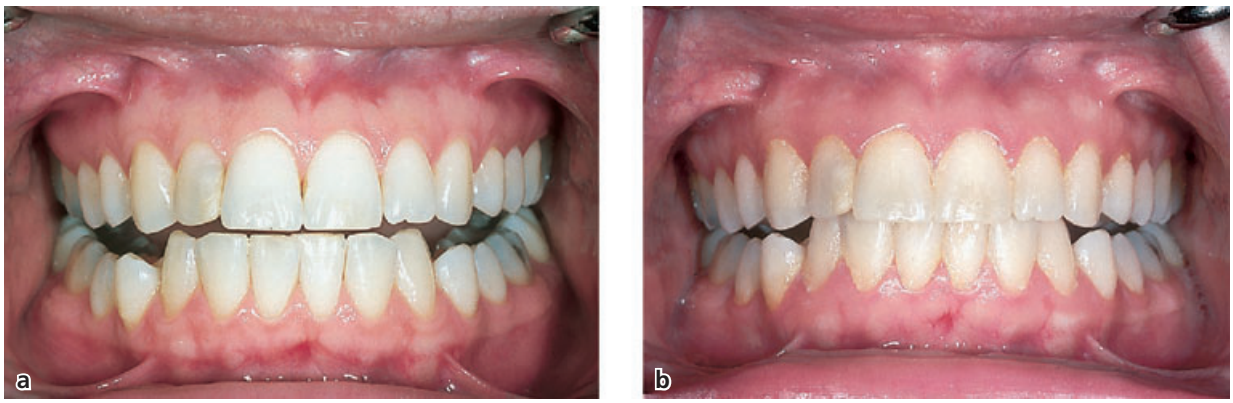

Fig. 8-1 Experimental gingivitis model (Löe *et al*. 1965). (a) Human volunteer with clean teeth and clinically healthy gingival tissues at the start of the period of experimental plaque accumulation. (b) Same human volunteer after 21 days of abolished oral hygiene practices leading to plaque deposits covering almost all tooth surfaces and consequently developing a generalized marginal gingival inflammation.

At first, a direct relationship was often assumed to exist between the total number of accumulated bacteria and the amplitude of the pathogenic effect; biologically relevant differences in the composition of plaque were not usually considered. This bacterial mass, termed *plaque*, was shown to produce a variety of irritants, such as acids, endotoxins, and antigens, which, over time, invariably dissolved teeth and destroyed the supporting tissues. Consequently, the need to discriminate among bacterial deposits from different patients or at healthy or diseased sites was not yet recognized in detail. Individuals with extensive periodontal disease were either suspected of having a weak resistance to bacterial plaque as a whole or were blamed for inadequate home care. Such a view of dental plaque as a biomass is referred to as the *non-specific plaque hypothesis* (Theilade 1986).

The propensity of inflamed sites to undergo permanent tissue destruction was recognized later to be more specific in nature, because not all gingivitis lesions seemed invariably to progress to periodontitis. Most periodontal sites in most subjects do not always show clinical signs of active tissue destruction with loss of connective tissue fiber attachment to the root surface, even though they may constantly be colonized by varying numbers and species of bacteria. Possible pathogens have been suggested among the organisms regularly found at elevated levels in periodontal lesions in relation to those observed under clinically healthy conditions. Longitudinal studies have indicated an increased risk for periodontal breakdown in sites colonized by some potentially pathogenic organisms. Treatment outcomes were better if these organisms could no longer be detected at follow-up examinations (see Chapter 9). If periodontal disease is indeed due to a limited number of bacterial species, the continuous and maximal suppression of plaque as a whole may not be the only possibility to prevent or treat periodontitis. Hence, specific elimination or reduction of presumptive pathogenic bacteria from plaque may become a valid alternative. Treatment may only be necessary in those patients diagnosed as having the specific infection and may be terminated once the pathogenic agents are eliminated. Such a view of periodontitis being caused by specific pathogens is referred to as the *specific plaque hypothesis* (Loesche 1979).

The term *infection* refers to the presence and multiplication of a microorganism in body tissues. The uniqueness of bacterial plaque-associated dental diseases as infections relates to the lack of massive bacterial invasion of tissues. Infections caused by the normal microbiota are sometimes called endogenous infections. Endogenous infections result when indigenous microbes move from their normal habitats into unusual anatomic regions. *Staphylococcus epidermidis*, for instance, is a non-pathogenic, commensal saprophyte on the skin. If this organism reaches the surface of a vascular prosthesis or an orthopedic implant, a serious infection may emerge. Infections caused by endogenous microbes are called *opportunistic infections* if they occur at the usual habitat of the microorganisms. Such infections may be the result of changing ecologic conditions or may be due to a decrease of host resistance. In the prevention of opportunistic infections due to overgrowth of indigenous organisms, continuous control of ecologic conditions regulating bacterial growth has high priority. The majority of microorganisms in periodontitis plaque can also be found occasionally in low proportions in health. These organisms may, therefore, be viewed as putative opportunistic pathogens. A small number of suspected pathogens, e.g. the Gram-negative anaerobe *Porphyromonas gingivalis*, are rare organisms in the mouth of healthy individuals. Some researchers have suggested that such bacteria may be considered exogenous pathogens. If some periodontal microorganisms were indeed exogenous pathogens, avoidance of exposure would become an important goal of prevention, and therapy should be aimed at the elimination of the microorganisms. Their mere presence would be an indication for intervention.

Dental plaque may accumulate supragingivally, i.e. on the clinical crown of the tooth, but also below the gingival margin, i.e. in the subgingival area of the sulcus or pocket. Differences in the composition of the subgingival microbiota have been attributed in part to the local availability of blood products, pocket depth, redox potential, and pO_2. Therefore, the question of whether the presence of specific microorganisms in patients or distinct sites may be the cause or the consequence of disease continues to be a matter of dispute (Socransky *et al*. 1987). Many microorganisms considered to be periodontopathogens are fastidious, strict anaerobes and, as such, may contribute little to the initiation of disease in shallow gingival pockets. If their preferred habitat were the deep periodontal pocket, they would be linked to the progression in sites with pre-existing disease, rather than to the initiation of disease in shallow sites. These microbiologic aspects are to be put in perspective with the host response. Further discussions are presented in Chapter 9.

General introduction to plaque formation

Growth and maturation patterns of bacterial plaque have been studied on natural hard oral surfaces, such as enamel and dentin, or artificial surfaces, such as metal or acrylic, using light and electron microscopy and bacterial culture (Theilade & Theilade 1985). Despite differences in surface roughness, free energy, and charge, the most important features of initial plaque development are similar on all these materials (Siegrist *et al*. 1991).

The ability to adhere to surfaces is a general property of almost all bacteria. It depends on an intricate,

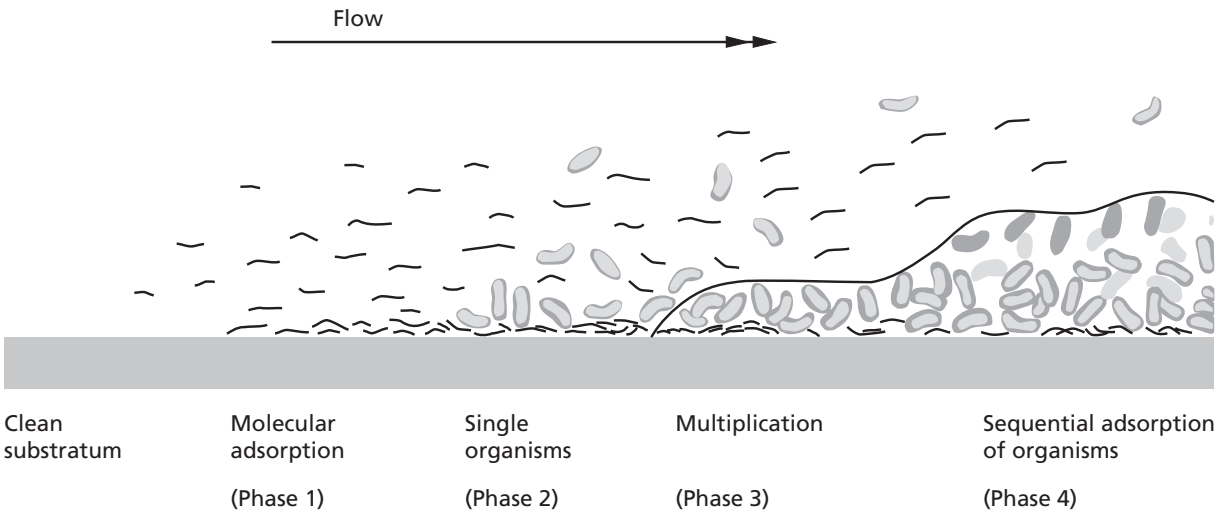

Fig. 8-2 Stages in the formation of a biofilm on a clean, hard and non-shedding surface following immersion into a fluid environment. Phase 1: Molecular adsorption to condition the biofilm formation. Phase 2: Bacterial adhesion by single organisms. Phase 3: Growth of extracellular matrix production and multiplication of the adhering bacteria. Phase 4: Sequential adsorption of further bacteria to form a more complex and mature biofilm. Adapted from Marshall (1992).

sometimes exquisitely specific, series of interactions between the surface to be colonized, the microbe, and an ambient fluid milieu (Mergenhagen & Rosan 1985).

Immediately upon immersion of a solid substratum into the fluid media of the oral cavity, or upon cleaning of a solid surface in the mouth, hydrophobic and macromolecules begin to adsorb to the surface to form a conditioning film (Fig. 8-2, Phase 1), termed the acquired pellicle. This film is composed of a variety of salivary glycoproteins (mucins) and antibodies. The conditioning film alters the charge and free energy of the surface, which in turn increases the efficiency of bacterial adhesion. Bacteria adhere variably to these coated surfaces. Some possess specific attachment structures such as extracellular polymeric substances and fimbriae, which enable them to attach rapidly upon contact (Fig. 8-2, Phase 2). Other bacteria require prolonged exposure to bind firmly. Behaviors of bacteria change once they become attached to surfaces. This includes active cellular growth of previously starving bacteria and synthesis of new outer membrane components. The bacterial mass increases due to continued growth of the adhering organisms, adhesion of new bacteria (Fig. 8-2, Phase 4), and synthesis of extracellular polymers. With increasing thickness, diffusion into and out of the biofilm becomes more and more difficult. An oxygen gradient develops as a result of rapid utilization by the superficial bacterial layers and poor diffusion of oxygen through the biofilm matrix. Completely anaerobic conditions eventually emerge in the deeper layers of the deposits. Oxygen is an important ecologic determinant because bacteria vary in their ability to grow and multiply at different levels of oxygen. Diminishing gradients of nutrients supplied by the aqueous phase, i.e. the saliva, are also created. Reverse gradients of fermentation products develop as a result of bacterial metabolism.

Dietary products dissolved in saliva are an important source of nutrients for bacteria in the supragingival plaque. Once a deepened periodontal pocket is formed, however, the nutritional conditions for bacteria change because the penetration of substances dissolved in saliva into the pocket is very limited. Within the deepened pocket, the major nutritional source for bacterial metabolism comes from the periodontal tissues and blood. Many bacteria found in periodontal pockets produce hydrolytic enzymes with which they can break down complex macromolecules from the host into simple peptides and amino acids. These enzymes may be a major factor in destructive processes of periodontal tissues.

Primary colonization is dominated by facultatively anaerobic Gram-positive cocci. They adsorb onto the pellicle-coated surfaces within a short time after mechanical cleaning. Plaque collected after 24 hours consists mainly of streptococci; *S. sanguis* is the most prominent of these organisms. In the next phase, Gram-positive rods, which are present in very low numbers initially, gradually increase and eventually outnumber the streptococci (Fig. 8-3). Gram-positive filaments, particularly *Actinomyces* spp., are the predominating species in this stage of plaque development (Fig. 8-4). Surface receptors on the deposited Gram-positive cocci and rods allow subsequent adherence of Gram-negative organisms with poor ability to attach directly to pellicle. *Veillonella*, fusobacteria, and other anaerobic Gram-negative bacteria can attach in this way (Fig. 8-5). The heterogeneity of plaque thus gradually increases and, with time, includes large numbers of Gram-negative organisms. A complex array of interrelated bacterial species is the result of this development. Exchange of nutrients

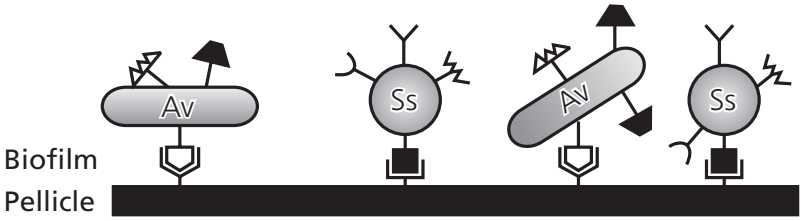

Fig. 8-3 Primary colonization by predominantly Gram-positive facultative bacteria. Ss: *Streptococcus sanguis* is most dominant. Av: *Actinomyces* spp. are also found in 24-hour plaque.

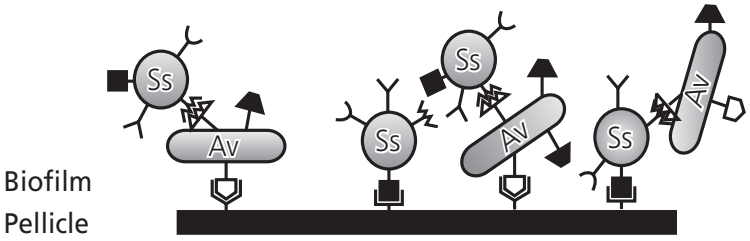

Fig. 8-4 Gram-positive facultative cocci and rods coaggregate and multiply.

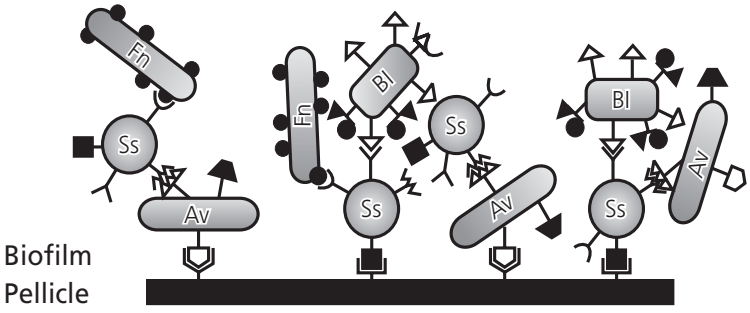

Fig. 8-5 Surface receptors on the Gram-positive facultative cocci and rods allow the subsequent adherence of Gram-negative organisms, which have a poor ability to adhere directly to the pellicle. Fn: *Fusobacterium nucleatum*; BI: *Prevotella intermedia*.

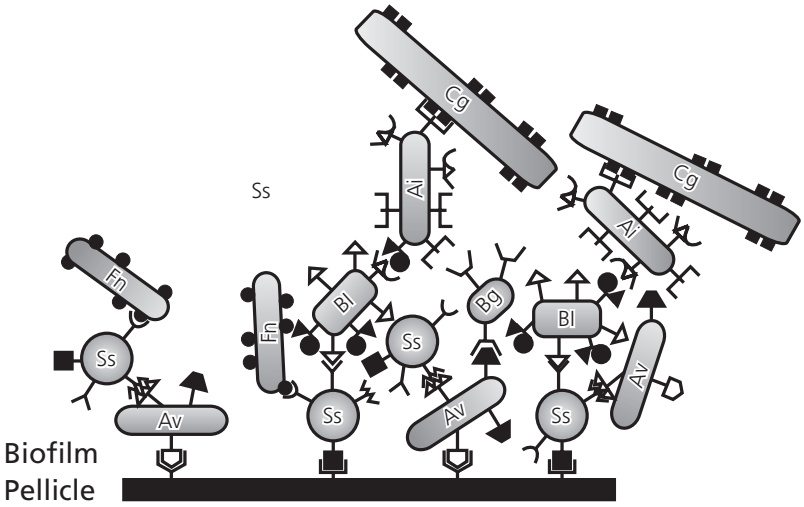

Fig. 8-6 The heterogeneity increases as plaque ages and matures. As a result of ecologic changes, more Gram-negative strictly anaerobic bacteria colonize secondarily and contribute to an increased pathogenicity of the biofilm. Bg: *Porphyromonas gingivalis*; Cg: *Capnocytophaga* sp.

between different species, but also negative interactions, e.g. the production of bacteriocins, play a role in the establishment of a stable bacterial community (Fig. 8-6). Due to the influences of local environmental factors, structurally different types of plaque evolve at different locations. Protection of the growing plaque from shear forces and local availability of certain nutrients are most important. A distinct composition of mature bacterial deposits can eventually be recognized at specific sites and under specific clinical conditions. Examples are the plaque on a smooth enamel surface versus fissure plaque, or the plaque in shallow and less shallow gingival crevices.

Accumulation of plaque along the gingival margin leads to an inflammatory reaction of the soft tissues. The presence of this inflammation has a profound influence on the local ecology. The availability of blood and gingival fluid components promotes growth of Gram-negative bacterial species with an increased periodontopathic potential. Bacterial samples from established gingivitis lesions have

increased numbers of these bacteria. Because of the capability enzymatically to digest proteins, many of these organisms do not depend upon a direct availability of dietary carbohydrates. Such bacteria do not produce extracellular polymers and develop only loosely adherent plaque in the developing periodontal pocket. Cultivation of samples from advanced periodontal lesions reveals a predominance of Gram-negative anaerobic rods. Under the microscope, particularly high numbers of anaerobic uncultivable spirochetes can be demonstrated. Further details on the microbial ecology of subgingival plaque are discussed in Chapter 9.

In summary, immediately following immersion of hard, non-shedding surfaces into the fluid environment of the oral cavity, adsorption of macromolecules will lead to the formation of a *biofilm*. Bacterial adhesion to this glycoprotein layer will first involve primary plaque formers, such as Gram-positive facultative cocci and rods. Subsequent colonization on to receptors of these organisms will involve Gram-negative, strictly anaerobic bacteria, while the primary plaque formers also multiply to form colonies. The heterogeneity of the complex biofilm increases with time, as the ecologic conditions gradually change.

Dental plaque as a biofilm

The term *biofilm* describes the relatively undefinable microbial community associated with a tooth surface or any other hard, non-shedding material (Wilderer & Charaklis 1989). In the lower levels of most biofilms a dense layer of microbes is bound together in a polysaccharide matrix with other organic and inorganic materials. On top of this layer is a looser layer, which is often highly irregular in appearance and may extend into the surrounding medium. The fluid layer bordering the biofilm may have a rather "stationary" sublayer and a fluid layer in motion. Nutrient components may penetrate this fluid medium by molecular diffusion. Steep diffusion gradients, especially for oxygen, exist in the more compact lower regions of biofilms. The ubiquity with which anaerobic species are detected from these areas of biofilms provides evidence for these gradients (Ritz 1969).

Accumulation of bacteria on solid surfaces is not an exclusive dental phenomenon. Biofilms are ubiquitous; they form on virtually all surfaces immersed in natural aqueous environments. Biofilms form particularly fast in flow systems where a regular nutrient supply is provided to the bacteria. Rapid formation of visible layers of microorganisms due to extensive bacterial growth accompanied by excretion of copious amounts of extracellular polymers is typical for biofilms. Biofilms effectively protect bacteria from antimicrobial agents. Treatment with antimicrobial substances is often unsuccessful unless the deposits are mechanically removed. Adhesion-mediated infections that develop on permanently or temporarily implanted materials, such as intravascular catheters, vascular prostheses or heart valves, are notoriously resistant to antibiotics and tend to persist until the device is removed. Similar problems are encountered in water conduits, wherein potentially pathogenic bacteria may be protected from chlorination, or on ship hulls, where biofilms increase frictional resistance and turbulence (Gristina 1987; Marshall 1992).

In summary, *dental plaque* as a naturally occurring microbial deposit *represents a true biofilm* which consists of bacteria in a matrix composed mainly of extracellular bacterial polymers and salivary and/or gingival exudate products.

Structure of dental plaque

Supragingival plaque

Supragingival plaque has been examined in a number of studies by light and electron microscopy to gain information on its internal structure (Mühlemann & Schneider 1959; Turesky *et al*. 1961; Theilade 1964; Frank & Brendel 1966; Leach & Saxton 1966; Frank & Houver 1970; Schroeder & De Boever 1970; Theilade & Theilade 1970; Eastcott & Stallard 1973; Saxton 1973; Rönström *et al*. 1975; Tinanoff & Gross 1976; Lie 1978). The introduction of the electron microscope in dental research was a significant development for studies of dental plaque, both because the size of many bacteria approaches the ultimate resolving power of the light microscope, and because the resins used for embedding allowed for sections thinner than the smallest bacterial dimension. The substructure of plaque could therefore be identified.

In studies of the internal details of plaque, samples are required in which the deposits are kept in their original relation to the surface on which they have formed. This may be accomplished by removing the deposits with the tooth. If plaque of known age is the object of study, the tooth surfaces are cleaned at a predetermined time before removal (McDougall 1963; Frank & Houver 1970; Schroeder & De Boever 1970). Pieces of natural teeth or artificial surfaces may also be attached to solid structures in the mouth and removed after a given interval. This method of plaque collection was already used at the beginning of the last century by Black (1911). The systematic use of artificial surfaces for collection of plaque was reintroduced during the 1950s. Thin plastic foils of Mylar® were attached to mandibular incisor teeth for known periods, after which they were removed for histologic, histochemical, and electron microscopic examination of the deposited material (Mandel *et al*. 1957; Mühlemann & Schneider 1959; Zander *et al*. 1960; Schroeder 1963; Theilade 1964). Other types of plastic materials such as Westopal®, Epon®, Araldite®, and *spray plast* have since been employed for this purpose (Berthold *et al*. 1971; Kandarkar 1973; Lie 1975; Listgarten *et al*. 1975; Rönström *et al*. 1975). Results from several such studies indicate that plaque formed

Fig. 8-7 Electron micrographic illustration of a 4-hour dental pellicle. The pellicle has formed on an artificial surface of plastic, which was painted on to the surface of the tooth. The plastic surface was exposed to the environment for a 4-hour period. A thin condensed layer of organic material is covering the film. The material has a relatively homogeneous appearance but varies in thickness over the surface. From Brecx *et al*. (1981).

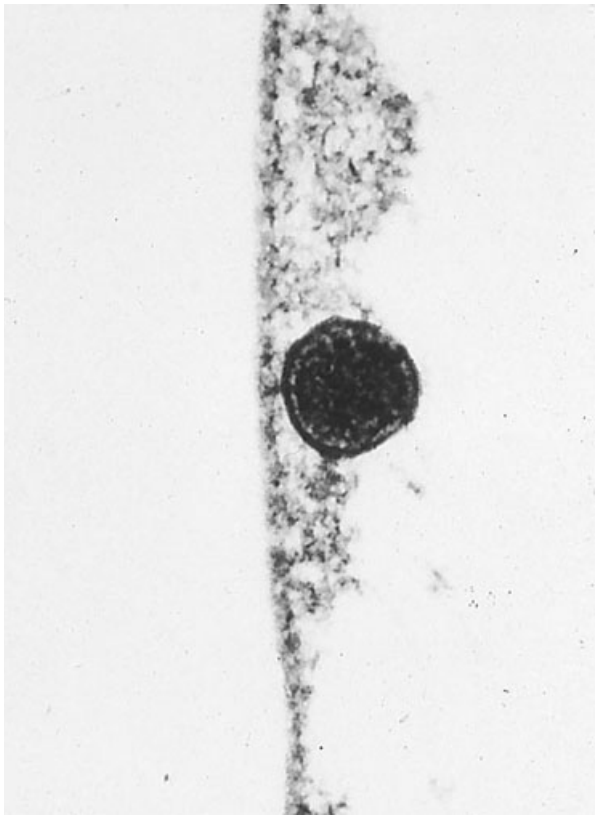

Fig. 8-8 Electron micrographic illustration of a 4-hour dental pellicle with a single bacterium included in the film. The microbe appears attached to the surface. The dental pellicle varies in thickness but has a homogeneous morphology. From Brecx *et al*. (1981).

on natural or artificial surfaces does not differ significantly in structure or microbiology (Hazen 1960; Berthold *et al*. 1971; Nyvad *et al*. 1982; Theilade *et al*. 1982a,b), indicating that at least some of the principal mechanisms involved in plaque formation are unrelated to the nature of the solid surface colonized. However, there are small, but important, differences in the chemical composition of the first layer of organic material formed on these artificial surfaces compared with that formed on natural tooth surfaces (Sönju & Rölla 1973; Sönju & Glantz 1975; Öste *et al*. 1981). Tooth surfaces, enamel as well as exposed cementum, are normally covered by a thin acquired pellicle of glycoproteins (Fig. 8-7). If removed, e.g. by mechanical instrumentation, it reforms within minutes. The pellicle is believed to play an active part in the selective adherence of bacteria to the tooth surface (Fig. 8-8). For details of the proposed mechanisms, see Chapter 9.

The first cellular material adhering to the pellicle on the tooth surface or other solid surfaces consists of coccoid bacteria with numbers of epithelial cells and polymorphonuclear leukocytes (Fig. 8-9). The bacteria are encountered either on (Fig. 8-10) or within the pellicle as single organisms (Fig. 8-11) or as aggregates of microorganisms (Fig. 8-12). Larger

Fig. 8-9 Electron micrographic illustration of a 4-hour dental pellicle, formed on a plastic surface attached to the buccal surface of a tooth. A condensed layer of organic material is observed on the surface and cell remnants are embedded in the film. From Brecx *et al*. (1981).

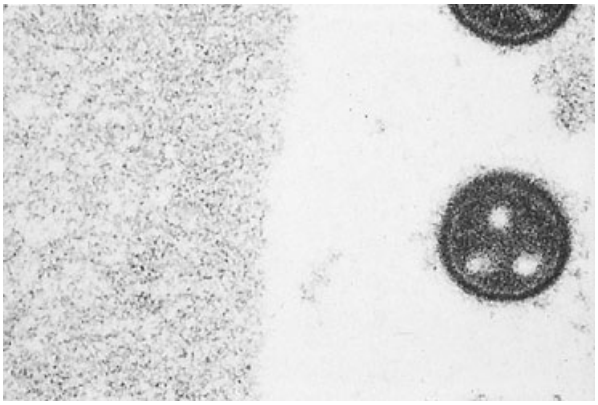

Fig. 8-10 High power electron micrographic illustration of a 4-hour pellicle with bacteria residing in the pellicle at a distance of around one micron from the condensed organic material. The pellicle is rather even in composition and, at the oral side, an irregular condensed organic material is seen close to the bacteria. From Brecx *et al*. (1981).

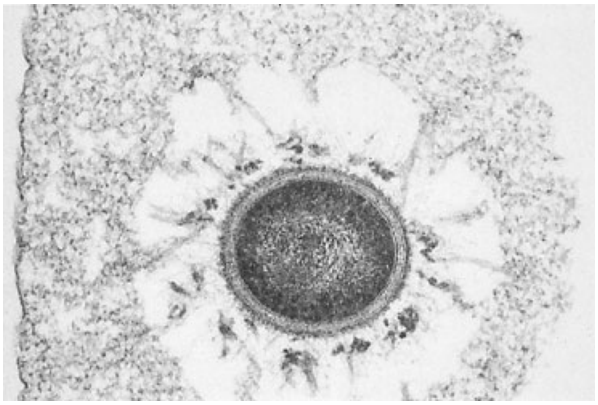

Fig. 8-11 High power electron micrographic illustration of a 4-hour pellicle with an embedded bacterium. The bacterium is deposited on the film surface together with the dental pellicle. Around the bacterium empty spaces are observed representing the radius of extrusions of filaments radiating from the microorganisms. From Brecx *et al*. (1981).

numbers of microorganisms may be carried to the tooth surface by epithelial cells.

The number of bacteria found on the surface a few hours after cleaning depends on the procedures applied to the sample before examination, the reason being that adherence to the solid surface is initially very weak. If no special precautions are taken during the preparatory processing, the early deposits are easily lost (Brecx *et al*. 1980). Apparently the adherence of microorganisms to solid surfaces takes place in two steps: (1) a reversible state in which the bacteria adhere loosely, and later (2) an irreversible state, during which their adherence becomes consolidated (Gibbons & van Houte 1980).

Another factor which may modify the number of bacteria in early plaque deposits is the presence of gingivitis, which increases the plaque formation rate so that the more complex bacterial composition is attained earlier (Saxton 1973; Hillam & Hull 1977; Brecx *et al*. 1980). Plaque growth may also be initiated

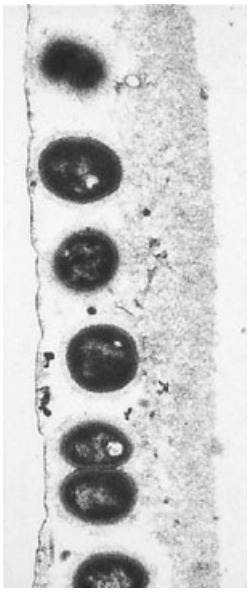

Fig. 8-12 Electron micrographic illustration of a 4-hour dental pellicle with bacteria attached to a plastic surface, which had been adhering to a buccal tooth surface and was exposed to the oral environment. A single row of bacteria attached to the surface is seen to the left. On top of the bacteria, a layer of condensed organic material representing the oral lateral portion of the dental pellicle is noted. From Brecx *et al*. (1981).

by microorganisms harbored in minute irregularities in which they are protected from the natural cleaning of the tooth surface.

During the first few hours, bacteria that resist detachment from the pellicle may start to proliferate and form small colonies of morphologically similar organisms (Fig. 8-13). However, since other types of organisms may also proliferate in an adjacent region, the pellicle becomes easily populated by a mixture of different microorganisms (Fig. 8-14). In addition, some organisms seem able to grow between already established colonies (Fig. 8-15). Finally, it is likely that clumps of organisms of different species will become attached to the tooth surface or to the already attached microorganism, contributing to the complexity of the plaque composition after a few days. At this time, different types of organisms may benefit from each other. One example is the corncob configurations resulting from the growth of cocci on the surface of a filamentous microorganism (Listgarten *et al*. 1973). Another feature of older plaque is the presence of dead and lysed bacteria which may provide additional nutrients to the still viable bacteria in the neighborhood (Theilade & Theilade 1970).

The material present between the bacteria in dental plaque is called the intermicrobial matrix and accounts for approximately 25% of the plaque volume. Three sources may contribute to the intermicrobial matrix: the plaque microorganisms, the saliva, and the gingival exudate.

The bacteria may release various metabolic products. Some bacteria may produce various extracellular carbohydrate polymers, serving as energy storage

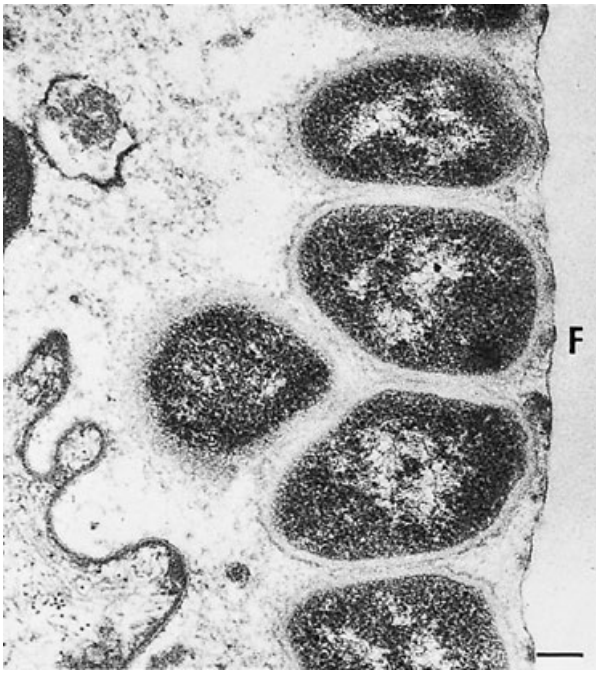

Fig. 8-13 Thin section of plaque colony consisting of morphologically similar bacteria deposited on plastic film (F) applied to the buccal surface of a premolar during an 8-hour period. Magnification ×35 000. Bar: 0.2 µm. From Brecx *et al*. (1980).

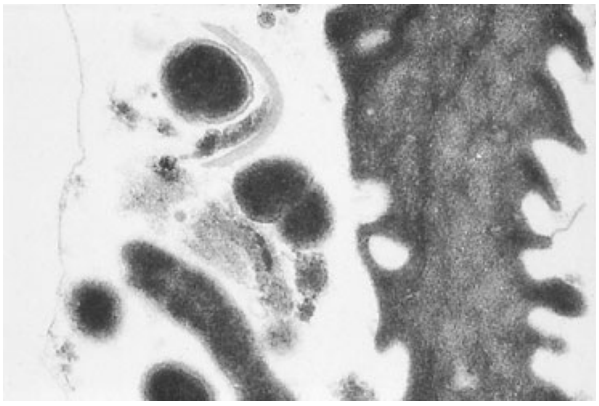

Fig. 8-14 Electron micrographic illustration of early plaque formation. The film surface on which the pellicle and bacteria adhere is located to the left. Bacteria of varying morphology are attached to the film. They are surrounded by organic pellicle material. An epithelial cell remnant is seen in close vicinity to the microbes. From Brecx *et al*. (1981).

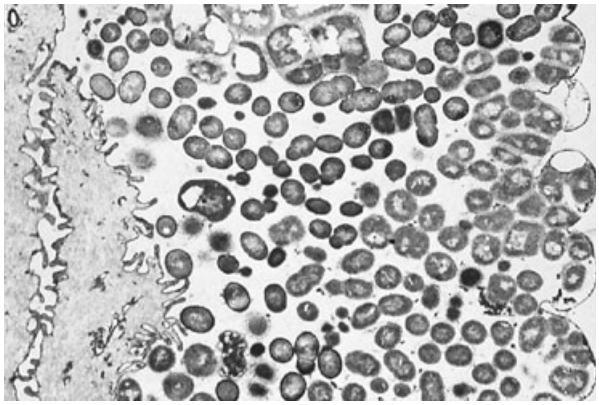

Fig. 8-15 Electron micrographic illustration of 24-hour dental plaque formed on a plastic film surface attached to the buccal surface of the tooth. A multilayer bacterial plaque is noted. A remnant of an epithelial cell has been trapped in the microbial mass. From Brecx *et al*. (1981).

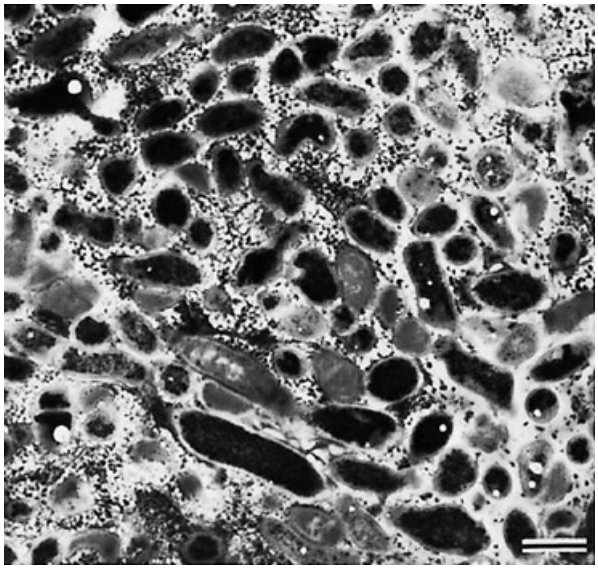

Fig. 8-16 Thin section of old plaque stained for the demonstration of polysaccharides by reacting them with electron-dense material appearing dark in the illustration. Many bacteria contain large amounts of intracellular polysaccharide, and the intermicrobial matrix contains extracellular polysaccharides. Magnification ×7000. Bar: 1 µm. From Theilade & Theilade (1970).

or as anchoring material to secure their retention in plaque (Fig. 8-16). Degenerating or dead bacteria may also contribute to the intermicrobial matrix. Different bacterial species often have distinctly different metabolic pathways and capacity to synthesize extracellular material. The intermicrobial matrix in plaque, therefore, varies considerably from region to region. A fibrillar component is often seen in the matrix between Gram-positive cocci (Fig. 8-17) and is in accordance with the fact that several oral streptococci synthesize levans and glucans from dietary sucrose. In other regions, the matrix appears granular or homogeneous (Fig. 8-18). In parts of the plaque with the presence of Gram-negative organisms, the intermicrobial matrix is regularly characterized by the presence of small vesicles surrounded by a trilaminar membrane, which is similar in structure to that of the outer envelope of the cell wall of the Gram-negative microorganisms (Fig. 8-19). Such vesicles probably contain endotoxins and proteolytic enzymes, and may also be involved in adherence between bacteria (Hofstad *et al*. 1972; Grenier & Mayrand 1987).

It must be remembered, however, that the transmission electron microscope does not reveal all organic components of the intermicrobial matrix. The more soluble constituents may be lost during the

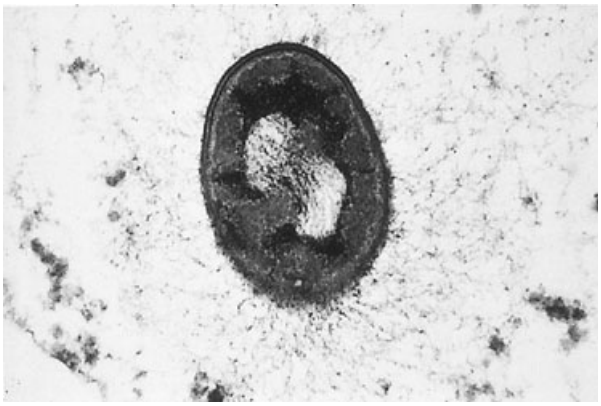

Fig. 8-17 High power electron micrographic illustration of a single bacterium attached to the pellicle by filaments which extend from the bacterial surface to the tooth surface. The surface had been exposed to the oral environment for an 8-hour period. From Brecx *et al*. (1981).

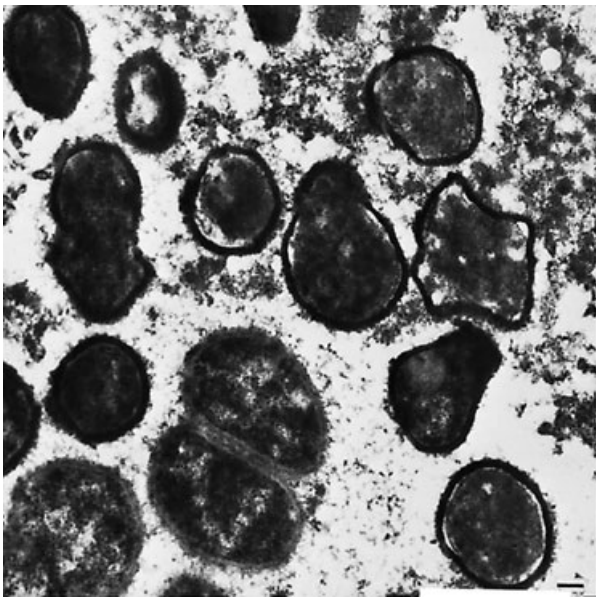

Fig. 8-18 Thin section of plaque with granular or homogeneous intermicrobial matrix. Magnification ×20 000. Bar: 0.1 µm. From Theilade & Theilade (1970).

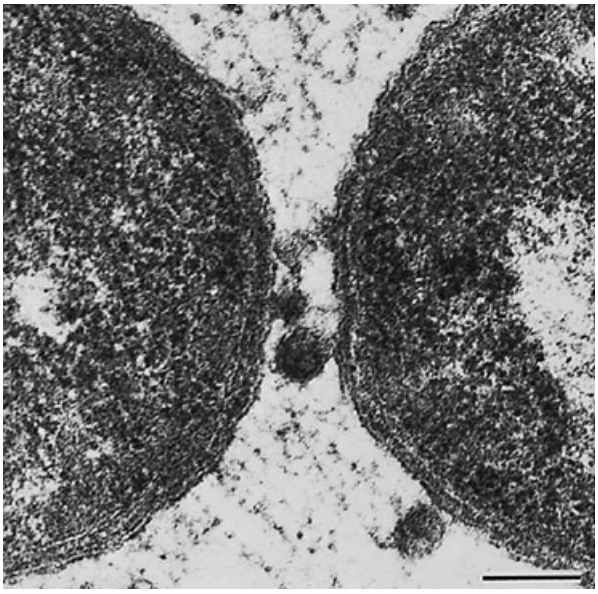

Fig. 8-19 Thin section of plaque with a region predominated by Gram-negative bacteria. Between them, vesicles are surrounded by a trilaminar membrane (two thin electron-dense layers with an electron-lucent layer in between). This substructure is also seen in the outermost endotoxin containing cell wall layer of the adjacent Gram-negative bacteria. Magnification ×110 000. Bar: 0.1 µm. From Theilade & Theilade (1970).

procedures required prior to sectioning and examination of the plaque sample. Biochemical techniques may be used to identify such compounds (Silverman & Klein-berg 1967; Krebel *et al*. 1969; Kleinberg 1970; Hotz *et al*. 1972; Rölla *et al*. 1975; Bowen 1976). Such studies indicate that proteins and carbohydrates constitute the bulk of the organic material while lipids appear in much lower amounts.

The carbohydrates of the matrix have received a great deal of attention, and at least some of the polysaccharides in the plaque matrix are well characterized: fructans (levans) and glucans. Fructans are synthesized in plaque from dietary sucrose and provide a storage of energy which may be utilized by microorganisms in times of low sugar supply. The glucans are also synthesized from sucrose. One type of glucan is dextran, which may also serve as energy storage. Another glucan is mutan, which is not readily degraded, but acts primarily as a skeleton in the matrix in much the same way as collagen stabilizes the intercellular substance of connective tissue. It has been suggested that such carbohydrate polymers may be responsible for the change from a reversible to an irreversible adherence of plaque bacteria.

The small amount of lipids in the plaque matrix are as yet largely uncharacterized. Part of the lipid content is found in the small extracellular vesicles, which may contain lipopolysaccharide endotoxins of Gram-negative bacteria.

Subgingival plaque

Owing to the difficulty of obtaining samples with subgingival plaque preserved in its original position between the soft tissues of the gingiva and the hard tissues of the tooth, there is only a limited number of studies on the detailed internal structure of human subgingival plaque (Schroeder 1970; Listgarten *et al*. 1975; Listgarten 1976; Westergaard *et al*. 1978). From these it is evident that in many respects subgingival plaque resembles the supragingival variety, although the predominant types of microorganisms found vary considerably from those residing coronal to the gingival margin.

Between subgingival plaque and the tooth an electron-dense organic material is interposed, termed a *cuticle* (Fig. 8-20). This cuticle probably contains the remains of the epithelial attachment lamina originally connecting the junctional epithelium to the

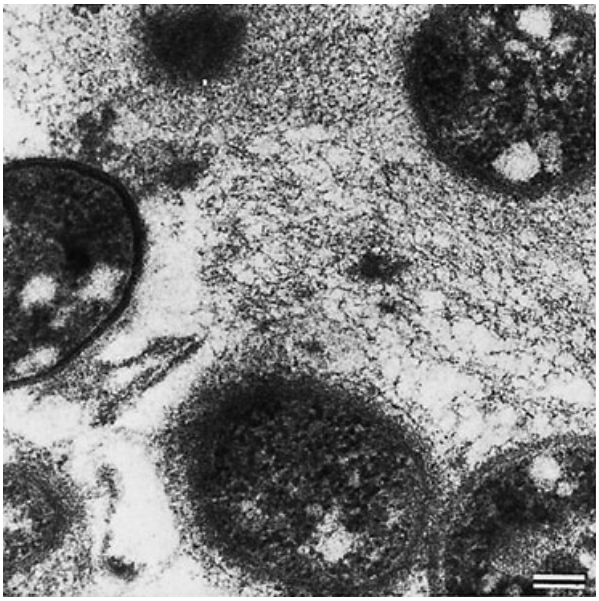

Fig. 8-20 Semithin section of subgingival plaque. An electron-dense cuticle bordering the enamel space is visible to the left. Filamentous bacteria are less than in supragingival plaque. The surface toward the gingival tissue contains many spirochetes (between arrows). Various host tissue cells can be seen on the right side. Magnification ×775. Bar: 10 µm. From Listgarten (1976).

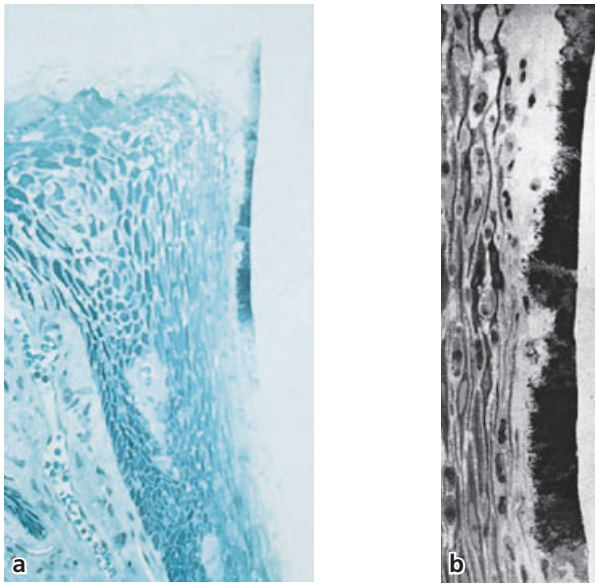

Fig. 8-21 (a) Light microscopic image of the dento-gingival region of a dog with experimental gingivitis. A thin layer of dento-gingival plaque can be seen, extending from the supragingival region approximately 0.5 mm into the gingival sulcus. (b) Higher magnification of a region of the plaque shown in (a). The subgingival plaque has a varying thickness and the epithelial cells are separated from the surface by a layer of leukocytes. There are also numerous leukocytes in the superficial portion of the sulcus epithelium. The apical termination of the plaque is bordered by leukocytes separating the epithelium from direct contact with the plaque bacteria.

tooth, with the addition of material deposited from the gingival exudate (Frank & Cimasoni 1970; Lie & Selvig 1975; Eide *et al*. 1983). It has also been suggested that the cuticle represents a secretory product of the adjacent epithelial cells (Schroeder & Listgarten 1977). Information is lacking concerning its chemical composition, but its location in the subgingival area makes it unlikely that salivary constituents contribute to its formation.

The subgingival plaque structurally resembles supragingival plaque, particularly with respect to plaque associated with gingivitis without the formation of deep pockets (Fig. 8-21). A densely packed accumulation of microorganisms is seen adjacent to the cuticular material covering the tooth surface (Fig. 8-22). The bacteria comprise Gram-positive and Gram-negative cocci, rods, and filamentous organisms. Spirochetes and various flagellated bacteria may also be encountered, especially at the apical extension of the plaque. The surface layer is often less densely packed and leukocytes are regularly interposed between the plaque and the epithelial lining of the gingival sulcus (Fig. 8-23).

When a periodontal pocket has formed, the appearance of the subgingival bacterial deposit becomes much more complex. In this case the tooth surface may either represent enamel or cementum from which the periodontal fibers are detached. Plaque accumulation on the portion of the tooth previously covered by periodontal tissues does not differ markedly from that observed in gingivitis (Fig. 8-24). In this layer, filamentous microorganisms dominate (Figs. 8-25, 8-26, 8-27), but cocci and rods also occur.

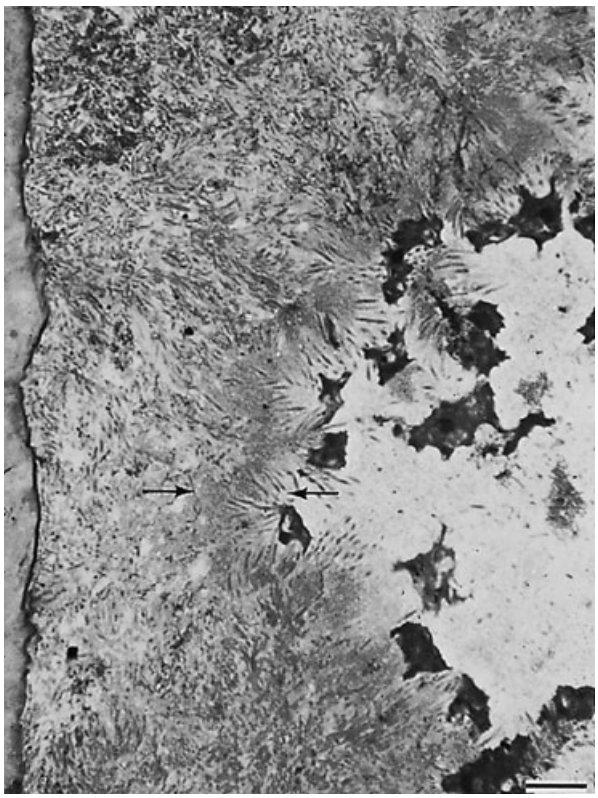

Fig. 8-22 Semithin section of supragingival plaque with layer of predominantly filamentous bacteria adhering to the enamel (to the left). Lighter staining indicates calcification of part of the plaque close to the tooth. Magnification ×750. Bar: 10 µm. From Listgarten (1976).

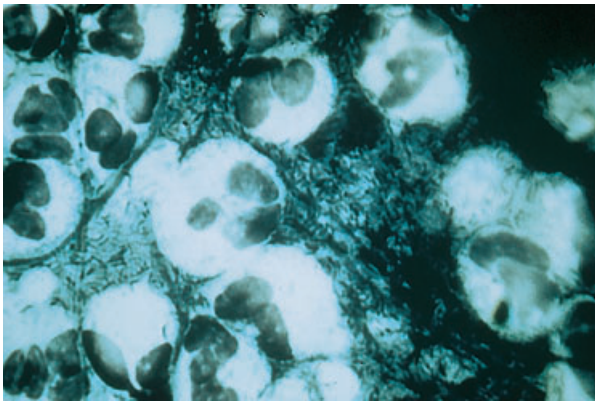

Fig. 8-23 Light microscopic image of a smear sample taken from the dento-gingival region in a subject who had abstained from mechanical oral hygiene during 3 weeks. Numerous leukocytes can be observed embedded in a dense accumulation of bacteria.

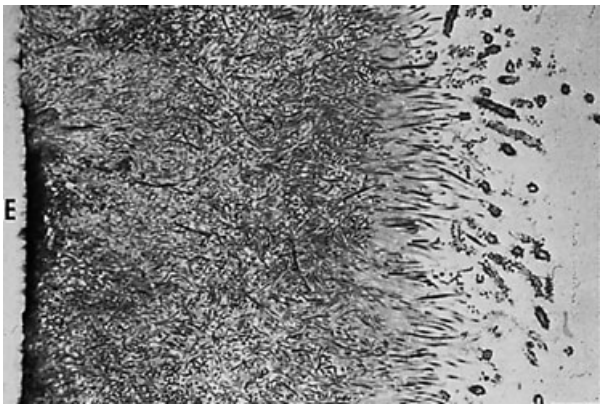

Fig. 8-24 Semithin section of supragingival plaque on enamel (E), which has been dissolved prior to sectioning. Magnification ×750. Bar: 10 µm. From Listgarten (1976).

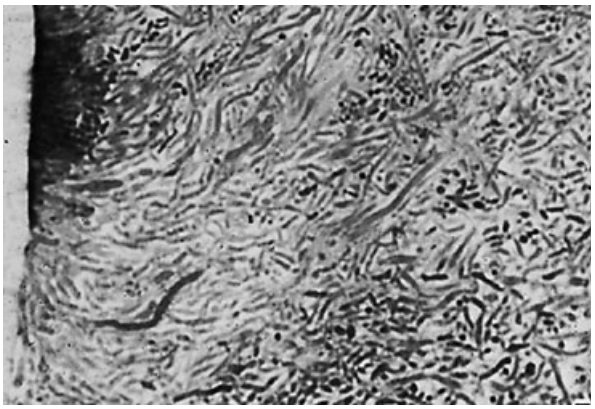

Fig. 8-25 See Fig. 8.24. Filamentous organisms predominate. At the surface some of these organisms are surrounded by cocci. This configuration resembles a corncob. Magnification ×1400. Bar: 1 µm. From Listgarten (1976).

However, in the deeper parts of the periodontal pocket, the filamentous organisms become fewer in number, and in the apical portion they seem to be virtually absent. Instead, the dense, tooth-facing part of the bacterial deposit is dominated by smaller

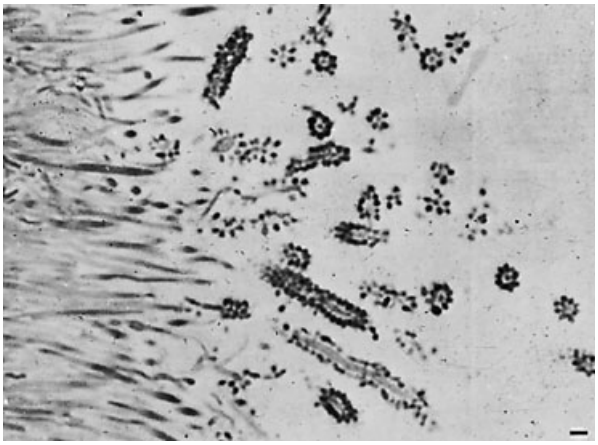

Fig. 8-26 The corncob formations seen at the plaque surface in Fig. 8-24 and 8-25. Magnification ×1300. Bar: 1 µm. From Listgarten (1976).

organisms without particular orientation (Listgarten 1976) (Fig. 8-28).

The surface layers of microorganisms in the periodontal pocket facing the soft tissue are distinctly different from the adherent layer along the tooth surface, and no definite intermicrobial matrix is apparent (Figs. 8-28, 8-29). The microorganisms comprise a larger number of spirochetes and flagellated bacteria. Gram-negative cocci and rods are also present. The multitude of spirochetes and flagellated organisms are motile bacteria and there is no intermicrobial matrix between them. This outer part of the microbial accumulation in the periodontal pocket adheres loosely to the soft-tissue pocket wall (Listgarten 1976).

In cases of juvenile periodontitis (Listgarten 1976; Westergaard *et al*. 1978) the bacterial deposits in deep pockets are much thinner than those found in adult forms of periodontal disease. Areas of the tooth surface in the periodontal pocket may sometimes even be devoid of adherent microbial deposits. The cuticular material has an uneven thickness (Figs. 8-30, 8-31). The adherent layer of microorganisms varies considerably in thickness and shows considerable variation in arrangement. It may exhibit a palisaded organization of the bacteria (Fig. 8-32). The microorganisms in this layer are mainly cocci, rods or filamentous bacteria, primarily of the Gram-negative type (Fig. 8-33). A surface layer with some Gram-positive cocci, frequently associated with filamentous organisms in the typical corncob configuration, may also be found.

Subgingivally located bacteria appear to have the capacity to invade dentinal tubules, the openings of which have become exposed as a consequence of inflammatory driven resorptions of the cementum (Adriaens *et al*. 1988). Such a habitat might serve as the source for bacterial recolonization of the subgingival space following treatment of periodontal disease. The mechanisms involved in such reversed invasion of the subgingival space are unknown.

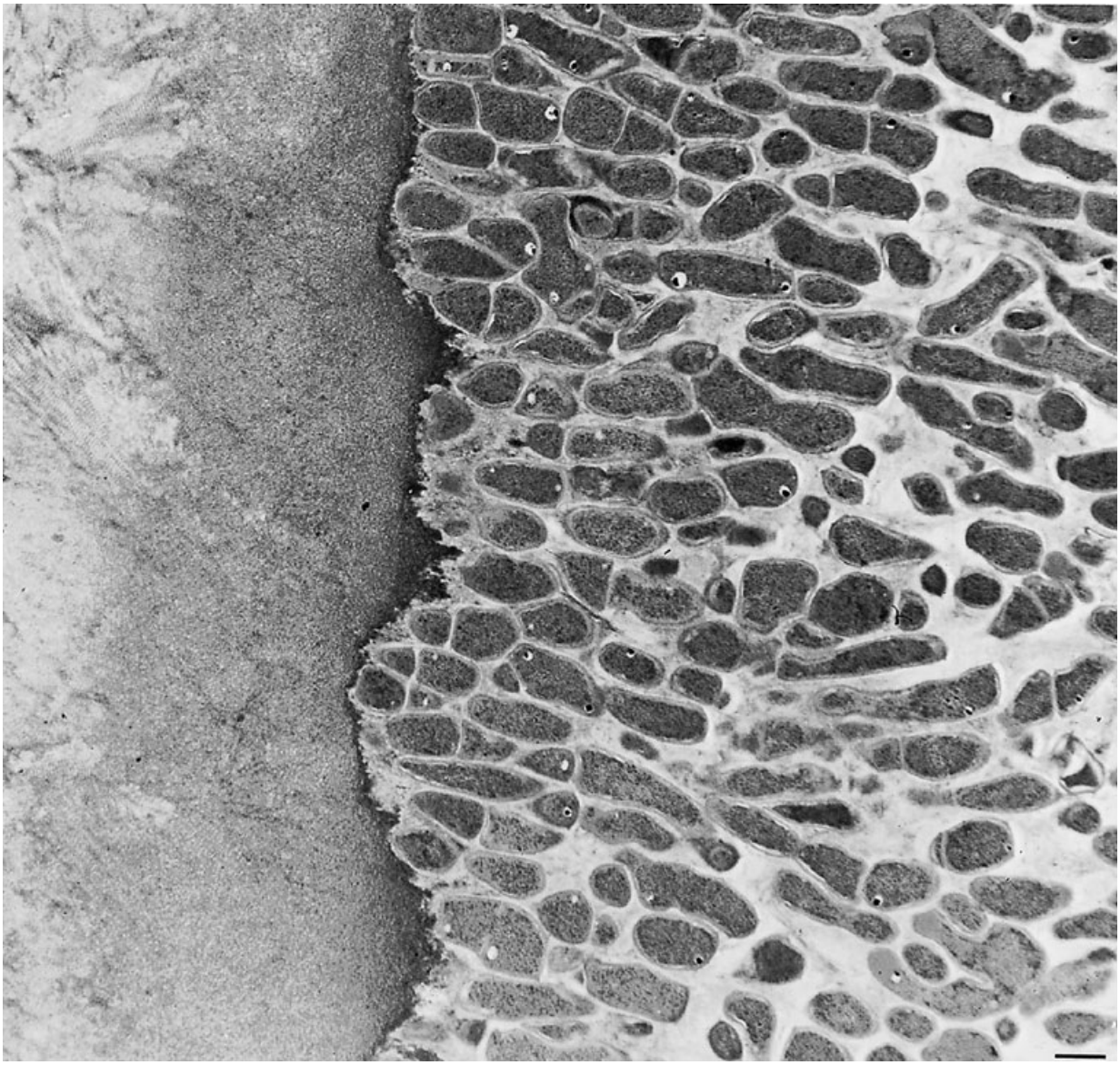

Fig. 8-27 Thin section of supragingival plaque on a root surface (to the left). The Gram-positive bacteria are oriented in a palisading arrangement. Magnification ×6400. Bar: 1 µm. From Listgarten (1976).

The sequential events taking place during the development of subgingival plaque have not been studied in man. However, in dogs, subgingival plaque may develop in the gingival sulcus within a few days, if oral hygiene is discontinued (Matsson & Attström 1979; Ten Napel *et al*. 1983). From these studies it has been established that early dental plaque in the dog has many structural similarities with that occurring in man. This applies to the supragingival plaque (Fig. 8-21a) as well as to the subgingival accumulation (Fig. 8-21b). The deposits may either appear as an apical continuation of the supragingival plaque, or as discrete aggregates at some distance from the supragingival deposit. Old established subgingival plaque shows considerable variation in bacterial composition between dogs: in some, a subgingival microbiota dominated by spirochetes is seen; in others, colonies of Gram-negative cocci and rods are found in the gingival crevice, whereas spirochetes are virtually absent (Soames & Davies 1975; Theilade & Attström 1985). A characteristic feature of subgingival plaque is the presence of leukocytes interposed between the surfaces of the bacterial deposit and the gingival sulcular epithelium (Fig. 8-34). Some bacteria may be found between the epithelial cells. Evidence of phagocytosis (by polymorphonuclear leukocytes) is frequently encountered (Fig. 8-35).

Although subgingival plaque formation in the dog may not develop identically to that in man, the dog may still serve as a convenient model for investigating the basic phenomena governing the formation of subgingival plaque (Schroeder & Attström 1979).

In summary, there are four distinct subgingival ecologic niches which are probably different in their composition:

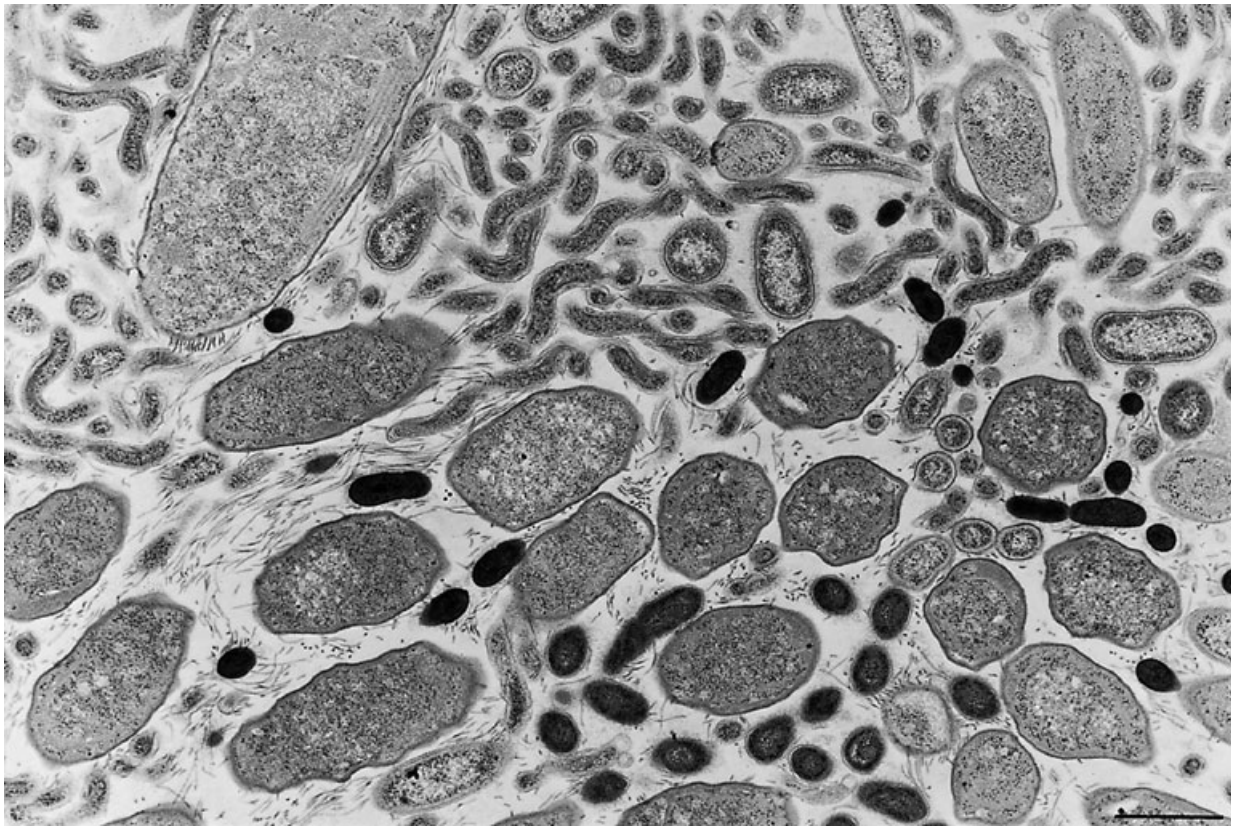

Fig. 8-28 Thin section of subgingival plaque from a deep periodontal pocket. Small microorganisms predominate, many of which are spirochetes. Magnification ×13 000. Bar: 1 µm. From Listgarten (1976).

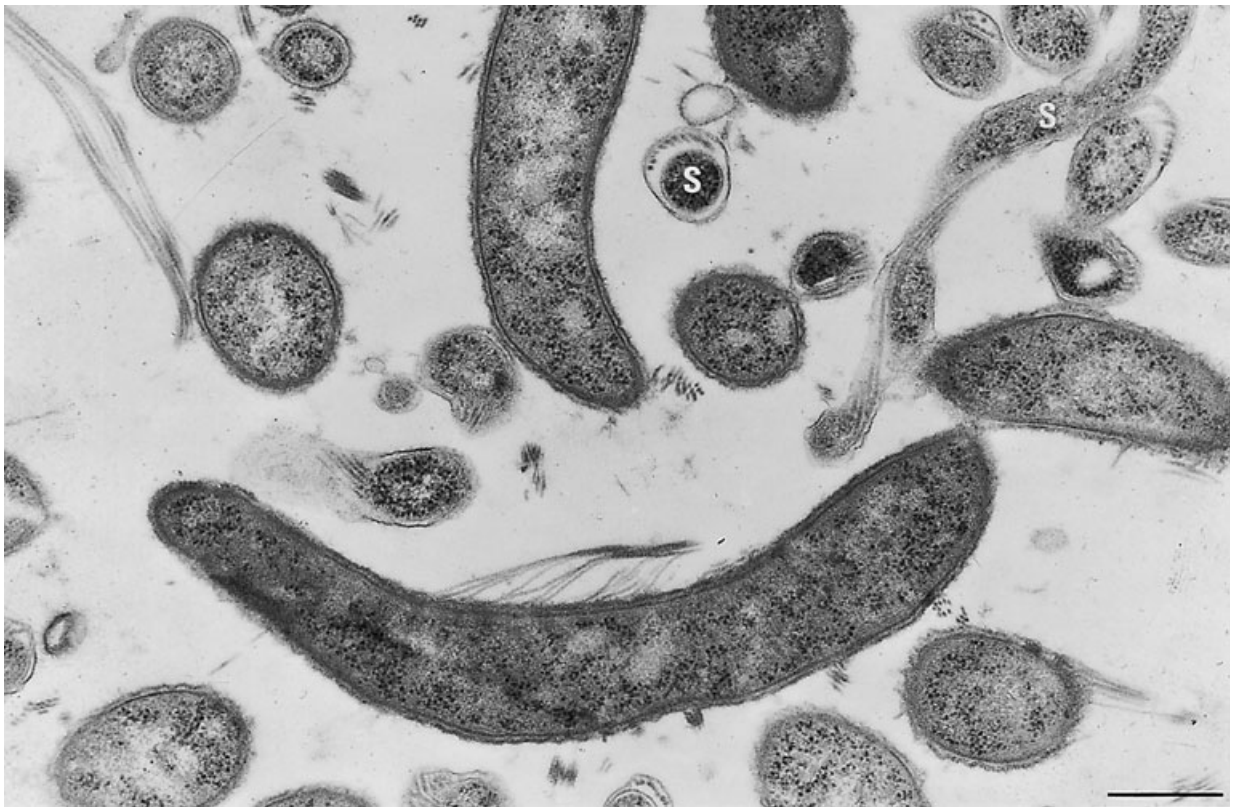

Fig. 8-29 Thin section of subgingival plaque from a deep periodontal pocket with many spirochetes (S), which are recognized by their axial filaments. In the lower part of the figure is a curved organism with flagella at its concave surface. Magnification ×25 000. Bar: 0.5 µm. From Listgarten (1976).

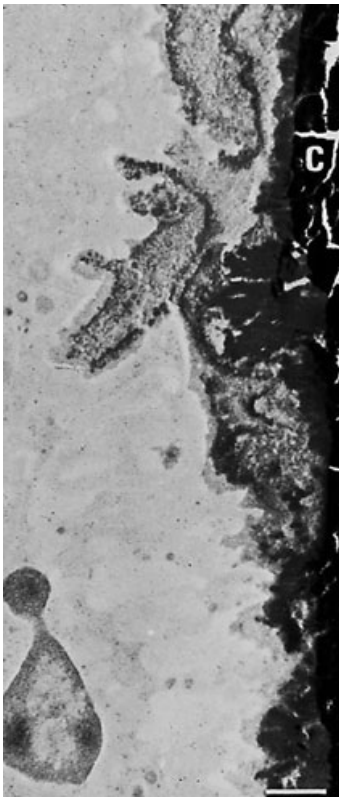

Fig. 8-30 Thin section of deposit in deep pocket of patient with juvenile periodontitis. The cementum (C) is covered with cuticular material and cellular remnants. Magnification ×5500. Bar: 1 µm. From Westergaard *et al*. (1978).

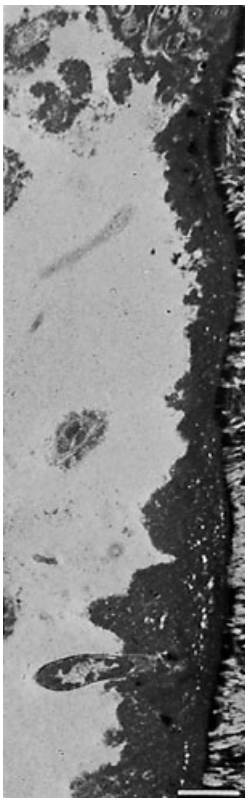

Fig. 8-31 Thin section of deposit in deep pocket of patient with juvenile periodontitis. A cuticle of uneven thickness is seen to the right on the cementum. A small colony of degenerating bacteria adheres to the cuticle in the upper part of the illustration, and below a single rod-shaped microorganism is partly embedded in the cuticle. Magnification ×5500. Bar: 1 µm. From Westergaard *et al*. (1978).

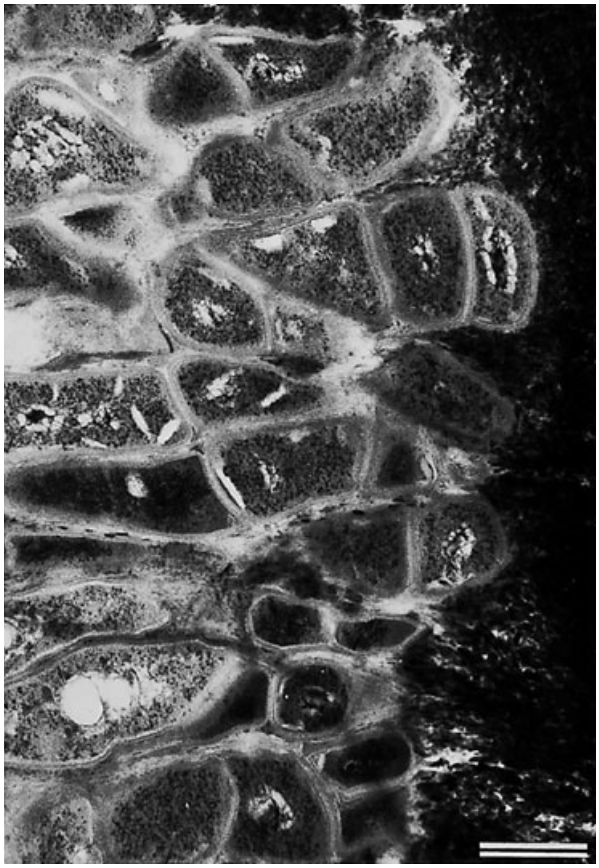

Fig. 8-32 Thin section of plaque in deep pocket of patient with juvenile periodontitis. Densely packed Gram-positive rods grow perpendicular to the cementum to the right in the illustration. Magnification ×23 000. Bar: 0.5 µm. From Westergaard *et al*. (1978).

1. The tooth (or implant) surface
2. The gingival exudate fluid medium
3. The surface of epithelial cells
4. The superficial portion of the pocket epithelium.

The composition of the bacteria in these niches has still not been completely investigated. The influence of the different bacterial compartments on the pathogenesis of the disease process is generally unknown.

Peri-implant plaque

Biofilms form not only on natural teeth, but also on artificial surfaces exposed to the oral environment. As a consequence, the formation of bacterial plaque on oral implants deserves some attention. Although a number of studies have characterized the plaque deposits of the human peri-implant sulcus or pocket using either dark field microscopy (Mombelli *et al*. 1988; Quirynen & Listgarten 1990) or microbiologic culturing techniques (Rams *et al*. 1984; Mombelli *et al*. 1987, 1988; Apse *et al*. 1989; Leonhardt *et al*. 1992), no studies have attempted to document the structure of the supramucosal or the peri-implant (submucosal) microbiota. However, the similarities between peri-implant and subgingival microbial deposits have

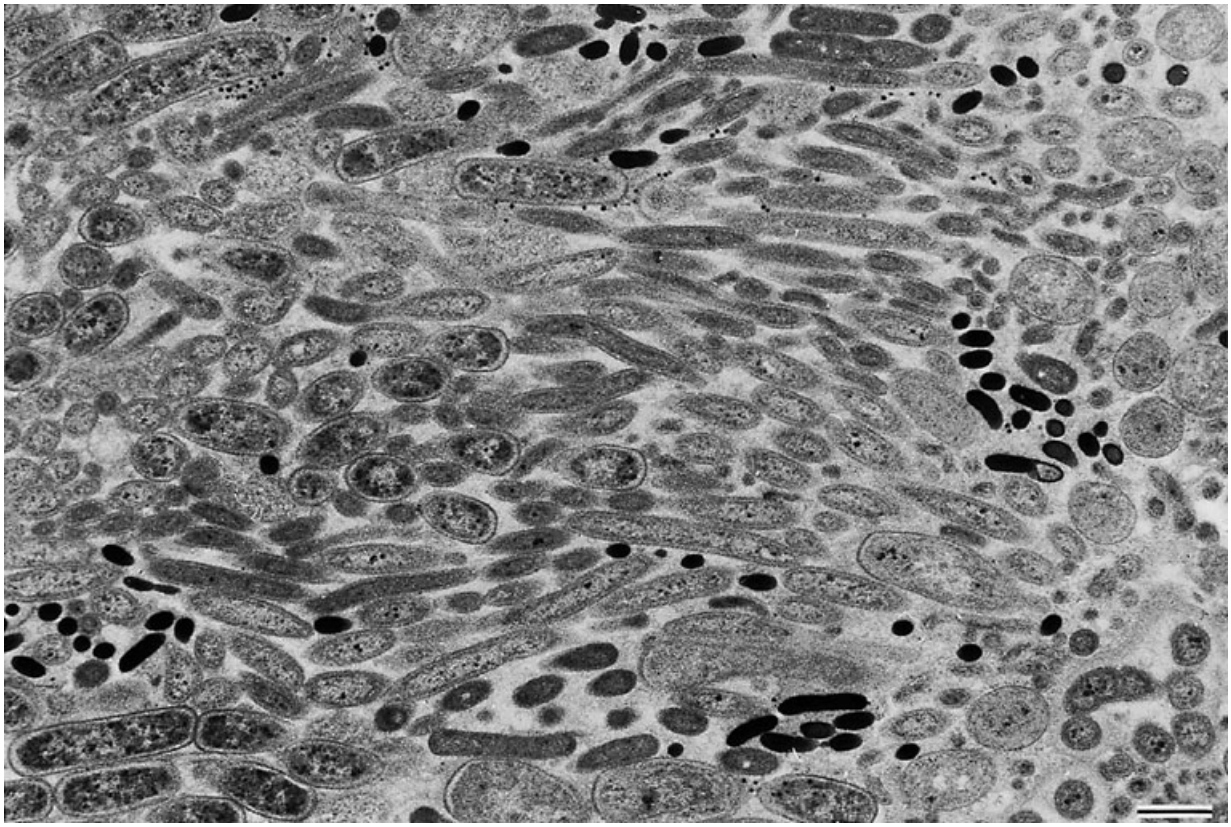

Fig. 8-33 Thin section of plaque in deep pocket of patient with juvenile periodontitis. The bacterial flora is characterized by cocci, rods or filamentous organisms, primarily of the Gram-negative type. Magnification ×9200. Bar: 1 µm. From Westergaard *et al*. (1978).

clearly been demonstrated in cross-sectional (Mombelli *et al*. 1987, 1995) and longitudinal studies (Mombelli *et al*. 1988; Pontoriero *et al*. 1994), and it may be anticipated that the structure of peri-implant plaque deposits may resemble that encountered in the subgingival environment. Micrographs from an implant retrieved because of a peri-implant infection may provide some evidence for the similarity between the structural image of the submucosal peri-implant microbiota (Fig. 8-36).

Dental calculus

Although calculus formation has been reported to occur in germ-free animals as a result of calcification of salivary proteins, dental calculus or tartar usually represents mineralized bacterial plaque.

Clinical appearance, distribution, and clinical diagnosis

Supragingivally, calculus can be recognized as a creamy-whitish to dark yellow or even brownish mass of moderate hardness (Fig. 8-37). The degree of calculus formation is not only dependent on the amount of bacterial plaque present but also on the secretion of the salivary glands. Hence, supragingival calculus is predominantly found adjacent to the excretion ducts of the major salivary glands, such as the lingual aspect of the mandibular anterior teeth and the buccal aspect of the maxillary first molars, where the parotid gland ducts open into the oral vestibule. The duct openings of the submandibular glands are located in the former region. It should be noted that calculus continually harbors a viable bacterial plaque (Zander *et al*. 1960; Theilade 1964; Schroeder 1969).

Subgingivally, calculus may be found by tactile exploration only, since its formation occurs apical to the gingival margin and, hence, is usually not visible to the naked eye. Occasionally, subgingival calculus may be visible in dental radiographs provided that the deposits present an adequate mass (Fig. 8-38). Small deposits or residual deposits following root instrumentation may barely be visualized radiographically. If the gingival margin is pushed open by a blast of air or retracted by a dental instrument, a brownish to black calcified hard mass with a rough surface may become visible (Fig. 8-39). Again, this mineralized mass reflects predominantly bacterial accumulations mixed with products from gingival crevicular fluid and blood. Consequently, subgingival calculus is found in most periodontal pockets, usually extending from the cemento-enamel junction and reaching close to the bottom of the pocket. However, a band of approximately 0.5 mm is usually found coronal to the apical extension of the periodontal pocket (Fig. 8-40). This zone appears to be free of mineralized deposits owing to the fact that gingival crevicular fluid is exuding from the periodontal soft

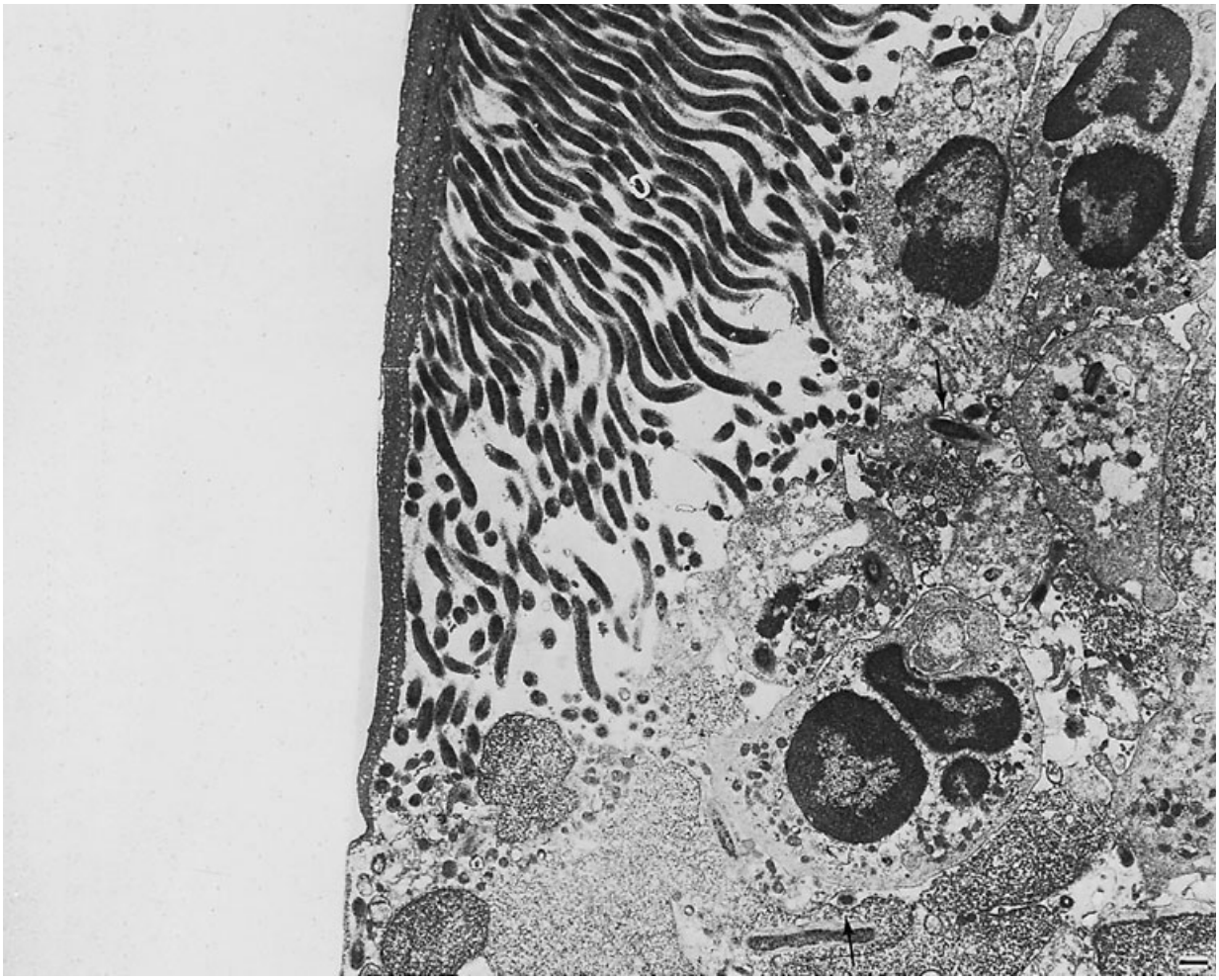

Fig. 8-34 Thin section of old subgingival plaque in a dog with long-standing gingivitis. The most apical colony consists primarily of spirochetes attached to a dense cuticle and surrounded by migrated leukocytes. Single microorganisms are seen between them (arrows). Magnification ×2800. Bar: 1 µm. From Theilade & Attström (1985).

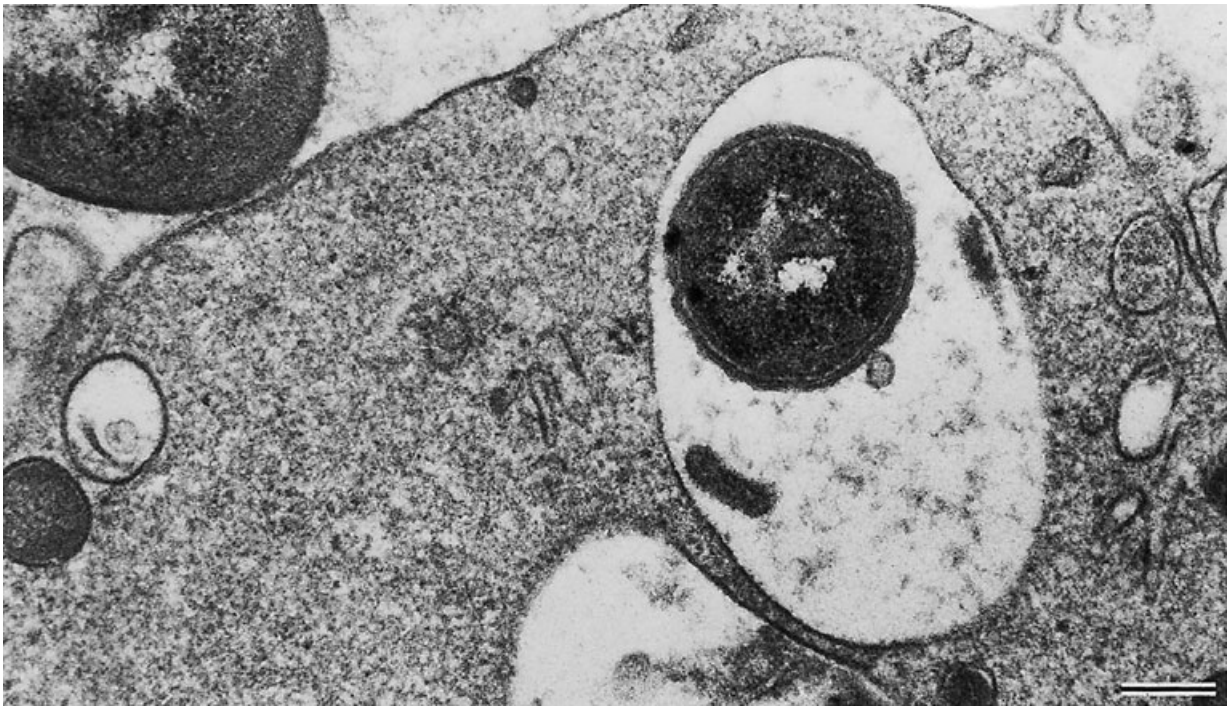

Fig. 8-35 Thin section of part of a leukocyte situated between subgingival plaque and the junctional epithelium of the dog. The large membrane-bound compartment of the leukocyte cytoplasm contains a phagocytized Gram-negative microorganism. Another bacterium is in close apposition to the cytoplasmic membrane of the leukocyte. Magnification ×21 500. Bar: 0.5 µm. From Theilade & Attström (1985).

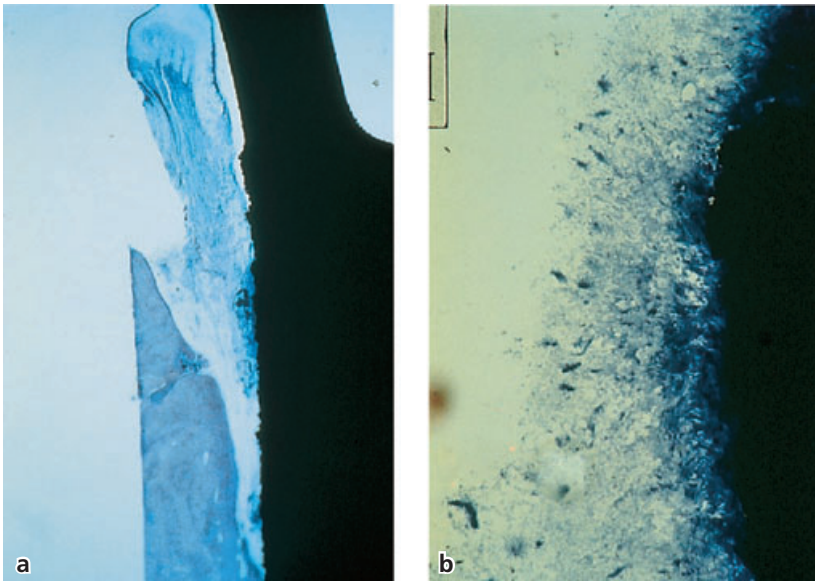

Fig. 8-36 Peri-implant infection. (a) Human explant of an ITI® dental implant affected by a peri-implantitis with an infrabony lesion. Adhering plaque closely resembles the structure of subgingival microbiota encountered in advanced periodontitis. (b) Higher magnification of plaque adhering to the implant surface.

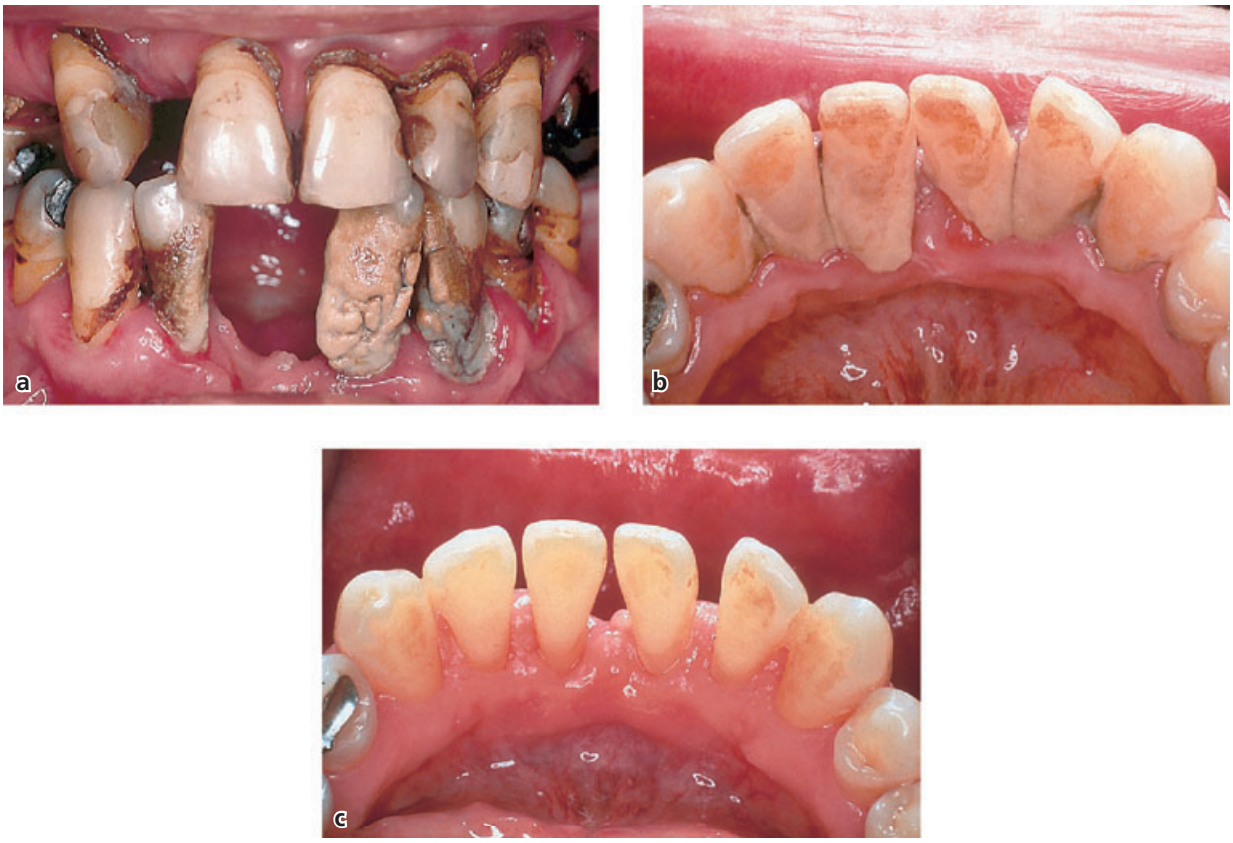

Fig. 8-37 Abundance of supragingival calculus deposits. (a) Gross deposits as a result of long-term neglect of oral hygiene. Two mandibular incisors have been exfoliated. (b) Supragingival plaque usually covering the lingual aspect of mandibular incisors. Note the intense inflammatory reaction adjacent to the deposits. (c) Same patient and region as in Fig. 8-37b following removal of the calculus. The gingival tissues demonstrate healing.

tissues and acting as a gradient against the microbial accumulation. Like supragingival calculus, subgingival calculus also provides an ideal environment for bacterial adhesion (Zander *et al*. 1960; Schroeder 1969).

Plaque mineralization varies greatly between and within individuals and, as indicated above, also within the different regions of the oral cavity. Not only the formation rate for bacterial plaque (amount of bacterial plaque per time and tooth surface), but also the formation rate for dental calculus (time period during which newly deposited supragingival plaque with an ash weight of 5–10% becomes calcified and yields an ash weight of approximately 80%) is subject to great variability. In some subjects, the time required for the formation of supra-

gingival calculus is 2 weeks, at which time the deposit may already contain approximately 80% of the inorganic material found in mature calculus (Fig. 8-41) (Mühlemann & Schneider 1959; Mandel 1963; Mühlemann & Schroeder 1964). In fact, evidence of mineralization may already be present after a few days (Theilade 1964). Nevertheless, the formation of dental calculus with the mature crystalline composition of old calculus may require months to years (Schroeder & Baumbauer 1966). Supragingival plaque becomes mineralized saliva and subgingival plaque in the presence of the inflammatory exudate in the pocket. It is, therefore, evident that subgingival calculus represents a secondary product of infection and not a primary cause of periodontitis.

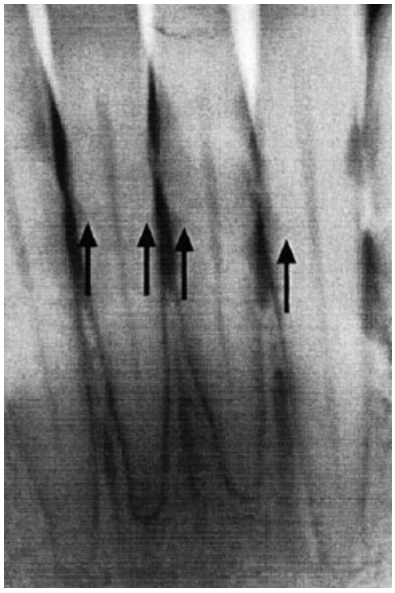

Fig. 8-38 Subgingival calculus may be visible (arrows) on radiographs if abundant deposits are present.

Attachment to tooth surfaces and implants

Dental calculus generally adheres tenaciously to tooth surfaces. Hence, the removal of subgingival calculus may be expected to be rather difficult. The reason for this firm attachment to the tooth surface is the fact that the pellicle beneath the bacterial plaque also calcifies. This, in turn, results in an intimate contact with enamel (Fig. 8-42), cementum (Fig. 8-43) or dentin crystals (Fig. 8-44) (Kopczyk & Conroy 1968; Selvig 1970). In addition, the surface irregularities are also penetrated by calculus crystals and, hence, calculus is virtually locked to the tooth. This is particularly the case on exposed root cementum, where small pits and irregularities occur at the sites

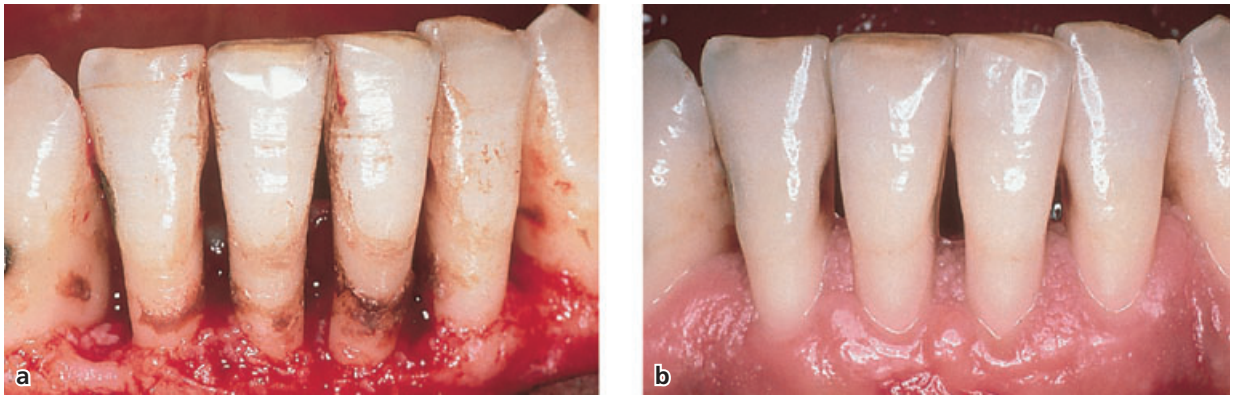

Fig. 8-39 (a) Subgingival calculus presents as a black-brownish hard mass if the gingival margin is retracted or reflected during a surgical procedure. (b) Healing of the site following removal of all hard deposits.

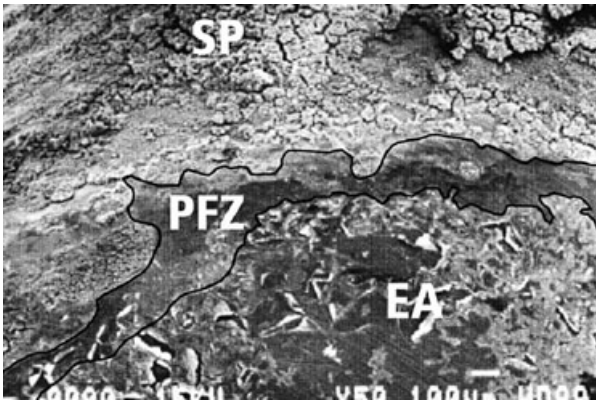

Fig. 8-40 Plaque- and calculus-free zone coronal to the epithelial attachment. SP: subgingival plaque bacteria; PFZ: plaque-free zone; EA: remnants of junctional epithelium.

Fig. 8-41 Seven-day-old calcified plaque. Observe the isolated calcification centers indicated by the black areas (van Kossa stain).

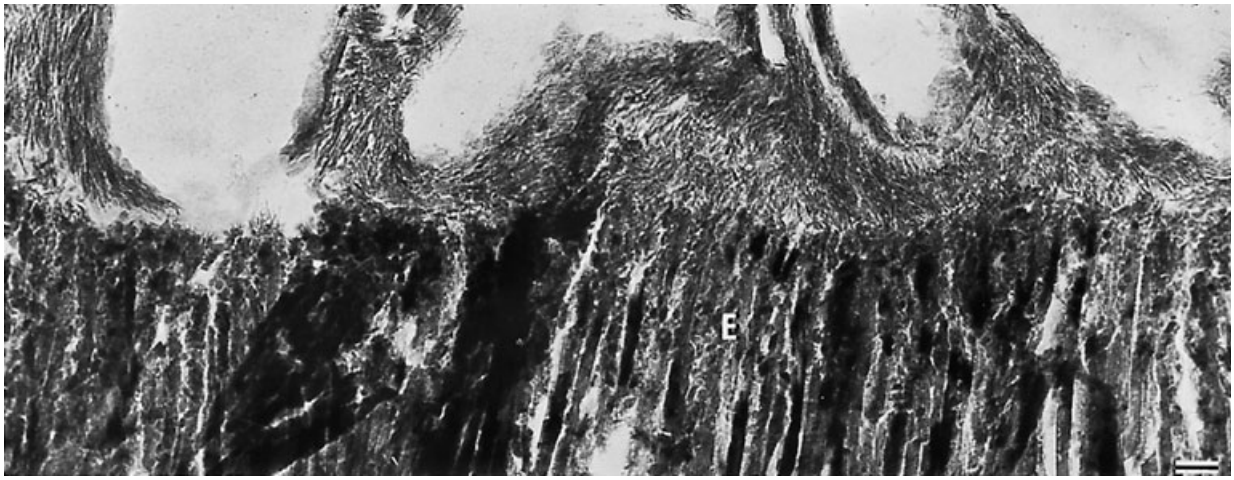

Fig. 8-42 Thin section of enamel surface (E) with overlying calculus. The enamel and calculus crystals are in intimate contact, and the latter extends into the minute irregularities of the enamel. Magnification ×37 500. Bar: 0.1 µm. From Selvig (1970).

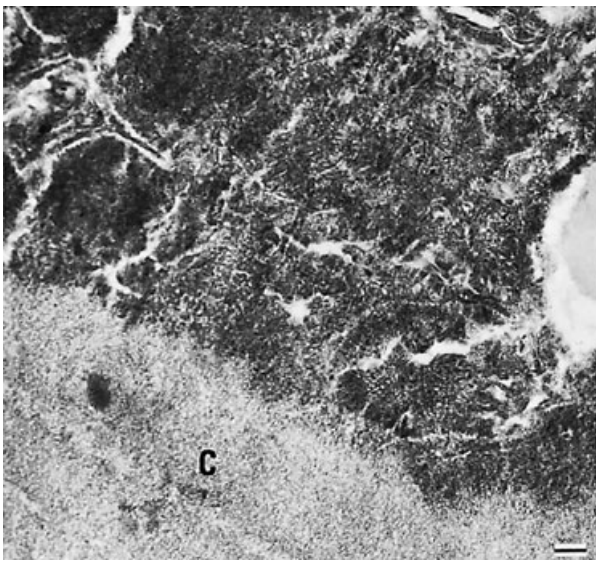

Fig. 8-43 Thin section of cementum surface (C) with overlying calculus. The calculus is closely adapted to the irregular cementum and is more electron-dense and therefore harder than the adjacent cementum. To the right in the illustration, part of an uncalcified microorganism. Magnification ×32 000. Bar: 0.1 µm. From Selvig (1970).

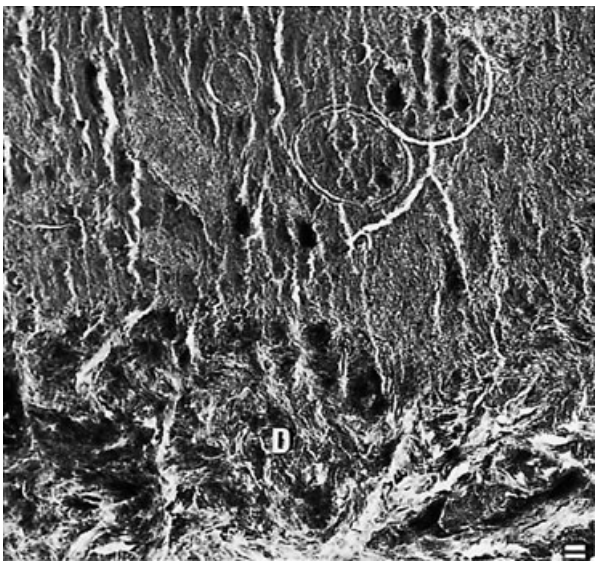

Fig. 8-44 Thin section of dentin (D) surface with overlying calculus. The interface between the calculus and dentin cannot be precisely determined because the calculus crystals fill the irregularities of the dentin surface, which is devoid of cementum as a result of a previous scaling of the root surface. The circular profiles in the calculus completely surround calcified bacteria. Magnification ×19 000. Bar: 1 µm. From Selvig (1970).

of the previous insertion of Sharpey's fibers (Bercy & Frank 1980). Uneven root surfaces may be the result of carious lesions and small areas of cementum may have been lost due to resorption, when the periodontal ligament was still invested into the root surface (Moskow 1969). Under such conditions it may become extremely difficult to remove all calculus deposits without sacrificing some hard tissues of the root.

Although some irregularities may also be encountered on oral implant surfaces, the attachment to commercially pure titanium generally is less intimate than to root surface structures. This in turn, would mean that calculus may be chipped off from oral implants (Fig. 8-45) without detriment to the implant surface (Matarasso *et al*. 1996).

Mineralization, composition, and structure

The mineralization starts in centers which arise intracellularly in bacterial colonies (Fig. 8-46) or extracellularly from matrix with crystallization nuclei (Fig. 8-47). Recent and old calculus consists of four different crystals of calcium phosphate (for review see Schroeder 1969):

1. $CaH(PO_4) \times 2H2O$ = brushite (**B**)
2. $Ca_4H(PO_4)_3 \times 2H2O$ = octa calcium phosphate (**OCP**)
3. $Ca_5(PO_4)_3 \times OH$ = hydroxyapatite (**HA**)
4. β-$Ca_3(PO_4)_2$ = whitlockite (**W**).

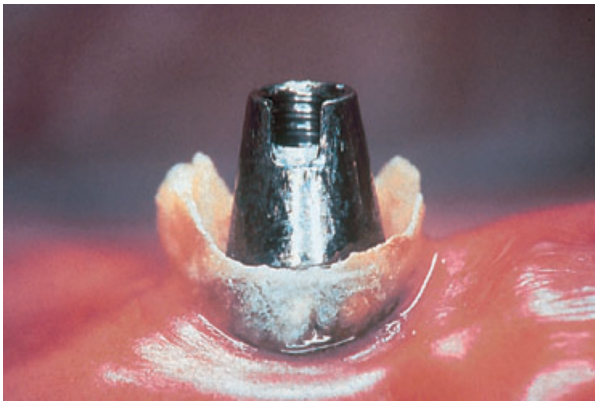

Fig. 8-45 Calculus deposit on an oral implant in a patient without regular maintenance care.

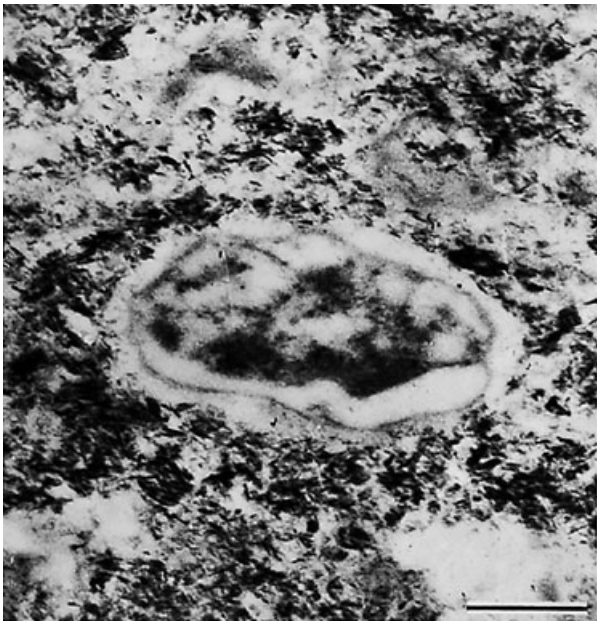

Fig. 8-46 Thin section of old plaque. A degenerating organism is surrounded by intermicrobial matrix in which initial mineralization has started by the deposition of small needle-shaped electron-dense apatite crystals. Magnification ×26 500. Bar: 0.5 µm. From Zander *et al*. (1960).

Supragingival calculus is clearly built up in layers and yields a great heterogeneity from one layer to another with regard to mineral content. On average, the mineral content is 37%, but ranges from 16% to 51%, with some layers yielding a maximal density of minerals of up to 80% exceptionally (Kani *et al*. 1983; Friskopp & Isacsson 1984). The predominant mineral in exterior layers is **OCP**, while **HA** is dominant in inner layers of old calculus. **W** is only found in small proportions (Sundberg & Friskopp 1985). **B** is identified in recent calculus, not older than 2 weeks, and appears to form the basis for supragingival calculus formation. The appearance of the crystals is characteristic for **OCP** as forming platelet-like crystals, for **HA** as forming sandgrain or rod-like crystals, while **W** presents with hexagonal (cuboidal, rhomboidal) crystals (Kodaka *et al*. 1988).

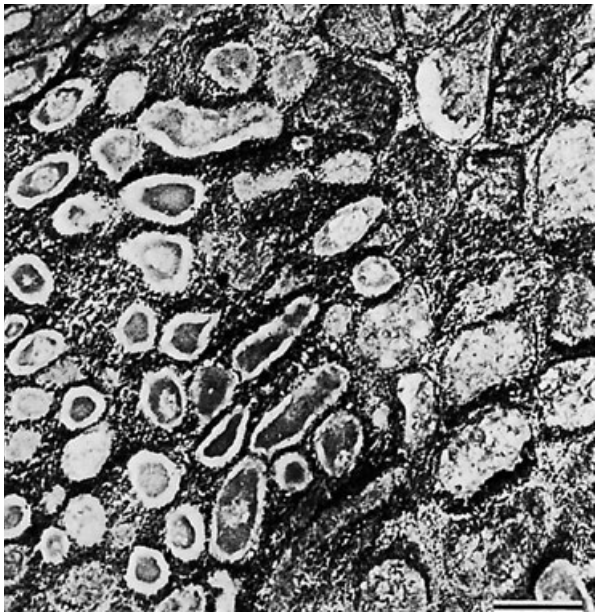

Fig. 8-47 Thin section of old mineralizing plaque. The intermicrobial matrix is totally calcified, and many microorganisms show intracellular crystal deposition. Magnification ×9500. Bar: 1 µm. From Theilade (1964).

Subgingival calculus appears somewhat more homogeneous since it is built up in layers with an equally high density of minerals. On average the density is 58% and ranges from 32% to 78%. Maximal values of 60–80% have been found (Kani *et al*. 1983; Friskopp & Isacsson 1984). The predominant mineral is always **W**, although **HA** has been found (Sundberg & Friskopp 1985). **W** contains small proportions (3%) of magnesia (McDougall 1985).

In the presence of a relatively low plaque pH and a concomitant high Ca/P ratio in saliva, **B** is formed which may later on develop into **HA** and **W**. When supragingival plaque mineralizes, **OCP** forms and is gradually changed into **HA**. In the presence of alkaline and anaerobic conditions and concomitant presence of magnesia (or Zn and CO_3), large amounts of **W** are formed, which are a stable form of mineralization.

Clinical implications

Although strong associations between calculus deposits and periodontitis have been demonstrated in experimental (Wærhaug 1952, 1955) and epidemiologic studies (Lövdal *et al*. 1958), it has to be realized that calculus is always covered by an unmineralized layer of viable bacterial plaque. It has been debated whether or not calculus may exert a detrimental effect on the soft tissues owing to its rough surface. However, it has clearly been established that surface roughness alone does not initiate gingivitis (Wærhaug 1956). On the contrary, in monkeys a normal epithelial attachment with the junctional epithelial cells forming hemidesmosomes and a basement membrane on calculus could be established (Listgarten &

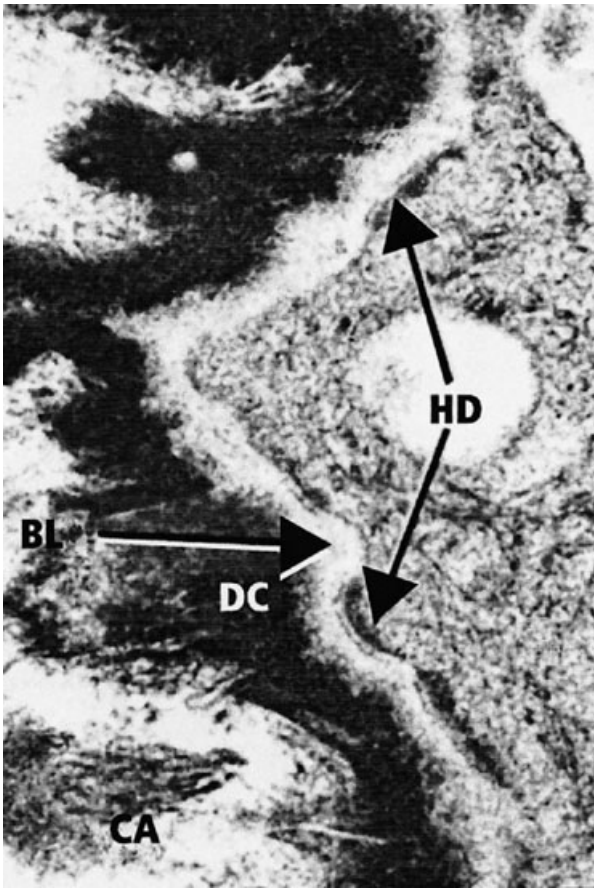

Fig. 8-48 Hemidesmosomal attachment of junctional epithelium on dental calculus in the absence of bacteria following application of chlorhexidine. CA: calculus; HD: hemidesmosomes; BL: basement lamina; DC: dental cuticle. ×32 000. Data from Listgarten & Ellegaard (1973).

Ellegaard 1973) if the calculus surface had been disinfected using chlorhexidine (Fig. 8-48). Furthermore, it has been demonstrated that autoclaved calculus may be encapsulated in connective tissue without inducing marked inflammation or abscess formation (Allen & Kerr 1965).

These studies clearly exclude the possibility of dental calculus being a primary cause of periodontal diseases. The effect of calculus seems to be secondary by providing an ideal surface configuration conducive to further plaque accumulation and subsequent mineralization.

Nevertheless, calculus deposits may have developed in areas with difficult access for oral hygiene or may – by the size of the deposits – jeopardize proper oral hygiene practices. Calculus may also amplify the effects of bacterial plaque by keeping the bacterial deposits in close contact with the tissue surface, thereby influencing both bacterial ecology and tissue response (Friskopp & Hammarström 1980).

Well controlled animal (Nyman *et al*. 1986) and clinical (Nyman *et al*. 1988; Mombelli *et al*. 1995) studies have shown that the removal of subgingival plaque on top of subgingival calculus will result in healing of periodontal lesions and the maintenance of healthy gingival and periodontal tissues, provided that the supragingival deposits are meticulously removed on a regular basis. One of these studies (Mombelli *et al*. 1995) clearly demonstrated that the diligent and complete removal of subgingival plaque on top of mineralized deposits after chipping off gross amounts of calculus showed almost identical results in the composition of the microbiota and the clinical parameters to those obtained with routine removal of subgingival calculus by root surface instrumentation. Again, it has to be realized that meticulous supragingival plaque control guarantees the depletion of the supragingival bacterial reservoir for subgingival recolonization. These studies have clearly elucidated the role of subgingival calculus as a plaque-retaining factor.

In summary, dental calculus represents mineralized bacterial plaque. It is always covered by unmineralized viable bacterial plaque, and hence, does not directly come into contact with the gingival tissues. Calculus, therefore, is a secondary etiologic factor for periodontitis. Its presence, however, makes adequate plaque removal impossible and prevents patients from performing proper plaque control. It is the most prominent plaque-retentive factor which has to be removed as a basis for adequate periodontal therapy and prophylactic activities.

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Chapter 9

Periodontal Infections

Sigmund S. Socransky and Anne D. Haffajee

Introduction

Periodontal diseases are infections that are caused by microorganisms that colonize the tooth surface at or below the gingival margin. It is estimated that about 700 different species are capable of colonizing the mouth and any individual may typically harbor 150 or more different species. Counts in subgingival sites range from about 10^3 in healthy, shallow sulci to $>10^8$ in deep periodontal pockets. Numbers in supragingival plaque can exceed 10^9 on a single tooth surface. Thus, while hundreds of millions or even billions of bacteria continually colonize the tooth at or below the gingival margin throughout life, most periodontal sites in most individuals do not exhibit new loss of the supporting structures of the teeth at any given time. This recognition is critical. The ecologic relationships between the periodontal microbiota and its host are, by and large, benign, in that damage to the supporting structures of the tooth is infrequent. Occasionally, a subset of bacterial species either is introduced, overgrows or exhibits new properties that lead to the destruction of the periodontium. The resulting stressed equilibrium is usually spontaneously corrected, or corrected by therapy. In either instance, microbial species continue to colonize above and below the gingival margin; hopefully, in a new and "peaceful" equilibrium.

Similarities of periodontal diseases to other infectious diseases

Our concepts of infectious diseases often appear to be influenced by our experiences with acute infections, particularly upper respiratory infections. In acute infections, an agent is acquired by exposure to an individual harboring that agent or from the environment. The agent establishes within tissues or on mucous membranes or skin. Within a short period of time, signs or symptoms of a disease appear at the site of introduction or elsewhere in the individual. A "battle" occurs between the parasite and the host resulting in increasingly obvious clinical signs and symptoms. This host–pathogen interaction often is resolved within a short period of time, usually, but not always, in favor of the host. Thus, daily experience suggests that colonization by a pathogen is rapidly followed by expression of disease. While certain infections follow this pattern, more commonly, colonization by a pathogenic species does not

lead to overt disease, at least immediately. For example, 15% of the American population is colonized by *Neisseria meningitidis* (Caugant *et al*. 1988), but only 0.5–1.1 cases of meningitis occur per 100 000 of the population (Summary of Notifiable Diseases – United States 2004, 2006). *Mycobacterium tuberculosis* colonizes about 5% of Americans (Sudre *et al*. 1992), but only 2.6 new cases of tuberculosis per 100 000 of US-born individuals are reported each year (Summary of notifiable diseases – United States 2004, 2006). Finally, about one third of the adult population is colonized by *Haemophilus influenzae* (Kilian & Frederiksen 1981) but only a tiny fraction exhibit disease. Even the highly virulent HIV virus may be detected in individuals for years prior to the development of clinical symptoms.

In a similar fashion, individuals may be colonized continuously by periodontal pathogens at or below the gingival margin and yet not show evidence of ongoing or previous periodontal destruction. Many of the organisms that colonize such sites are members of species thought to be periodontal pathogens. In spite of their presence, periodontal tissue damage does not take place. This is not an anomaly. This phenomenon is consistent with other infectious diseases in which it may be observed that a pathogen is necessary but not sufficient for a disease to occur.

Infectious diseases in a given organ system are caused by one or more of a relatively finite set of pathogens. Further, different species have different tissue specificities and cause diseases in different sites in the body. Lung infections may be caused by a wide range of species that includes *Streptococcus pneumoniae*, *M. tuberculosis*, *Klebsiella pneumoniae*, *Legionella pneumophilia*, and others. Infections of the intestine are caused by *Salmonella typhi*, *Shigella dysenteriae*, *Vibrio cholerae*, *Escherichia coli*, and *Campylobacter* species. In a similar fashion periodontal diseases appear to be caused by a relatively finite group of periodontal pathogens acting alone or in combination. Such species include *Aggregatibacter* (formerly *Actinobacillus*) *actinomycetemcomitans*, *Tannerella forsythia*, *Campylobacter rectus*, *Eubacterium nodatum*, *Fusobacterium nucleatum*, *Peptostreptococcus micros*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Prevotella nigrescens*, *Streptococcus intermedius*, and *Treponema* sp. (Haffajee & Socransky 1994).

There is a number of other common themes observed in different infectious diseases, particularly those that affect mucous membranes, such as the need to attach to one or more surfaces, the need to "sense" the environment and turn on or off various virulence factors, and the need to overcome or evade host defense mechanisms. Infectious agents have evolved a set of common strategies to perform these tasks and the host has developed a series of responses to combat these infections. Thus, periodontal diseases are infectious diseases that have many properties that are similar to bacterial infections in other parts of the body and to a large extent can be combatted in similar fashions.

Unique features of periodontal infections

Although periodontal diseases have certain features in common with other infectious diseases, there are several features of these diseases that are quite different. In certain ways, periodontal diseases may be among the most unusual infections of the human. The major reason for this uniqueness is *the unusual anatomic feature that a mineralized structure, the tooth, passes through the integument, so that part of it is exposed to the external environment while part is within the connective tissues.* The tooth provides a surface for the colonization of a diverse array of bacterial species. Bacteria may attach to the tooth itself, to the epithelial surfaces of the gingiva or periodontal pocket, to underlying connective tissues, if exposed, and to other bacteria which are attached to these surfaces. In contrast to the outer surface of most parts of the body, the outer layers of the tooth do not "shed" and thus microbial colonization (accumulation) is facilitated. Thus, a situation is set up in which microorganisms colonize a relatively stable surface, the tooth, and are continually held in immediate proximity to the soft tissues of the periodontium. This poses a potential threat to those tissues and indeed to the host itself.

The organisms that cause periodontal diseases reside in biofilms that exist on tooth or epithelial surfaces. The biofilm provides a protective environment for the colonizing organisms and fosters metabolic properties that would not be possible if the species existed in a free-living (planktonic) state. Periodontal infections and another biofilm-induced disease, dental caries, are arguably the most common infectious diseases affecting the human. The onset of these diseases is usually delayed for prolonged periods of time after initial colonization by the pathogen(s). The course of these diseases typically runs for years. The etiologic agents in most instances appear to be members of the indigenous microbiota and, thus, the infections might be thought of as endogenous. The source of the infecting agents for any given individual is usually unknown, although transfer from parents or significant others is thought to play a primary role (Petit *et al*. 1993a,b; Saarela *et al*. 1993; van Steenbergen *et al*. 1993; Preus *et al*. 1994). The major characteristics of these diseases are that they are caused by organisms that reside in biofilms outside the body. Their treatment is complex in that physical, antimicrobial, and ecologic approaches are required.

The presence of a tooth increases the complexity of the host–parasite relationship in a number of ways. The bacteria colonizing the tooth are, by and large, outside the body where they are less able to be controlled by the potent mechanisms which operate within the tissues. The environment within plaque

may be conducive for microbial survival, but it is unlikely to be a particularly effective environment for the host to seek out and destroy microorganisms. Factors, such as *hydrogen ion concentration* (pH), *oxidation reduction potential* (Eh), and *proteolytic enzymes*, can affect the performance of host defense mechanisms. In addition, the tooth provides "sanctuaries" in which microorganisms can hide, persist at low levels during treatment and then re-emerge to cause further problems. Bacteria in dentinal tubules, flaws in the tooth, or areas that were demineralized by bacteria are not easily approached by the much larger host cells. In a similar fashion, non-cellular host factors must face diffusion barriers, lytic enzymes, and absorption by the mineral structure of the tooth. Mechanical debridement other than vigorous removal of tooth material cannot reach organisms within the tooth. Chemotherapeutic agents will also have difficulty in reaching the organisms.

Taken together, the infections that affect the tooth and its supporting structures present a formidable problem for both the host and the therapist. The unique anatomic features of this "organ system" must be borne in mind as we attempt to unravel the etiology and pathogenesis of periodontal diseases and plan treatment or prevention strategies for their control.

Historical perspective

The search for the etiologic agents of periodontal diseases has been in progress for over a century. The search started in the "golden age of microbiology" (approx. 1880–1920), when the etiologic agents of many medically important infections were determined. It is not surprising that parallel investigations of the etiology of periodontal diseases were initiated in this era. However, these investigations were not as successful as some of the investigations of extraoral infectious diseases. It seems worthwhile to review briefly the findings of the early era and to understand the effect that the inconclusive nature of many of the studies had on the concepts of etiology and treatment of disease. The references for this section may be found in Socransky and Haffajee (1994).

The early search

Investigators in the period from 1880–1930 suggested four distinct groups of microorganisms as possible etiologic agents; amoeba, spirochetes, fusiforms, and streptococci. The basis of this determination was primarily the seeming association of these organisms with periodontal lesions. The identification of a suspected pathogen was heavily influenced by the nature of the techniques available. The major techniques at that time were wet mount or stained smear microscopy and limited cultural techniques. The different techniques suggested different etiologic agents. A situation not unlike that found today. While a greater variety of improved techniques is available, different techniques can and do emphasize the importance of different organisms.

Amoeba

Certain groups of investigators used stained smears to seek amoeba in bacterial plaque. They found higher proportions of amoeba in lesions of destructive periodontal diseases than in samples taken from sites in healthy mouths or mouths with gingivitis. Local therapies for this organism included the use of dyes or other antiseptic agents to decrease the numbers of amoebae in the oral cavity. Other approaches employed agents such as the emitic, emitin, administered systemically or locally. The role of amoeba in periodontal disease was questioned by some authors because amoeba were found in sites with minimal or no disease and could not be detected in many sites with destructive disease and because of the failure of emitin to ameliorate the symptoms of the disease.

Spirochetes

Other investigators used wet mount preparations or specific stains for spirochetes when they examined dental plaque. They reported higher proportions of spirochetes and other motile forms in lesions of destructive disease when compared with control sites in the same or other individuals. This finding led to the suggestion that spirochetes may be etiologic agents of destructive periodontal disease. Therapies were proposed that sought to control disease by the elimination or suppression of these microorganisms including the systemic administration of Neosalvarsan (compound 606), the anti-spirochetal agent used to treat syphilis, coupled with the use of subgingival scaling to control destructive periodontal disease. Other investigators employed bismuth compounds to treat oral spirochetal infections. Many investigators claimed success in controlling advanced destructive periodontal disease by combining local and systemic therapy. Others questioned the relationship of spirochetes to periodontal diseases.

Fusiforms

The third group of organisms that were frequently suggested to be etiologic agents of destructive periodontal diseases, including Vincent's infection, were the spindle-shaped fusiforms. These organisms were originally recognized on the basis of their frequent appearance in microscopic examination of subgingival plaque samples. The organisms were first related to periodontal disease by Plaut (1894). Vincent (1899) distinguished certain pseudomembranous lesions of the oral cavity and throat from diphtheria and recognized the important role of fusiforms and spirochetes in this disease. In honor of this investigator the

infection became known as Vincent's infection. The important role of spirochetes and fusiforms in Vincent's infection was widely recognized in the succeeding 2 decades.

As a footnote to this section, it is worth noting that acute necrotizing ulcerative gingivitis (ANUG) appears to have been declining in many "first world countries" for many decades. Many older practitioners can remember periods when they would see several cases of ANUG a month or even a week. Detection of this disease is much less common today. In reviewing the earlier literature, we were struck with how common the disease appeared to be from about 1915–1930. Most of us are aware of the devastation this disease caused in the combat troops of World War I, when the disease was commonly called trench mouth (due to its frequent occurrence in troops stationed in the trenches of the battlegrounds). What we are less aware of is how common the disease became in countries out of the war zone (e.g. the US) after World War I. For example, Daley (1927a,b) examined over 1000 patients who came to Tufts Dental College in Boston for operative dentistry (not periodontal problems). He found Vincent's infection in one of three people using clinical criteria and stained smears seeking the presence of fusiforms and spirochetes. Daley carefully described the lesions in terms acceptable today; i.e. as ulcerated lesions that bled easily on probing and had a distinctive fetid odor. He further pointed out that the disease was rare in Boston prior to 1917; at which time the troops began to return home. He described an outbreak stemming from a local barracks which led to 75 cases being treated at Tufts within 48 hours. Daley and others in the era felt that the severe outbreak after the war was due to the transmission of more virulent bacteria among an unprotected (not immune) population. Assuming that the disease described in this era was ANUG, it is interesting to note that there was a virtual epidemic. This is particularly intriguing in that it supports the notion that periodontal pathogens can be readily transmitted from one person to another as modern molecular techniques are documenting today.

Streptococci

The fourth group of microorganisms that were proposed as etiologic agents of periodontal diseases in this era were the streptococci. These microorganisms were proposed on the basis of cultural examination of samples of plaque from subgingival sites of periodontal disease. The selection of the streptococci may have been predicated upon the fact these were the only species that could be consistently isolated from periodontitis lesions using the cultural techniques of that era. Since there were no methods available at that time for the specific control of streptococci, workers turned to non-specific agents such as the intramuscular injection of mercury or to the use of vaccines for the control of periodontal diseases.

Vaccines

For the first 3 decades of the twentieth century, vaccines were commonly employed by physicians and dentists in attempts to control bacterial infections. Three types of vaccines were employed for the control of periodontal diseases. These included vaccines prepared from pure cultures of streptococci, and other oral organisms, autogenous vaccines, and stock vaccines such as Van Cott's vaccine, Goldenberg's vaccine or Inava Endocorps vaccine. These vaccines were administered systemically or locally in the periodontal tissues.

Autogenous vaccines were prepared from the dental plaque of patients with destructive periodontal diseases. Plaque samples were removed from the diseased site, "sterilized" by heat, and/or by immersion in iodine or formalin solutions, then re-injected into the same patient, either in the local periodontal lesion or systemically. Proponents of all three techniques claimed great efficacy for the vaccination methods employed, while others using the same techniques were more skeptical.

Other forms of therapy directed against oral microorganisms

The difficulty in controlling microorganisms in the absence of specific antimicrobial agents gave rise to a series of rather remarkable treatment procedures. For example, ultraviolet light was widely used to attempt to control the oral microbiota and to improve the well-being of the local tissue (for review see Rasmussen 1929). Other measures were somewhat more dramatic and in some instances rather frightening. Dental practitioners used electrochemical techniques, caustic agents such as phenol, sulfuric, trichloracetic or chromic acids, nascent copper, castor oil soap (sodium ricolineate), and even radium was used to combat root canal infections. In the last instance radium at levels of up to 0.135 millicuries was placed in canals to "sterilize" them. As might be expected, the reports were glowing. The recent interest in controlling the epithelium in order to maximize reattachment had antecedents in this era. One technique which appears to have been commonly employed was the use of sodium sulfide to "dissolve" the epithelial lining of the pocket and permit reattachment.

Invasion – the early years

One of the more interesting phenomena of research is the fact that research workers keep rediscovering the same phenomena in a cyclical fashion. Invasion of the periodontal tissues by bacteria was thought to be important in the pathogenesis of periodontal

diseases in the early 1900s, forgotten and then rediscovered.

Beckwith *et al*. (1925) used stains specific for bacteria to study biopsy specimens from prisoners at San Quentin who had periodontitis. They regularly observed bacteria both within the epithelium and in the underlying tissues. Bacteria in the epithelium were usually streptococci or "diphtheroids". Gram-negative rods were observed in the connective tissue. They noted the rare occurrence of spiral forms in the tissues, although they were routinely detected in the plaque overlying the tissues. Other investigators also showed invasion into periodontal tissues. Invasion of spirochetes deep into the lesions of Vincent's infection was clearly documented. It was thought that the spirochetes moved into the connective tissues first and were followed by fusiform-shaped species.

Comment

In this early period, literally hundreds of papers were published which suggested certain specific etiologic agents of periodontal diseases or advocated specific therapies directed at microbial control. In spite of this enthusiasm, the concept of the infectious nature of periodontal diseases and the recognition that treatment should be directed at the causative agents, disappeared. Reasons for the demise of this promising area of research could have included the possibility of incorrect etiologic agents, inadequate therapies and multiplicity of diseases. A more likely scenario was the failure of early researchers (and this is still true today) to recognize that periodontal diseases represent an array of infections, each requiring different specific therapies. Indeed, a similar situation exists today where a given adjunctive antibiotic therapy is effective in some individuals and not others. Finally, competing theories explaining the etiology of periodontal diseases in this era appeared to, temporarily at least, gain popularity, due primarily to their nebulous and untestable nature. Such hypotheses as "diffuse alveolar atrophy", "continuing eruption", "lack of function", and "constitutional defects" became acceptable alternatives (to some) to the recognition of the infectious nature of periodontal diseases.

The decline of interest in microorganisms

The initial enthusiasm for the hunt for the etiologic agents of destructive periodontal diseases slowly subsided and by the mid 1930s there were virtually no workers involved in this quest. This state was eloquently described by Belding and Belding (1936) in the aptly titled "Bacteria – Dental Orphans". During the period from the mid 1920s to the early 1960s, the attitude toward the etiology of periodontal diseases changed. In the first 2 decades of this period it was thought that periodontal disease was due to some constitutional defect on the part of the patient, to trauma from occlusion, to disuse atrophy or to some combination of these factors. Bacteria were thought to be merely secondary invaders in this process or, at most, contributors to the inflammation observed in periodontal destruction.

Non-specific plaque hypothesis

Treatment of patients based on the notion of constitutional defects or trauma from occlusion was not effective in controlling periodontal diseases. Clinicians recognized that plaque control was essential in the satisfactory treatment of periodontal patients. During the late 1950s, a group of clinicians, sometimes referred to as "plaque evangelists", heavily emphasized the need for plaque control in the prevention and treatment of periodontal diseases. Thus, once again bacteria were thought to play a role in the etiology of destructive periodontal disease, but as non-specific causative agents. According to this "non-specific plaque" hypothesis, any accumulations of microorganisms at or below the gingival margin would produce irritants leading to inflammation. The inflammation in turn was responsible for the periodontal tissue destruction. The specific species of microorganisms that accumulated on the teeth was not considered to be particularly significant, providing that their numbers were sufficiently large to trigger a destructive process.

Mixed anaerobic infections

Beginning in the late 1920s, a series of oral and medical microbiologists believed that periodontal disease was the result of "mixed infections". This hypothesis had been considered since the late 1800s when microscopic observations by Vincent in France suggested that certain forms of periodontal disease, particularly ANUG, were due to a combination of microorganisms dominated by fusiforms and spirochetes. These infections were known as fuso-spirochetal infections. In the early 1930s, investigators found that mixtures of microorganisms isolated from lung infections or subgingival plaque would induce lesions when injected subcutaneously into various experimental animals. A combination of a fusiform, a spirochete, an anaerobic vibrio and an alpha hemolytic streptococcus could cause transmissible infections in the guinea pig. Later investigators failed to reproduce their results either with the above combination of microorganisms or with many other combinations they tested. They did demonstrate, however, that mixed infections were due to bacteria (rather than a virus).

Macdonald and co-workers (1956) were later able to produce transmissible mixed infections in the guinea pig groin using combinations of pure cultures. The critical mixture of four organisms included a *Bacteroides melaninogenicus* strain, a Gram-positive anaerobic rod and two other Gram-negative

anaerobic rods. This combination of organisms was completely different from those used by earlier investigators to cause transmissible infections. These results led to the concept that mixed infections might be "bacteriologically non-specific but biochemically specific". In other words, any combination of microorganisms capable of producing an array of destructive metabolites could lead to transmissible infections in animals and, by extension, to destructive periodontal infections in humans. Later experiments suggested that members of the *B. melaninogenicus* group were the key species in these infections.

Return to specificity in microbial etiology of periodontal diseases

In the 1960s, interest in the specific microbial etiology of periodontal disease was rekindled by two groups of experiments. The first demonstrated that periodontal disease could be transmitted in the hamster from animals with periodontal disease to animals without periodontal disease by caging them together. Swabs of plaque or feces from diseased animals were effective in transmitting the disease to animals free of disease. It was demonstrated that a pure culture of a Gram-positive pleomorphic rod that later became known as *Actinomyces viscosus* was capable of causing destructive periodontal disease in animals free of disease. Other species isolated from the plaque of hamsters with periodontal disease did not have this capability.

At about the same time, it was demonstrated that spirochetes with a unique ultrastructural morphology could be detected in practically pure culture in the connective tissue underlying lesions of ANUG and within the adjacent epithelium. Control tissue taken from healthy individuals and individuals with other forms of disease did not exhibit a similar tissue invasion. To date, the spirochete associated with ANUG has not been cultivated.

Such findings suggested that there might be more specificity to the microbial etiology of periodontal disease than had been accepted for the previous 4 decades. However, the emphasis of clinicians in the 1960s was on the mechanical control of plaque accumulation. This approach was consistent with the prevailing concept that periodontal disease was due to a non-specific accumulation of bacteria on tooth surfaces. This concept is very much in evidence today and still serves as the basis of preventive techniques in most dental practices. It is also clear that non-specific plaque control is not able to effectively prevent all forms of periodontal disease.

The transmissibility studies stimulated a new concept of periodontal diseases. The organisms which were responsible for the periodontal destruction observed in the hamster clearly differed from other organisms by their ability to form large amounts of bacterial plaque both in the hamster and in *in vitro* test systems. A concept emerged that microorganisms that were capable of forming large amounts of plaque *in vivo* and *in vitro* should be considered as prime suspects in the etiology of periodontal diseases. Human isolates of *Actinomyces* species were shown to have this ability *in vitro* and led to plaque formation and periodontal destruction in animal model systems. These findings reinforced the notion that organisms that formed abundant plaque were responsible for destructive periodontal disease. Unfortunately, later research findings revealed major discrepancies in this hypothesis.

Changing concepts of the microbial etiology of periodontal diseases

By the end of the 1960s it was generally accepted that dental plaque was in some way associated with human periodontal disease. It was believed that the presence of bacterial plaque initiated a series of as yet undefined events that led to the destruction of the periodontium. The composition of plaque was thought to be relatively similar from patient to patient and from site to site within patients. Variability was recognized, but the true extent of differences in bacterial composition was not appreciated. It was thought that the major event triggering destructive periodontal disease was an increase in mass of bacterial plaque, possibly accompanied by a diminution of host resistance. Indeed, in the mid 1960s the classic studies of Loe *et al*. (1965, 1967) and Theilade *et al*. (1966) convincingly demonstrated that plaque accumulation directly preceded and initiated gingivitis. Many investigators believed that gingivitis was harmful, and led to the eventual destruction of the periodontal tissues, probably by host-mediated events.

Yet, certain discrepancies continued to baffle clinicians and research workers alike. If all plaques were more or less alike and induced a particular tissue response in the host, why was periodontal destruction localized, taking place adjacent to one tooth but not another? If plaque mass was a prime trigger for periodontal destruction, why did certain subjects accumulate much plaque, frequently accompanied by gingivitis, but fail, even after many years to develop destruction of the supporting structures? On the other hand, why did some individuals with little detectable plaque or clinical inflammation develop rapid periodontal destruction? If inflammation was the main mediator of tissue destruction, why were so many teeth retained in the presence of continual gingivitis? One explanation may have been that there were inconsistencies in the host response, or disease required the superimposition of local factors such as trauma from occlusion, overhanging fillings etc. Other explanations can be derived from extensive studies of the microbiota adjacent to periodontal tissues.

The recognition of differences in the composition of bacterial plaque from subject to subject and site to site within subjects led to a series of investigations.

Some studies attempted to determine whether specific microorganisms were found in lesion sites as compared to healthy sites. Others studies sought differences in the microorganisms in subgingival plaque samples taken from subjects with clinically different forms of periodontal disease or periodontal health. Newman *et al*. (1976, 1977) and Slots (1976) demonstrated that the microbial composition of subgingival plaque taken from diseased sites differed substantially from the samples taken from healthy sites in subjects with localized aggressive periodontitis (LAP). Tanner *et al*. (1979) and Slots (1977) demonstrated that the microbiota recovered from lesion sites from subjects with chronic periodontitis differed from the microbiota from healthy sites in the same subjects and also from lesion sites in LAP subjects. These studies, along with the demonstration that subjects with LAP could be treated successfully with local debridement and systemic antibiotics, provided the initial impetus to perform larger-scale studies attempting to relate specific microorganisms to the etiology of different periodontal diseases.

Current suspected pathogens of destructive periodontal diseases

Criteria for defining periodontal pathogens

For more than a century, the classical "Koch's postulates" have been used to define a causal relationship between an infectious agent and a disease. These postulates were: (1) the agent must be isolated from every case of the disease, (2) it must not be recovered from cases of other forms of disease or non-pathogenically, and (3) after isolation and repeated growth in pure culture, the pathogen must induce disease in experimental animals (Carter 1987). The criteria for defining pathogens of destructive periodontal diseases initially were based on Koch's postulates but have been amended and extended in recent years. These criteria include association, elimination, host response, virulence factors, animal studies, and risk assessment. The discrimination of a pathogen from a non-pathogenic species is not based on a single criterion but rather on a "weight of evidence" evaluation.

The criterion of association is really the same as Koch's first two postulates; i.e. the species should be found more frequently and in higher numbers in cases of the infection than in individuals without overt disease or with different forms of disease. However, periodontal microbiologists do not expect to find the pathogen in "all cases of the disease" because they currently cannot distinguish "all cases of a given disease". The criterion of elimination is based on the concept that elimination of a species should be accompanied by a parallel remission of disease. If a species is eliminated by treatment and the disease progresses, or if the level of a species remains high or increases in a site and the disease stops, doubt would be cast on that species' role in pathogenesis. This criterion (like all of the others) has certain problems in that therapy rarely (if ever) eliminates or suppresses only one species at a time. The criterion of host response, particularly the immunological response, appears to be of value in defining periodontal pathogens. If a species (or its antigens) gains access to underlying periodontal tissues and causes damage, it seems likely that the host will produce antibodies or a cellular immune response that is directed specifically to that species. Thus, the host response could act as a pointer to the pathogen(s). Biochemical determinants (virulence factors) may also provide valuable clues to pathogenicity. Potentially damaging metabolites produced, or properties possessed, by certain species may be suggestive that those species could play a role in the disease process.

Animal model systems provide suggestive evidence that a microbial species may play a role in human disease. Particularly noteworthy are studies of experimentally induced disease in dogs or monkeys, which can be manipulated to favor selection of single or subsets of species that may or may not induce pathology. These models usually suggest a possible etiologic role of a species indigenous to the test animal that may have analogues in the human subgingival microbiota. Finally, technological developments, such as checkerboard DNA–DNA hybridization (Fig. 9-1) and polymerase chain reaction (PCR), now permit assessment of specific microorganisms in large numbers of subgingival plaque samples. This allows prospective studies to be performed in which the risk of periodontal disease progression conferred by the presence of an organism at given levels may be assessed.

Periodontal pathogens

The World Workshop in Periodontology (Consensus Report, 1996) designated *A. actinomycetemcomitans*, *P. gingivalis*, and *T. forsythia* as periodontal pathogens. Tables 9-1, 9-2, and 9-3 summarize some of the data that indicate an etiologic role of these species in periodontal diseases, categorized according to the criteria defined above. The summary is by no means exhaustive but does indicate that a growing literature suggests some reasonable candidates as etiologic agents of destructive periodontal diseases.

Aggregatibacter (formerly *Actinobacillus*) *actinomycetemcomitans*

One of the clearest associations between a suspected pathogen and destructive periodontal disease is provided by *A. actinomycetemcomitans.* This species has recently been renamed *Aggregatibacter actinomycetemcomitans* from its former name of *Actinobacillus actinomycetemcomitans* (Norskov-Lauritsen & Kilian 2006). *A. actinomycetemcomitans* is a small, non-motile,

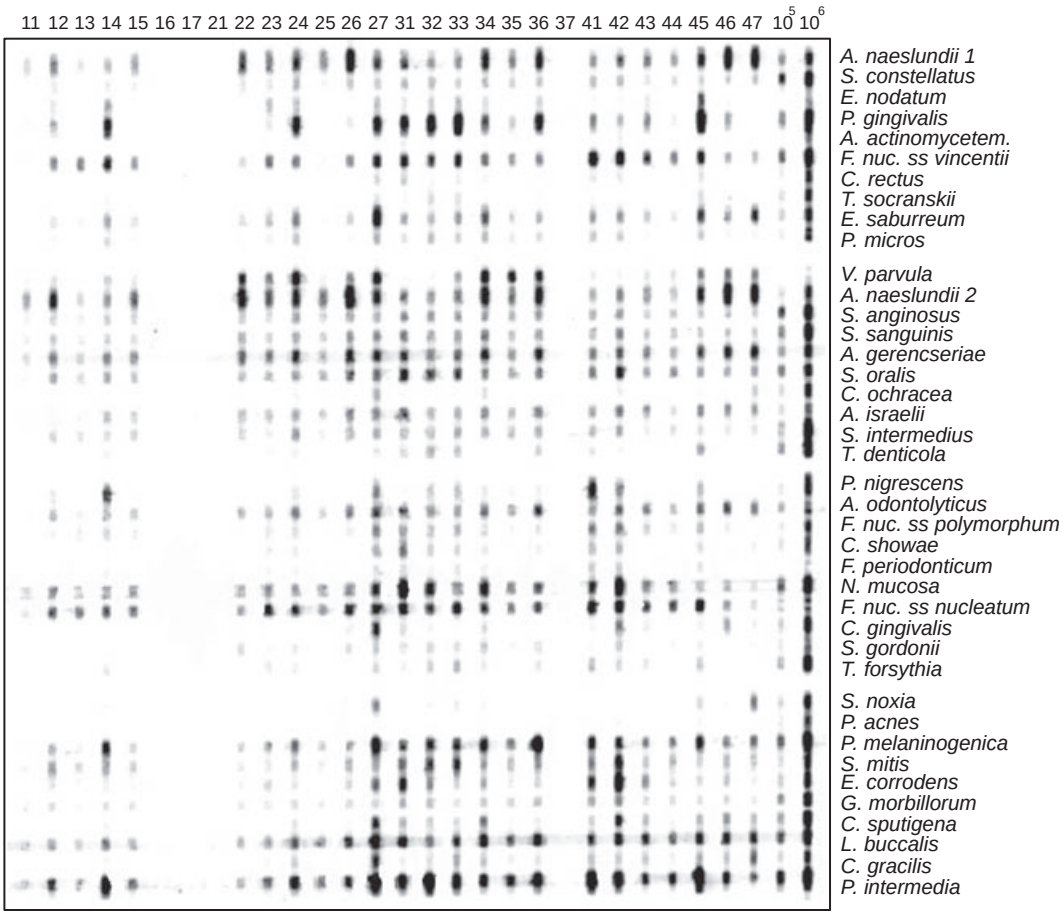

Fig. 9-1 Example of checkerboard DNA–DNA hybridization being used to detect 40 bacterial species in 28 subgingival plaque samples from a single patient. The vertical lanes are the plaque samples numbered from 11 (upper right central incisor) to 47 (lower right second molar). In this subject, teeth 16, 17, 21, and 37 were missing. The two vertical lanes on the right are standards containing either 10^5 or 10^6 cells of each test species. The horizontal lanes contained the indicated DNA probes in hybridization buffer. A signal at the intersection of the vertical and horizontal lanes indicates the presence of a species. The intensity of the signal is related to the number of organisms of that species in the sample. In brief, samples of plaque were placed into individual Eppendorf tubes and the DNA released from the microorganisms by boiling in NaOH. After neutralization, the released DNA was transferred to the surface of a nylon membrane using the 30 channels of a Minislot device (Immunetics, Cambridge, MA). The DNA was fixed to the membrane by UV light and baking and placed in a Miniblotter 45 (Immunetics) with the lanes of DNA at right angles to the 45 channels of the Miniblotter device. Whole genomic DNA probes labelled with digoxigenin were placed in hybridization buffer into 40 of the lanes and hybridized overnight. After stringency washing, the signals were detected using phosphatase-conjugated antibody to digoxigenin and chemifluorescence substrates. Signals were compared to the standards using a Storm Fluorimager and converted to counts.

Table 9-1 Summary of some of the types of data that suggest that *Aggregatibacter actinomycetemcomitans* may be an etiologic agent of destructive periodontal diseases (for literature citations see text and Haffajee & Socransky 1994)

Factor	Data
Association	Elevated in lesions of localized juvenile periodontitis (LJP), prepubertal or adolescent periodontal disease
	Lower in health, gingivitis and edentulous subjects or sites
	Elevated in some adult periodontitis lesions
	Elevated in active lesions of juvenile periodontitis
	Detected in prospective studies
	Detected in apical ares of pocket or in tissues from LJP lesions
Elimination	Elimination or suppression resulted in successful therapy
	Recurrent lesions harbored the species
Host response	Elevated antibody in serum or saliva of LJP patients
	Elevated antibody in serum or saliva of chronic periodontitis patients
	Elevated local antibody in LJP sites
Virulence factors	Leukotoxin; collagenase; endotoxin; epitheliotoxin; fibroblast inhibitory factor; bone resorption inducing factor; induction of cytokine production from macrophages; modification of neutrophil function; degradation of immunoglobulins; cytolethal distending toxin (Cdt); induces apoptotic cell death
	Invades epithelial and vascular endothelial cells *in vitro* and buccal epithelial cells *in vivo*
Animal studies	Induced disease in gnotobiotic rats
	Subcutaneous abscesses in mice

Table 9-2 Summary of some of the types of data that suggest that *Porphyromonas gingivalis* may be an etiologic agent of destructive periodontal diseases (for literature citations see text and Haffajee & Socransky 1994)

Factor	Data
Association	Elevated in lesions of periodontitis Lower in sites of health, gingivitis and edentulous subjects Elevated in actively progressing lesions Elevated in subjects exhibiting periodontal disease progression Detected in cells or tissues of periodontal lesions Presence indicates increased risk for alveolar bone loss and attachment level loss
Elimination	Elimination resulted in successful therapy Recurrent lesions harbored the species Successful treatment lowered level and/or avidity of antibody
Host response	Elevated antibody in serum or saliva in subjects with various forms of periodontitis Altered local antibody in periodontitis
Virulence factors	Collagenase; endotoxin; proteolytic trypsin-like activity; fibrinolysin; hemolysin; other proteases including gingipain; phospholipase A; degrades immunoglobulin; fibroblast inhibitory factor; H_2S; NH_3; fatty acids; factors that adversely affect PMNs; capsular polysaccharide; bone resorption inducing factor; induction of cytokine production from various host cells; generates chemotactic activities; inhibits migration of PMNs across epithelial barriers; Invades epithelial cells *in vitro*
Animal studies	Important in experimental pure or mixed subcutaneous infections Induced disease in gnotobiotic rats Studies in sheep, monkeys and dogs Immunization diminished disease in experimental animals

Table 9-3 Summary of some of the types of data that suggest that *Tannerella forsythia* may be an etiologic agent of destructive periodontal diseases (for literature citations see text and Haffajee & Socransky 1994)

Factor	Data
Association	Elevated in lesions of periodontitis Lower in sites of health or gingivitis Elevated in actively progressing lesions Elevated in periodontal abscesses Increased in subjects with refractory periodontitis Detected in epithelial cells of periodontal pockets Presence indicates increased risk for alveolar bone loss, tooth and attachment level loss
Elimination	Elimination resulted in successful therapy Recurrent lesions harbored the species Reduced in successfully treated peri-implantitis
Host response	Elevated antibody in serum of periodontitis subjects and very high in a subset of subjects with refractory periodontitis
Virulence factors	Endotoxin; fatty acid and methylglyoxal production; induces apoptotic cell death; cytokine production from various host cells; invades epithelial cells *in vitro* and *in vivo*
Animal studies	Increased levels in ligature-induced periodontitis and peri-implantitis in dogs Induced disease in gnotobiotic rats

Gram-negative, saccharolytic, capnophilic, round-ended rod that forms small, convex colonies with a "star-shaped" center when grown on blood agar plates (Fig. 9-2). This species was first recognized as a possible periodontal pathogen by its increased frequency of detection and higher numbers in lesions of localized aggressive periodontitis (Newman *et al*. 1976; Slots 1976; Newman & Socransky 1977; Slots *et al*. 1980; Mandell & Socransky 1981; Zambon *et al*. 1983a; Chung *et al*. 1989) when compared with numbers in plaque samples from other clinical conditions including periodontitis, gingivitis, and health. Soon thereafter, it was demonstrated that the majority of subjects with localized aggressive periodontitis (LAP) had an enormously elevated serum antibody response to this species (Genco *et al*. 1980; Listgarten *et al*. 1981; Tsai *et al*. 1981; Altman *et al*. 1982; Ebersole *et al*. 1982, 1987) and that there was local synthesis of antibody to this species (Schonfeld & Kagan 1982; Ebersole *et al*. 1985; Smith *et al*. 1985; Tew *et al*. 1985a). When subjects with this form of disease were treated successfully, the species was eliminated or lowered in level; treatment failures were associated with failure to lower the numbers of the species in treated sites (Slots & Rosling 1983; Haffajee *et al*. 1984; Christersson *et al*. 1985; Kornman & Robertson 1985;

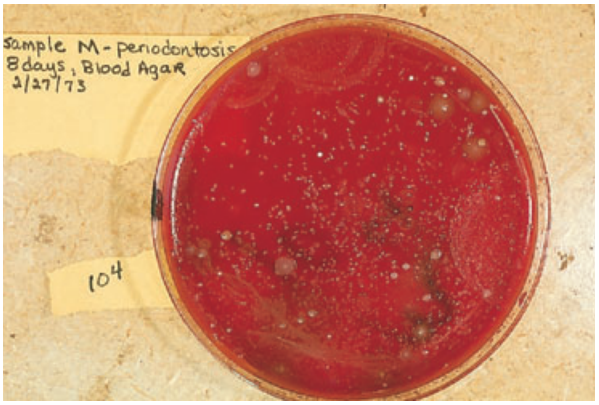

Fig. 9-2 Photograph of a primary isolation plate of a subgingival plaque sample from a diseased site in a subject with LAP. A dilution of the plaque sample was grown for 7 days at 35°C on an enriched blood agar plate in an atmosphere of 80% N_2, 10% H_2, and 10% CO_2. The majority of the small, round, convex colonies on this plate were isolates of *Aggregatibacter actinomycetemcomitans*.

Mandell *et al*. 1986; Preus 1988; Shiloah *et al*. 1998; Tinoco *et al*. 1998). The species produced a number of potentially damaging metabolites, including a leukotoxin (Baehni *et al*. 1979) and a cytolethal distending toxin (Saiki *et al*. 2001; Shenker *et al*. 2001), and induced disease in experimental animals (Irving *et al*. 1978). *A. actinomycetemcomitans* has been shown, *in vitro*, to have the ability to invade cultured human gingival epithelial cells (Blix *et al*. 1992; Sreenivasan *et al*. 1993), human vascular endothelial cells (Schenkein *et al*. 2000) and buccal epithelial cells *in vivo* (Rudney *et al*. 2001). Further, studies have shown that *A. actinomycetemcomitans* induced apoptotic cell death (Arakawa *et al*. 2000; Kato *et al*. 2000).

Perhaps the strongest association data came from studies of "active lesions" in which the species was elevated in actively progressing periodontal lesions when compared with non-progressing sites (Haffajee *et al*. 1984; Mandell 1984; Mandell *et al*. 1987; Haubek *et al*. 2004) and in prospective studies of as yet undiseased siblings of LAP subjects (DiRienzo *et al*. 1994). *A. actinomycetemcomitans* was also elevated in studies of disease progression in young Indonesian subjects (Timmerman *et al*. 2001). Collectively, the data suggest that *A. actinomycetemcomitans* is a probable pathogen of LAP. However, this should not be interpreted as meaning that it is the sole cause of this clinical condition, since a subset of subjects with LAP did not exhibit this species in samples of their subgingival plaque and had no elevated antibody response to the species (Loesche *et al*. 1985; Moore 1987).

The possibility that a subset of *A. actinomycetemcomitans* clonal types was primarily responsible for LAP was raised in studies at the University of Pennsylvania. Strains of *A. actinomycetemcomitans* were isolated from members of 18 families with at least one member with active LAP as well as from from 32 control subjects. Restriction fragment length polymorphisms (RFLP) indicated 13 distinct RFLP groups of *A. actinomycetemcomitans* (DiRienzo & McKay 1994). Isolates from LAP subjects fell into predominantly RFLP pattern II, while RFLP patterns XIII and XIV were seen exclusively in isolates from periodontally healthy subjects. Further, disease progression was related strongly to the presence of RFLP group II (DiRienzo *et al*. 1994).

Haubek *et al*. (1996) demonstrated that strains of *A. actinomycetemcomitans* isolated from families, initially of African origin living in geographically different areas, were characterized by a 530 base pair deletion in the leukotoxin gene operon leading to a significantly increased production of leukotoxin. They speculated that this virulent clonal type may account for an increased prevalence of LAP in African Americans and other individuals of African descent. A key isolate of this clonal type, strain JP2, was first isolated from an 8-year-old African American child with prepubertal periodontitis (Tsai *et al*. 1979; Kilian *et al*. 2006). There was a strong association between the presence of the JP2 clonal type of *A. actinomycetemcomitans* and early onset periodontitis in Moroccan school children, but no association between the presence of *A. actinomycetemcomitans* without the 530 bp deletion and early onset periodontitis (Haubek *et al*. 2001). Further, the odds ratio for disease progression in a subject in this population infected with the JP2 clone was 14.5 (Haubek *et al.* 2004). These observations were corroborated in a Brazilian population, where highly leukotoxic strains of *A. actinomycetemcomitans* were more prevalent in aggressive periodontitis than in chronic periodontitis (Cortelli *et al*. 2005). This deletion in the leukotoxin operon was not detected in any strains of *A. actinomycetemcomitans* isolated from adult Chinese subjects (Mombelli *et al.* 1999; Tan *et al*. 2001) or Asian subjects in the United States (Contreras *et al*. 2000). Subjects harboring *A. actinomycetemcomitans* with the 530 bp deletion were 22.5 times more likely to convert to LAP than subjects who had *A. actinomycetemcomitans* variants containing the full-length leukotoxin promoter region (Bueno *et al*. 1998). Interestingly, strains of *A. actinomycetemcomitans* with the RFLP type II pattern described by DiRienzo & McKay (1994) that were found frequently in LAP subjects included strains of the JP2 clonal type (Kilian *et al*. 2006). The above data suggest that *A. actinomycetemcomitans* is a major pathogen of LAP and that the JP2 clonal type is a key pathogen in certain human populations.

A. actinomycetemcomitans has also been implicated in adult forms of destructive periodontal disease, but its role is less clear. The species has been isolated from chronic periodontitis lesions, but less frequently and in lower numbers than from lesions in LAP subjects (Rodenburg *et al*. 1990; Slots *et al*. 1990a). In addition, its numbers in plaque samples from lesions in adults were often not as high as those observed for other suspected pathogens in the same plaque samples. There appear to be at least six serotypes of

A. actinomycetemcomitans (a, b, c, d, e, and f) and these serotypes appear to be clonal in nature (Kilian *et al*. 2006). The most frequently isolated serotype of *A. actinomycetemcomitans* from lesions of LAP in American subjects was serotype b (Zambon *et al*. 1983b), whereas serotype a was more commonly detected in samples from chronic periodontitis subjects (Zambon *et al*. 1983a). This finding was corroborated indirectly by examination of serum antibody levels to the two serotypes. Most elevated responses to *A. actinomycetemcomitans* in LAP subjects were to serotype b while elevated responses to serotype a were more common in adult subjects with chronic periodontitis (Listgarten *et al*. 1981). Some subjects in each group exhibited elevated serum antibody responses to both serotypes. In Finnish subjects, serotypes a and b were more frequently isolated from subjects with periodontal disease and serotype c from periodontally healthy subjects (Asikainen *et al*. 1991). However, this pattern of serotype distribution was not observed in Korea (Chung *et al*. 1989) or Japan (Saito *et al*. 1993; Yoshida *et al*. 2003), where *A. actinomycetemcomitans* serotype c was frequently observed in plaque samples from sites of periodontal pathology. Serotypes d, e, and f, have been recognized more recently (Dogan *et al*. 1999; Mombelli *et al*. 1999) and are found less frequently than serotypes a, b and c. For example, serotypes d, e or f were not detected in a Brazilian population (Teixeira *et al*. 2006) and serotypes d or e were not found in Taiwanese subjects <35 years of age with different forms of periodontitis (Yang *et al*. 2004a).

Antibody data and data from the treatment of *A. actinomycetemcomitans* infected patients with adult or refractory periodontitis provide the most convincing evidence of a possible etiologic role of *A. actinomycetemcomitans* in adult forms of periodontal disease. Thirty-six of 56 adults with destructive periodontal disease examined at multiple time periods at the Forsyth Institute exhibited an elevated serum antibody response to *A. actinomycetemcomitans* serotypes a and/or b. Elevated responses to other suspected periodontal pathogens were far less common. Van Winkelhoff *et al*. (1992) treated 50 adult subjects with "severe generalized periodontitis" and 40 subjects with refractory periodontitis who were culture positive for *A. actinomycetemcomitans* using mechanical debridement and systemically administered amoxicillin and metronidazole. Only one of 90 subjects was culture positive for *A. actinomycetemcomitans* 3–9 months post-therapy (van Winkelhoff *et al*. 1992) and one of 48 subjects was culture positive 2 years post-therapy (Pavicic *et al*. 1994). There was a significant gain in attachment level and decrease in probing pocket depth in virtually all patients after therapy.

It is suspected that *A. actinomycetemcomitans* initially colonizes the oral cavity by attachment to the surfaces of the oral epithelium (Fine *et al*. 2006). There is a specific protein adhesin, Aae, that binds to a carbohydrate receptor on buccal epithelial cells of humans and Old World monkeys. It is thought that *A. actinomycetemcomitans* moves from the buccal epithelial cells to the supragingival plaque, possibly binding to the tooth by fimbriae comprised of repeating subunits of a 6.5 kDa protein, Flp 1. The fimbiriae, along with an extracellular carbohydrate polymer, PGA, mediate attachment to hard surfaces (Fine *et al*. 2006). Alternatively, *A. actinomycetemcomitans* may attach to other colonizing bacterial species by coaggregation (Kolenbrander 2000). At some point these organisms may move from the supragingival to the subgingival environment. From this vantage point, they may then attach to and invade the epithelial lining of the periodontal pocket and possibly penetrate the underlying connective tissues (Rudney *et al*. 2001). *A. actinomycetemcomitans* has been shown to be present in the intima of vessel walls (Marques de Silva *et al*. 2005) and has been cultured from atheromatous plaques (Kozarov *et al*. 2005). Finally, *A. actinomycetemcomitans* may leave the oral cavity and cause or contribute to endocarditis, since it has been frequently found in lesions of this condition (Paturel *et al*. 2004).

Porphyromonas gingivalis

P. gingivalis is a second consensus periodontal pathogen that continues to be intensely investigated. Isolates of this species are Gram-negative, anaerobic, non-motile, asaccharolytic rods that usually exhibit coccal to short rod morphologies. *P. gingivalis* is a member of the much investigated "black-pigmented *Bacteroides*" group (Fig. 9-3). Organisms of this group form brown to black colonies (Oliver & Wherry 1921) on blood agar plates and were initially grouped into a single species, *B. melaninogenicus* (*Bacterium melaninogenicum*; Burdon 1928). The black-pigmented *Bacteroides* have a long history of association with periodontal diseases since the early efforts of Burdon (1928) through the mixed infection studies of Macdonald *et al*. (1960) to the current intense interest.

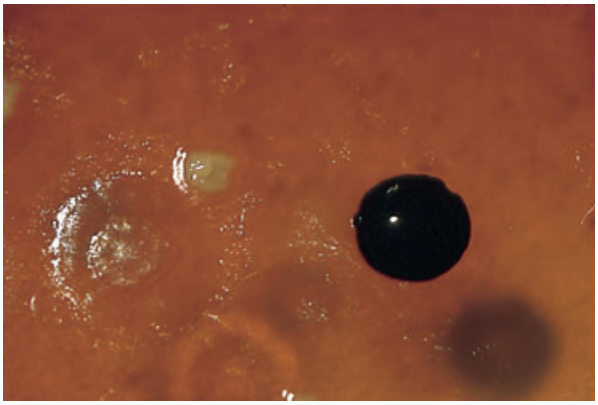

Fig. 9-3 Photograph of part of a primary isolation plate of a subgingival plaque sample from a subject with chronic periodontitis. The medium and growth conditions were as described in Fig. 9-2. The black-pigmented colony was an isolate of *Porphyromonas gingivalis*.

In the late 1970s, it was recognized that the black-pigmented *Bacteroides* contained species that were asaccharolytic (eventually *P. gingivalis*), and either had an intermediate level of carbohydrate fermentation (which eventually led to a group of species including *Prevotella intermedia*) or were highly saccharolytic (leading to the group that includes *Prevotella melaninogenica*).

Early interest in *Porphyromonas gingivalis* and other black-pigmented *Bacteroides* arose primarily because of their essential role in certain experimental mixed infections (Macdonald *et al*. 1956, 1963; Socransky & Gibbons 1965) and their production of an unusually large array of virulence factors (Table 9-2) (Haffajee & Socransky 1994; Deshpande & Khan 1999; Holt & Ebersole 2005). Members of these species produce collagenase, gingipain, an array of proteases (including those that destroy immunoglobulins), hemolysins, endotoxin, fatty acids, ammonia, hydrogen sulfide, indole etc. *P. gingivalis* can inhibit migration of PMNs across an epithelial barrier (Madianos *et al*. 1997), has been shown to affect the production or degradation of cytokines by mammalian cells (Darveau *et al*. 1998; Fletcher *et al*. 1998; Sandros *et al*. 2000). and produces extracellular vesicles that contribute to the loss of membrane-bound CD14 receptors on human macrophage-like cells (Duncan *et al*. 2004).

Studies initiated in the late 1970s and extending to the present have strengthened the association of *P. gingivalis* with disease and demonstrated that the species is uncommon and in low numbers in health or gingivitis but more frequently detected in destructive forms of disease (Table 9-2) (Haffajee & Socransky 1994; O'Brien-Simpson *et al*. 2000; Takeuchi *et al*. 2001; van Winkelhoff *et al*. 2002; Lau *et al*. 2004; Yang *et al*. 2004b). In diseased subjects, there was a strong positive relationship with pocket depth (Kawada *et al*. 2004; Socransky & Haffajee 2005). This species has also been shown to be increased in numbers and or frequency of detection in deteriorating periodontal sites (Dzink *et al*. 1988; Lopez 2000; Kamma *et al*. 2001) or in subjects exhibiting periodontal disease progression (Albandar *et al*. 1997). The species has been shown to be reduced in successfully treated sites but was commonly encountered in sites that exhibited recurrence of disease or persistence of deep periodontal pockets post-therapy (Bragd *et al*. 1987; Haffajee *et al*. 1988a; van Winkelhoff *et al*. 1988; Berglundh *et al*. 1998; Shiloah *et al*. 1998; Winkel *et al*. 1998; Takamatsu *et al*. 1999; Chaves *et al*. 2000; Mombelli *et al*. 2000; Fujise *et al*. 2002; Kawada *et al*. 2004). *P. gingivalis* has been associated with an increased risk of periodontal disease severity and progression (Beck *et al*. 1990, 1992, 1997; Grossi *et al*. 1994, 1995).

P. gingivalis has been shown to induce elevated systemic and local immune responses in subjects with various forms of periodontitis (Table 9-2) (Haffajee & Socransky 1994; Mahanonda *et al*. 1991; O'Brien-Simpson *et al*. 2000). Indeed, there has been an effort in many laboratories, not only to compare the level of antibody response in subjects with and without disease, but to examine relative avidities of antibody (Lopatin & Blackburn 1992; Whitney *et al*. 1992; Mooney *et al*. 1993), subclass of antibody (Lopatin & Blackburn 1992; Wilton *et al*. 1992), the effect of treatment (Chen *et al*. 1991; Johnson *et al*. 1993), and the nature of the antigens which elicit the elevated responses (Ogawa *et al*. 1989; Yoshimura *et al*. 1989; Curtis *et al*. 1991; Papaioannou *et al*. 1991; Duncan *et al*. 1992; Schifferle *et al*. 1993). Noteworthy in this regard were the observations of Ogawa *et al*. (1989), which indicated that an average of approximately 5% of plasma cells in lesions of advanced periodontitis formed antibody to the fimbriae of *P. gingivalis*. The consensus of the antibody studies is that many, but not all, subjects who had experienced periodontal attachment loss exhibited elevated levels of antibody to antigens of *P. gingivalis*, suggesting that this species gained access to the underlying tissues and may have initiated or contributed to the observed pathology.

P. gingivalis-like organisms were also strongly related to destructive periodontal disease in naturally occurring or ligature-induced disease in dogs, sheep or monkeys (Table 9-2). The species or closely related organisms were higher in number in lesion sites than in non-lesion sites in naturally occurring disease. When disease was induced by ligature in dogs or monkeys, the level of the species rose at the diseased sites concomitant with the detection of disease. Of great interest were the observations of Holt *et al*. (1988) who demonstrated that a microbiota suppressed by systemic administration of rifampin (and without detectable *P. gingivalis*) would not cause ligature-induced disease, but the re-introduction of *P. gingivalis* to the microbiota resulted in initiation and progress of the lesions. Ligature-induced periodontitis and peri-implantitis in dogs was also accompanied by a significant increase in the detection of *P. gingivalis* (Nociti *et al*. 2001). Like *A. actinomycetemcomitans*, *P. gingivalis* has been shown to be able to invade human gingival epithelial cells *in vitro* (Lamont *et al*. 1992; Duncan *et al*. 1993; Sandros *et al*. 1993), buccal epithelial cells *in vivo* (Rudney *et al*. 2001), endothelial cells (Takahashi *et al*. 2006) and has been found in higher numbers on or in epithelial cells recovered from the periodontal pocket than in associated plaque (Dzink *et al*. 1989) or healthy sites (Colombo *et al*. 2006). Attachment to and invasion of epithelial cells appears to be mediated by the *P. gingivalis* fimbriae (Njoroge *et al*. 1997; Weinberg *et al*. 1997; Nakajawa *et al*. 2006).

There have been several studies that have attempted to immunize experimental animals against periodontal disease induced by *P. gingivalis*. Studies in monkeys and gnotobiotic rats have indicated that immunization with whole organisms or specific antigens affected the progress of the periodontal lesions. In most instances, periodontal breakdown was

decreased (Evans *et al*. 1992; Persson *et al*. 1994a). However, in one study, the disease severity was increased after immunization (Ebersole *et al*. 1991). In the monkey model, the percentage of *P. gingivalis* cells in subgingival plaque was inversely related to the serum antibody titer to this species (Persson *et al*. 1994b). Reductions in alveolar bone loss in the monkey model could also be achieved by immunization with the cysteine protease porphypain-2 from *P. gingivalis* (Moritz *et al*. 1998; Page 2000). In more recent years, investigators have used a mouse "oral challenge" (by cells of *P. gingivalis*) model to study the effects of immunization by various fractions of *P. gingivalis* on alveolar bone loss induced by this species. Immunization by hemagglutinin B (Katz *et al*. 1999), capsular polysaccharide (Gonzalez *et al*. 2003), heat shock protein (Lee *et al*. 2006), gingipain R (Gibson & Genco 2001), and the active sites of RgpA and Kgp proteinases (O'Brien-Simpson *et al*. 2005) protected against alveolar bone loss in the mouse model. Thus, altering the host–*P. gingivalis* equilibrium by raising the level of specific antibodies to *P. gingivalis* antigens markedly affected disease outcome. Such data reinforce the importance of this bacterial species in periodontal disease, at least in the animal model systems employed.

Tannerella forsythia

The third consensus periodontal pathogen, *T. forsythia*, was first described in 1979 (Tanner *et al*. 1979) as a "fusiform" *Bacteroides*. This species was difficult to grow, often requiring 7–14 days for minute colonies to develop. The organism is a Gram-negative, anaerobic, spindle-shaped, highly pleomorphic rod. The growth of the organism was shown to be enhanced by co-cultivation with *F. nucleatum* and indeed it commonly occurred with this species in subgingival sites (Socransky *et al*. 1988). The need for co-cultivation could be overcome by providing N-acetylmuramic acid in the medium (Wyss 1989). Inclusion of this factor markedly enhanced growth and the resulting cells were regularly shaped, short, Gram-negative rods rather than the pleomorphic cells observed in the absence of this factor (Tanner & Izard 2006). A feature that *T. forsythia* cells shares with certain other Gram-negative species is the presence of a serrated S-layer that is easily visible by electron microscopy (Tanner *et al*. 1986) that may contribute to the pathogenicity of the species in periodontal diseases (Sabet *et al*. 2003). The S-layer has been isolated and shown to mediate hemagglutination, adhesion/invasion of epithelial cells, and murine subcutaneous abscess formation. The S-layer is composed of two glycoproteins of molecular mass 200 and 210 kDa (Lee *et al*. 2006). This species has been shown to produce trypsin-like proteolytic activity (BANA test positive) (Loesche *et al*. 1992) and methylglyoxal (Kashket *et al*. 2002), and induce apoptotic cell death (Arakawa *et al*. 2000). In addition, *T. forsythia* in co-cultures of macrophage and epithelial cells leads to the expression of pro-inflammatory cytokines, chemokines, PGE_2, and MMP9 (Bodet *et al*. 2006).

Initially, *T. forsythia* was thought to be a relatively uncommon subgingival species. However, the studies of Gmur *et al*. (1989) using monoclonal antibodies to enumerate the species directly in plaque samples, suggested that the species was more common than previously found in cultural studies and its levels were strongly related to increasing pocket depth. Lai *et al*. (1987) reported similar findings using fluorescent-labeled polyclonal antisera and demonstrated that *T. forsythia* was much higher in subgingival than supragingival plaque samples. Data of Tanner *et al*. (1998) suggested that *T. forsythia* was a major species found at sites that converted from periodontal health to disease. There was a greater risk of periodontal attachment loss in adolescents who were colonized by *T. forsythia* than adolescents in whom the species was not detected (Hamlet *et al*. 2004). *T. forsythia* was in much higher counts, proportions, and prevalence in subjects with various forms of periodontitis than in periodontally healthy subjects (van Winkelhoff *et al*. 2002; Yang *et al*. 2004b; Haffajee *et al*. 2006a). *T. forsythia* was found in higher numbers in sites of destructive periodontal disease or periodontal abscesses than in gingivitis or healthy sites (Lai *et al*. 1987; Herrera *et al*. 2000; Papapanou *et al*. 2000; Lau *et al*. 2004). In addition, *T. forsythia* was detected more frequently and in higher numbers in actively progressing periodontal lesions than inactive lesions (Dzink *et al*. 1988) (Table 9-3). Further, subjects who harbored *T. forsythia* were at greater risk for alveolar bone loss, attachment loss and tooth loss compared with subjects in whom this species was not detected (Machtei *et al*. 1999).

Since these early studies, a large number of additional studies have demonstrated the association of *T. forsythia* with periodontal disease using techniques such as PCR and DNA hybridization (Tanner & Izard 2006). *T. forsythia* has also been shown to be present in the oral cavities of monkeys, cats, and dogs, and species related to *T. forsythia* have been found in insects such as termites (Tanner & Izard 2006). An as yet uncultivated clone similar to *T. forsythia* has been found more frequently in subjects who were periodontally healthy than subjects with periodontitis (Leys *et al*. 2002).

T. forsythia has been shown to be decreased in frequency of detection and counts after successful periodontal therapy, including scaling and root planing (SRP) (Haffajee *et al*. 1997; Takamatsu *et al*. 1999; Cugini *et al*. 2000; Darby *et al*. 2001, 2005; van der Velden *et al*. 2003; Teles *et al*. 2006), periodontal surgery (Levy *et al*. 2002), or systemically administered antibiotics (Feres *et al*. 2000; Winkel *et al*. 1998, 2001; Haffajee *et al*. 2006b; Teles *et al*. 2006). *T. forsythia* was found at higher levels at sites which showed breakdown after periodontal therapy than

sites which remained stable or gained attachment (Shiloah *et al*. 1998; Fujise *et al*. 2002). Ligature-induced periodontitis and peri-implantitis in dogs were accompanied by a significant increase in the frequency of detection of *T. forsythia* (Nociti *et al*. 2001). Finally, subjects with a low severity of chronic periodontitis who exhibited a persistent presence of *T. forsythia* at periodontal sites had a 5.3 times greater chance of having at least one site in their mouths losing attachment compared with subjects with occasional or no presence of this species (Tran *et al*. 2001).

Studies using checkerboard DNA–DNA hybridization techniques to examine subgingival plaque samples not only confirmed the high levels of *T. forsythia* detected using fluorescent-labeled antisera but demonstrated that *T. forsythia* was the most common species detected on or in epithelial cells recovered from periodontal pockets (Dibart *et al*. 1998). It was infrequently detected in epithelial cell samples from healthy subjects. Double-labeling experiments demonstrated that *T. forsythia* was both on and in periodontal pocket epithelial cells and indicated the species' ability to invade. Listgarten *et al*. (1993) found that the species most frequently detected in "refractory" subjects was *T. forsythia.* Serum antibody to *T. forsythia* has been found to be elevated in a number of periodontitis patients (Taubman *et al*. 1992) and was often extremely elevated in a subset of refractory periodontal disease subjects. The observation that *T. forsythia* shares antigens with *P. gingivalis* suggests that protective antibody formed to one species may provide protection against both species (Vasel *et al*. 1996).

The role of *T. forsythia* in periodontal diseases has been clarified and strengthened by studies in numerous laboratories involving non-cultural methods of enumeration, such as DNA probes, PCR or immunologic methods. For example, Grossi *et al*. (1994, 1995) considered *T. forsythia* to be the most significant microbial risk factor that distinguished subjects with periodontitis from those who were periodontally healthy.

Spirochetes

Spirochetes are Gram-negative, anaerobic, helical-shaped, highly motile microorganisms that are common in many periodontal pockets (Fig. 9-4). The role of spirochetes in the pathogenesis of destructive periodontal diseases deserves extended comment. Clearly, a spirochete has been implicated as the likely etiologic agent of acute necrotizing ulcerative gingivitis by its presence in large numbers in tissue biopsy specimens from affected sites (Listgarten & Socransky 1964; Listgarten 1965). The role of spirochetes in other forms of periodontal disease is less clear. The organisms have been considered as possible periodontal pathogens since the late 1800s and in the 1980s enjoyed a resurgence of interest for use as possible diagnostic indicators of disease activity and/or therapeutic efficacy (Keyes & Rams 1983; Rams & Keyes 1983). The major reason for the interest in this group of organisms has been their increased numbers in sites with increased pocket depth. Healthy sites exhibit few, if any, spirochetes, sites of gingivitis but no attachment loss exhibit low to moderate levels, while many deep pockets harbor large numbers of these organisms. Further, spirochetes such as *Treponema denticola*, have been shown to be at the forefront of periodontal lesions as demonstrated in sections of undisturbed subgingival plaque using immunohistochemical localization (Kigure *et al*. 1995; Noiri *et al*. 2001). The localization of spirochetes next to the epithelial lining of the periodontal pocket may facilitate both attachment of these species to epithelial cells and invasion into the adjacent tissues.

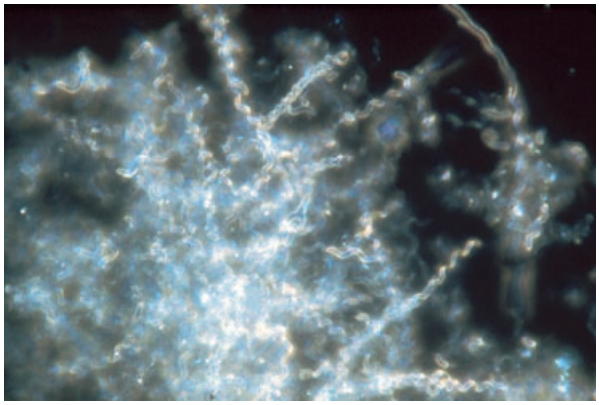

Fig. 9-4 Photomicrograph of a sample of subgingival plaque from a subject with advanced chronic periodontitis viewed by darkfield microscopy. The sample was dominated by large spirochetes with the typical corkscrew appearance.

The major difficulty encountered in defining the role of spirochetes has been the difficulty in distinguishing individual species. This is due in large part to difficulty in cultivating spirochetes in general and, in particular, species of spirochetes that are currently uncultivable. There are currently 10 cultivable species of spirochetes (Ellen & Galimanas 2005). At least 50 taxa of subgingival spirochetes can be recognized using 16S rRNA analysis (Dewhirst *et al*. 2000). The cultivable spirochetes require very complex media for their cultivation. These contain infusions of animal organs, trypsin digests of casein, various fatty acids and accessory growth factors, and serum (Ellen & Galimanas 2005). Wyss *et al*. (1999) have developed more defined media for the cultivation of some of the species of oral spirochetes. In spite of the ability to cultivate certain species of oral spirochetes, it has been difficult to use these media to enumerate the spirochetes in subgingival plaque samples. Therefore, in many of the earlier studies of plaque samples, spirochetes were combined either in a single group or groups based on cell size; i.e. small, medium or large. Thus, while there may be pathogens among the spirochetes, their role may have been obscured by unintentionally pooling their numbers with

non-pathogenic spirochetes. This would be similar to combining in a single count, organisms with coccal morphologies, such as *P. gingivalis*, *Veillonella parvula*, and *Streptococcus sanguinis*.

In spite of the limitations of combining spirochetes into a single morphogroup, spirochetes as a group or as individual species have been related to periodontal disease (Ellen & Galimanas 2005). Spirochetes have been associated with an increased risk at a site for the development of gingivitis (Riviere & DeRouen 1998) and periodontitis (Riviere *et al*. 1997). The need to evaluate the role of individual species of spirochetes in periodontal diseases is reinforced by studies of serum antibody responses to different species. When antibody responses to individual species were examined in subjects with chronic or aggressive periodontitis or a healthy periodontium, different responses were observed to different species. Certain spirochetal species elicited an elevated response in one or more of the groups with destructive periodontal disease (Mangan *et al*. 1982; Tew *et al*. 1985c; Lai *et al*. 1986), while others were related to depressed antibody responses in certain patient groups (Steinberg & Gershoff 1968; Tew *et al*. 1985c). Such data suggest that pooling spirochete species into a collective group may obscure meaningful host–parasite interactions.

More recently, specific species of spirochetes have been related to periodontal breakdown using antibody-based or molecular techniques. *Treponema denticola* was found to be more common in periodontally diseased than healthy sites, more common in subgingival than supragingival plaque (Simonson *et al*. 1988; Riviere *et al*. 1992; Albandar *et al*. 1997; Haffajee *et al*. 1998; Yuan *et al*. 2001), and more common in healthy sites that progressed to gingivitis (Riviere & DeRouen 1998). *Tr. denticola* was shown to decrease in successfully treated periodontal sites, but not change or increase in non-responding sites (Simonson *et al*. 1992). Cultural studies suggested that *Tr. denticola* and a "large treponeme" were found more frequently in patients with severe periodontitis than in healthy or gingivitis sites (Moore *et al*. 1982).

Riviere *et al*. (1991,a,b,c, 1992) employed a monoclonal antibody directed against *Treponema pallidum*, the etiologic agent of syphilis, to examine supra- and subgingival plaque samples and/or tissues from healthy, periodontitis and ANUG subjects. This antibody cross-reacted with antigens of uncultivated spirochetes in many of the plaque samples. These "pathogen-related oral spirochetes" (PROS) were the most frequently detected spirochetes in supra- and subgingival plaques of periodontitis patients and were the most numerous spirochetes in periodontitis lesion sites. Their presence in periodontally healthy sites was related to an increased risk of development of periodontitis (Riviere *et al*. 1997). The PROS were also detected in plaque samples from ANUG (Riviere *et al*. 1991c) and tissue biopsies from ANUG lesions using immunohistochemical techniques (Riviere *et al*. 1991a). PROS were also shown to have the ability to penetrate a tissue barrier in *in vitro* systems (Riviere *et al*. 1991b). This property was shared with *Tr. pallidum* but not with other cultivated species of oral spirochetes such as *Tr. denticola*, *Tr. socranskii*, *Tr. pectinovorum* or *Tr. vincentii*. In later studies, the PROS were shown by molecular techniques to share 16S rRNA gene sequences with *Tr. vincentii* and *Tr. medium* (Choi *et al*. 1996; Riviere *et al*. 1999). These studies and others suggested that certain specific species of spirochetes were important in the pathogenesis of ANUG and certain forms of periodontitis. Precise evaluation of the role of individual spirochete species appears to be realistic based on their detection in plaque samples by immunologic, PCR or DNA probe techniques. Indeed, enumeration of even uncultivable spirochete taxa is possible using oligonucleotide probes (Tanner *et al*. 1994) or specific antibody as described above. Studies performed using such techniques permit better distinction of species of spirochetes and a clearer understanding of their possible role in disease.

The mechanisms of pathogenicity of the spirochetes have been under active investigation in recent years. Spirochetes demonstrate pathogenicity in animal abscess model systems (Kesavalu *et al*. 1999; Kimizuka *et al*. 2003), and produce a wide range of potential virulence factors (Ellen 2005). Among the virulence factors that may play a major role is a subtilisin family protease, dentilisin, that is encoded by the *prtP* gene. This enzyme affects a wide range of protein substrates including fibronectin, laminin, and fibrinogen (Ishihara *et al*. 1996). It is thought that spirochetes may prolong tissue remodeling and wound healing following periodontal treatment; thus, the chronic periodontal lesion may represent an "ever-healing" wound that is sustained during chronic infection (Ellen & Galimanas, 2005).

Successful treatment of periodontal infections is accompanied by a decrease in the numbers and proportions of oral spirochetes as a group and individual species. Indeed, this reduction is so consistent that it has been used in some studies as a measure of compliance in determining whether subjects used the prescribed antibiotics (Loesche *et al*. 1993).

Prevotella intermedia/Prevotella nigrescens

At present the data for other species as etiologic agents of destructive periodontal diseases are more limited, but certain organisms appear to merit further investigation (Zambon 1996). *Pr. intermedia* is the second black-pigmented *Bacteroides* to receive considerable interest (Fig. 9-5). The levels of this Gram-negative, short, round-ended anaerobic rod have been shown to be particularly elevated in acute necrotizing ulcerative gingivitis (Loesche *et al*. 1982), certain forms of periodontitis (Tanner *et al*. 1979; Dzink *et al*. 1983; Moore *et al*. 1985; Maeda *et al*. 1998; Herrera *et al*. 2000; Papapanou *et al*. 2000; Lee *et al*.

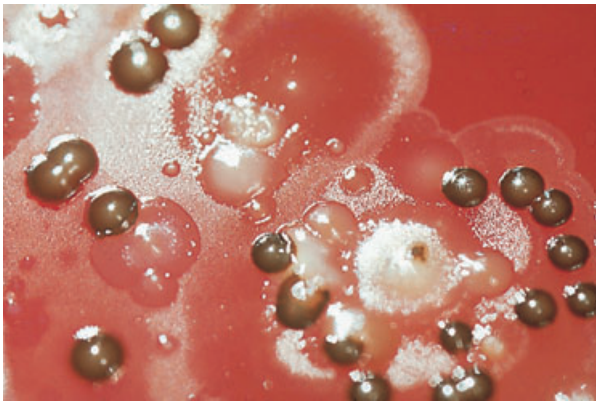

Fig. 9-5 Photograph of part of a primary isolation plate of a subgingival plaque sample from a subject with chronic periodontitis. The medium and growth conditions were as described in Fig. 9-2. The dark-pigmented colonies were isolates of *Prevotella intermedia*.

2003; van Winkelhoff *et al*. 2002; Alves *et al* 2006; Boutaga *et al*. 2006), and progressing sites in chronic periodontitis (Tanner *et al*. 1996; Lopez 2000), and it has been detected by immunohistological methods in the intercellular spaces of periodontal pocket biopsies from rapidly progressive periodontitis subjects (Hillmann *et al*. 1998). Isolates of this species can induce alveolar bone loss in rats (Yoshida-Minami *et al*. 1997). *Pr. intermedia* was reduced more markedly in subgingival plaque samples from subjects who received adjunctive systemically administered amoxicillin plus metronidazole than subjects receiving a placebo (Rooney *et al*. 2002). Persistence of *Pr. intermedia/nigrescens* after standard mechanical therapy has been shown to be associated with a large proportion of sites exhibiting bleeding on probing (Mombelli *et al*. 2000). Berglundh *et al*. (1998) demonstrated that improved clinical parameters after the use of mechanical therapy and systemically administered amoxicillin and metronidazole were associated with a decrease of periodontal pathogens including *Pr. intermedia.*

This species appears to have a number of the virulence properties exhibited by *P. gingivalis* and was shown to induce mixed infections on injection in laboratory animals (Hafstrom & Dahlen 1997). Like *P. gingivalis*, *Pr. intermedia/nigrescens* appears to induce an increased release of MMP-8 and MMP-9 in gingival pockets as well as MMP-9 in plasma (Soder *et al*. 2006). It has also been shown to invade oral epithelial cells *in vitro* (Dorn *et al*. 1998) and induce expression of nitric oxide synthase in tissue culture cells (Kim *et al*. 2004). Elevated seroantibodies to this species have been observed in some but not all subjects with refractory periodontitis (Haffajee *et al*. 1988b). Elevated IgG antibody to *Pr. intermedia* was associated with coronary heart disease (CHD) in past and current smokers, while elevated IgG antibody to *Pr. nigrescens* was associated with CHD in never smokers (Beck *et al*. 2005). Strains of *Pr. intermedia* that show identical phenotypic traits have been separated into two species, *Pr. intermedia* and *Pr. nigrescens* (Shah & Gharbia 1992). This distinction makes earlier studies of this "species" difficult to interpret since data from two different species may have been inadvertently pooled. However, new studies which discriminate the species in subgingival plaque samples might strengthen the relationship of one or both species to periodontal disease pathogenesis.

Fusobacterium nucleatum

F. nucleatum is a Gram-negative, anaerobic, spindle-shaped rod that has been recognized as part of the subgingival microbiota for over 100 years (Plaut 1894; Vincent 1899). This species was the most common isolate found in cultural studies of subgingival plaque samples, comprising approximately 7–10% of total isolates from different clinical conditions (Dzink *et al*. 1985, 1988; Moore *et al*. 1985). *F. nucleatum* was prevalent in subjects with periodontitis (Papapanou *et al*. 2000; Colombo *et al*. 2002; Socransky *et al*. 2002; Boutaga *et al*. 2006) and periodontal abscesses (Herrera *et al*. 2000) and was reduced after successful periodontal therapy (van der Velden *et al*. 2003; Haffajee *et al*. 2006b). Although there were differences detected in levels of this species between active and inactive periodontal lesions (Dzink *et al*. 1988), the differences may have been minimized by the inadvertent pooling of subspecies of *F. nucleatum*. Support for this contention may be derived from the antibody responses in subjects with different forms of periodontal disease to different homology groups of *F. nucleatum* (Tew *et al*. 1985b). The role of *F. nucleatum* in periodontal diseases is being clarified by examining the relationship of individual subspecies, such as *F. nucleatum* ss *nucleatum*, *F. nucleatum* ss *polymorphum*, *F. nucleatum* ss *vincentii*, and *F. periodonticum*, to disease status and progression.

IgG and IgM titers in serum against the lipopolysaccharide (LPS) of *F. nucleatum* were higher in subjects with periodontitis than in healthy individuals (Onoue *et al*. 2003). Invasion of this species into human gingival epithelial cells *in vitro* was accompanied by an increased secretion of IL-8 from the epithelial cells (Han *et al*. 2000). The species can induce apoptotic cell death in mononuclear and polymorphonuclear cells (Jewett *et al*. 2001), induces epithelial cells to produce collagenase 3 (Uitto *et al*. 2005), and produces a 65 kDa serine protease (Bachrach *et al*. 2004). In addition, *F. nucleatum* induces cytokine, elastase, and oxygen radical release from leukocytes (Sheikhi *et al*. 2000). Perhaps the most important role of *F. nucleatum* in the subgingival ecosystem is its function as a "bridging" species, facilitating coaggregation among species as described below.

Campylobacter rectus

C. rectus is a Gram-negative, anaerobic, short, motile vibrio. The organism is unusual in that it utilizes

hydrogen or formate as its energy source. It was first described as a member of the "vibrio corroders", a group of short nondescript rods that formed small convex, "dry spreading" or "corroding" (pitting) colonies on blood agar plates. These organisms were eventually shown to include members of a new genus *Wolinella* (most species have been redefined as *Campylobacter*), and *Eikenella corrodens*. *C. rectus* has a 150-kDa protein on its cell surface that forms a paracrystalline lattice or S-layer that surrounds the bacterium (Wang *et al*. 1998, 2000). *C. rectus* may help to initiate periodontitis by increasing the expression of proinflammatory cytokines and the S-layer may help to moderate this response facilitating the survival of the species at the site of infection. *C. rectus* is widely distributed in subgingival sites, even in the primary, mixed and permanent dentitions of children (Umeda *et al*. 2004; Hayashi *et al*. 2006). *C. rectus* has been shown to be present in higher numbers in samples from diseased sites as compared with healthy sites (Moore *et al*. 1983, 1985; Lippke *et al*. 1991; Lai *et al*. 1992; Papapanou *et al*. 1997; Macuch & Tanner 2000; Dogan *et al*. 2003; Ihara *et al*. 2003; Suda *et al*. 2004; Nonnenmacher *et al*. 2005) and it was found in higher numbers and more frequently at sites exhibiting active periodontal destruction (Dzink *et al*. 1985, 1988; Tanner & Bouldin 1989; Rams *et al*. 1993) or converting from periodontal health to disease (Tanner *et al*. 1998). In addition, *C. rectus* was found less frequently and in lower numbers after successful periodontal therapy (Tanner *et al*. 1987; Haffajee *et al*. 1988a; Levy *et al*. 1999; Colombo *et al*. 2005). *C. rectus* was also found in combination with other suspected pathogens in sites of subjects with refractory periodontal diseases (Haffajee *et al*. 1988b) and was in higher levels in subjects with aggressive periodontitis than in subjects with other forms of periodontitis (Gajardo *et al*. 2005). Like *A. actinomycetemcomitans*, *C. rectus* has been shown to produce a leukotoxin. These are the only two oral species known to possess this characteristic (Gillespie *et al*. 1992). The species is also capable of stimulating human gingival fibroblasts to produce IL-6 and IL-8 (Dongari-Bagtzoglou & Ebersole 1996). Higher serum antibody levels to *C. rectus* GroEL was detected in patients with periodontitis when compared with control subjects (Fukui *et al*. 2006).

C. rectus has been associated with a number of systemic conditions. Elevated IgM antibody to *C. rectus* in fetal chord blood has been associated with an increased rate of prematurity (Madianos *et al*. 2001) and increased levels of *C. rectus* along with *Peptostreptococcus micros* in subgingival plaque samples of pregnant females was associated with an increased risk of pre-term low birth weight (Buduneli *et al*. 2005). IgG antibody to these same two species was also associated with increased carotid intima–medial thickness (Beck *et al*. 2005). Finally, *C. rectus*, as well as other oral species, has been detected in atherosclerotic vessels (Fiehn *et al*. 2005) and in occluded arteries in patients with Buerger disease (Iwai *et al*. 2005).

Eikenella corrodens

E. corrodens is a Gram-negative, capnophilic, asaccharolytic, regular, small rod with blunt ends. It has been recognized as a pathogen in other forms of disease, particularly osteomyelitis (Johnson & Pankey 1976), infections of the central nervous system (Emmerson & Mills 1978; Brill *et al*. 1982), and root canal infections (Goodman 1977). This species was found more frequently in sites of periodontal destruction as compared with healthy sites in some (Savitt & Socransky 1984; Muller *et al*. 1997; Yuan *et al*. 2001), but not all studies (Papapanou *et al*. 2000). In addition, *E. corrodens* was found more frequently and in higher levels in actively breaking down periodontal sites (Dzink *et al*. 1985; Tanner *et al*. 1987) and in sites of subjects who responded poorly to periodontal therapy (Haffajee *et al*. 1988b). Successfully treated sites harbored lower proportions of this species (Tanner *et al*. 1987). *E. corrodens* has been found to be elevated in lesions in LAP subjects (Suda *et al*. 2002) as well as in association with *A. actinomycetemcomitans* in such lesions (Mandell 1984; Mandell *et al*. 1987). In tissue culture systems, *E. corrodens* has been shown to stimulate the production of matrix metalloproteinases (Dahan *et al*. 2001) and IL-6 and IL-8 (Yumoto *et al*. 1999, 2001). While there is some association of this species with periodontal disease, to date it has not been particularly strong (Chen *et al*. 1989).

Peptostreptococcus micros

Pe. micros is a Gram-positive, anaerobic, small, asaccharolytic coccus. It has long been associated with mixed anaerobic infections in the oral cavity and other parts of the body (Finegold 1977). Two genotypes can be distinguished, with the smooth genotype being more frequently associated with periodontitis lesions than the rough genotype (Kremer *et al*. 2000). *Pe. micros* has been detected more frequently and in higher numbers at sites of periodontal destruction as compared with gingivitis or healthy sites (Moore *et al*. 1983, 1985; Herrera *et al*. 2000; Papapanou *et al*. 2000; Choi *et al*. 2000; Riggio *et al*. 2001; van Winkelhoff *et al*. 2002; Lee *et al*. 2003; Nonnenmacher *et al*. 2005; Boutaga *et al*. 2006; Gomes *et al*. 2006), was elevated in actively breaking down sites (Dzink *et al*. 1988), and at higher mean levels in current smokers compared with non-smokers (van Winkelhoff *et al*. 2001). The levels and frequency of detection of the species were decreased at successfully treated periodontal sites (Haffajee *et al*. 1988a). Studies of systemic antibody responses to suspected periodontal pathogens indicated that subjects with severe generalized periodontitis had elevated antibody levels to this species when compared with

healthy subjects or subjects with LAP (Tew *et al*. 1985a). *Pe. micros* produces proteases (Grenier & Bouclin 2006) and, in a mouse skin model system, it was shown that this species in combination with either *Pr. intermedia* or *Pr. nigrescens* could produce transmissible abscesses (van Dalen *et al*. 1998). In a study of chronic periodontitis subjects with and without acute myocardial infarction, it was found that *Pe. micros* was much higher in the plaque samples of the subjects exhibiting myocardial infarction (Dogan *et al*. 2005).

Selenomonas species

Selenomonas species have been observed in plaque samples using light microscopy for many decades. The organisms may be recognized by their curved shape, tumbling motility, and, in good preparations, by the presence of a tuft of flagella inserted in the concave side. The *Selenomonas* spp. are Gram-negative, curved, saccharolytic rods. The organisms have been somewhat difficult to grow and speciate. However, Moore *et al*. (1987) described six genetically and phenotypically distinct groups isolated from the human oral cavity. *Selenomonas noxia* was found at a higher proportion of shallow sites (pocket depth (PD) <4 mm) in chronic periodontitis subjects compared with similar sites in periodontally healthy subjects (Haffajee *et al*. 1998). Further, *S. noxia* was found to be associated with sites that converted from periodontal health to disease (Tanner *et al*. 1998).

Eubacterium species

Certain *Eubacterium* species have been suggested as possible periodontal pathogens due to their increased levels in diseased sites, particularly those of severe periodontitis (Uematsu & Hoshino 1992). *E. nodatum*, *Eubacterium brachy*, and *Eubacterium timidum* are Gram-positive strictly anaerobic, small somewhat pleomorphic rods. They are often difficult to cultivate, particularly on primary isolation, and appear to grow better in roll tubes than on blood agar plates. To date, there is greater evidence supporting a possible etiologic role in periodontitis for *E. nodatum* than the other *Eubacterium* species. Moore *et al*. (1982, 1985) used the roll tube cultural technique to examine the proportions of bacterial species in subgingival plaque samples from subjects with various forms of periodontitis, gingivitis, and health. They found that *E. nodatum* was absent or in low proportions in periodontal health and various forms of gingivitis, but was present in higher proportions in moderate periodontitis (2%), generalized early onset periodontitis (8%), LAP (6%), early onset periodontitis (5%), and adult (chronic) periodontitis (2%). *E. nodatum* was in the top 2–14 species enumerated in these different periodontal states. Uematsu and Hoshina (1992) found *Eubacterium* species to be the predominant species in subgingival plaque samples from subjects with advanced periodontitis using cultural techniques. More recent studies have confirmed an association of *E. nodatum* with periodontitis using molecular techniques. Using species-specific oligonucleotide probes, Booth *et al*. (2004) found that *E. nodatum* was at significantly higher counts in patients than in matched control subjects. The species was also at higher levels in deep compared with shallow pockets. Papapanou *et al*. (2000) found higher counts of *E. nodatum* in 131 periodontitis patients than in 74 periodontally intact controls using checkerboard DNA–DNA hybridization. Colombo *et al*. (2002) also used checkerboard DNA–DNA hybridization to evaluate the microbiota in 25 untreated Brazilian subjects with chronic periodontitis and found a significant positive correlation of *E. nodatum* with mean pocket depth and attachment level. Samples of subgingival plaque were taken from 21 832 periodontal sites in 635 chronic periodontitis and 189 periodontally healthy subjects and examined by checkerboard DNA–DNA hybridization (Haffajee *et al*. 2006a). It was found that *E. nodatum* was strongly associated with chronic periodontitis both in the presence of high levels of *P. gingivalis* and *T. forsythia* and in subjects where these species were in lower proportions. It has also been demonstrated that the percentage of sites colonized by *E. nodatum* was significantly higher in current smokers than non-smokers (Haffajee & Socransky 2001). Some of the *Eubacterium* species elicited elevated antibody responses in subjects with different forms of destructive periodontitis (Tew *et al*. 1985a,b; Vincent *et al*. 1986; Martin *et al*. 1988).

The "milleri" streptococci

Streptococci were frequently implicated as possible etiologic agents of destructive periodontal diseases in the early part of the twentieth century. Cultural studies of the last 2 decades have also suggested the possibility that some of the streptococcal species were associated with, and may contribute to, disease progression. At this time, evidence suggests that the "milleri" streptococci, *Streptococcus anginosus*, *Streptococcus constellatus*, and *S. intermedius*, might contribute to disease progression in subsets of periodontal patients. The species was found to be elevated at sites which demonstrated recent disease progression (Dzink *et al*. 1988). Walker *et al*. (1993) found *S. intermedius* to be elevated in a subset of patients with refractory disease at periodontal sites which exhibited disease progression. Colombo *et al* (1998a) found that subjects exhibiting a poor response to SRP and then to periodontal surgery with systemically administered tetracycline had higher levels and proportions of *S. constellatus*, than subjects who responded well to periodontal therapy. Refractory subjects also exhibited elevated serum antibody to *S. constellatus* when compared with successfully treated subjects (Colombo *et al*. 1998b). In a study of 161 subjects with

acute coronary syndrome (ACS) and 161 control subjects, it was suggested that the oral bacterial load of species including *S. intermedius* and *S. anginosus* may be a risk factor for ACS (Renvert *et al*. 2006). The data on streptococci are somewhat limited, but a continued examination of their role in disease seems warranted.

Other species

It has long been recognized that many taxa in subgingival plaque were not being cultivated based on microscopic observations that revealed cell morphotypes that were never recovered in culture. In addition, there were marked differences between total viable counts (representing cultivable species) and total microscopic counts representing all organisms (Socransky *et al*. 1963; Olsen & Socransky 1981; Moore & Moore 1994). Currently, the best model for exploring microbial diversity is based on isolating DNA from the target environment, amplifying the rDNA using consensus primers and PCR, cloning the amplicons into *Escherichia coli*, and sequencing the cloned 16S rDNA inserts (Pace *et al*. 1986; Hugenholtz & Pace 1996). The resulting sequences are compared with those of known species and phylotypes in sequence databases, such as GenBank and the Ribosomal Database Project (Cole *et al*. 2005). These culture-independent molecular phylogenetic methods have been used to deduce the identity of novel phylotypes from periodontitis subjects (Choi *et al*. 1994; Spratt *et al*. 1999). To date, based on sequence analysis of 16S rRNA clonal libraries from specimens of the oral cavity, over 700 bacterial taxa have been detected, of which over half have not yet been cultivated *in vitro* (Dewhirst *et al*. 2000; Paster *et al*. 2001, 2002; Becker *et al*. 2002; Kazor *et al*. 2003). "New" putative pathogens were tentatively identified in a study in which the presence of 39 bacterial species were determined that were implicated in health or disease based on 16S rRNA clonal analysis. Samples from 66 subjects with chronic periodontitis and 66 age-matched healthy controls were examined for the presence of target species. Associations and relative risks were determined for these species. Several novel taxa, in addition to the classical putative pathogens, were suggested as potential periodontal pathogens or health-related species (Kumar *et al*. 2003).

Interest has grown in groups of cultivable species not commonly found in the subgingival plaque as initiators or possibly contributors to the pathogenesis of periodontal disease, particularly in individuals who have responded poorly to periodontal therapy. Species not commonly thought to be present in subgingival plaque can be found in a proportion of such subjects or even in subjects who have not received periodontal treatment. Studies have examined enteric organisms and staphylococcal species as well as other unusual mouth inhabitants. Slots *et al*. (1990b) used cultural techniques to examine plaque samples from over 3000 chronic periodontitis patients and found that 14% of these patients harbored enteric rods and pseudomonads. *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, and *Enterobacter agglomerans* comprised more than 50% of the strains isolated. Systemically administered ciprofloxacin improved the treatment response of patients whose periodontal pockets were heavily infected with enteric rods (Slots *et al*. 1990a). This group of investigators also examined 24 subjects with periodontal disease in the Dominican Republic and found that the prevalence of enteric rods in these subjects was higher than levels found in subjects in the US (Slots *et al*. 1991). In the 16 of 24 subjects in whom this group of organisms was detected, they averaged 23% of the cultivable microbiota. Rams *et al*. (1990, 1992) also identified a number of species of staphylococci and enterococci in subjects with various forms of periodontal disease. The presence of unusual species in periodontal lesions suggests the possibility that they may play a role in the etiology of periodontal diseases. However, such roles must be evaluated in the same manner as the species discussed earlier in this section.

In addition to the cultivable and uncultivable bacterial species, a number of studies have suggested that specific viruses, including cytomegalovirus, the Epstein Barr virus, papillomavirus, and herpes simplex virus, may play a role in the etiology or progression of periodontal lesions, possibly by changing the host response to the local subgingival microbiota (for a comprehensive review, see Slots 2005). A suspected role of various viruses was based primarily on association of the viruses with lesion sites when compared with periodontally healthy sites and the effect of successful therapy on reducing the detection frequency of these viruses in treated sites (Klemenc *et al*. 2005; Slots 2005; Slots *et al*. 2006).

Mixed infections

To this point, attention has been paid to the possible role of individual species as risk factors for destructive periodontal diseases. However, the complex mixture of species colonizing the subgingival area can provide a spectrum of relationships with the host, ranging from beneficial (the organisms prevent disease), to harmful (the organisms cause disease). At the pathogenic end of the spectrum, it is conceivable that different relationships exist between pathogens. The presence of two pathogens at a site could have no effect or could diminish the potential pathogenicity of one or the other of the species. Alternatively, pathogenicity could be enhanced either in an additive or synergistic fashion. It seems likely that mixed infections occur in subgingival sites since so many diverse species inhabit this habitat. Evidence to support this concept has been derived mainly from studies in animals in which it was shown that combinations of species were capable of inducing

experimental abscesses, even though the components of the mixtures could not (Smith 1930; Proske & Sayers 1934; Cobe 1948; Rosebury *et al*. 1950; Macdonald *et al*. 1956; Socransky & Gibbons 1965). It is not clear whether the combinations suggested in the experimental abscess studies are pertinent to human periodontal diseases. Studies in humans suggest that combinations of *P. gingivalis* and *T. forsythia* may be significant in determining diseased sites and disease progression after treatment (Fujise *et al*. 2002). In addition, it has been observed that species such as *P. gingivalis*, *T. forsythia*, and *A. actinomycetemcomitans* may be components of a polymicrobial intracellular microbiota within human buccal epithelial cells (Rudney *et al*. 2005). At the very least, some species may set the stage for specific pathogens by providing essential nutrients, sites of attachment (co-aggregation), or means to evade or subvert host defenses (e.g. by producing protective capsules or enzymes that destroy host antibody). The relationship of microbial "complexes" to periodontal diseases will be discussed further below.

The nature of dental plaque – the biofilm way of life

Biofilms colonize a widely diverse set of moist surfaces, including the oral cavity, the bottom of boats and docks, the inside of pipes, as well as rocks in streams. Infectious disease investigators are interested in biofilms that colonize a wide array of artificial devices that have been implanted in the human, including catheters, hip and voice prostheses, and contact lenses. Biofilms consist of one or more communities of microorganisms, embedded in a glycocalyx, that are attached to a solid surface. The biofilm allows microorganisms to stick to and multiply on surfaces. Thus, attached bacteria (sessile) growing in a biofilm display a wide range of characteristics that provide a number of advantages over single cell (planktonic) bacteria. The interactions among bacterial species living in biofilms take place at several levels including physical contact, metabolic exchange, small signal molecule mediated communication, and exchange of genetic information (Kolenbrander *et al*. 2006). References to pertinent biofilm literature may be found in the following publications: Newman & Wilson (1999); Socransky & Haffajee (2001); Marsh (2005).

The nature of biofilms

Biofilms are fascinating structures. They are the preferred method of growth for many, perhaps most species of bacteria. This method of growth provides a number of advantages to colonizing species. A major advantage is the protection that the biofilm provides to colonizing species from competing microorganisms, from environmental factors such as host defense mechanisms, and from potentially toxic substances in the environment, such as lethal chemicals or antibiotics. Biofilms also can facilitate processing and uptake of nutrients, cross-feeding (one species providing nutrients for another), removal of potentially harmful metabolic products (often by utilization by other bacteria), as well as the development of an appropriate physicochemical environment (e.g. a properly reduced oxidation reduction potential).

A crude analogy to the development of a biofilm might be the development of a city. Successful human colonization of new environments requires several important factors including a stable nutrient supply, an environment conducive to proliferation, and an environment with limited potential hazards. Cities (like biofilms) develop by an initial "attachment" of humans to a dwelling site followed by multiplication of the existing inhabitants and addition of new inhabitants. Cities and biofilms typically spread laterally and then in a vertical direction often forming columnar habitation sites. Cities and biofilms offer many benefits to their inhabitants. These include shared resources and inter-related activities. Inhabitants of cities or biofilms are capable of "metabolic processes" and synthetic capabilities that could not be performed by individuals in an unattached (planktonic) or nomadic state. An important benefit provided by a city or biofilm is protection both from other potential colonizers of the same species, from exogenous species, and from sudden harmful changes in the environment. Individuals in the "climax community" of a flourishing city/biofilm can facilitate joint activities and live in a far more stable environment than individuals who live in isolation. Cities, like biofilms, require a means to bring in nutrients and raw materials, and to remove waste products. In cities, these are usually roads, water or sewage pipes, in biofilms they may be water channels such as those described below. Cities have maximum practical sizes based on physical constraints and nutrient/waste limits; so do biofilms. Cities that are mildly perturbed, e.g. by a snow storm or a local fire, usually reform a climax community that is similar to that which was present in the first place; as do biofilms. However, major perturbations in the environment such as prolonged drought or a radioactive cloud can lay waste to a city. Major perturbations in the environment such as a toxic chemical can severely affect the composition or existence of a biofilm. Communication between individuals in a city is essential to allow inhabitants to interact optimally. This is usually performed by vocal, written or pictorial means. Communication between bacterial cells within a biofilm is also necessary for optimum community development and is performed by production of signaling molecules such as those found in "quorum sensing" or perhaps by the exchange of genetic information. The long-term survival of the human species as well as a species in a biofilm becomes more likely if that species (or the human) colonizes multiple sites. Thus, detachment of cells from biofilms and establishment in new sites is as impor-

tant for survival of biofilm dwellers as the migration of individuals and establishment of new cities is for human beings. Thus, we may regard mixed species biofilms as primitive precursors to the more complex organizations observed for eukaryotic species.

Properties of biofilms

Structure

Biofilms are composed of microcolonies of bacterial cells (15–20% by volume) that are non-randomly distributed in a shaped matrix or glycocalyx (75–80% by volume). Earlier studies of thick biofilms (>5 mm) that develop in sewage treatment plants indicated the presence of voids or water channels between the microcolonies that were present in these biofilms. The water channels permit the passage of nutrients and other agents throughout the biofilm acting as a primitive "circulatory" system. Nutrients make contact with the sessile (attached) microcolonies by diffusion from the water channel to the microcolony rather than from the matrix. Microcolonies occur in different shapes in biofilms which are governed by shear forces due to the passage of fluid over the biofilm. At low shear force, the colonies are shaped liked towers or mushrooms, while at high shear force, the colonies are elongated and capable of rapid oscillation. Individual microcolonies can consist of a single species, but more frequently are composed of several different species.

Exopolysaccharides – the backbone of the biofilm

The bulk of the biofilm consists of the matrix or glycocalyx and is composed predominantly of water and aqueous solutes. The "dry" material is a mixture of exopolysaccharides, proteins, salts, and cell material. Exopolysaccharides (EPS), which are produced by the bacteria in the biofilm, are the major components of the biofilm making up 50–95% of the dry weight. They play a major role in maintaining the integrity of the biofilm as well as preventing desiccation and attack by harmful agents. In addition, they may also bind essential nutrients such as cations to create a local nutritionally rich environment favoring specific microorganisms. The EPS matrix could also act as a buffer and assist in the retention of extracellular enzymes (and their substrates) enhancing substrate utilization by bacterial cells. The EPS can be degraded and utilized by bacteria within the biofilm. One distinguishing feature of oral biofilms is that many of the microorganisms can both synthesize and degrade the EPS.

Physiological heterogeneity within biofilms

Cells of the same microbial species can exhibit extremely different physiologic states in a biofilm even though separated by as little as 10 μm. Typically, DNA indicating the presence of bacterial cells is detected throughout the biofilm, but protein synthesis, respiratory activity, and RNA are detected primarily in the outer layers.

The use of micro-electrodes has shown that pH can vary quite remarkably over short distances within a biofilm. Two-photon excitation microscopy of *in vitro* plaque made up of ten intra-oral species showed that, after a sucrose challenge, microcolonies with a pH <3.0 could be detected adjacent to microcolonies with pH values >5.0. The number of metal ions can differ sufficiently in different regions of a biofilm so that difference in ion concentration can produce measurable potential differences. Bacterial cells within biofilms can produce enzymes such as beta-lactamase against antibiotics, catalases, and superoxide dismutases against oxidizing ions released by phagocytes. These enzymes are released into the matrix producing an almost impregnable line of defense. Bacterial cells in biofilms can also produce elastases and cellulases which become concentrated in the local matrix and produce tissue damage. Measurement of oxygen and other gases has demonstrated that certain microcolonies are completely anaerobic even though composed of a single species and grown in ambient air. Carbon dioxide and methane can reach very high concentrations in specific microcolonies in industrial biofilms. Thus, studies to date indicate that sessile cells growing in mixed biofilms can exist in an almost infinite range of chemical and physical microhabitats within microbial communities.

Quorum sensing and exchange of genetic information

Some of the functions of biofilms are dependent on the ability of the bacteria and microcolonies within the biofilm to communicate with one another. Quorum sensing in bacteria "involves the regulation of expression of specific genes through the accumulation of signaling compounds that mediate intercellular communication" (Prosser 1999). Quorum sensing is dependent on cell density. With few cells, signaling compounds may be produced at low levels, however, auto-induction leads to increased concentration as cell density increases. Once the signaling compounds reach a threshold level (quorum cell density), gene expression is activated. Quorum sensing may give biofilms their distinct properties. For example, expression of genes for antibiotic resistance at high cell densities may provide protection. Quorum sensing also has the potential to influence community structure by encouraging the growth of beneficial species (to the biofilm) and discouraging the growth of competitors. It is also possible that physiological properties of bacteria in the community may be altered through quorum sensing. Quoring-sensing signaling molecules produced by

putative periodontal pathogens such as *P. gingivalis*, *Pr. intermedia*, and *F. nucleatum* have been detected (Frias *et al*. 2001). Of particular importance may be a recently discovered molecule, autoinducer-2, which is thought to be a universal signal mediating messages among the species in mixed species communities (Kolenbrander *et al*. 2006). This family of molecules has been detected in the cell-free culture supernatants of multiple oral bacterial species. Kolenbrander *et al*. (2006) indicated that commensal bacterial species such as *Streptococcus oralis* and *Actinomyces naeslundii* produce and respond to low levels of autoinducer-2, while pathogens, such as *F. nucleatum*, *Pr. intermedia* and *P. gingivalis*, produce and respond to high levels of these substances. They hypothesized that when the pathogens become established in a mixed species community, their production of high levels of autoinducer-2 may foster the growth of the pathogenic community and minimize the growth of commensal species.

Signaling is not the only way of transferring information in biofilms. The high density of bacterial cells growing in biofilms facilitates exchange of genetic information between cells of the same species and across species or even genera. Conjugation, transformation, plasmid transfer, and transposon transfer have all been shown to occur in naturally occurring or *in vitro* prepared mixed species biofilms (described in greater detail in a later section). Of particular interest, was the demonstration of transfer of a conjugative transposon conferring tetracycline resistance from cells of one genus, *Bacillus subtilis*, to a *Streptococcus* species present in dental plaque grown as a biofilm in a constant depth film fermenter.

Attachment of bacteria

The key characteristic of a biofilm is that the microcolonies within the biofilm attach to a solid surface. Thus, adhesion to a surface is the essential first step in the development of a biofilm. In the mouth, there is a wide variety of surfaces to which bacteria can attach including the oral soft tissues, the pellicle-coated teeth, other bacteria, as well as prosthetic replacements such dentures and implants. Many bacterial species possess surface structures such as fimbriae and fibrils that aid in their attachment to different surfaces. Fimbriae have been detected on a number of oral species including *Actinomyces naeslundii*, *P. gingivalis*, *A. actinomycetemcomitans* and some strains of streptococci such as *Streptococcus salivarius*, *Streptococcus parasanguinis*, and members of the *Streptococcus mitis* group. Fibrils can be found on a number of oral bacterial species. They are morphologically different and shorter than fimbriae and may be densely or sparsely distributed on the cell surface. Oral species that possess fibrils include *S. salivarius*, the *S. mitis* group, *Pr. intermedia*, *Pr. nigrescens*, and *Streptococcus mutans*.

Mechanisms of increased antibiotic resistance of organisms in biofilms

Antibiotics have been and continue to be used effectively in the treatment of periodontal infections. However, the indiscriminate use of antimicrobials and biocides has the potential of leading to the development of resistant bacteria. It has also been suggested that resistance from one type of antimicrobial, such as a biocide, can be transferred to a different type of antimicrobial, such as an antibiotic. Thus, it is important to understand the factors leading to antimicrobial resistance in biofilms such as dental plaque.

It has been recognized for considerable periods of time that organisms growing in biofilms are more resistant to antibiotics than the same species growing in a planktonic (unattached) state. While the mechanisms of resistance to antibiotics of organisms growing in biofilms are not entirely clear, certain general principles have been described. Almost without exception, organisms grown in biofilms are more resistant to antibiotics than the same cells grown in a planktonic state. Estimates of 1000–1500 times greater resistance for biofilm-grown cells than planktonic grown cells have been suggested, although these estimates have been considered to be too high by some investigators. The mechanisms of increased resistance in biofilms differ from species to species, from antibiotic to antibiotic, and for biofilms growing in different habitats. One important mechanism of resistance appears to be the slower rate of growth of bacterial species in biofilms which makes them less susceptible to many but not all antibiotics. It has been shown in many studies that the resistance of bacteria to antibiotics, biocides or preservatives is affected by their nutritional status, growth rate, temperature, pH, and prior exposure to sub-effective concentrations of antimicrobials. Variations in any of these parameters can lead to a varied response to antibiotics within a biofilm. The matrix performs a "homeostatic function", such that cells deep in the biofilm experience different conditions, such as hydrogen ion concentration or redox potentials, than cells at the periphery of the biofilm or cells growing planktonically. Growth rates of these deeper cells will be decreased allowing them to survive better than faster growing cells at the periphery when exposed to antimicrobial agents. In addition, the slower growing bacteria often over-express "non-specific defense mechanisms", including shock proteins and multidrug efflux pumps, and demonstrate increased exopolymer synthesis.

The exopolymer matrix of a biofilm, although not a significant barrier in itself to the diffusion of antibiotics, does have certain properties that can retard diffusion. For example, strongly charged or chemically highly reactive agents can fail to reach the deeper zones of the biofilm because the biofilm acts as an ion-exchange resin, removing such molecules

from solution. In addition, extracellular enzymes, such as beta-lactamases, formaldehyde lyase, and formaldehyde dehydrogenase, may become trapped and concentrated in the extracellular matrix, thus inactivating susceptible, typically positively charged, hydrophilic antibiotics. Some antibiotics such as the macrolides, which are positively charged but hydrophobic, are unaffected by this process. Thus, the ability of the matrix to act as a physical barrier is dependent on the type of antibiotic, the binding of the matrix to that agent, and the levels of the agent employed. Since reaction between the agent and the matrix will reduce the levels of the agent, a biofilm with greater bulk will deplete the agent more readily. Further, hydrodynamics and the turnover rate of the microcolonies will also impact on antibiotic effectiveness.

Alteration of genotype and/or phenotype of the cells growing within a biofilm matrix is receiving increased attention. Cells growing within a biofilm express genes that are not observed in the same cells grown in a planktonic state and they can retain this resistance for some time after being released from the biofilm. For example, it was demonstrated that cells of *Pseudomonas aeruginosa* liberated from biofilms were considerably more resistant to tobramycin than planktonic cells, suggesting that the cells became intrinsically more resistant when growing in a biofilm and retained some of this resistance even outside the biofilm.

The presence of a glycocalyx, a slower growth rate, and development of a biofilm phenotype cannot provide a total explanation for the phenomenon of antibiotic resistance. These features probably delay elimination of the target bacteria, allowing other selection events to take place. Recently, the notion of a subpopulation of cells within a biofilm that are "super-resistant" was proposed. Such cells could explain the remarkably elevated levels of resistance to certain antibiotics that have been suggested in the literature.

Techniques for the detection and enumeration of bacteria in oral biofilm samples

The enumeration of specific bacterial species in oral biofilm samples is a challenging task, in part, because of the large number of bacterial species present in such samples and, in part, because of the fastidious nature of many of the resident species. Ideal methods of enumeration should be able to quantify multiple species, be sensitive, specific, inexpensive, and high throughput. Quantification is essential because the differences in the microbiota between periodontal health and disease, and between pre- and post-periodontal therapy, are quantitative rather than presence or absence of one or more species. The early light microscopy techniques were not satisfactory because they could not distinguish bacterial species only morphotypes. Cultural techniques are specific in their ability to distinguish species, but are so expensive that the number of samples that can be examined is severely limited. Antibody-based techniques such as immunofluorescence and enzyme-linked immunosorbent assay (ELISA) are very specific and can provide quantitative data. However, antisera to only a limited range of species have been developed and these techniques are somewhat cumbersome, diminishing the number of species and samples that may be conveniently examined. Molecular techniques, including PCR and DNA hybridization, have the advantage of being specific and readily extensible to a wide range of bacterial taxa. PCR is convenient and able to detect low numbers of cells but suffers from the inability to provide quantitative data. Real-time PCR overcomes this limitation, but is expensive and time-consuming, precluding examination of large numbers of species and samples. DNA hybridization using formats such as that described in Fig. 9-1, are sensitive, specific, inexpensive, and high throughput, providing at the moment, perhaps the most useful technique for quantifying a wide range of species in large numbers of biofilm samples.

There has been considerable interest in enumerating the uncultivable or as yet to be cultivated taxa in addition to the cultivable taxa in subgingival biofilms. Recent studies have employed amplification of the 16S rRNA genes directly from plaque samples using PCR and consensus primers. The products were cloned into *Escherichia coli* and the sequences of the inserts determined. These studies provided a remarkably different view of the composition of the subgingival microbiota compared with other techniques such as culture, immunofluorescence, ELISA, PCR, real-time PCR, and DNA hybridization. The results of the cloning–sequencing studies must at present be viewed with considerable caution because these methods failed to detect or detected infrequently known prominent taxa such as *P. gingivalis*, *T. forsythia*, and members of the genera *Fusobacterium* and *Actinomyces*. For more detail on microbiological techniques used to examine biofilm samples see Socransky and Haffajee (2005).

The oral biofilms that lead to periodontal diseases

The section on biofilm biology presented above provided a background to help understand the ecology of the incredibly complex communities of organisms that colonize the tooth surface and lead to periodontal diseases. Figure 9-6 presents a clinical photograph of a subject with less than optimal home care. Evident in this photograph is stain on the tooth surfaces that may have resulted from smoking, coffee or tea drinking. Of greater concern, is the occurrence of a thin film of bacterial plaque on many of the tooth surfaces along with the quite obvious plaque formation in regions such as the mesial buccal surfaces of the

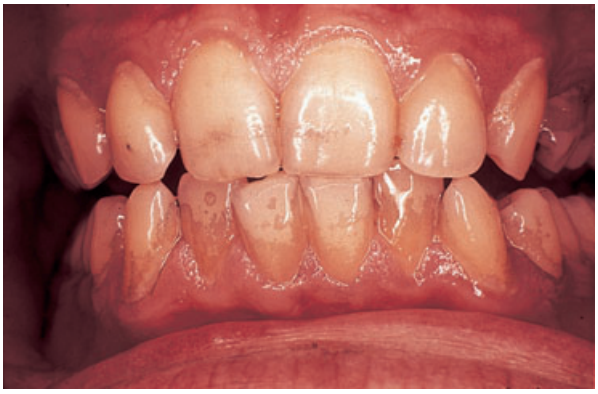

Fig. 9-6 Clinical photograph of a subject exhibiting tooth stain and supragingival dental plaque.

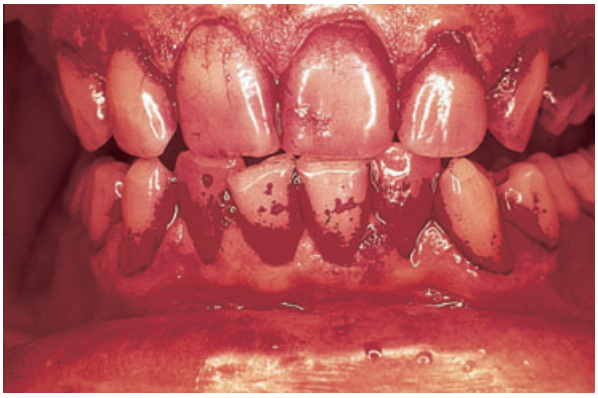

Fig. 9-7 Clinical photograph of the subject in Fig. 9-6 after staining with disclosing solution.

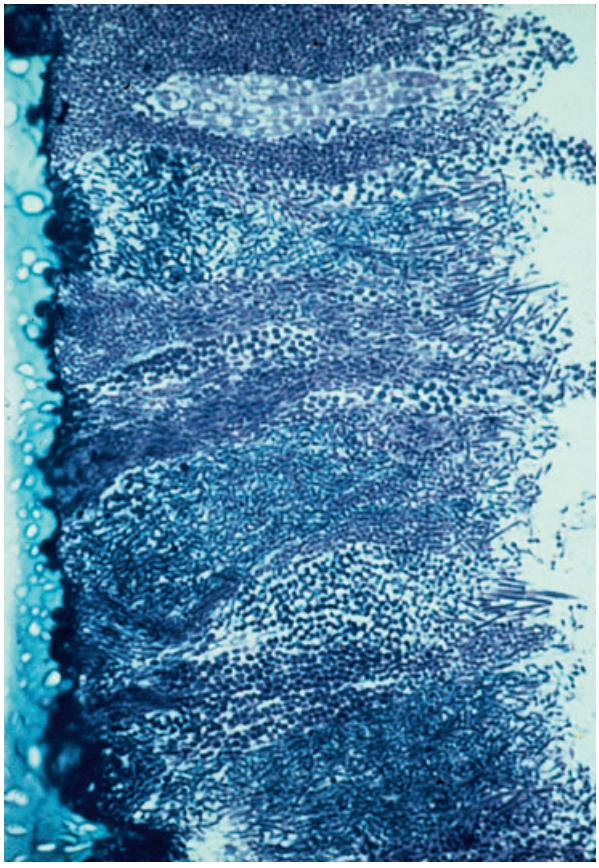

Fig. 9-8 Histological section of human supragingival plaque stained with toluidine blue–methylene blue. The supragingival plaque was allowed to develop for 3 days on an epon crown in a human volunteer. The crown surface is at the left and the saliva interface is towards the right. (Courtesy of Dr. Max Listgarten, University of Pennsylvania.)

upper left and lower right canines. These biofilm (plaque) regions are highlighted in Fig. 9-7, which shows the same dentition after staining with a disclosing solution. The thin films such as those on the lower incisors might consist of biofilm communities that are 50–100 cells thick. Thicker plaques, such as those on the upper left and lower right canines, might consist of biofilms that are 300 or more cell layers in thickness. The number of organisms that reside on the mesial surface of the upper left or lower right canine probably exceeds 300 million. This number is remarkable in that it is similar to the entire human population of the United States. These microbial communities are very complex. Over 700 bacterial species have been detected in the human oral cavity, and over 400 of these can be found in the periodontal pocket (Paster *et al*. 2006). It is thought that about half of these species may be as yet uncultivated. In any given plaque sample, it is not uncommon to detect 30 or more bacterial species. Thus, the biofilms that colonize the tooth surface may be among the most complex biofilms that exist in nature. This complexity is due in large part to the non-shedding surface of the tooth which permits persistent colonization and the opportunity for very complex ecosystems to develop. In addition, the relatively high nutrient abundance as well as the remarkable ability of oral species to coaggregate with one another may facilitate this complexity.

Figure 9-8 is a section of human supragingival dental plaque grown on an epon crown in a human volunteer (Listgarten *et al*. 1975; Listgarten 1976, 1999). The section demonstrates many of the features of biofilms outlined earlier. Bacterial species adhered to the solid surface, multiplied, and, in this section, formed columnar microcolonies. The heterogeneity of colonizing species is evident even at a morphological level and would be emphasized if the cells within the section had been characterized by cultural or molecular techniques. The surface layers of the biofilm exhibit morphotypes that are not evident in deeper layers and emphasize the role that coaggregation plays in the development of biofilms. Not evident in this section are the water channels in biofilms described earlier. This might be due to preparation or fixation artifacts (Costerton *et al*. 1999) or it might be because the plaque is typical of a "dense" bacterial model. Water channels have been observed in plaque grown in the human oral cavity by confocal microscopy (Wood *et al*. 2000). This dental biofilm has all of the properties of biofilms in other habitats in nature. It has a solid substratum, in this case an epon crown

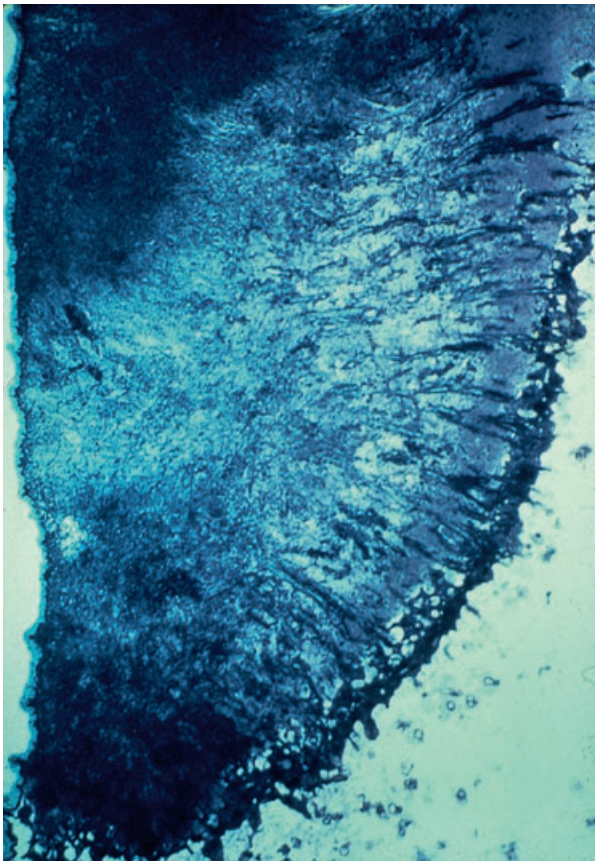

Fig. 9-9 Histological section of human subgingival dental plaque stained with toluidine blue–methylene blue. The tooth surface is to the left and the epithelial lining of the periodontal pocket is to the right. Bacterial plaque attached to the tooth surface is evident towards the upper left of the section, while a second zone of organisms can be observed lining the periodontal pocket wall. (Courtesy of Dr. Max Listgarten, University of Pennsylvania.)

but more typically a tooth, it has the mixed microcolonies growing in a glycocalyx, and it has the bulk fluid interface provided by saliva.

A second biofilm ecosystem is shown in Fig. 9-9. This is a section of human subgingival plaque. The section is at lower magnification than Fig. 9-8 to permit visualization of regions within the biofilm. The plaque attached to the tooth surface is evident in the upper left portion of the section. This tooth-associated biofilm is an extension of the biofilm found above the gingival margin and may be quite similar in microbial composition. A second, possibly epithelial cell-associated biofilm, may be observed lining the epithelial surface of the pocket. This biofilm contains primarily spirochetes and Gram-negative bacterial species (Listgarten *et al*. 1975; Listgarten 1976, 1999). *P. gingivalis* and *Tr. denticola* have been detected in large numbers in the epithelial cell-associated biofilms within the periodontal pocket, by immunocytochemistry (Kigure *et al*. 1995). *T. forsythia* might also be numerous in this zone, since high levels of this species have been detected, using DNA probes, in association with the epithelial cells lining the periodontal pocket (Dibart *et al*. 1998). Between the tooth-associated and epithelial cell-associated biofilms, a less dense zone of organisms may be observed. These organisms may be "loosely attached" or they might be in a planktonic state. The critical feature of Fig. 9-9 is that there appear to be tooth-associated and epithelial cell-associated regions in subgingival plaque as well as a possible third weakly attached or unattached zone of microorganisms. It is strongly suspected that these regions differ markedly in microbial composition, physiological state, and their response to different therapies.

Microbial complexes

The association of bacteria within mixed biofilms is not random, rather there are specific associations among bacterial species. Socransky *et al*. (1998) examined over 13 000 subgingival plaque samples from 185 adult subjects and used cluster analysis and community ordination techniques to demonstrate the presence of specific microbial groups within dental plaque (Fig. 9-10). Six closely associated groups of bacterial species were recognized. These included specific species of *Actinomyces*, a yellow complex consisting of members of the genus *Streptococcus*, a green complex consisting of *Capnocytophaga* species, *A. actinomycetemcomitans* serotype a, *E. corrodens* and *Campylobacter concisus*, and a purple complex consisting of *V. parvula* and *Actinomyces odontolyticus*. These groups of species are early colonizers of the tooth surface whose growth usually precedes the multiplication of the predominantly Gram-negative orange and red complexes (Fig. 9-10). The orange complex consists of *Campylobacter gracilis*, *C. rectus*, *C. showae*, *E. nodatum*, *F. nucleatum* subspecies, *F. periodonticum*, *Pe. micros*, *Pr. intermedia*, *Pr. nigrescens*, and *S. constellatus*, while the red complex consists of *T. forsythia*, *P. gingivalis*, and *Tr. denticola.* The last two complexes are comprised of the species thought to be the major etiologic agents of periodontal diseases.

Similar relationships have been demonstrated in *in vitro* studies examining interactions between different pairs of oral bacterial species (Kolenbrander *et al*. 2006). These studies of oral bacteria have indicated that cell-to-cell recognition is not random but that each strain has a defined set of partners (Fig. 9-11). Further, functionally similar adhesins found on bacteria of different genera may recognize the same receptors on other bacterial cells. Most human oral bacteria adhere to other oral bacteria. This cell-to-cell adherence is known as coaggregation. It is interesting that the relationships among species determined by pair-wise *in vitro* coaggregation studies depicted in Fig. 9-11 are similar to the microbial complexes (Fig. 9-10) determined by examination of *in vivo* samples suggesting that coaggregation may be a powerful ecological determinant of community development. Figure 9-11 also suggests some of the mechanisms that might control the observed microbial succession

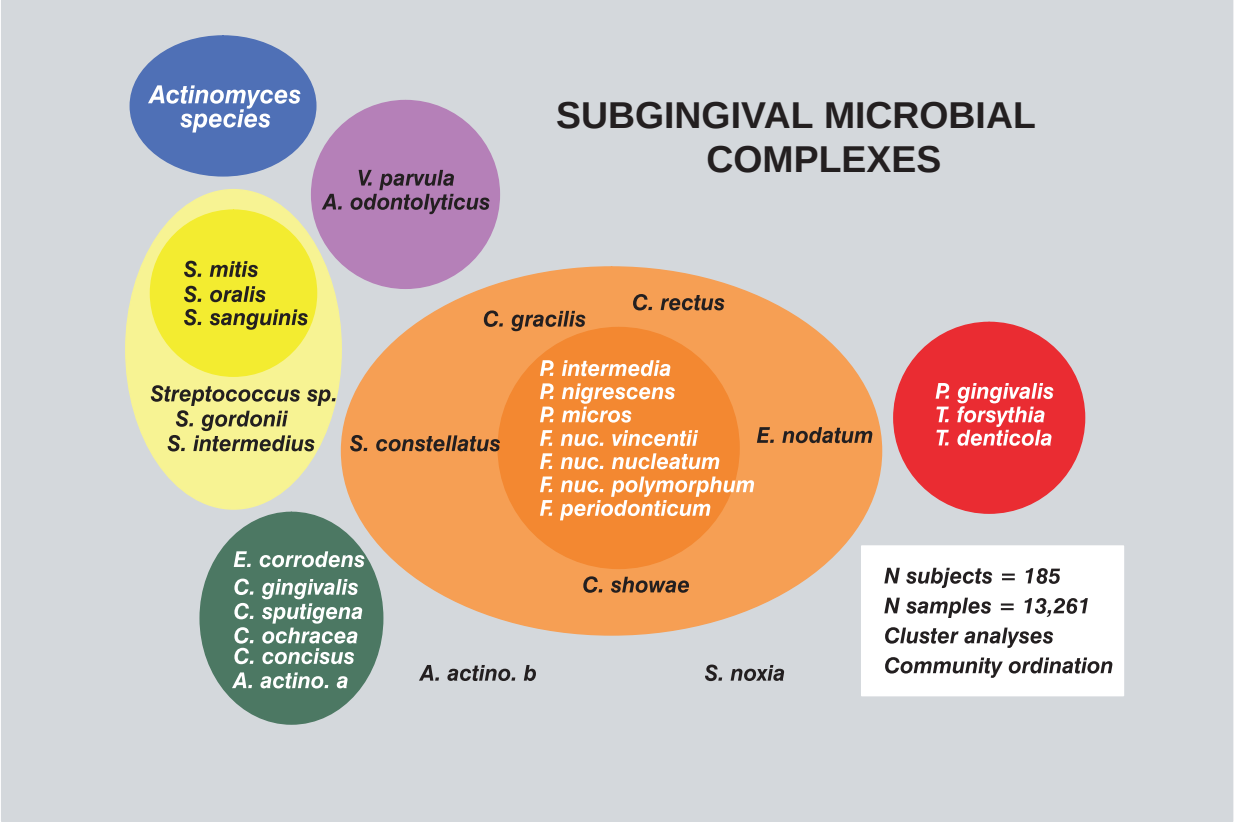

Fig. 9-10 Diagram of the association among subgingival species (adapted from Socransky *et al*. 1998). The data were derived from 13 261 subgingival plaque samples taken from the mesial aspect of each tooth in 185 adult subjects. Each sample was individually analyzed for the presence of 40 subgingival species using checkerboard DNA–DNA hybridization. Associations were sought among species using cluster analysis and community ordination techniques. The complexes to the left are comprised of species thought to colonize the tooth surface and proliferate at an early stage. The orange complex becomes numerically more dominant later and is thought to bridge the early colonizers and the red complex species which become numerically more dominant at late stages in plaque development.

in plaque development that will be discussed below. For example, the ability of many streptococcal species, particularly *S. mitis* and *S. oralis* (Nyvad & Kilian 1987; Li *et al*. 2004), to attach to different receptors found in tooth pellicle as well as to each other may contribute to their critical role as early colonizers of the tooth surface. The streptococci provide receptors for a wide range of species, including other early colonizing species and bridging species, such as *F. nucleatum*, that in turn may coaggregate with late colonizers including many periodontal pathogens.

Factors that affect the composition of subgingival biofilms

Although this chapter emphasizes the effect that microorganisms have on their habitat, the periodontal tissues, it is important to understand that the habitat has a major effect on the composition, metabolic activities, and virulence properties of the colonizing microorganisms. The importance of this axiom, that the microorganisms affect the habitat and the habitat affects the microorganisms, has recently begun to be fully appreciated. Thus, modifications of the supra- and subgingival microbiota certainly affect the outcome, periodontal health or disease; but changes in the host or local habitat also affect the composition and activities of the microbiota. Understanding this relationship should help to lead us into better approaches to diagnosing the etiology and contributing factors of a patient's disease and to optimizing appropriate therapy. In this section, we will provide examples of some of the factors that are known to modify subgingival microbial composition.

Periodontal disease status

Perhaps the most influential factor on the composition of the subgingival microbiota is the periodontal disease status of the host. Figure 9-12 presents the counts, proportions and percentage of sites colonized at $>10^5$ of 40 subgingival taxa in subjects with chronic periodontitis or periodontal health (Haffajee *et al*. 2006a). Clearly, the major difference between health and disease, *on average*, was the increased counts, proportions, and prevalence of the red complex species, *T. forsythia*, *P. gingivalis*, and *Tr. denticola* in subjects with periodontal disease. In addition, other putative periodontal pathogens of the orange complex were also more prevalent and in higher levels in periodontitis subjects. However, individuals with

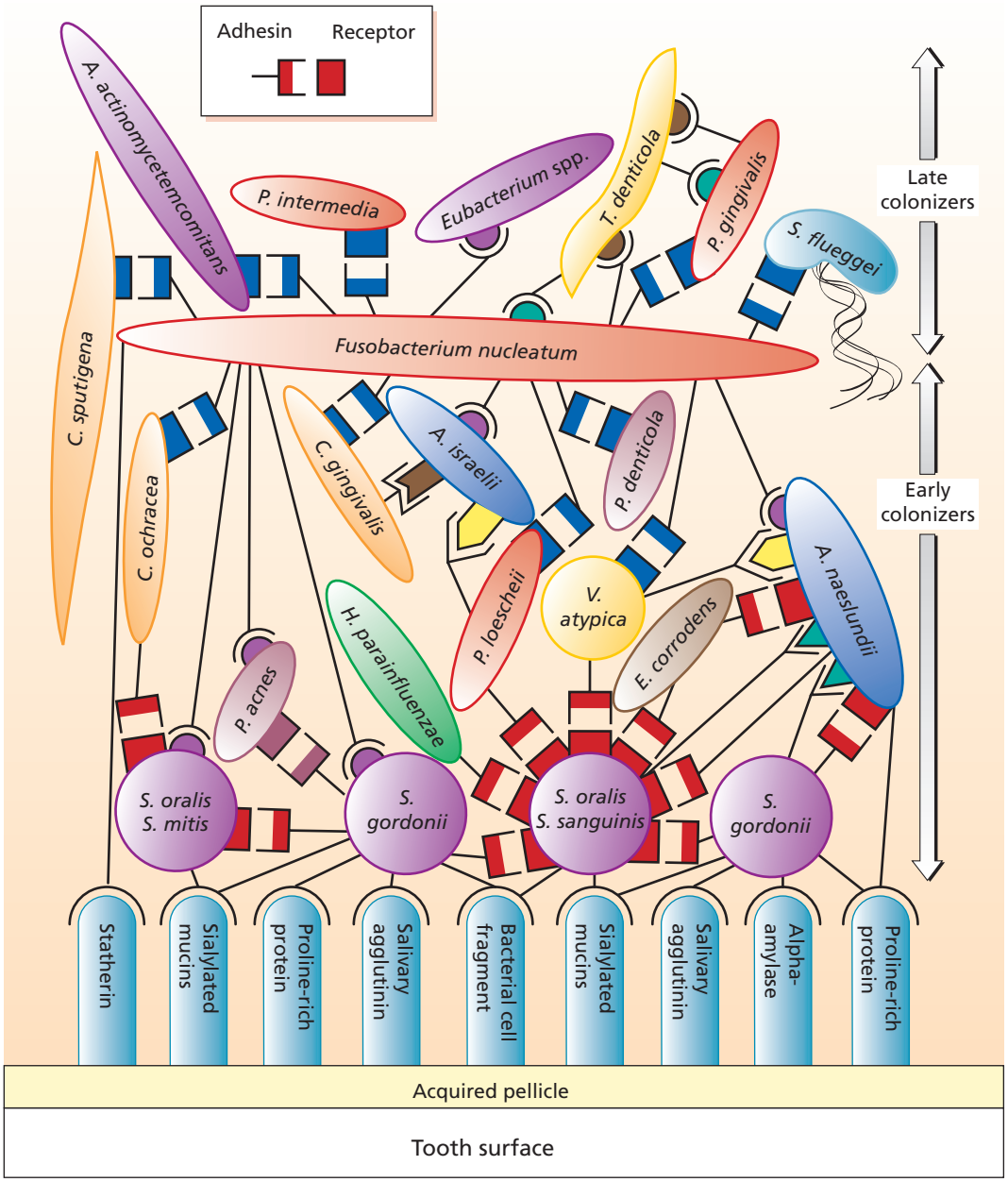

Fig. 9-11 Spatiotemporal model of oral bacterial colonization, showing recognition of salivary pellicle receptors by early colonizing bacteria and coaggregations between early colonizers, fusobacteria and late colonizers of the tooth surface (Kolenbrander *et al*. 2002). Each coaggregation depicted is known to occur in a pairwise test. Collectively, these interactions are proposed to represent development of dental plaque. Starting at the bottom, primary colonizers bind via adhesins (round-tipped black line symbols) to complementary salivary receptors (blue–green vertical round-topped columns) in the acquired pellicle coating the tooth surface. Secondary colonizers bind to previously bound bacteria. Sequential binding results in the appearance of nascent surfaces that bridge with the next coaggregating partner cell. Several kinds of coaggregations are shown as complementary sets of symbols of different shapes. One set is depicted in the box at the top. Proposed adhesins (symbols with a stem) represent cell surface components that are heat inactivated (cell suspension heated to 85°C for 30 minutes) and protease sensitive; their complementary receptors (symbols without a stem) are unaffected by heat or protease. Identical symbols represent components that are functionally similar but may not be structurally identical. Rectangular symbols represent lactose-inhibitable coaggregations. Other symbols represent components that have no known inhibitor. The bacterial species shown are *Aggregatibacter actinomycetemcomitans*, *Actinomyces israelii*, *Actinomyces naeslundii*, *Capnocytophaga gingivalis*, *Capnocytophaga ochracea*, *Capnocytophaga sputigena*, *Eikenella corrodens*, *Eubacterium* spp., *Fusobacterium nucleatum*, *Haemophilus parainfluenzae*, *Porphyromonas gingivalis*, *Prevotella denticola*, *Prevotella intermedia*, *Prevotella loescheii*, *Propionibacterium acnes*, *Selenomonas flueggei*, *Streptococcus gordonii*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus sanguinis*, *Treponema* spp., and *Veillonella atypica*. (Published with permission of Paul Kolenbrander, Kolenbrander *et al*. 2006 and Blackwell Publishing.)

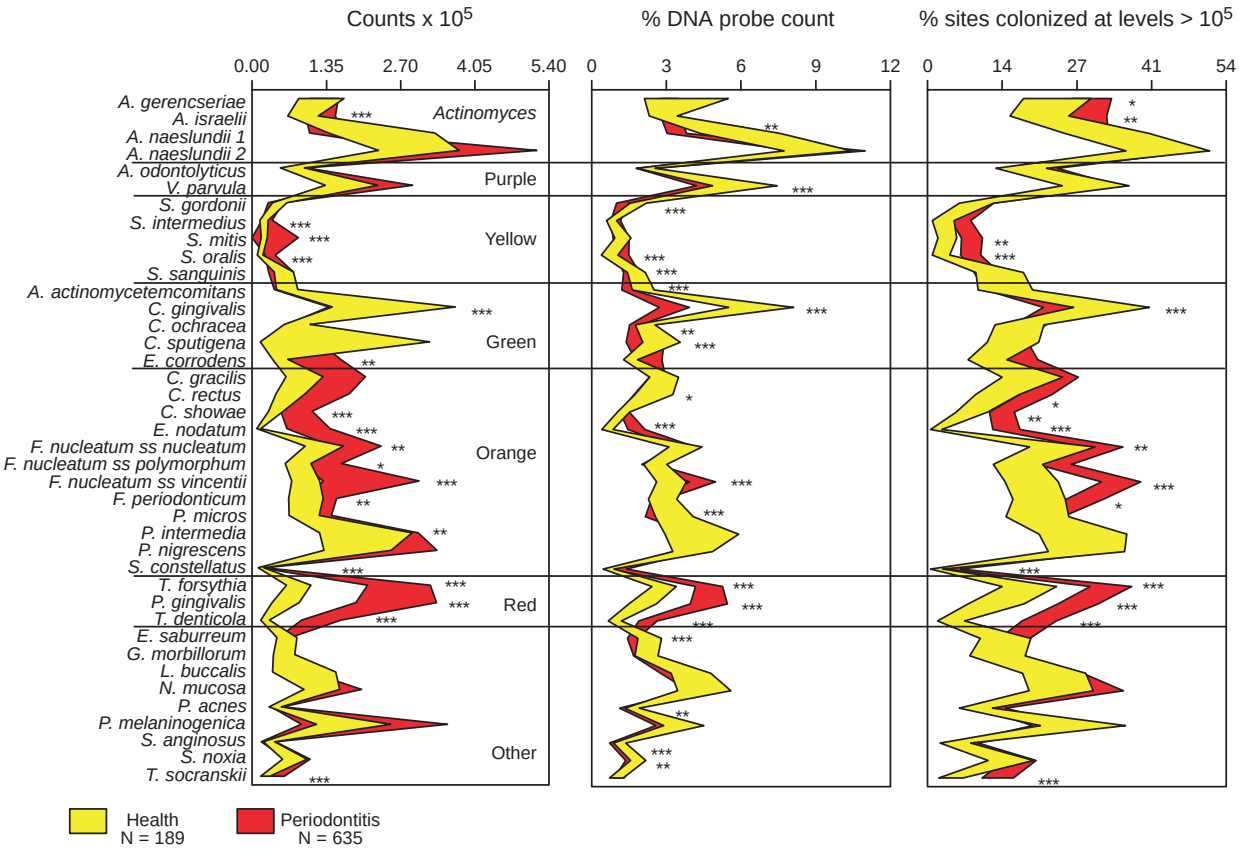

Fig. 9-12 Plots of mean counts (left panel), percents of the total DNA probe count (middle panel) and percentage of sites colonized by 40 bacterial species at counts >10^5 (right panel) in subgingival plaque samples taken from 189 periodontally healthy and 635 chronic periodontitis subjects. The "bands" represent the mean values ± the 95% confidence intervals after adjusting for 40 comparisons. Mean values for each species were computed by averaging up to 28 samples in each subject, and then averaging across subjects in the two clinical groups. Significance of differences between groups was sought using the non-parametric Mann Whitney test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ after adjusting for multiple comparisons (Socransky *et al.* 1991). The species were ordered and grouped according to the complexes described by Socransky *et al.* (1998). The yellow profile represents the mean data for the healthy subjects and the red profile represents the data for the periodontitis subjects. Reprinted with permission from Blackwell Publishing (Haffajee *et al.* 2006a, *Oral Microbiology and Immunology*, **21**, 1–14).

different forms of disease have different subgingival microbial profiles. Even subjects with the "same" periodontal disease in terms of both clinical appearance and severity can exhibit quite different subgingival microbiotas (Fig. 9-13).

The local environment

One host factor that markedly influenced the subgingival environment was pocket depth. Figure 9-14 demonstrates that the mean counts of subgingival species differed at sites of different pocket depths. Red complex species, *T. forsythia*, *P. gingivalis*, as well as *Tr. denticola* (data not shown), increased strikingly in numbers with increasing pocket depth. All orange complex species also demonstrated this relationship. *S. sanguinis* and *A. naeslundii* genospecies 2 were typical of the majority of species in the other four complexes that showed little relationship to pocket depth. Thus, red and orange complex species were not only related to periodontal disease status in a subject, but to disease status at the periodontal site. The species of the red and orange complexes were also elevated at sites exhibiting gingival inflammation, as measured by gingival redness, bleeding on probing, and suppuration (Fig. 9-15). Other species such as *A. naeslundii* genospecies 2 and *S. sanguinis* did not show this relationship.

One remarkable feature of the microbiota of "healthy sites" (defined as sites with pocket depth <4 mm) in subjects with periodontitis was that their microbiota differed markedly from that found in healthy sites in periodontally healthy subjects (Fig. 9-16). The data in Fig. 9-16 once again demonstrate the strong relationship of orange and red complex species with pocket depth in the subjects with periodontitis. However, the figure also demonstrates that subjects who were periodontally healthy had clearly lower levels of periodontal pathogens, such as *E. nodatum*, *P. gingivalis*, *T. forsythia*, and *Tr. denticola*, in their shallow sulci/pockets than were detected in the shallow pockets in periodontitis subjects. This suggests that the "healthy sites" in the subjects with periodontitis would be at more risk for destructive disease initiation and progression than similar sites in periodontally healthy individuals and may

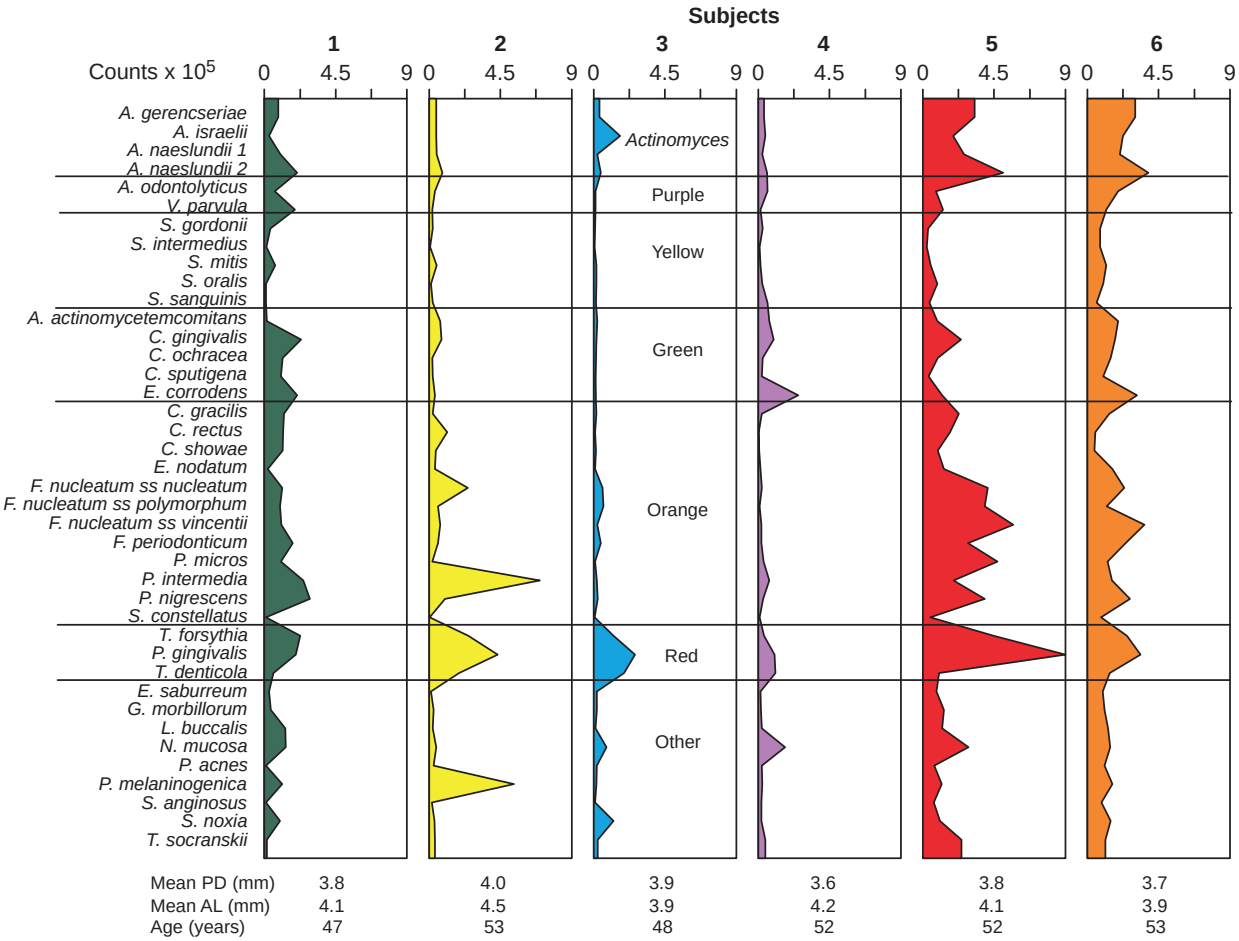

Fig. 9-13 Mean counts ($\times 10^5$) of the 40 test species in samples from six chronic periodontitis subjects with similar clinical and demographic features. Mean values for each species were computed by averaging up to 28 samples in each subject. Each panel represents an individual subject and the mean clinical features of the subjects are presented below each panel. The species were ordered and grouped according to microbial complexes (Socransky *et al*. 1998).

warrant therapy to lower the levels of colonizing pathogens.

Host factors

In addition to the impact of local factors on the composition of subgingival biofilms, host level factors can also affect biofilm composition. Some of these factors include the genetic background of the subject, environmental factors such smoking and diet, systemic conditions such as diabetes and obesity, and even geographic location. For example, subjects who are positive for a specific genotype of the polymorphic IL-1 gene cluster have been found to have increased levels of periodontal disease (Kornman *et al*. 1997) and increased counts of species of the red and orange complexes at sites with pocket depth >6 mm (Socransky & Haffajee 2005). Another condition that has been associated with a heightened inflammatory response, obesity, was associated with increased counts of red complex species in subgingival plaque samples, in particular, increased counts of *T. forsythia* in very obese subjects (Socransky & Haffajee 2005). There are numerous studies in the literature indicating that subjects who are current smokers have significantly more periodontal disease than past or never smokers and respond less well to mechanical periodontal therapies (Haffajee & Socransky 2000). In addition, it has been shown that current smokers have a larger proportion of their "healthy" sites (pocket depth <4 mm) colonized by red and orange complex species compared to similar sites in subjects who have never smoked (Socransky & Haffajee 2005). Individuals with Sjogren's syndrome, an autoimmune disease, that leads to a variety of host changes including a decrease in salivary flow rates, exhibit decreased levels of supra- and subgingival plaque, but increased proportions of *V. parvula* and *N. mucosa* in supra- and subgingival biofilms (Socransky & Haffajee 2005). Even the geographic location of a subject can influence the composition of subgingival biofilms (Fig. 9-17). Samples of subgingival plaque from the four deepest sites in each subject with chronic periodontitis from five different countries evaluated using checkerboard DNA–DNA hybridization, demonstrated that the proportions of species such as *P. gingivalis*, *Tr. denticola*, and *E. nodatum* differed markedly among subjects. The

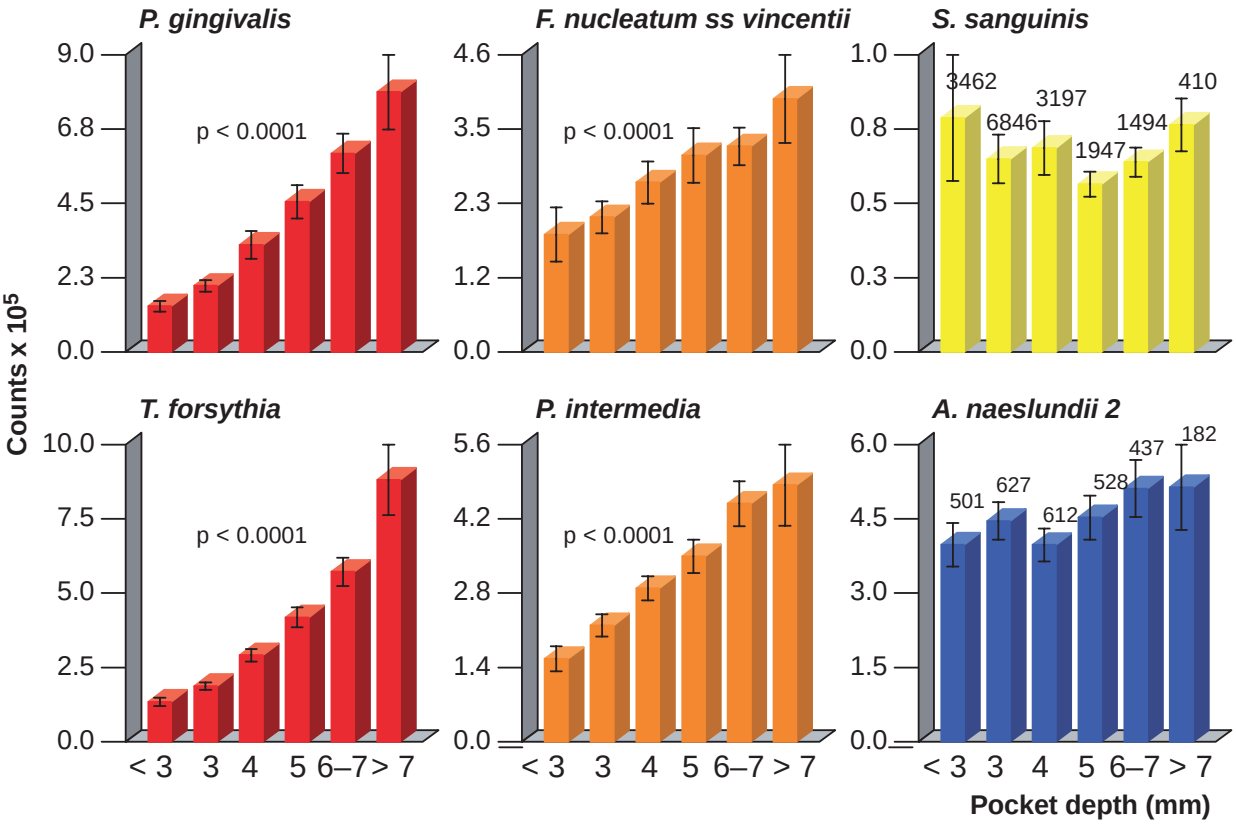

Fig. 9-14 Bar charts of the mean counts (× 10^5, ± SEM) of six subgingival species at selected pocket depths in samples from 635 chronic periodontitis subjects. *T. forsythia* and *P. gingivalis* are representative of the red complex, *F. nucleatum* ss *vincentii* and *Pr. intermedia* are representative of the orange complex species, and *S. sanguinis* and *A. naeslundii* genospecies 2 are typical of other cluster groups. The mean counts of each species at each pocket depth category were computed for each subject and then averaged across subjects. The numbers above the bars in the *S. sanguinis* panel represent the number of sampled sites in each pocket depth category, while the numbers above the bars in the *A. naeslundii* panel represent the number of subjects who provided data for each pocket depth category. Significance of differences among pocket depth categories was tested using the Kruskal-Wallis test and adjusted for 40 comparisons.

differences may have been due to oral hygiene habits, diet, socioeconomic status, genetic background, or transmission among individuals in the community.

Transmission

In planning control of periodontal pathogens, it is essential to clarify their source. If an individual were fortunate enough not to encounter virulent periodontal pathogens, he or she would exhibit minimal periodontal disease even if susceptible. However, most individuals have acquired strains of suspected periodontal pathogens at some time in their lives. For the most part, it appears that subgingival species found in humans are unique to that environment. The subgingival species of the human, by and large, are not commonly encountered in the environment (e.g. soil, air, water) or indeed in the subgingival microbiota of other animal species. Thus, survival of subgingival species in the human requires the transmission of periodontal pathogens from the oral cavity of one individual to the oral cavity of another. Two types of transmission are recognized; "vertical", that is transmission from parent to offspring, and "horizontal", i.e. passage of an organism between individuals outside the parent–offspring relationship.

Evidence for both forms of transmission has been provided using molecular epidemiology techniques. For many of these techniques, the investigator isolates DNA from strains of a given species recovered from different individuals. The DNA is cut with restriction endonucleases, run on agarose gel electrophoresis and the resulting fingerprint patterns compared, either directly, or with the help of various DNA probes. When these techniques were employed on isolates from subgingival plaque, it was demonstrated that *A. actinomycetemcomitans* and *P. gingivalis* strains isolated from parents and children within the same family exhibited identical restriction endonuclease patterns. Different patterns were found for strains isolated from different families (DiRienzo & Slots 1990; Alaluusua *et al*. 1993; Petit *et al*. 1993a,b). In other studies it was found that *A. actinomycetemcomitans* and *P. gingivalis* strains isolated from husband and wife had the same restriction endonuclease patterns or ribotypes indicating that these species could be transmitted within married couples (Saarela *et al*. 1993; van Steenbergen *et al*. 1993).

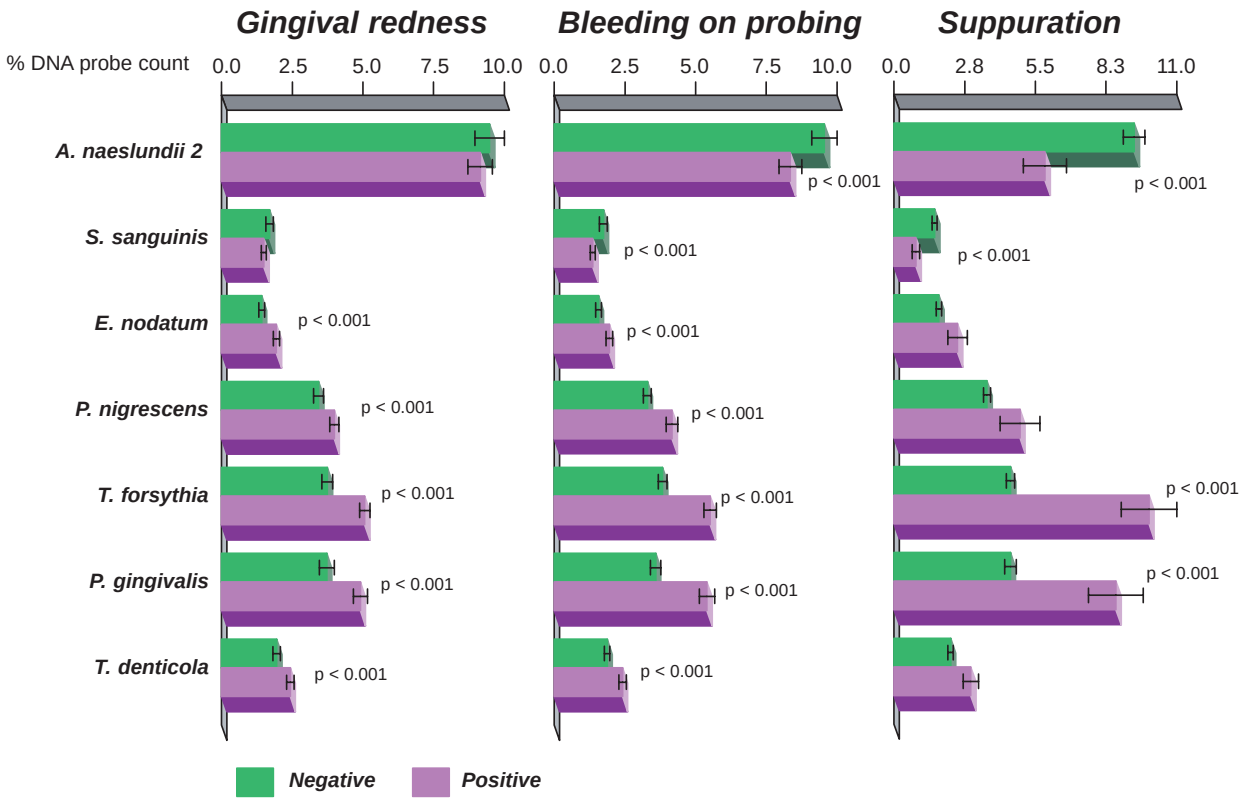

Fig. 9-15 Bar charts of the mean proportions (± SEM) of seven subgingival species at sites positive or negative for gingival redness, BOP and suppuration. *T. forsythia*, *P. gingivalis*, and *T. denticola* are representative of the red complex, *E. nodatum* and *Pr. nigrescens* are representative of the orange complex species, while *A. naeslundii* genospecies 2 and *S. sanguinis* represent other cluster groups. The mean proportions of each species at positive or negative sites for each parameter were computed for each subject and then averaged across subjects. The green bars represent the sites negative for the clinical parameters and the purple bars represent the positive sites. Significance of differences in proportions of species between positive and negative sites was determined using the Wilcoxon signed ranks test and adjusted for 40 comparisons.

The above data should not be surprising in view of the fact that periodontal pathogens have to come from somewhere, and the most likely source would appear to be a family member, whether spouse, sibling or parent. However, while intra-family transmission has been demonstrated, it appears likely that transmission of pathogens also occurs between unrelated individuals. Earlier, the transmission of ANUG was described both within troops in trenches in World War I and in communities outside the war zone after World War I. Another example of transmission between members of different families is provided by the detection of the JP2 clone of *A. actinomycetemcomitans* in individuals of African descent who were located in Africa or had relocated to Europe or the Americas (Kilian *et al*. 2006). Such reports suggest that periodontal pathogens can be transmitted, on occasion, between unrelated individuals. Thus, while there has been an intuitive feeling that the oral microbiota is relatively stable within an individual, it seems likely that new species or different clonal types of the same species can be introduced into an individual at various stages of his or her life. If the newly acquired strain is more virulent than the pre-existing strain of that species, then a change in disease pattern could occur.

Transmission of bacteria is not restricted to passage of strains from one subject to another, but frequently occurs from one type of intraoral biofilm to another. For example, it is thought that a species such as *A. actinomycetemcomitans* may colonize the buccal mucosa long before it can be found in supra- or subgingival biofilms (Fine *et al*. 2006). When a species moves from one oral surface to another, different modes of attachment are employed. For example, for *A. actinomycetemcomitans* a protein adhesin, Aae, may mediate attachment to buccal epithelial cells, while fimbriae and a polysaccharide mediate attachment to tooth surfaces as discussed previously. In a similar fashion streptococcal species, such as *S. mitis*, that are found in high proportions on soft tissue surfaces may be important in dental plaque development on the tooth surfaces from 0–6 hours as described Li *et al*. (2004) and from 1–2 days as described by Socransky and Haffajee (2005). In more mature plaques, these species become a small proportion of the microbiota (Socransky & Haffajee 2005).

There is one more level of intraoral transmission that should be considered and that is the horizontal transfer of genetic material from one bacterial species to another (Roberts & Mullany 2006). This particular mechanism is important not only in providing

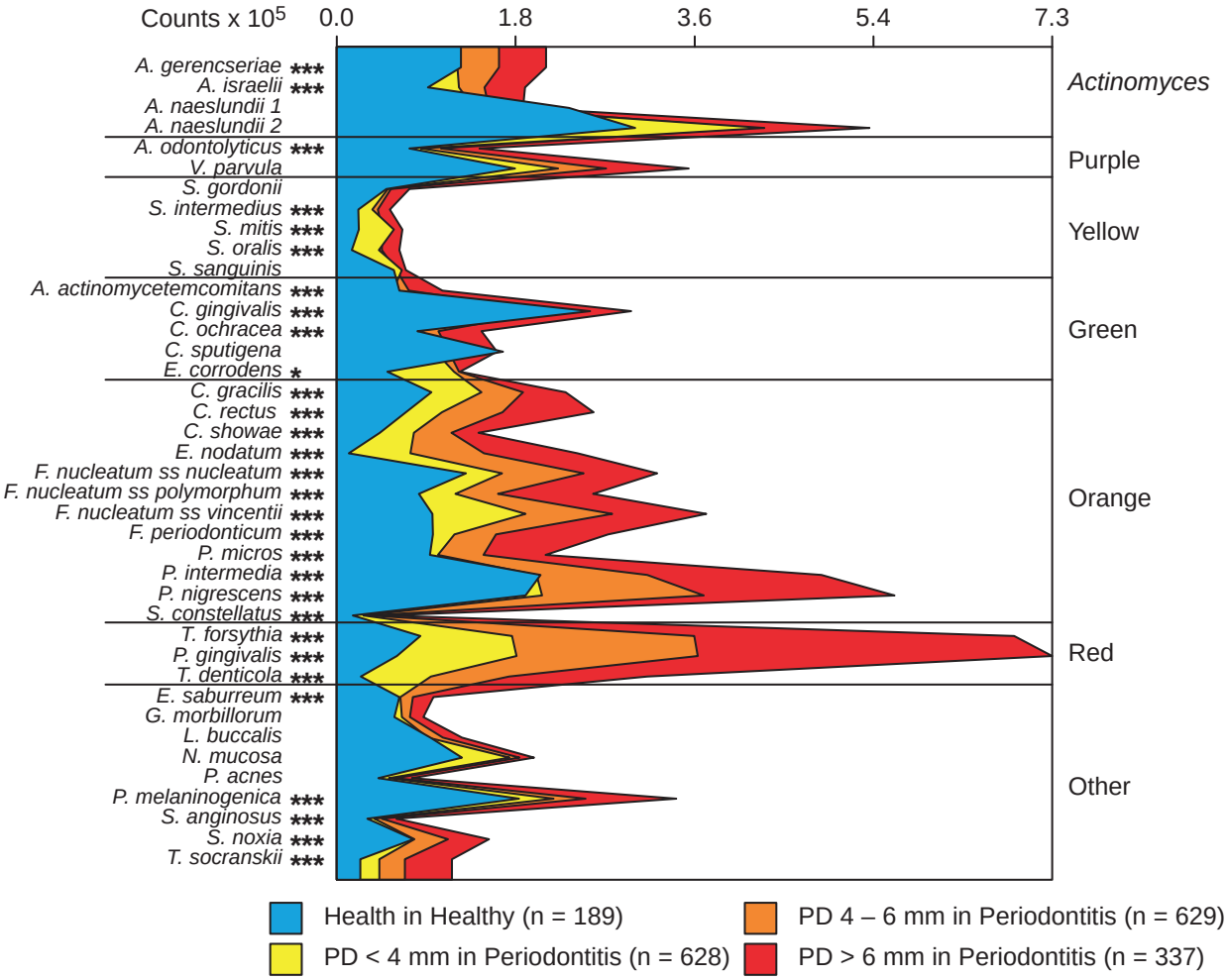

Fig. 9-16 Mean counts ($\times 10^5$) of 40 species in subgingival plaque samples from periodontal pockets/sulci <4, 4–6 and >6 mm in 635 chronic peridontitis subjects and from periodontally healthy sites in 189 periodontally healthy subjects. Subgingival plaque samples were taken at baseline and analyzed for their content of 40 subgingival species using checkerboard DNA–DNA hybridization. Counts of each species were averaged in each subject for each pocket depth category and then averaged across subjects for each category separately. The species were ordered according to microbial complexes (Socransky *et al*. 1998). Significance of differences among pocket depth categories was sought using the Kruskal Wallis test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ after adjusting for multiple comparisons (Socransky *et al*. 1991).

potential virulence traits to a pathogenic species, but also in providing information that codes for factors such as adhesins or mechanisms of antibiotic resistance. Mechanisms of horizontal gene transfer include plasmids, conjugative transposons, bacteriophage, and transformation (for review of horizontal gene transfer within the oral cavity see Roberts and Mullany, 2006).

Microbial composition of supra- and subgingival biofilms

The bacteria associated with periodontal diseases reside within biofilms both above and below the gingival margin. The supragingival biofilm is attached to the tooth surface and is predominated by *Actinomyces* species in most plaque samples. Figure 9-18 provides the counts, proportions, and prevalence (percentage of sites colonized) of 40 taxa grouped according to microbial complexes (Socransky *et al*. 1998) in supragingival plaque samples from periodontally healthy and periodontitis subjects. The *Actinomyces* predominate in both health and disease. Further, all taxa examined could be found (on average) in both health and disease, although counts, proportions, and prevalence (percentage of sites colonized) of periodontal pathogens were significantly higher in the periodontally diseased subjects.

As described above, the nature of subgingival biofilms was more complex with both a tooth-associated and tissue-associated biofilm separated by loosely bound or planktonic cells. Figure 9-12 presented the counts, proportions, and prevalence of 40 taxa in subgingival plaque samples from periodontally diseased and periodontally healthy individuals (Haffajee *et al*. 2006a). Similar to supragingival plaque, the dominant species subgingivally were the *Actinomyces*, but significantly higher counts, proportions, and

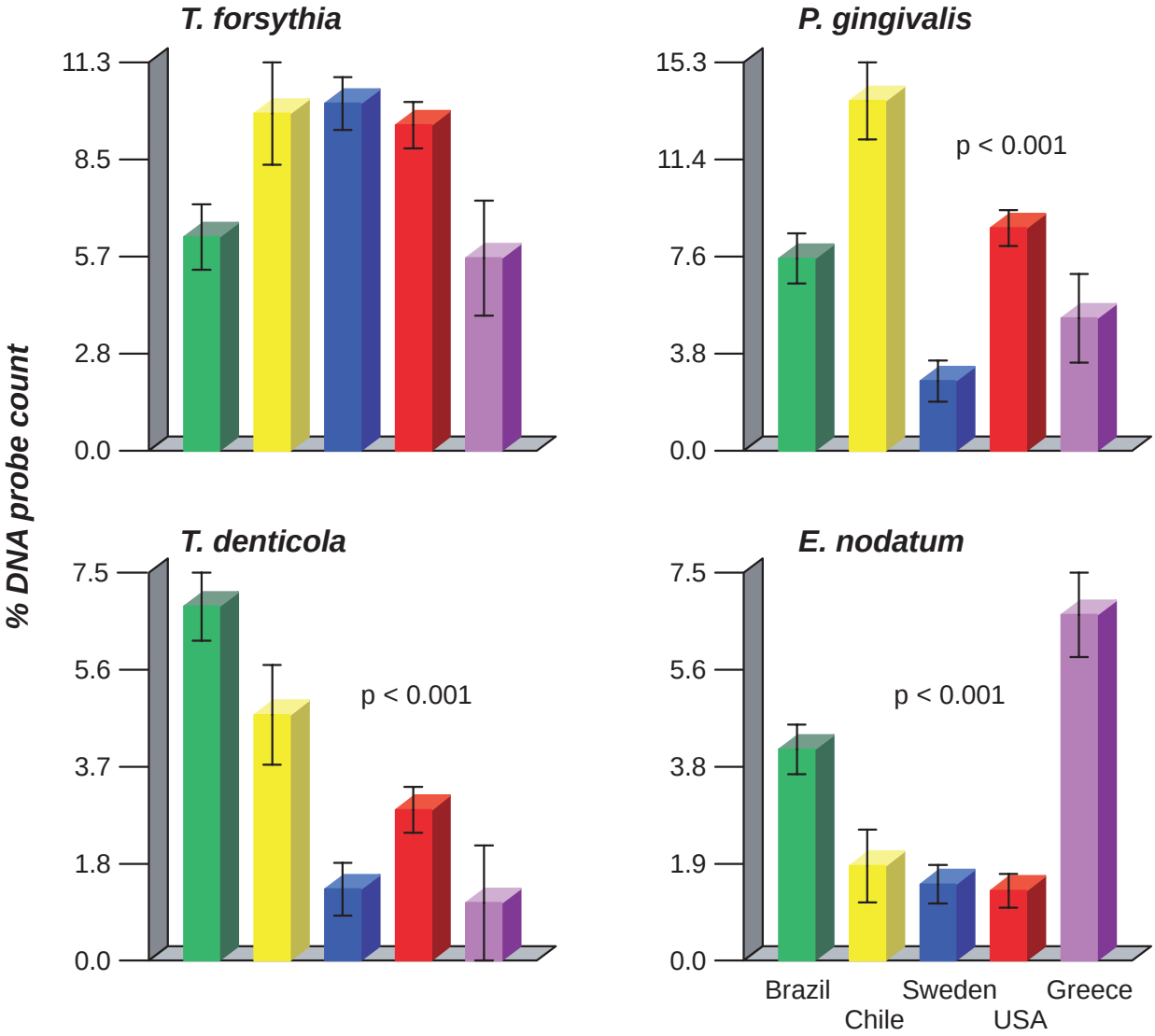

Fig. 9-17 Bar charts of adjusted mean percents (± SEM) of the total DNA probe count of the red complex species, *T. forsythia*, *P. gingivalis*, and *Tr. denticola* and the orange complex species, *E. nodatum*, in baseline subgingival plaque samples taken from the four deepest, sampled periodontal pockets in 58 Brazilian, 26 Chilean, 92 Swedish, 114 American, and 20 Greek chronic periodontitis subjects. The bars represent the mean percents after adjusting for age, mean pocket depth, gender and smoking status. The whiskers indicate the standard error of the mean. Significance of differences among groups for each species was sought using ANCOVA adjusting for age, mean pocket depth, gender and smoking status. The p values were adjusted for 40 comparisons.

prevalence of red and orange complex species were found in the samples from the periodontitis subjects. In particular, there were significantly higher levels, proportions, and prevalence of *P. gingivalis*, *T. forsythia*, and *Tr. denticola* in both supra- and subgingival plaque of periodontitis subjects when compared with similar samples from periodontally healthy individuals. Figure 9-19 summarizes the major differences in microbial complexes between supra- and subgingival plaque in health and periodontitis. As one moves from the supragingival to the subgingival environment and from health to disease, there is a significant decrease in the *Actinomyces* species and an increase in the proportion of members of the red complex.

Development of supra- and subgingival biofilms

Prior to the advent of molecular techniques, few studies had comprehensively examined the microbial shifts that occurred during supra- or subgingival plaque development. Ritz (1967) described the changes that occur in plaque that formed on the labial surfaces of the six upper and six lower anterior teeth from 1–9 days using selective media techniques. The data indicated that streptococci were predominant at 1 day, comprising an average of 46% of the colonies detected. *Neisseria* and *Nocardia* were also high in mean proportions at 1 day but decreased in counts and proportions over time. *Actinomyces* were initially

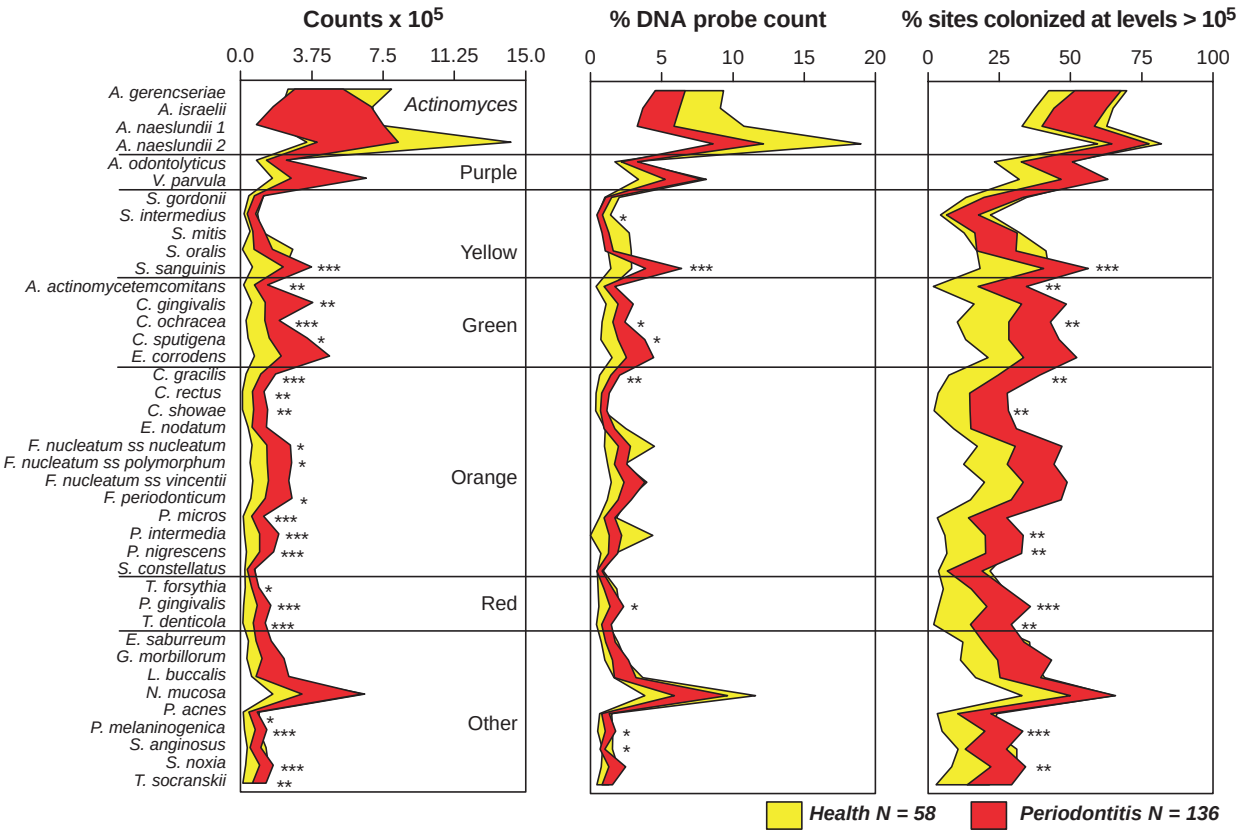

Fig. 9-18 Plots of mean counts (left panel), percents of the total DNA probe count (middle panel) and percentage of sites colonized by 40 bacterial species at counts >10^5 (right panel) in supragingival plaque samples taken from 58 periodontally healthy and 136 chronic periodontitis subjects. The "bands" represent the mean values ± the 95% confidence intervals after adjusting for 40 comparisons. Mean values for each species were computed by averaging up to 28 samples in each subject, and then averaging across subjects in the two clinical groups. Significance of differences between groups was sought using the non-parametric Mann Whitney test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ after adjusting for multiple comparisons. The species were ordered and grouped according to microbial complexes. The yellow profile represents the mean data for the healthy subjects and the red profile represents the data for the periodontitis subjects.

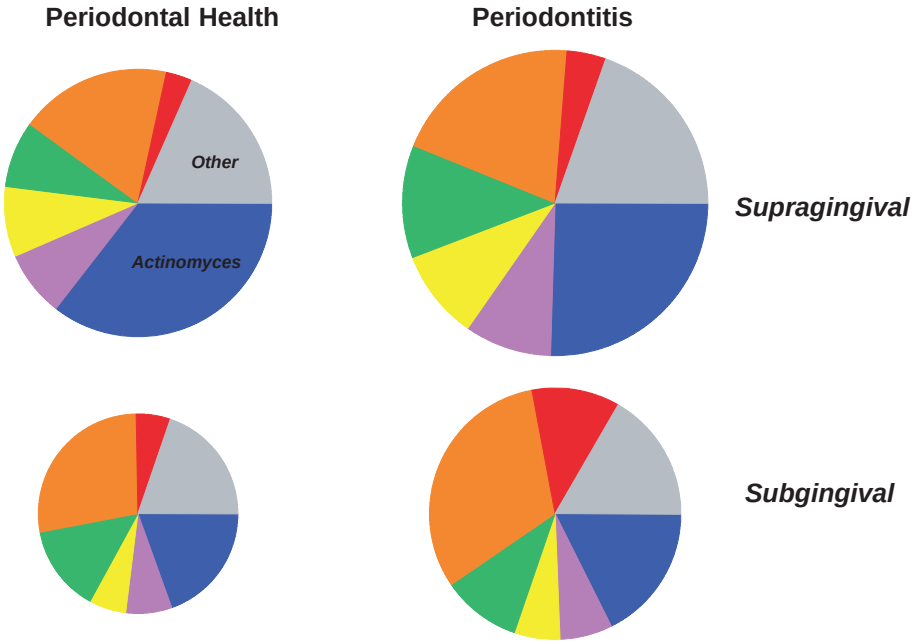

Fig. 9-19 Pie charts of the mean percentage DNA probe count of microbial groups in supragingival plaque samples from 58 periodontally healthy and 136 periodontitis subjects and subgingival plaque samples from 189 periodontally healthy and 635 periodontitis subjects. The species were grouped into seven microbial groups based on the description of Socransky *et al*. (1998). The areas of the pies were adjusted to reflect the mean total DNA probe counts at each of the sample locations. The significance of differences in mean percentages of the supra- and subgingival complexes in health and disease was tested using the Kruskal Wallis test. All complexes differed significantly among groups at $p < 0.001$ after adjusting for seven comparisons. The "other" category represents probes to species that did fall into a complex as well as probes to new species whose relationships with other species has not yet been ascertained.

low in proportion (0.18%) but rose to 23% of the microbiota by 9 days. Ritz (1967) felt that there was microbial succession in plaque development with aerobic or facultative species reducing the environment for the subsequent growth of anaerobic species. In a study of five "rapid" and six "slow" plaque formers, a single plaque sample was taken from each subject at days 1, 3, 7, and 14 and evaluated using cultural techniques (Zee *et al*. 1996). Gram-positive bacteria were the predominant cultivable species in both clinical groups, but Gram-negative species increased in proportion more rapidly in the "rapid" plaque formers. At 14 days, the "rapid" plaque formers had a mean of 38% Gram-negative rods compared with 17% in the 14 day samples from the "slow" plaque formers. The majority of cultivable Gram-negative rods were in the genera *Fusobacterium* and *Capnocytophaga*. Striking in their data was the decrease in proportion of Gram-positive cocci from 50–60% at day 1 to <15% at day 14. This decrease was accompanied by an increase in the proportion of *Actinomyces* species and Gram-negative rods.

The introduction of molecular techniques provided a more comprehensive description of biofilm development. Li *et al*. (2004) used checkerboard DNA–DNA hybridization to examine the early development (0–6 hours) of supragingival biofilm on the buccal/labial surfaces of 20 restoration-free tooth surfaces in 15 subjects. Figure 9-20 presents the mean counts of the 40 test species at 0, 2, 4, and 6 hours. Certain species, such as *S. mitis* and *S. oralis*, appeared to be "pioneer" species in supragingival biofilm development since they were the predominant species at 4 and 6 hours. These findings are in accord with *in vivo* cultural studies that demonstrated the early colonization of enamel and root surfaces using cultural techniques (Nyvad & Kilian 1987). The development of the biofilm in the Li *et al*. (2004) study did not appear to be due to simple adsorption of species from saliva, because the microbial profile of saliva samples from the same subjects differed markedly from the biofilm that developed on the teeth (Fig. 9-20).

The development of supragingival and subgingival biofilm, over a 7-day period, in periodontally healthy and diseased subjects has been described (Socransky & Haffajee 2005). Figure 9-21 presents the total DNA probe counts of supra- and subgingival biofilm samples from chronic periodontitis subjects taken pre and post tooth cleaning and at 1, 2, 4, and 7 days in the absence of home care procedures. There was a marked reduction in supra- and subgingival total counts after tooth cleaning, demonstrating that plaque levels could be significantly reduced even in individuals who performed "reasonable" home care procedures. The total numbers of organisms increased

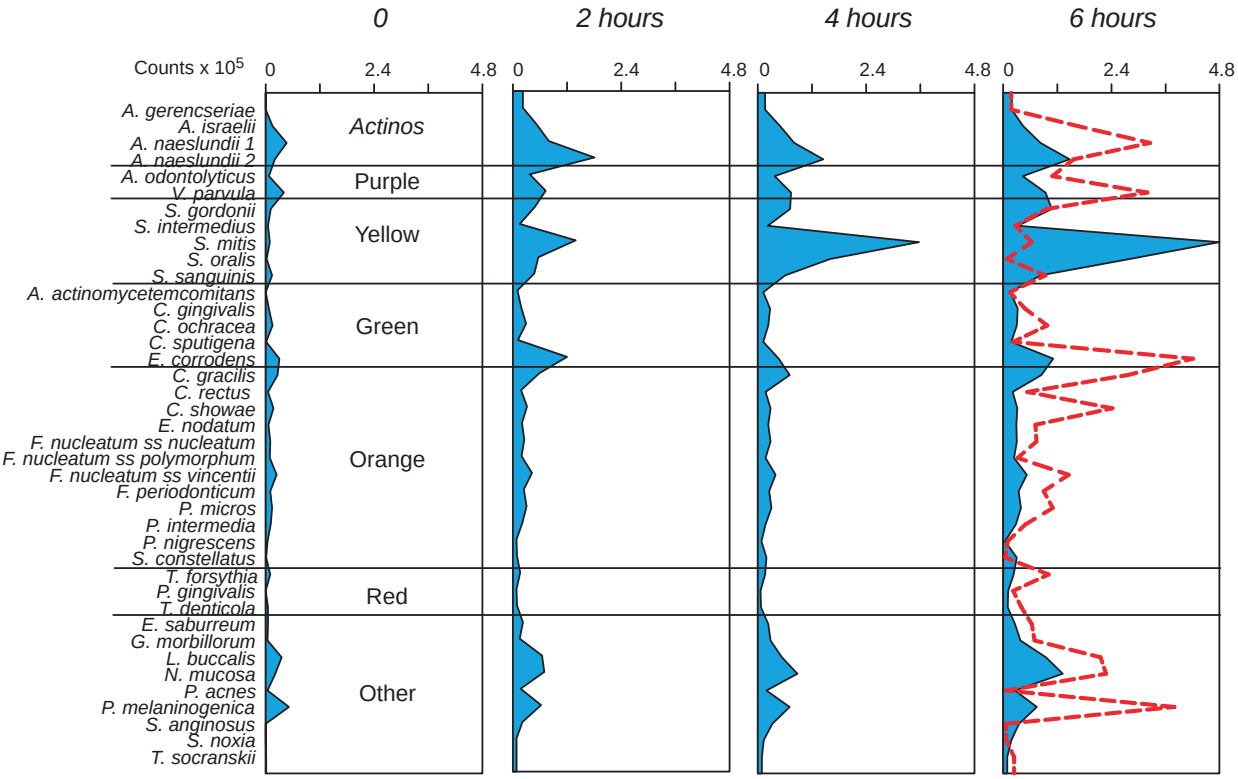

Fig. 9-20 Microbial profiles of the mean counts (× 10^5) of 40 taxa in plaque biofilm samples pooled from at least 20 buccal surfaces immediately post cleaning (0), 2, 4, and 6 hours in 15 subjects. Samples were analyzed for their content of 40 bacterial species using checkerboard DNA–DNA hybridization. Counts of individual species were computed in each subject and then averaged across subjects for each time point. The red dashed profile superimposed on the 6-hour biofilm profile represents the microbial profile of saliva samples from the same subjects taken at baseline. The species are ordered according to the complexes described by Socransky *et al*. (1998). The data were adapted from Li *et al*. (2004).

rapidly, in the absence of oral hygiene, in both the supra- and subgingival areas reaching pre-cleaning levels by 2 days subgingivally and by 4 days supragingivally. These findings were in accord with other studies that demonstrated the rapid return of tooth-associated biofilms after their removal (Sharawy *et al*. 1966; Furuichi *et al*. 1992; Ramberg *et al*. 2003). However, as indicated by the Li *et al*. (2004) study, not all species returned at the same rate.

Figure 9-22 (left panel) presents the mean counts of 4 of 40 tested species in subgingival biofilm samples from chronic periodontitis subjects at the six time points described above. All of the species were reduced in counts after tooth cleaning, but *S. oralis* increased rapidly, exceeding baseline (pre-cleaning) levels at 1–2 days. Levels of *F. nucleatum* ss *nucleatum* and *Pr. intermedia* increased more slowly and exceeded baseline levels at between 2 and 4 and 4 and 7 days respectively. The periodontal pathogen, *P. gingivalis*, had not reached baseline values by 7 days. The shifts in the proportions of the same species are presented in Fig. 9-22 (right panel). Proportions of *S. oralis* increased rapidly by 2 days and then declined, while proportions of the two orange complex species, *F. nucleatum* ss *nucleatum* and *Pr. intermedia*, declined initially and slowly increased over the 7-day period. Proportions of *P. gingivalis* decreased over time and were at their lowest levels at 7 days. These findings are instructive in terms of the role that mechanical debridement plays in controlling periodontal infections. While the total number of bacteria returns rapidly after mechanical debridement, reductions in the proportions of certain species, such as *P. gingivalis* and other members of the red and orange complexes, occur and can be maintained for prolonged periods of time. However, it is important to recognize that pathogenic species are not usually eliminated by this form of therapy and can return to pre-treatment levels in periods varying from weeks to years.

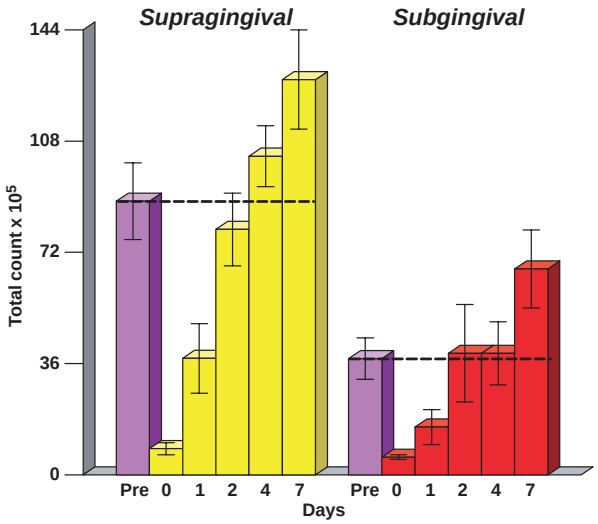

Fig. 9-21 Mean total DNA probe counts (× 10^5, ± SEM) of supra and subgingival plaque samples taken prior to, immediately post-cleaning, and after 1, 2, 4, and 7 days of no oral hygiene in 16 subjects with chronic periodontitis. The dashed horizontal lines are provided to indicate the pre-cleaning levels.

Prerequisites for periodontal disease initiation and progression

It is a common feature of many infectious diseases that a pathogenic species may colonize a host and yet

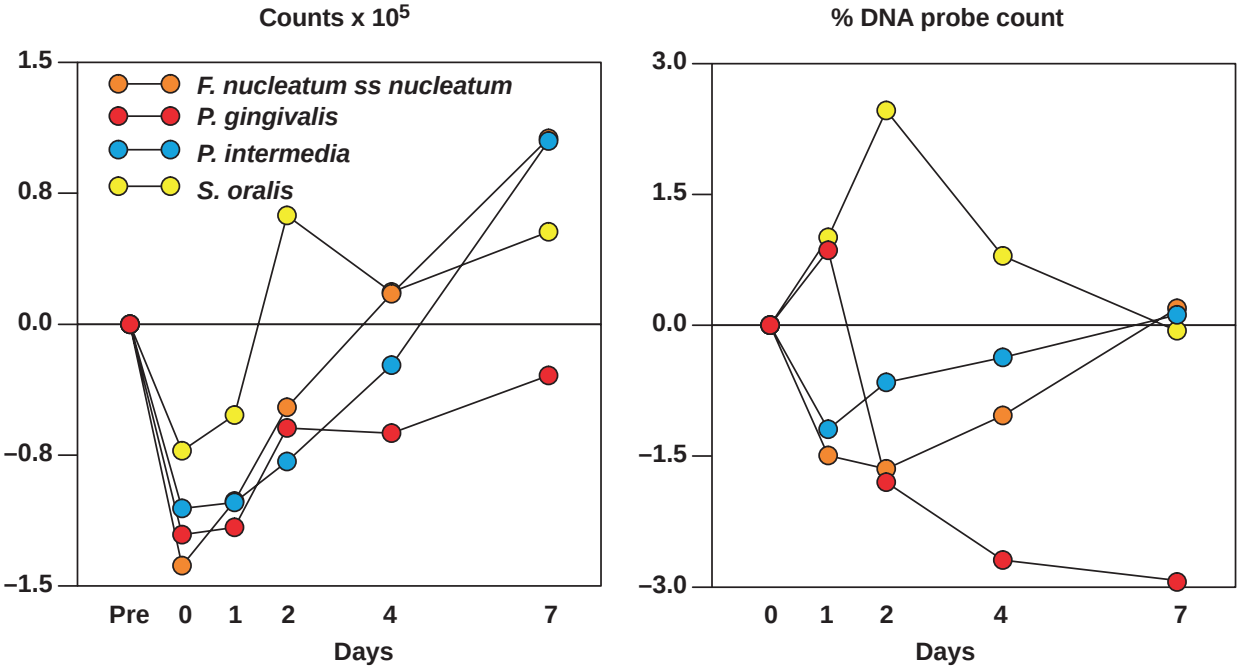

Fig. 9-22 Change in mean counts (× 10^5) (left panel) and percentage of DNA probe count (right panel) of four species in subgingival plaque samples from pre cleaning to immediately post cleaning, and after 1, 2, 4, and 7 days of no oral hygiene in 16 subjects with chronic periodontitis.

the host may not manifest clinical features of that disease for periods of time varying from weeks to decades or ever. Thus, it appears that periodontal disease progression is dependent on the simultaneous occurrence of a number of factors (Socransky & Haffajee 1992, 1993). The host must be susceptible both systemically and locally. The local environment has to contain bacterial species which enhance the infection or at very least do not inhibit the pathogen's activity. The environment also must be conducive to the expression of virulence factors by the pathogen. This might take the form of affecting the regulation of virulence factor expression or stressing the organism so that it manifests properties which lead to tissue damage. The pathogen(s) must achieve sufficient numbers to initiate or cause progression of the infection in that particular individual in the given local environment. Fortunately, the simultaneous occurrence of all these factors does not happen frequently or periodontal disease would be more prevalent and severe in the population.

The virulent periodontal pathogen

Detection of suspected periodontal pathogens in plaque samples from periodontally healthy mouths (Dahlen *et al*. 1989; McNabb *et al*. 1992; Haffajee *et al*. 1998) or healthy sites in periodontally diseased mouths (Socransky *et al*. 1991) raises the question as to whether all strains of a pathogenic species are virulent. A major recognition of the last decade was that all clonal types of a pathogenic species are not equally virulent. For many medically important pathogenic species, a very small proportion of clonal types account for the majority of the disease that is observed (briefly reviewed in Socransky & Haffajee 1991, 1992). The clear association of the virulent JP2 clone of *A. actinomycetemcomitans* in LAP was discusssed above and in greater detail in Fine *et al.* (2006) and Kilian *et al*. (2006). Studies of the pathogenic potential of different strains of *P. gingivalis* in animal model systems support the notion of strain differences in virulence (Grenier & Mayrand 1987a; van Steenbergen *et al*. 1987; Marsh *et al*. 1989; Neiders *et al*. 1989; Sundqvist *et al*. 1991; Baker *et al*. 2000). Certain clonal types of *P. gingivalis* were detected more frequently in samples from periodontitis subjects than control periodontally healthy subjects, suggesting an association of more virulent clonal types with disease (Griffen *et al*. 1999). These studies highlight the fact that there are major differences in virulence of different isolates of *P. gingivalis* and suggest that in some instances when suspected pathogens are found in periodontally healthy sites, the strains may be avirulent. *P. gingivalis fim*A gene encoding fimbrillin, a subunit of fimbriae, has been classified into six genotypes based on their nucleotide sequences. Amano *et al*. (2000) examined the *P. gingivalis fim*A genotypes in dental plaque samples from 380 periodontally healthy adults and 139 periodontitis patients. Type I and type V genotypes were most common in *P. gingivalis*-positive periodontally healthy adults, while type II and type IV were far more common in subjects with periodontitis. Such data suggest that *fim*A genotype may be an important factor influencing the pathogenicity of *P. gingivalis*.

Another requirement for a pathogen to express virulence is that the organism possess all of the necessary genetic elements. Some of these elements might be missing in a strain inhabiting the gingival crevice area, but could be received from other strains of that species (or possibly other species) via phage, plasmids or transposons (Roberts & Mullany 2006). Thus, periodontally healthy sites might be colonized with periodontal pathogens without a full complement of genes needed to lead to tissue destruction.

Finally, the pathogen must be in the right location in a site (e.g. at the apical area of the pocket or adjacent to the epithelium) in sufficient numbers to initiate disease. There are probably minimum numbers of a pathogen needed to initiate disease.

The local environment

If periodontal disease progression is a comparatively infrequent phenomenon, most of the resident species are likely to be host-compatible and in some instances may be actively beneficial to the host. Thus, microbial interactions play a role in the nature of species that colonize a site and ultimately on the outcome health or disease. Some interactions might be harmful, leading to mixed infections as discussed earlier. Others might be more beneficial to the host. Host-compatible species could colonize sites that otherwise would be colonized by pathogens. They might "dilute" the number of pathogens in a pocket, compete for or alter binding sites for pathogens, or destroy virulence factors produced by pathogens (Socransky & Haffajee 1991).

One carefully studied interbacterial antagonism has implications for our understanding of the ecology of destructive periodontal diseases. Hillman and coworkers (1982, 1985, 1987) became interested in the long-term stability of LAP lesions after treatment with surgery and systemic tetracycline. They surmised that a microbiota was established after treatment that was antagonistic to the return of the presumed pathogen *A. actinomycetemcomitans.* This proved to be the case. It was shown that certain species such as *S. sanguinis*, *Streptococcus uberis* and *A. naeslundii* genospecies 2 produced factors that were inhibitory to the growth of *A. actinomycetemcomitans* (Hillman *et al*. 1985). These species were absent or in low numbers in lesion sites of LAP prior to therapy but in elevated numbers after therapy. The mechanism of inhibition was shown to be hydrogen peroxide formation by the "beneficial" species, (Hillman & Socransky 1987) which either directly, or via a host peroxidase system (Tenovuo & Pruitt 1984), inhibited the pathogen. Stevens *et al*. (1987) and

Hammond *et al*. (1987) demonstrated the reverse antagonism. *A. actinomycetemcomitans* was shown to specifically inhibit the growth of *S. sanguinis*, *S. uberis*, and *A. naeslundii* genospecies 2 (but not other species) by the production of a bacteriocin. This mutual antagonism is highly specific and its outcome may strongly influence whether a subject or a site will exhibit disease due to *A. actinomycetemcomitans.* Such interactions demonstrate the potent role resident microbial species play in permitting or preventing the establishment or spread of pathogenic species. The tremendous controlling pressure of the resident microbiota is reinforced by the difficulty encountered when an investigator attempts to implant a human oral isolate into the microbiota of a conventional animal or purposely attempts to implant strains isolated from one human into the subgingival plaque of another.

The local subgingival environment can affect disease pathogenesis in other ways. One of the more intriguing ways centers around the recognition that virulent strains of pathogenic species do not always express their virulence factors (Socransky & Haffajee 1991). Often, a global "regulon" simultaneously turns on or off the production of multiple virulence factors. The regulon is affected by specific factors in the local environment, such as temperature, osmotic pressure, or the concentration of iron, magnesium or calcium. The effect of environment on protein expression has been shown in subgingival species. For example, the level of iron in the environment will affect the expression of outer membrane proteins of *P. gingivalis* and will also affect virulence of the strain in animal model systems (McKee *et al*. 1986, Barua *et al*. 1990, Bramanti & Holt 1990). Even the presence of specific other species might lead to expression of virulence genes by pathogenic species. For example, the production of a surface protein by *Streptococcus cristatus* caused repression of the *P. gingivalis fim*A gene, possibly influencing the development a pathogenic plaque (Xie *et al*. 2000). The effect of environment on virulence factor expression seems a fertile area for investigation. It may help to explain the long lag phase that occurs prior to disease initiation. Conceivably, a pathogen may reside quietly in an area for years as a compatible member of the microbiota. However, some stress generated by a change in the environment might influence that organism to express long-hidden, rather damaging factors.

Host susceptibility

For a period of time considerably longer than the search for microbial etiologic agents of periodontal diseases, dental practitioners have hypothesized that differences in disease pattern or severity may be due to differences in host susceptibility (in earlier years termed resistance). In spite of these hypotheses, it is remarkable how few "host susceptibly factors" have been identified. With increased research in this area and better methods for comparing populations, a number of host or environmental factors have been suggested that may impact on the initiation and rate of progression of periodontal diseases. Such factors include defects in polymorphonuclear leukocyte levels or function, a poorly regulated immunological response, smoking, diet, and various systemic diseases (Genco *et al*. 1986; Bergstrom & Eliasson 1987; Greenspan *et al*. 1989; Williams *et al*. 1990; de Pommereau *et al*. 1992; Greenspan & Greenspan 1993; Seppala *et al*. 1993; Thorstensson & Hugoson 1993).

HIV infection

Debilitating systemic illness can alter the host's ability to cope with infections and may exacerbate existing infections. In early studies, it appeared that periodontal diseases were more prevalent and severe in HIV-positive individuals than in patients who were not infected with HIV (Greenspan *et al*. 1989; Williams *et al*. 1990; Greenspan & Greenspan 1993). In some HIV-positive subjects, unusual necrotic, rapidly destructive periodontal lesions were observed. These observations led to speculation that either unusual pathogenic species were involved or that the modification of host resistance was so severe that it led to extreme tissue destruction. Examination of plaque samples taken from periodontitis sites in HIV-positive individuals indicated that the subgingival microbiota was very similar to that seen in non-HIV-infected periodontitis subjects, except that occasionally unusual organisms were encountered (Murray *et al*. 1989, 1991; Zambon *et al*. 1990; Rams *et al*. 1991; Moore *et al*. 1993). Further, suspected periodontal pathogens, including *P. gingivalis*, *Pr. intermedia*, *F. nucleatum*, and *A. actinomycetemcomitans*, were found more frequently in periodontitis sites in HIV-infected subjects than in either gingivitis or, in particular, healthy sites in these subjects (Murray *et al*. 1989). Rams *et al*. (1991) in a study of 14 HIV-infected individuals with periodontitis found that *A. actinomycetemcomitans*, *C. rectus*, *Pe. micros*, and *Pr. intermedia* each averaged 7–16% of the cultivable microbiota in patients positive for the species. In addition, levels of spirochetes were high, while levels of *Candida albicans* and Gram-negative enteric rods were low. Thus, the microbiota of lesions in HIV-positive individuals was quite similar to that in HIV-negative subjects. However, not all HIV-positive subjects exhibit periodontal disease, and certainly not the extremely rapid form of disease. In addition, patients with the mild or rapid forms of disease are successfully treated using conventional periodontal therapies including local debridement, antiseptic mouthwashes, and local and/or systemically administered antimicrobial agents (Williams *et al*. 1990; Winkler & Robertson 1992; Greenspan & Greenspan 1993).

Diabetes

Another systemic illness which has been associated with increased prevalence and incidence of periodontal disease is diabetes. Many studies (de Pommereau *et al*. 1992; Seppala *et al*. 1993; Thorstensson & Hugoson 1993), but not all (Barnett *et al*. 1984; Rylander *et al*. 1987), indicated that periodontitis is more severe in juvenile or adult diabetic subjects than non-diabetic controls. Microbiologic studies of diabetic subjects have indicated that similar periodontal pathogens were found in diseased sites of diabetic subjects as in non-diabetic periodontal patients. *A. actinomycetemcomitans*, *Capnocytophaga* sp., and "anaerobic vibrios" were found to be elevated in subgingival plaque samples from juvenile diabetic subjects (Mashimo *et al*. 1983), while Sastrowijoto *et al*. (1989) found that *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia* were elevated in diseased sites of adult diabetic subjects. Mandell *et al*. (1992) found that a number of suspected periodontal pathogens were elevated at disease sites in poorly controlled insulin-dependent diabetics, including *Pr. intermedia*, *Pr. melaninogenica*, *C. gracilis*, *E. corrodens*, *F. nucleatum*, and *C. rectus*, when compared with healthy sites in the same subject. Similar species were found in adult periodontitis patients with non-insulin-dependent diabetes. *Pr. intermedia* was the most frequently detected species, while *C. rectus* and *P. gingivalis* were also very common (Zambon *et al*. 1988).

The intriguing aspect of the studies of HIV-positive and diabetic subjects, is that periodontal lesions, for the most part, appeared to be related to already suspected periodontal pathogens and not to some novel species. Studies such as these suggest that altered host susceptibility may change the rate of disease progression in affected individuals, but by and large the periodontal pathogens are likely to be the same as those found in uncompromised subjects.

Smoking

The deleterious effects of cigarette smoking on the periodontium have been reported in numerous studies (briefly reviewed in Haffajee & Socransky 2000). It has been shown that cigarette smokers have more bone loss, attachment loss, deeper periodontal pockets, and less gingival bleeding than non-smokers. As described in an earlier section, suspected or known periodontal pathogens were more prevalent; i.e. colonized a larger proportion of sites, in current smokers than in past or never smokers. On average, this increased extent of colonization was from 10–25%; i.e. three to seven teeth (of 28) in each subject. The species that differed significantly between smokers and non-smokers were primarily species of the red and orange complexes. The increased extent of colonization appeared to occur primarily at shallow periodontal pockets (<4 mm) rather than deeper pockets. The difference in prevalence of these species helps to explain the greater extent of periodontal destruction in smokers than in non-smokers, since more sites are at risk (colonized by potential pathogens) in subjects who smoke. The reason for this difference in colonization pattern is not clear. Cigarette smoke could directly affect the pathogens or their local habitats. Tobacco usage also could affect the host's ability to control the infection by diminishing the local and systemic immune response. Whatever the reason, the widespread colonization of potential pathogens even at clinically healthy sites is likely to lead to future tissue damage at these sites. Further, the greater extent of colonization by periodontal pathogens could complicate periodontal therapy, since elimination or control of species would be more difficult.

Mechanisms of pathogenicity

Essential factors for colonization of a subgingival species

For a periodontal pathogen to cause disease, it is essential that the pathogen be able to (1) colonize the subgingival area and (2) produce factors that either directly damage the host tissue or lead to the host tissue damaging itself. To colonize subgingival sites, a species must be able to (1) attach to one or more of the available surfaces, (2) multiply, (3) compete successfully against other species desiring that habitat, and (4) defend itself from host defense mechanisms.

Adhesins

To establish in a periodontal site, a species must be able to attach to one or more surfaces, including the tooth (or host-derived substances binding to the tooth), the sulcular or pocket epithelium, or other bacterial species attached to these surfaces. Studies of bacterial adhesion have demonstrated specificity in the involved mechanisms. At the simplest level there are one or more specific receptors on the host cell or other surfaces to which specific "adhesin" molecule(s) on the bacterial surface may attach. It has been demonstrated that there is a multiplicity of receptors on tooth surfaces, epithelial or other mammalian cells, and other bacteria. Some of the adhesins that have been identified on subgingival species include fimbriae (Cisar *et al*. 1984; Clark *et al*. 1986; Sandberg *et al*. 1986, 1988; Isogai *et al*. 1988) and cell-associated proteins (Murray *et al*. 1986, 1988; Mangan *et al*. 1989; Weinberg & Holt 1990). Receptors on tissue surfaces include galactosyl residues (Cisar *et al*. 1984; Murray *et al*. 1988; Sandberg *et al*. 1988; Mangan *et al*. 1989), sialic acid residues (Murray *et al*. 1986), proline-rich proteins or statherin (Clark *et al*. 1986), and type I or

IV collagens (Naito & Gibbons 1988; Winkler *et al*. 1988).

Coaggregation

While many species attach directly to host surfaces, other species attach to bacteria attached to such surfaces. This phenomenon is called coaggregation. It has been shown that there is specificity in the attachment of one species to another in *in vitro* systems and *in vivo* (Kaufman & DiRienzo 1989; Kolenbrander *et al*. 2006). In some instances, coaggregation between non-coaggregating species may be mediated by cellular constituents (e.g. vesicles) of a third species (Ellen & Grove 1989; Grenier & Mayrand 1987b). Further, the mechanism of attachment of cells of a given pair of species appears to be mediated by specific receptor–adhesin interactions. Many of these interactions are lectin-like in that they are based on the attachment of a specific protein on the surface of one species to a specific carbohydrate on the surface of the other (Kinder & Holt 1989; Kolenbrander & Andersen 1989; Kolenbrander *et al*. 1989; Abeygunawardana *et al*. 1990), but other mechanisms exist (Kolenbrander & Andersen 1990; Kolenbrander *et al*. 1989). For example, the *S. sanguinis–A. naeslundii* genospecies 2 interaction was shown to be due to the attachment of a fimbrial-associated lectin on *A. naeslundii* genospecies 2 to a polysaccharide with a repeating heptasaccharide on *S. sanguinis* (Abeygunawardana *et al*. 1990). In certain instances more than one type of adhesin–receptor interaction has been detected between a species pair. It is of interest that the same galactose-binding adhesin of *F. nucleatum* to *P. gingivalis* and *A. actinomycetemcomitans* also binds the cell to human epithelial cells and fibroblasts (Weiss *et al*. 2000).

The initial stages of plaque development involves the adhesion of organisms to the tooth surfaces or pellicle proteins on the tooth surfaces. The early colonizers are dominated by members of the genus *Streptococcus* (Fig. 9-20), followed by the *Actinomyces*, the two genera that commonly exhibit intra-generic coaggregation. This intra-generic coaggregation may help to explain the detection of the yellow complex, which is made up of *Streptococcus* species, and the species forming the *Actinomyces* cluster demonstrated in Fig. 9-10. In addition, there are also frequent coaggregations between species of these two genera. If the *Streptococcus–Actinomyces* coaggregations were random, thousands of potential interactions could result. However, only six specific coaggregation groups of streptococci and six coaggregation groups of *Actinomyces* have been detected (Kolenbrander *et al*. 2006). Sequential colonization of different species during plaque development may be mediated in part by coaggregation. This leads to the concept of bridging species; i.e. one or more species that coaggregate with early colonizers and are in turn attached to by late colonizing species. The colonization would be mediated by specific adhesin–receptor interactions between the early colonizers and the bridging species and a second set of receptor–adhesin interactions between the bridging species and late colonizers. Members of the genus *Fusobacterium* appear to be the major bridging species in dental plaque due to their ability to adhere to a very wide range of dental plaque species.

Multiplication

The gingival crevice and/or periodontal pocket might be considered a lush area for microbial growth, but it is in fact a rather stringent environment for a bacterial species to live in. The mean temperature of the area averages about 35°C and ranges from 30–38°C (Haffajee *et al*. 1992), eliminating whole classes of potential colonizing organisms such as thermophiles and psychrophiles. The pH of 7.0–8.5 is rather restricted (Forscher *et al*. 1954; Kleinberg & Hall 1969; Cimasoni 1983), and numerous microbial species find this range unacceptable. Oxidation reduction potential measurements vary from an Eh of about –300 to +310 mv at pH 7.0 (Onisi *et al*. 1960; Kenney & Ash 1969). The wide range of Eh provides suitable microenvironments for numerous bacterial species, although extremes of Eh in a local environment could be limiting to certain species.

The selective physical environment of the gingival crevice area is accompanied by limited nutritional availability. Three sources of nutrient are available to subgingival organisms (diet, host, and other subgingival species). Certain nutrients essential to some bacterial species must be formed by other species in that area. The vitamin K analogues required by certain *Porphyromonas* and *Prevotella* species (Gibbons & Macdonald 1960) and the hydrogen or formate required by *Campylobacter* species are produced by other species colonizing the subgingival ecosystem. However, the precursors to such substances and certain specific growth factors such as hemin (Evans 1951; Gibbons & Macdonald 1960) must be derived from the host. Gingival crevice fluid (GCF) is not particularly rich in nutrients, creating a major competition for the small amounts available. However, inflammation and damage to the host tissues, as a consequence of the colonizing species, lead to an increase in GCF and breakdown products of tissue, fostering the growth of resident species. Finally, nutrients delivered in relative abundance to the outer layers of plaque may not reach deeper layers.

Interbacterial relationships

Bacterial interactions play important roles in species survival. Some inter-species relationships are favorable, in that one species provides growth factors for, or facilitates attachment of, another. Other relationships are antagonistic due to competition for nutrients and binding sites or to the production of

substances which limit or prevent growth of a second species.

A number of types of inter-species interactions have been described. The inter-species agglutinations described above are an important means of bacterial attachment for some species. Bacterial attachment may also be influenced by the production of extracellular enzymes by one set of organisms which uncover binding sites fostering the attachment of a second set of organisms. For example, *S. mitis* and *S. sanguinis* bind in comparable levels to intact epithelial cells, as do strains of *P. gingivalis* and *Pr. intermedia*. However, if epithelial cells are exposed to bacterial neuraminidase the attachment of the streptococci is diminished, but attachment of the *P. gingivalis* and *Pr. intermedia* strains is enhanced (Gibbons 1989). It is suspected that removal of sialic acid reveals galactosyl residues that foster attachment of the suspected pathogens. This mechanism may account for the greater level of such species on cells from periodontal pockets than from healthy sulci (Dzink *et al*. 1989).

Other beneficial interactions are mediated by one species providing growth conditions favorable to another. Such conditions include altered physicochemical parameters such as *Eh* (Socransky *et al*. 1964), *pH* (Kleinberg & Hall 1969), or *temperature* (Haffajee *et al*. 1992). One of the more important environmental parameters is the oxygen level. Subgingival species differ in their ability to grow in the presence or absence of oxygen. Obligate aerobes require oxygen for growth and cannot multiply in its absence. Obligately anaerobic species are killed by even low levels of oxygen, while facultative species can grow in either situation. Dental plaque provides a spectrum of environments with high levels of oxygen available on outer surfaces and adjacent to periodontal tissues, but low levels of oxygen and a low oxidation reduction potential within the plaque. The differences in microenvironments are due in part to location within the periodontal pocket and in part due to the intense reducing abilities of many subgingival species. The survival of some anaerobic species may be due to the presence of facultative or aerobic species that utilize oxygen and/or detoxify its potentially cell damaging activated radicals, such as the hydroxyl radicals. Subgingival species also provide specific growth factors utilized by other species, including branched chain fatty acids and polyamines (Socransky *et al*. 1964), analogues of vitamin K (Gibbons & Macdonald 1960), lactate (Rogosa 1964), formate or hydrogen (Tanner & Socransky 1984).

Colonization of a pathogenic species in the presence of a species that produces substances antagonistic to its survival presents a different challenge to a pathogen. Antagonistic substances vary from those that affect binding (e.g. the enzymes that favored *Pr. intermedia* above probably adversely affected *S. mitis*) to those that kill the species. Factors that kill other species include bacteriocins (Rogers *et al*. 1979; Hammond *et al*. 1987; Stevens *et al*. 1987), hydrogen peroxide (Holmberg & Hallander 1973; Hillman *et al*. 1985), and organic acids (Mashimo *et al*. 1985). These factors may be considered as virulence factors since they suppress the growth of competing species or different clonal types of the same species (Hillman & Socransky 1989). Defense against such factors varies. The simplest way to avoid such factors is to find sites that are not colonized by antagonistic species. A second method is to produce factors that destroy the antagonistic species. For example, *S. sanguinis* produces hydrogen peroxide which inhibits the growth of *A. actinomycetemcomitans* (Hillman *et al*. 1985), while *A. actinomycetemcomitans* produces a bacteriocin that inhibits *S. sanguinis* (Hammond *et al*. 1987; Stevens *et al*. 1987). Thus, the bacteriocin that protects the suspected pathogen *A. actinomycetemcomitans* from the deleterious effect of the more commonly detected *S. sanguinis* must be considered to be a virulence factor.

Overcoming host defense mechanisms

Subgingival plaque microorganisms appear to overgrow and lead to severe disease in immune-compromised hosts particularly those with neutrophil disorders (Genco *et al*. 1986; Shenker 1987; Winkler *et al*. 1989). Such findings suggest that host defense mechanisms are important in limiting the numbers of bacteria in subgingival plaque and preventing tissue damage.

A bacterial species has a number of host-derived obstacles to overcome when colonizing a subgingival site. These include the flow of saliva and gingival crevice fluid and mechanical displacement by chewing and speaking. Substances in saliva and gingival crevice fluid may aid in the prevention of colonization by blocking the binding of bacterial cells to mammalian surfaces. Such factors include specific antibodies, salivary glycoproteins, mucins, and proline-rich proteins which may act as non-specific blocking agents (Gibbons 1984).

Once a bacterial cell has successfully attached to a surface in the subgingival area, other host mechanisms come into play. Desquamation of epithelial cells presents a new cleansing mechanism, which is overcome by certain species by their ability to bind to underlying epithelial cells (Freter 1985). Other species are able to invade the epithelial cells (Finlay & Falkow 1989; Rudney *et al*. 2001, 2005) and may multiply intracellularly and spread to adjacent cells.

Specific antibody in the subgingival area could act by preventing bacterial attachment or, in some instances, by making the bacterial cell susceptible to various phagocytic or killing mechanisms. A number of subgingival species have evolved mechanisms for evading the effect of specific antibody. Species including *P. gingivalis*, *Pr. intermedia*, *Pr. melaninogenica*, and *Capnocytophaga* species possess IgG and IgA proteases that can destroy antibody (Kilian 1981; Saito

et al. 1987; Grenier *et al*. 1989). Other species are capable of evading antibody by changing their surface antigens (Gibbons & Qureshi 1980) or possibly by mimicking the host's antigens (Ellen 1985).

Polymorphonuclear leukocytes affect subgingival species in at least two ways: by phagocytosing and ultimately killing bacterial cells or by releasing their lysosomal enzymes into the crevice or pocket. A number of bacterial mechanisms exist that might counteract these effects, including the production of leukotoxin by *A. actinomycetemcomitans* (Baehni *et al*. 1979) and capsules by *P. gingivalis* and other species that inhibit phagocytosis (Okuda & Takazoe 1988). In addition, a number of species have developed strategies to interfere with the killing mechanisms of the polymorphonuclear leukocytes (Boehringer *et al*. 1986; Seow *et al*. 1987, 1989; Sela *et al*. 1988; Yoneda *et al*. 1990).

If a species enters the underlying connective tissue, it has moved into the area where the host's defense mechanisms are the most formidable. Polymorphonuclear leukocytes and antibodies are joined by macrophages and various types of lymphocytes, completing an awesome array of antagonistic cells and their biologically active substances. To be successful in this area a species would have to have evolved sophisticated mechanisms to evade, hide from or destroy opposition. Some of the periodontal pathogens may have devised such mechanisms. For example, it has been shown that *A. actinomycetemcomitans* leukotoxin affects not only polymorphonuclear leukocytes and monocytes (Baehni *et al*. 1979) but also kills mature T and B lymphocyte cell lines (Simpson *et al*. 1988) or facilitates a non-lethal suppression of immune cells (Rabie *et al*. 1988). Other species such as *Pr. intermedia*, *Porphyromonas endodontalis*, and *Tr. denticola* have been shown to produce substances that suppress immune mechanisms (Shenker *et al*. 1984, Ochiai *et al*. 1989, Shenker & Slots 1989).

Finally, artificial agents, including antiseptics and antibiotics, have been developed that augment the host's natural defense mechanisms against bacterial pathogens. In turn the microorganisms have evolved mechanisms of resistance to these agents and added insult to injury by having the ability to pass these resistance factors to one another, even across species (Guiney & Bouic 1990).

Factors that result in tissue damage

The set of properties that results in a species causing periodontal tissue loss in destructive periodontal diseases is poorly understood. Some or all tissue damage may result from an immunopathologic reaction triggered by a species which is sustained until the species is eliminated or suppressed. However, the fact that disease progression is rare, is associated with specific species, and that inflammation without attachment loss is common, suggest specificity in the properties of organisms that lead to tissue damage. Two general mechanisms of pathogenesis have been hypothesized. The first involves invasion by subgingival species. The second suggests a "long-range" attack where cells of the pathogenic species remain in the pocket but fragments of cells as well as other "virulence factors" enter the underlying periodontal tissues and either directly damage the tissues or cause "immune pathology" (Allenspach-Petrzilka & Guggenheim 1982; Fillery & Pekovic 1982; Gillette & Johnson 1982; Sanavi *et al*. 1985; Saglie *et al*. 1986, 1988; Christersson *et al*. 1987; Liakoni *et al*. 1987; Listgarten 1988). More details on the mechanisms of pathogenesis may be found in Chapter 11.

Invasion

The possibility of invasion in periodontal infections gained credence with the unequivocal demonstration of invasion by a spirochete with an unique ultrastructural morphology during active episodes of acute necrotizing ulcerative gingivitis (Listgarten & Socransky 1964; Listgarten 1965). Other instances of invasion have been reported in tissues obtained from advanced periodontitis (Frank & Voegel 1978; Vitkov *et al*. 2005), LAP (Gillett & Johnson 1982; Christersson *et al*. 1987), and progressing periodontal lesions (Saglie *et al*. 1988).

As discussed earlier, strains of *A. actinomycetemcomitans* and *P. gingivalis* have been shown to be capable of invading epithelial cells derived from human periodontal pockets or gingival sulci. Other studies demonstrated that *T. forsythia* was present in high numbers in preparations of human periodontal pocket epithelial cells and cells of this species could be detected within the epithelial cells. The property of invasion of epithelial cells is a common property of a wide range of mucosal pathogens including members of the genera *Salmonella*, *Shigella*, *Yersinia*, *Escherichia*, and *Listeria*. The mechanisms of attachment to and subsequent entry differ from species to species. It is thought that fimbriae-mediated adhesion may be a prerequisite for bacterial invasion in periodontitis (Vitkov *et al*. 2005). The ability to enter into and survive within human cells confers an advantage to potential pathogens in that they are protected from many of the host's defense mechanisms.

Adherence to underlying tissues, such as basement membrane and various types of collagen, has been demonstrated (Winkler *et al*. 1987, 1988; Naito & Gibbons 1988). Strains of *F. nucleatum* and *P. gingivalis* adhere well to preparations of basement membrane and type IV collagen. *P. gingivalis* also adheres well to type I collagen, a property that may be useful in invasion of deeper tissues.

Deeper invasion may be important in progression of disease and could be facilitated by the property of motility. The flexible, sinuous spirochete has the physical tools to move through amorphous jelly-like

intercellular matrix. If other virulence factors were present, it is likely that spirochetes and other motile forms such as *Selenomonas* and *Campylobacter* would have unique invasive capacities.

Factors that cause tissue damage

The microbial substances that lead to damage of the periodontal tissues are poorly understood, in large part because so many potential "virulence factors" have been described for subgingival species and their roles inadequately evaluated. Virulence factors can be arbitrarily divided into three categories: substances that damage tissue cells (e.g. hydrogen sulphide), substances that cause cells to release biologically active substances (e.g. lipopolysaccharide), and substances that affect the intercellular matrix (e.g. collagenase). There is an unfortunate overlap in this categorization, since some substances elicit more than one response. Further, factors that affect the cells involved in host defense mechanisms may inhibit protective responses and/or lead to the production of substances that can directly damage the tissues.

Some of the suspected virulence factors produced by three periodontal pathogens are summarized in Tables 9-1 to 9-3. Enzymes produced by subgingival species appear to be able to degrade virtually all of the macromolecules found in periodontal tissues. The periodontal pathogen, *P. gingivalis*, produces an unusually wide array of proteases, including those that degrade collagen (Gibbons & Macdonald 1961; Smalley *et al*. 1988; Winkler *et al*. 1988; Jin *et al*. 1989), immunoglobulins (Kilian 1981; Saito *et al*. 1987; Grenier *et al*. 1989), and fibronectin (Wikstrom & Linde 1986; Smalley *et al*. 1988; Lantz *et al*. 1990). Of particular interest are the cysteine proteinases commonly referred to ARG-gingipain and LYS-gingipain which are important to the organism in order to break down proteins to peptides and amino acids necessary for its growth (Abe *et al*. 1998; Genco *et al*. 1999; Kadowaki *et al*. 2000). These proteinases are also important in the processing/maturation of cell surface proteins of *P. gingivalis* such as *fim*A fimbrillin. Other species produce additional or other lytic enzymes. It might be argued that enzymes produced by bacterial species might not be necessary to the pathogenesis of periodontal diseases since similar enzymes can be derived from host tissue. However, if a specific lytic enzyme is essential to disease progression, current data suggest that some subgingival species would form it.

A wide variety of cell preparations or substances have been shown to adversely affect the growth and/or metabolism of mammalian cells in tissue culture. Some of the substances are low molecular weight end-products of metabolism such as hydrogen sulphide, ammonia, fatty acids or indole (Socransky 1970; Singer & Buckner 1981; van Steenbergen *et al*. 1986). Other factors are less defined and are present in the extracellular milieu of bacterial cultures or extracts of the bacterial cells themselves. The importance of this group of inhibitory factors in the pathogenesis of disease is unclear. However, even minor inhibitions of cell metabolism might adversely affect structural integrity of the periodontal tissues.

It has been known for some time that certain bacterial products can induce organ cultures or tissue cells, including cells involved in host defense, to elaborate biologically active substances. One such factor derived from cultured white blood cells was initially described as osteoclast activating factor, since it accelerated bone resorption in tissue culture systems (Horton *et al*. 1972), but was later recognized as interleukin-1β (Dewhirst *et al*. 1985). Production of this factor was shown to be induced in a number of ways including stimulation by bacterial lipopolysaccharides or whole cells (Uchida *et al*. 2001). Numerous other biologically active mediators including prostaglandins, tumor necrosis factor, thymocyte activating factor, IL-8 (Uchida *et al*. 2001), and chemotactic factors have been shown to be formed in response to the addition of bacterial cells or their products to mammalian cells in tissue culture (Bomvan Noorloos *et al*. 1986; Millar *et al*. 1986; Garrison *et al*. 1988; Hanazawa *et al*. 1988; Lindemann 1988; Lindemann *et al*. 1988; Takada *et al*. 1988; Sismey-Durrant *et al*. 1989; Uitto *et al*. 1989). *P. gingivalis* can perturb the cytokine network not only by stimulating the release of cytokines from host cells, but by removing them from its local environment (Fletcher *et al*. 1997).

Virulence determinants in the genomics era

The study of mechanisms of virulence by oral subgingival species has been ongoing for many years and should exhibit a quantum leap due to the sequencing of the genomes of a number of subgingival species. To date, 308 bacterial genomes have been sequenced, 15 of these represent 13 distinct oral species (Duncan 2005; Kolenbrander *et al*. 2006). The knowledge of the sequences can lead to the development of microarrays to monitor gene expression by suspected periodontal pathogens while colonizing or invading oral tissues. Microarrays are already available for *P. gingivalis*, *S. mutans*, *A. actinomycetemcomitans*, *Tr. denticola*, and *F. nucleatum*. The search of the sequence genomes of periodontal species will undoubtedly reveal a large number of potential virulence factors. Unfortunately, it is an expensive and time-consuming process to evaluate whether the proposed factors actually play a role in human disease.

Effect of therapy on subgingival biofilms

There is an axiom in ecology that perturbations of a complex ecosystem are generally followed by a return

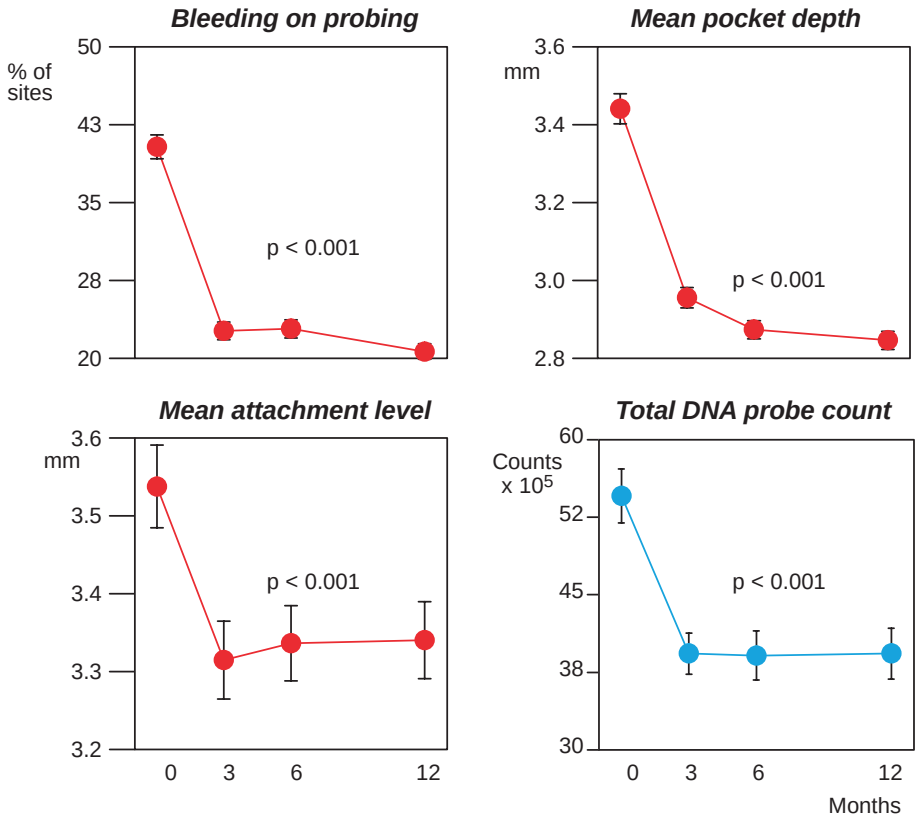

Fig. 9-23 Mean (± SEM) percentage of sites with bleeding on probing, mean pocket depth and attachment level and mean total DNA probe counts at baseline (pre-therapy), and at 3, 6, and 12 months post therapy in 493 chronic periodontitis subjects. The data for each clinical parameter were measured at up to 168 sites in each subject and averaged within a subject and then across subjects at each time point separately. For the microbiological data, mean values were computed by summing the DNA probe counts for each species in up to 28 subgingival plaque samples in each subject, and then averaging across subjects at the four time points separately. The significance of differences over time was determined using the Friedman test.

to an ecosystem of essentially the same composition. Thus, if a clinician alters a complex ecosystem, such as the subgingival biofilm, the expectation of an ecologist would be that, in general, the microbiota would return to a microbiota with a composition similar to that observed pre-therapy. Indeed as discussed earlier, within 4–7 days of biofilm removal by SRP the total numbers of microorganisms at a site had returned to pre-cleaning levels in the absence of home care procedures. Thus, key questions are whether the *composition* of the subgingival biofilm in periodontitis subjects is altered by periodontal therapy to one that is more compatible with health, and if it is, whether the beneficial changes are maintained for prolonged periods of time. Figure 9-23 presents the mean changes in the percentage of sites with bleeding on probing, mean probing pocket depth, and mean clinical attachment level before therapy and at 3, 6, and 12 months post therapy in 493 chronic periodontitis subjects who received different forms of periodontal therapy. All had received SRP and instruction in proper home care and some had received, in addition, periodontal surgery and/or systemically administered antibiotics. The major improvement in the clinical parameters occurred between baseline and 3 months post therapy with little change or modest improvement occurring from 3–12 months. Also depicted in this figure are the changes in mean total DNA probe counts at the same time points. The microbiological changes followed the same pattern as the clinical changes and were characterized by marked reductions in total bacterial counts between baseline and 3 months with minimal change thereafter.

Figure 9-24 presents the change in microbial composition of the subgingival biofilm from baseline to 12 months in the subjects presented in Fig. 9-23. There was a major reduction in the counts, proportions, and percentage of sites colonized at levels $>10^5$ for many of the test species. In particular, species of the red and orange complexes, the species associated with the etiology and pathogenesis of periodontal diseases, were significantly reduced by the various forms of therapy and the reductions were still evident 12 months after therapy. Thus, an improvement in mean clinical parameters was accompanied by a mean reduction in total bacterial counts and specifically reductions in the levels of many periodontal patho-

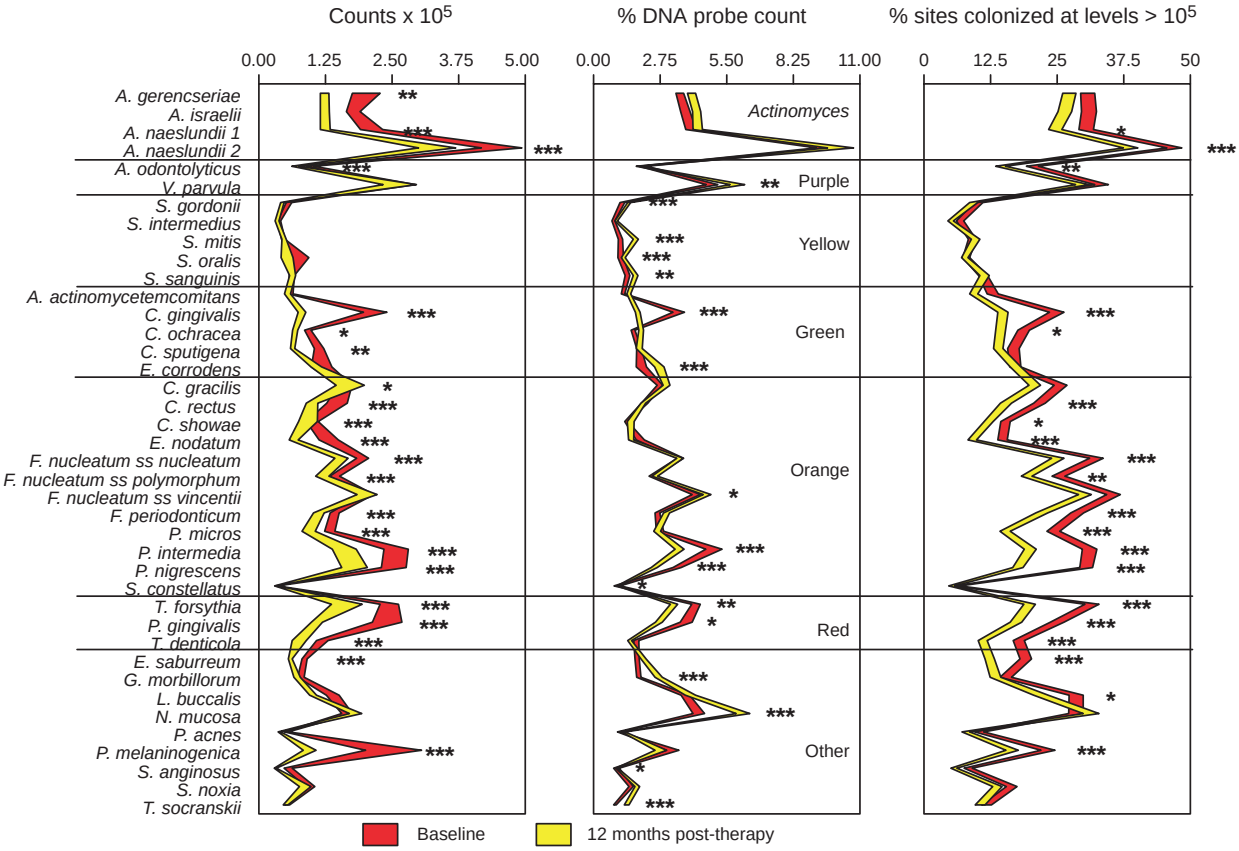

Fig. 9-24 Plots of mean counts (left panel), percents of the total DNA probe count (middle panel) and percentage of sites colonized by 40 bacterial species at counts >10^5 (right panel) in subgingival plaque samples taken from the subjects in Fig. 9-23 at baseline and 12 months post therapy. The "bands" represent the mean values ± SEM. Mean values for each species were computed by averaging up to 28 samples in each subject, and then averaging across subjects at the two time points. Significance of differences between groups was sought using the non-parametric Wilcoxon signed ranks test; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ after adjusting for multiple comparisons (Socransky *et al*. 1991). The species were ordered and grouped according to the complexes described by Socransky *et al*. (1998). The red profiles represent baseline data and the yellow profiles represent data at 12 months. Reprinted with permission from Blackwell Publishing (Haffajee *et al*. 2006b, *Periodontology 2000* **43**, 219–258).

gens. However, not all sites within a subject responded equally well to therapy. Figure 9-25 presents the change in the 40 test species from before therapy to 12 months post therapy at sites that showed improvement in attachment level of >2 mm, sites that showed loss of attachment >2 mm, and sites where the change in attachment level was between these two extremes. There were significant reductions from baseline to 12 months in the mean counts of many of the test species at sites that exhibited change in attachment level ≤2 mm or a "gain" of >2 mm. Not surprisingly the majority of these species were those of the red and orange complexes. In contrast, sites that showed loss of attachment at 12 months post therapy exhibited few changes in the counts of any of the test species, underscoring the association between clinical improvement and reductions in the levels of periodontal pathogens.

As mentioned earlier, not all periodontal therapies work equally well in all subjects, a finding likely related to, among other factors, the nature of the subgingival microbiota prior to therapy. Two systematic reviews have suggested that adjunctive systemically administered antibiotics can provide better clinical outcomes when compared with scaling and root planing only (Herrera *et al*. 2002; Haffajee *et al*. 2003). Figure 9-26 presents the 12-month microbiological findings in subjects who received SRP only (left panel) and those who received different systemically administered antibiotics as adjuncts to SRP (right panel). While, overall, both therapeutic modalities provided clinical improvements and reductions in bacterial counts, subjects receiving the adjunctive antibiotics exhibited a better clinical response as well as more species, particularly those of the red and orange complexes, with significant reductions which were maintained to 12 months post therapy. The reader may wonder why antibiotics have an effect on the composition of the subgingival microbiota, when these species are living in a protected biofilm environment as described earlier in this chapter. Among the possible explanations would be the disruption of the subgingival biofilm by scaling and root planing during or before antibiotic administration, the

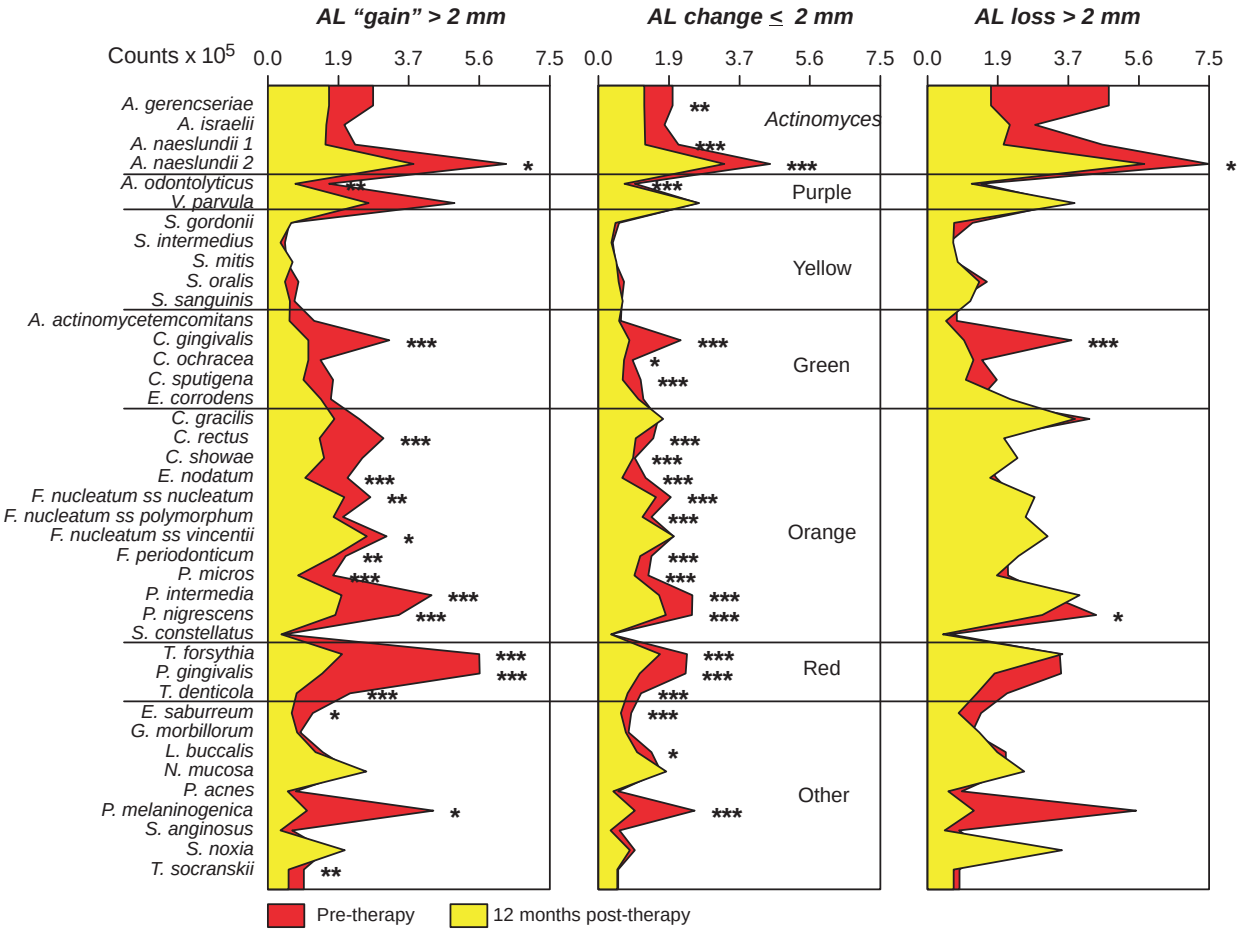

Fig. 9-25 Plots of mean counts ($\times 10^5$) of 40 taxa in subgingival plaque samples at baseline and 12 months at sites that exhibited attachment level "gain" >2 mm, (left panel), change ≤2 mm (middle panel) or loss >2 mm (right panel) from baseline to 12 months. Counts of each species at sites in each of the three attachment level change categories were determined, averaged within a subject, and then averaged across subjects in the three site categories at pre-therapy and 12 months post-therapy separately. Significance of differences between counts at baseline and 12 months was determined using the Wilcoxon signed ranks test and adjusted for multiple comparisons; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Species were ordered according to microbial complexes. The red panels represent the pre-therapy values and the yellow panels represent the 12 months post-therapy values. Reprinted with permission from Blackwell Publishing (Haffajee *et al.* 2006b, *Periodontology 2000* **43**, 219–258).

location of the red and orange complex species adjacent to the epithelial lining of the periodontal pocket (the site of entry of antibiotics into the periodontal pocket), and the possibility that antibiotics may affect pathogens that are located within mammalian tissue cells. Whatever the reason, it is clear that adjunctive systemic antibiotics lowered the levels of periodontal pathogens and improved clinical parameters significantly more than scaling and root planing alone and may be useful in the treatment of some periodontal infections.

Final comment

Infections of any organ system are caused by a relatively finite set of pathogens sometimes working individually or, occasionally, in small mixtures. For example, lung infections may be caused by any of a variety of organisms, including *M. tuberculosis*, *S. pneumoniae*, and *K. pneumoniae*. No single therapy is effective against all lung infections. Each of these infections requires the use of a different chemotherapeutic agent and the selection of the agent is based on the findings of diagnostic tests. The analogy to periodontal infections is clear. There is no single cause of these infections, no one treatment can control all the infections, and the choice of treatment should be guided by the nature of the infecting microbiota. Obviously a great deal of additional research is needed to define precisely the contribution of each periodontal pathogen to periodontal disease progression, to devise tests for their presence and to determine the best therapy for each pathogen's suppression. However, when the most appropriate anti-infective therapy is applied to a given subject or site, disease progression should, at least, be stopped and the potential for long-term periodontal stability should be markedly enhanced.

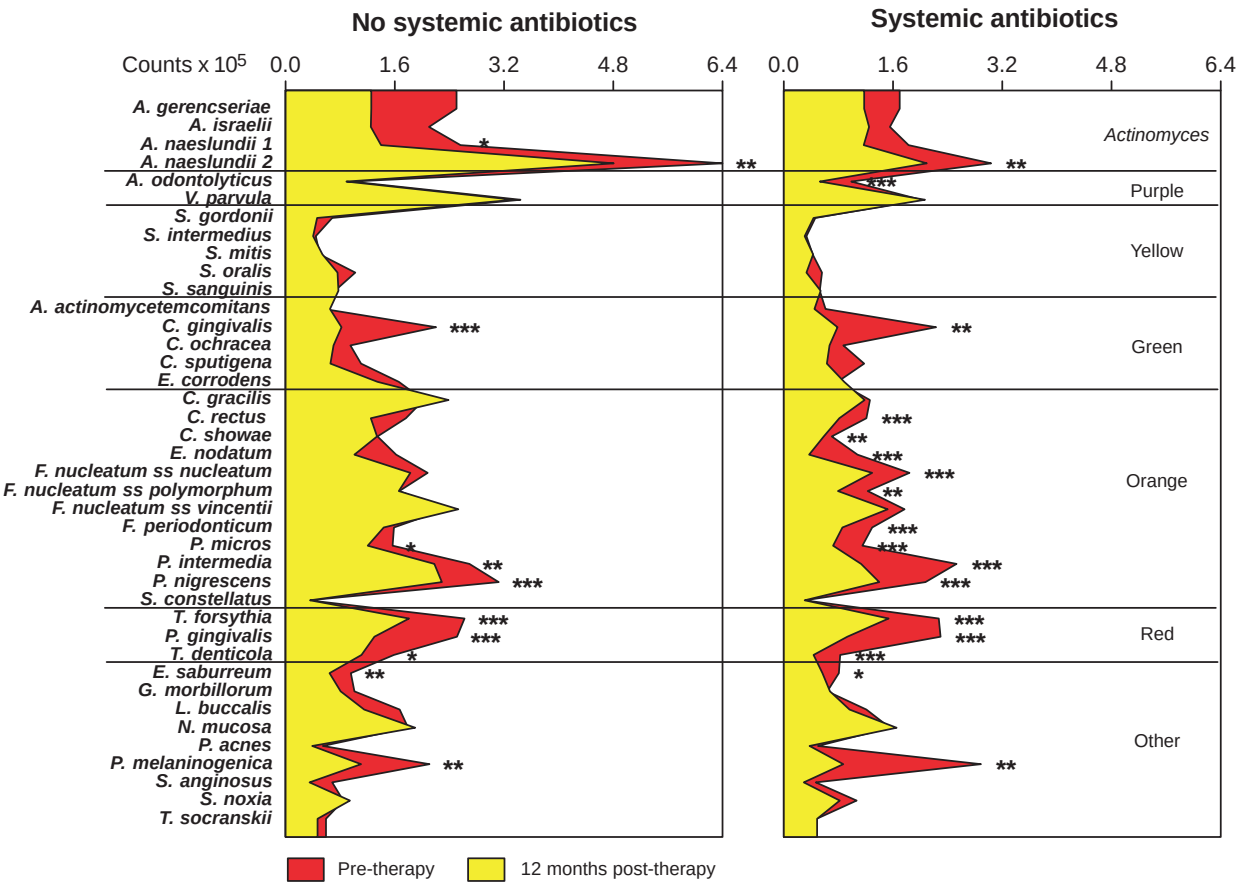

Fig. 9-26 Profiles of mean counts (× 10^5) of 40 taxa in subgingival plaque samples taken pre-therapy and 12 months post-therapy from subjects who did not (left panel) or did receive systemic antibiotics (right panel) as part of their periodontal therapy. Plaque samples were taken from the mesial aspect of each tooth and analyzed separately for their content of 40 species. Data for each species were averaged within in each subject and then across subjects in the two treatment groups for each time point separately. Significance of differences between pre-therapy and 12 months post-therapy was sought using the Wilcoxon test and adjusted for multiple comparisons; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. Species were ordered according to microbial complexes. The red panels represent the pre-therapy values and the yellow panels represent the 12 months post-therapy values. Reprinted with permission from Blackwell Publishing (Haffajee *et al*. 2006b, *Periodontology 2000* **43**, 219–258).

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Chapter 10

Peri-implant Infections

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Introduction

The introduction of dental implants as a procedure to replace natural teeth lost due to dental caries, trauma or periodontal diseases has been a major advance in the management of edentulous and partially edentulous individuals. The insertion of these "new surfaces" also presents a new opportunity for bacterial colonization. One might surmise that the presence of these implant surfaces with different physical properties from teeth might select for bacterial species that are unique to this habitat, leading to a microbiota that may be substantially different from that found on natural teeth. This chapter will examine the nature of the microbiota on implant surfaces in individuals who have clinically healthy implants in the edentulous or in the partially edentulous dentition. After examining the microbiota associated with healthy implants, the nature of the microbiota associated with peri-implantitis will be described.

Early biofilm development on implant surfaces

When an implant is inserted into the oral cavity, it provides a new and physically different surface for the colonization of microorganisms that might already be resident in the oral cavity or enter the oral cavity during biofilm development. The scanning electron micrographs provided in Fig. 10-1 indicate that implant surfaces are readily colonized by a variety of different bacterial morphotypes. The colonization of osseointegrated implants was studied using an immunoblot technique for the detection of antigens to six different species: *Porphyromonas gingivalis*, *Prevotella intermedia*, *Actinomyces naeslundii* genospecies 2 (formerly *Actinomyces viscosus)*, *Fusobacterium nucleatum*, *Treponema socranskii*, and *Treponema denticola* (Koka *et al*. 1993). Supra- and subgingival plaque samples were collected from teeth close to the implants before implant exposure and at

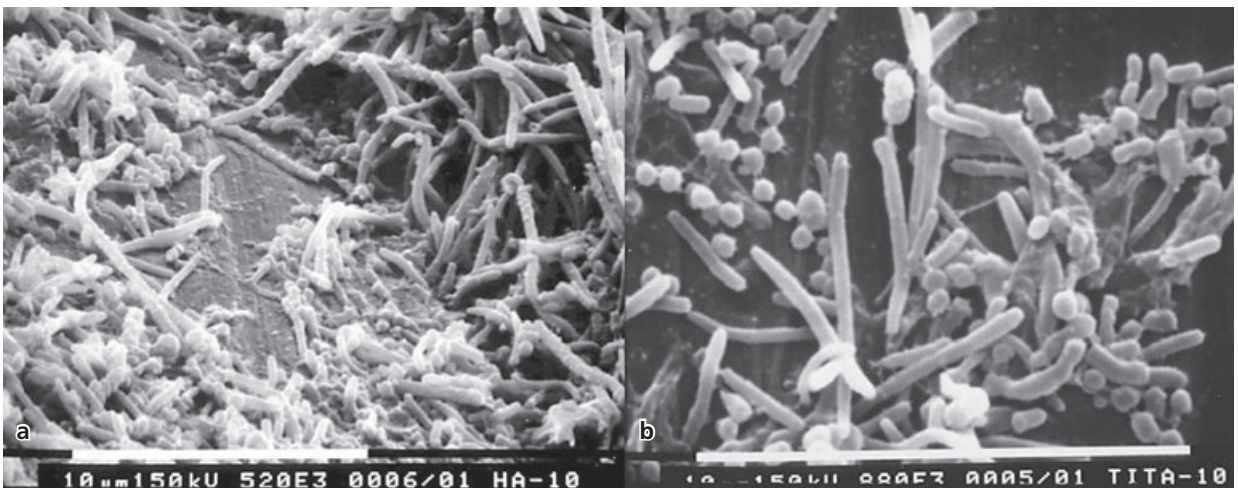

Fig. 10-1 Scanning electron micrographs of the subgingival microbiota on a titanium smooth collar of a hydroxyapatite plasma spray-coated dental implant (a) and on the smooth collar of a titanium dental implant (b). Courtesy of Dr. Charles Cobb.

14 and 28 days after exposure. Samples were taken from the implants 14 and 28 days after the second-stage surgery. The six test species were present in supragingival biofilm samples from the teeth at baseline, but *F. nucleatum* and *Tr. denticola* were not found in subgingival samples at this time point. The frequency of detection on teeth of most of the test species remained constant during the 28 days of observation. *Tr. denticola* was not detected at any time point in subgingival plaque samples from both teeth and implants. All six species were recovered from supragingival plaque samples from implant fixtures after 14 days of exposure, while only *A. naeslundii* genospecies 2 could be detected in the subgingival samples of implants at this time point. After 28 days of implant exposure, all but one species (*Tr. denticola*) could be recovered from subgingival plaque samples of implants. The data suggested that implants in partially edentulous subjects were colonized by periodontal pathogens as early as 14 days after exposure to the oral environment and that establishment of a complex subgingival microbiota occurred as early as 28 days after exposure.

Biofilm development on teeth and implants was also compared during a 3-week study of experimental gingivitis and experimental peri-implant mucositis using phase contrast microscopy (Pontoriero *et al*. 1994). Biofilm samples revealed similar proportions of coccoid cells, motile rods, and spirochetes on both teeth and implants at baseline and after 3 weeks of plaque accumulation. The results were similar to those reported by Löe *et al*. (1965) and Theilade *et al*. (1966) of experimental gingivitis in dentate subjects, in which higher proportions of motile rods and spirochetes and lower proportions of coccoid cells were detected after 3 weeks of plaque accumulation. The authors suggested that plaque accumulated at similar rates on both teeth and implant surfaces.

The development of biofilms on the surface of implants was examined in partially edentulous subjects who required implants (Quirynen *et al*. 2006). Samples were taken from implant and teeth sites using paper points at 2, 4, 12, and 26 weeks after implant exposure and evaluated for their content of 40 bacterial species using checkerboard DNA–DNA hybridization. The mean counts (x 10^5) of the 40 test species evaluated in the samples from the teeth and implant surfaces at the different time points are presented in Fig. 10-2. Higher counts of red and orange complex species (for a description of the microbial complexes, see Chapter 9) were detected on the tooth surfaces at all time points, particularly at 2 weeks. At

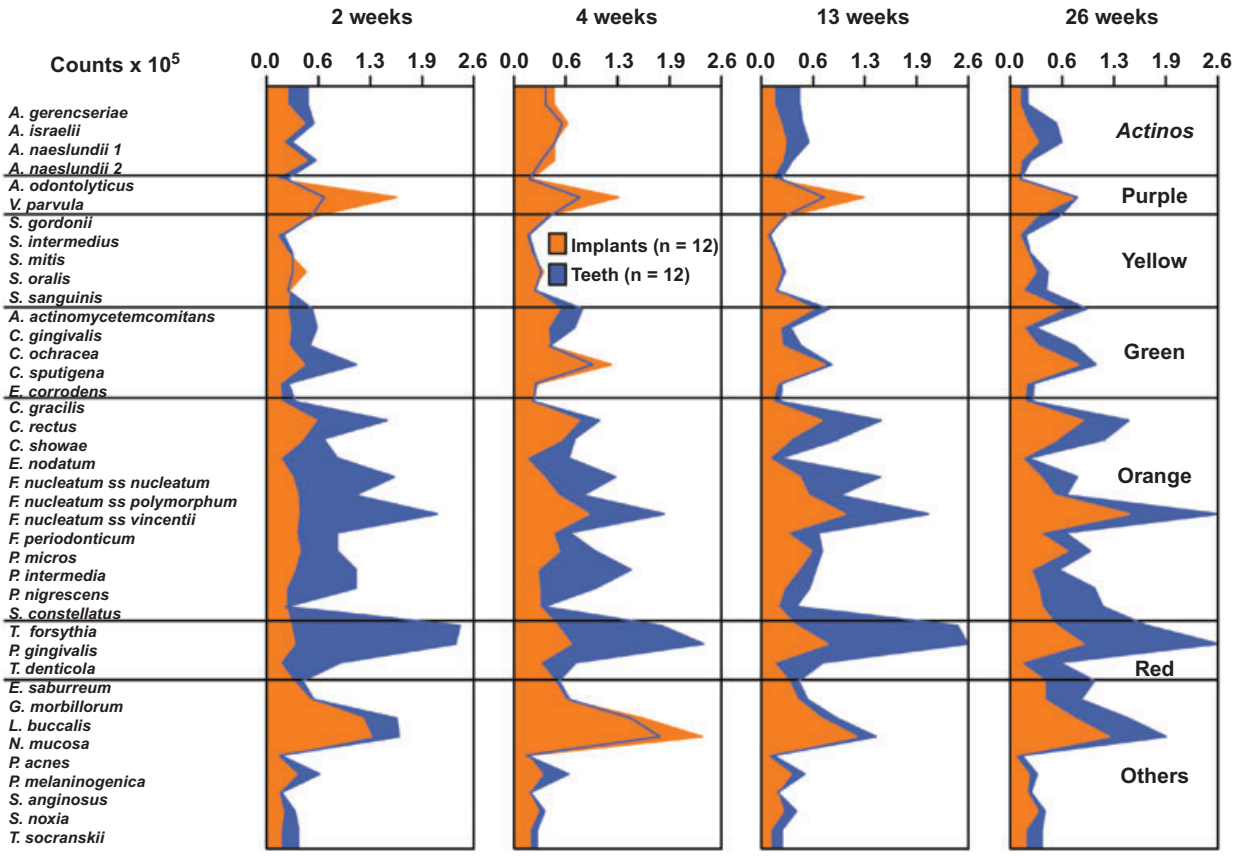

Fig. 10-2 Mean counts (×10^5) of 40 species in samples from 48 implants and 48 teeth in 12 subjects at 2, 4, 13, and 26 weeks after implant exposure. Mean counts of each species were computed by averaging the data for each site category separately in each subject, and then averaging across subjects at each time point separately. Significance of differences between site categories was sought using the Mann Whitney test. No significant differences were found after adjusting for multiple comparisons (Socransky *et al*. 1991). The species were ordered and grouped according to the complexes described by Socransky *et al*. (1998).

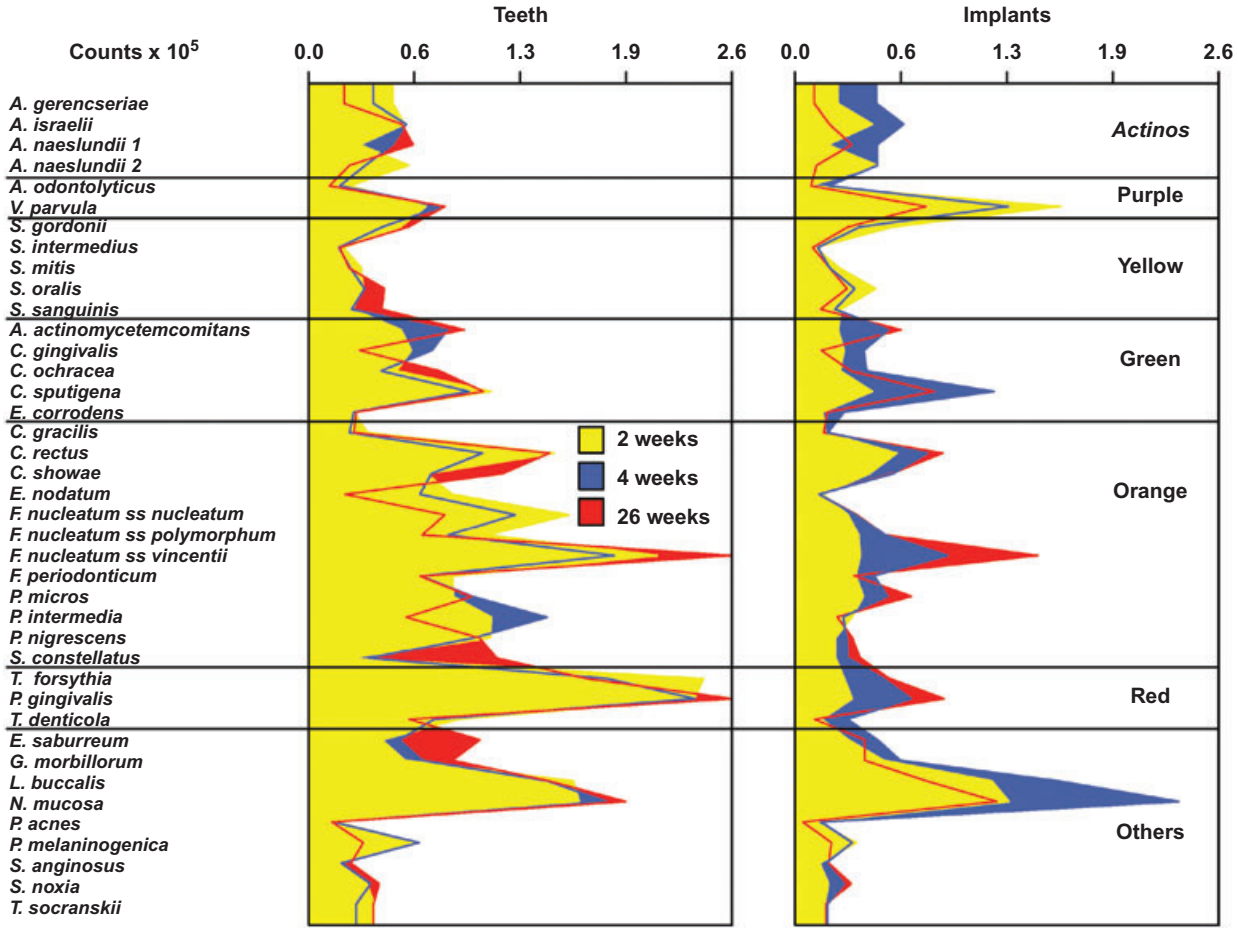

Fig. 10-3 Mean counts ($\times 10^5$) of 40 species at 2, 4, and 26 weeks after implant exposure in samples from 48 teeth (left panel) and 48 implants (right panel) from 12 subjects. Mean counts of each species were computed by averaging the data for each site category separately in each subject, and then averaging across subjects at each time point separately. Significance of differences over time was sought using the Friedman test. No significant differences were detected after adjusting for multiple comparisons (Socransky *et al.* 1991). The species were ordered and grouped according to the complexes described by Socransky *et al.* (1998).

later time points the differences between the different sampled sites were less marked, although red and some orange complex species were still at higher levels in the samples from the teeth. Figure 10-3 presents the mean counts of the 40 test bacteria at tooth (left panel) and implant sites (right panel) at 2, 4, and 26 weeks after implant exposure. There was little change in the mean microbial profiles at the tooth sites over time. However, at the implant sites, there was an increase in counts of certain species including *F. nucleatum* ss *vincentii*, *Peptostreptococcus micros*, *Prevotella nigrescens*, and *P. gingivalis*. Figures 10-2 and 10-3 are interesting because they suggest that species thought to be "early colonizers" on teeth, dentures, and soft tissues (Socransky & Haffajee 2005; Kolenbrander *et al.* 2006), such as *Streptococcus mitis* and *Streptococcus oralis*, appear on implants by 2 weeks and are maintained at their initial levels for periods of 2 to 26 weeks. Other species, such as members of the genus *Fusobacterium*, *Pe. micros*, and *P. gingivalis*, may be detected at early time intervals, but their levels increase more slowly over time. Some species thought to be periodontal pathogens, such as *Eubacterium nodatum* and *Tr. denticola* (Haffajee *et al.* 2006), were initially present in low numbers on implants with little evidence of an increase by 6 months at these clinically healthy implant sites.

The above studies indicated that the early development of biofilms on implant surfaces was similar to that observed on natural teeth and other restorative materials that were placed in the oral cavity. It is likely that in the first step, proteins of saliva may form a pellicle on the surface of the implant providing receptors for the adhesins that occur on oral bacterial species. In this regard, Edgerton *et al.* (1996) examined *in vitro*, experimental salivary pellicles formed on titanium surfaces. Several salivary components previously described in enamel pellicles were also found on titanium, including high-molecular weight mucins, α-amylase, secretory IgA, and proline-rich proteins. However, cystatins and low-molecular weight mucins, commonly found on enamel, were not detected on titanium surfaces. These differences in pellicle composition could result in qualitative differences in early biofilm formation on implants compared to teeth. Data comparing the initial bacterial colonization on titanium, hydroxy-

apatite, and amalgam surfaces suggested that this may not be the case (Leonhardt *et al*. 1995). Biofilm accumulation was examined at 10 minutes and 1, 3, 6, 24, and 72 hours in healthy volunteers who wore intraoral removable splints containing small sections of the three different materials. No significant differences were found in the species colonizing the three surfaces at any time point. It was concluded that although the salivary pellicle that formed on titanium surfaces might differ from that on enamel surfaces, these differences did not seem to influence the bacterial composition of the early biofilms formed on these surfaces.

It has been shown in studies of biofilm development on natural teeth that attachment of bacteria occurred within minutes (Socransky *et al*. 1977) and that increases in specific species could be detected in time periods as short as 2–6 hours (Li *et al*. 2004). It is likely that biofilm development on the implant follows a similar course and that "maturation" is well under way by 2 weeks. Data supporting this conjecture were provided by Quirynen *et al*. (2005b) who examined biofilm development on implant surfaces 1 week after their insertion and showed that there were quite marked differences in the microbiotas on the implants with either shallow or deep pockets compared with the microbiota found in shallow and deep pockets adjacent to the natural teeth. The differences had decreased by 2 weeks and were markedly reduced by 6 months, as shown in Figs. 10-2 and 10-3. It must be pointed out that colonization of a pristine implant surface may be different from that of a previously cleaned tooth. The pristine surfaces of the implant are devoid of an indigenous microbiota and may require initial colonization by early colonizers to set the stage for the subsequent complex community (Kolenbrander *et al*. 2006). The cleaned tooth is likely to have remnants of an attached microbiota (Li *et al*. 2004; Socransky & Haffajee 2005) that can immediately multiply and provide surfaces for attachment of later colonizing species. This may also account for the longer time period required for the biofilm developing on implant surfaces to reach a more complex climax community.

Time of implant exposure and climax community complexity

Studies on early plaque development clearly demonstrated development of multi-species supra- and subgingival biofilms on implant fixtures within weeks of their exposure to the oral cavity (Fig. 10-1). However, microbiological data from fully and partially edentulous subjects suggested that the complete maturation of the implant biofilm might take months, if not years to occur. The microbial changes that took place over time on 68 implants inserted in 22 subjects with a history of advanced aggressive periodontitis were examined by De Boever and De Boever (2006). Microbial samples were collected at various time points after installation of transmucosal implants and processed using DNA probes. The frequency of detection of *P. gingivalis* and *Tannerella forsythia* at levels $>10^5$ increased from 0% of implants at 1 month after insertion to 10% and 4% respectively at the end of the 6-month follow-up (Fig. 10-4).

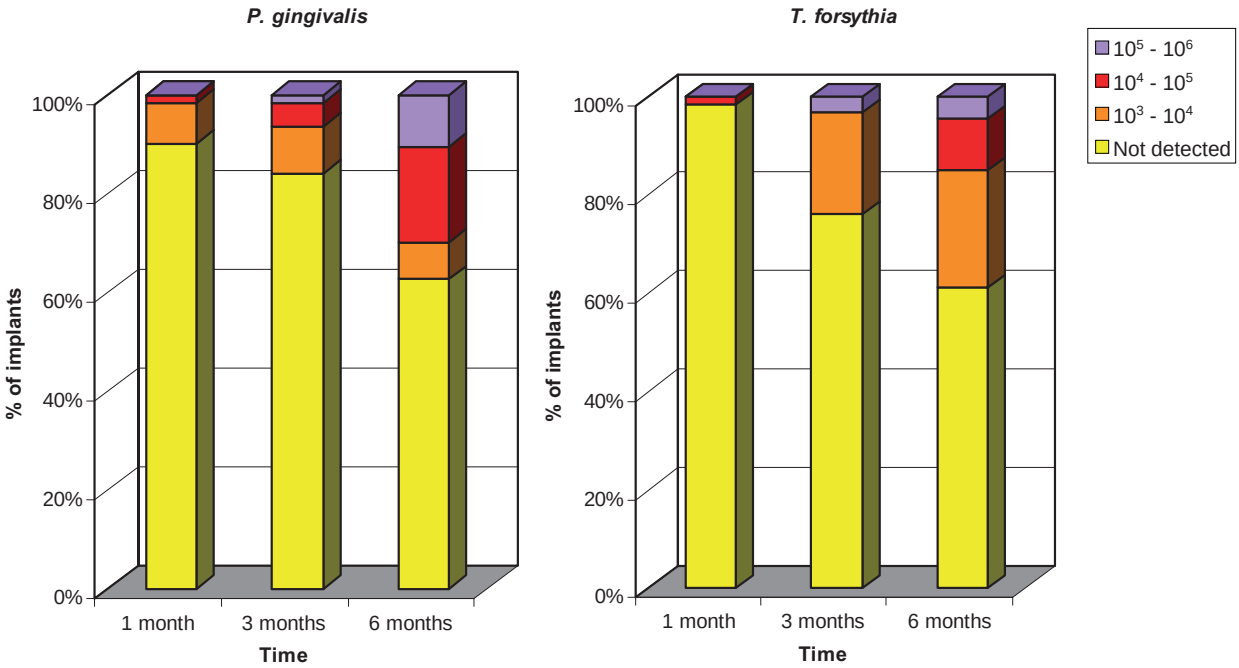

Fig. 10-4 Stacked bar charts of the frequency of detection of *P. gingivalis* (left panel) and *T. forsythia* (right panel) at different levels on 68 implants inserted in 22 advanced aggressive periodontitis subjects at different time points. The bar colors indicate the different levels of detection of *P. gingivalis* and *T. forsythia* using DNA probes. Data adapted from De Boever & De Boever (2006).

The levels of subgingival species over time on implants inserted in subjects with a history of periodontitis were examined using cultural techniques (Leonhardt *et al*. 1993). The mean percentage of total viable counts increased between 2 and 36 months for periodontal pathogens including *P. gingivalis* (0.3% to 1.8%), *Pr. intermedia* (1.1% to 1.9%), and *Aggregatibacter actinomycetemcomitans* (formerly known as *Actinobacillus actinomycetemcomitans*) (0.1% to 1.0%). In a second study, the colonization of implant fixtures over a period of 12 months was examined (van Winkelhoff *et al*. 2000). The percentage of subjects positive for the orange complex species *Pr. intermedia* (60%), *Pe. micros* (90%), and *F. nucleatum* (85%) were already high 1 month after implant exposure, while the red complex species, *T. forsythia*, was detected in 55% of subjects at 6 months.

Microbial colonization on implants that had been in place for up to 5 years was examined using darkfield microscopy in subjects treated for generalized aggressive periodontitis and up to 3 years in subjects treated for chronic periodontitis (Mengel *et al*. 2001; Mengel & Flores-de-Jacoby 2005). A clear increase in the complexity of the subgingival peri-implant microbiota over time was observed, with an increase in the proportions of motile rods, fusiforms, spirochetes, and filaments and a decrease in the proportion of coccoid cells. Interestingly, in the aggressive periodontitis group, there was a marked increase in the proportions of spirochetes, fusiforms, and motile rods between the 4- and 5-year time-points (Fig. 10-5) which was preceded by an increase in mean Gingival Index scores, mean pocket depth, and mean attachment level (Fig. 10-6). This change in the local habitat, in terms of increased inflammation and deeper pockets, may have been responsible for the observed shifts in the peri-implant microbiota.

Indirect evidence of an increase in biofilm complexity over time has been provided by studies comparing the microbiota on implants exposed to the oral environment for different lengths of time. Implants present in the oral cavity for 3–4 years were significantly more frequently colonized by *A. actinomycetemcomitans* and/or *P. gingivalis*/*Pr. intermedia* (44.4% of sites), compared to implants present for only 1–2 years (2.6%) (George *et al*. 1994). The implant microbiota in partially edentulous subjects harbored increased proportions of spirochetes and motile rods at implant sites with longer intraoral exposure times (Papaioannou *et al*. 1995). A statistically significant

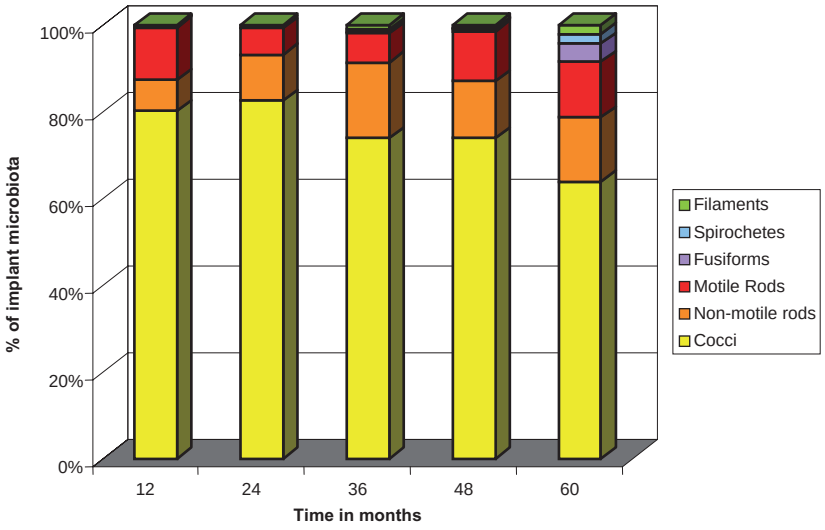

Fig. 10-5 Stacked bar chart of the distribution of bacterial morphotypes on ten implants from five aggressive periodontitis subjects at different time points. The bar colors indicate the percentage of the microbiota comprised by the different morphotypes identified using darkfield microscopy. Data adapted from Mengel *et al*. (2001).

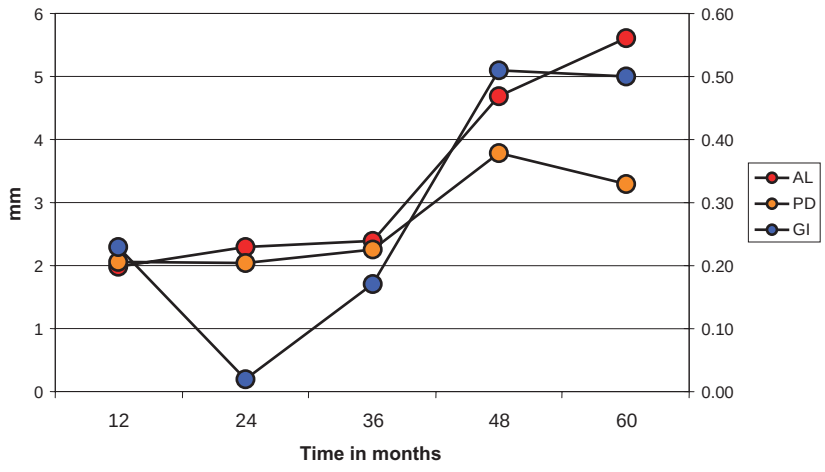

Fig. 10-6 Mean attachment level (AL), pocket depth (PD), and gingival index (GI) values around ten implants from five aggressive periodontitis subjects at different time points. The left Y-axis represents the scale for AL and PD in mm, while the right Y-axis presents the scale for the GI. Data adapted from Mengel *et al*. (2001).

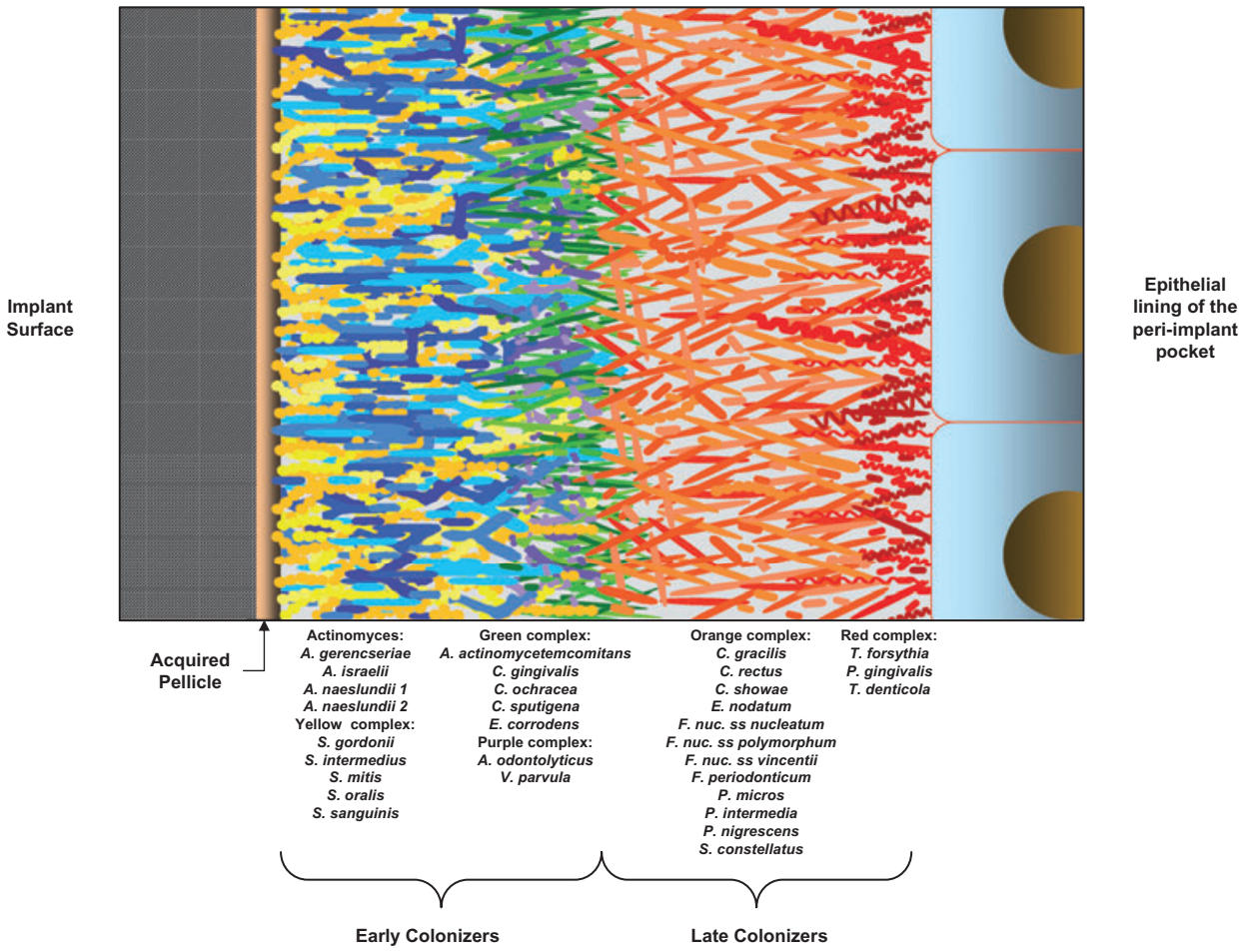

Fig. 10-7 Simplified diagrammatic representation of the microbial succession that may take place subgingivally on a "pristine" implant surface exposed to the oral environment. Microbial species are colored according to the microbial complexes described by Socransky *et al.* (1998).

increase in the proportion of motile rods around implants from 1 year (2.7%) to 2 years (5%) after implant loading has also been reported (Sbordone *et al*. 1999). The sequence of colonization of microbial complexes at implants with different loading times, determined using checkerboard DNA–DNA hybridization, was found to be similar to that described on tooth surfaces (Lee *et al*. 1999a). Levels of yellow and green complex species (early colonizers) were relatively stable at all loading times examined. Orange complex species were detected at lower levels than the streptococci, and their levels appeared to peak 12–24 months after loading. Red complex species were either absent or detected at low levels on implants exposed for only 3 months and only increased at later times. *P. gingivalis* and *T. forsythia* were detected at their highest levels between 7 to 12 months after loading.

Studies on early colonization of "pristine" implant surfaces and on the impact of length of time of implant presence on the composition of the microbiota suggest a pattern and sequence of microbial succession on these surfaces quite similar to the one described for tooth surfaces (Socransky & Haffajee 2005; Kolenbrander *et al*. 2006). A salivary acquired pellicle forms on implant surfaces, providing the binding sites for adhesins on the surface of early colonizers such as members of the yellow complex (streptococci species) and *Actinomyces* spp. Multiplication and coaggregation of these early colonizers will result in a dense accumulation of bacteria attached to the implant surface and/or to each other. A second wave of early colonizers will adhere to the coaggregates attached to the implant surface. These include members of the green and purple complexes, which will, in turn, form their own coaggregates. Members of the orange complex will form a more "loosely attached" mass of microorganisms interspersed between the implant-associated biofilm and the epithelial-associated biofilm, composed in large part by red complex species. Species that participate in multiple coaggregates, such as the fusobacteria, will act as coaggregation bridges between early and late colonizers (Fig. 10-7).

The microbiota on implants in edentulous subjects

Early reports characterizing the microbiota on successful implants in fully edentulous subjects

using darkfield microscopy described coccoid bacteria as the main morphotype, with a low proportion of spirochetes, fusiforms, and motile and curved rods. Results obtained using cultural techniques confirmed these findings and described high levels of Gram-positive facultative cocci, high levels of *Actinomyces* and *Veillonella* spp., low total anaerobic counts, low levels of Gram-negative anaerobic rods, low frequency of *Fusobacterium* spp. and "black-pigmented *Bacteroides*", and no detection of *P. gingivalis* (Mombelli *et al*. 1987, 1988; Mombelli & Mericske-Stern 1990). The levels of *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia* were measured on successful implants exposed to the oral environment for 3–38 months (Ong *et al*. 1992). *P. gingivalis* was not cultured from any sample, while *A. actinomycetemcomitans* was present in only one sample and *Pr. intermedia* was detected in 7/37 sampled sites. These data suggested that the microbiota colonizing clinically healthy implant fixtures in fully edentulous subjects was very similar to the microbiota associated with healthy periodontal sites in periodontally healthy subjects (Socransky & Haffajee 2005).

It was suggested that extraction of all of the teeth resulted in elimination of *P. gingivalis* and *A. actinomycetemcomitans* from the oral microbiota (Danser *et al*. 1994, 1995, 1997). *A. actinomycetemcomitans* and *P. gingivalis* could not be detected in samples from the oral mucosa and saliva 1–3 months after full-mouth extraction, even in subjects where these microorganisms were detected prior to tooth extraction (Danser *et al*. 1994). The prevalence of these pathogens in denture-wearing subjects with a history of periodontitis and an average of 9.3 years of edentulism was also investigated. *A. actinomycetemcomitans* was not detected and *P. gingivalis* was found in only 2/26 subjects in samples obtained from saliva, the oral mucous membranes, and biofilm accumulating on the dentures (Danser *et al*. 1995). These observations implied that the subgingival environment was the primary habitat of these periodontal pathogens and that the intraoral surfaces of edentulous subjects did not constitute a reservoir for these species. Indeed, the same group of investigators did not detect these periodontal pathogens in samples from the oral mucosa or from the peri-implant pockets in edentulous subjects with a past history of periodontitis who had received implants as part of the reconstruction of their dentition (Danser *et al*. 1997). The data suggested that even after the reestablishment of a "subgingival" environment by implant insertion, there was no intraoral reservoir of the two test species to re-colonize the peri-implant sulcus. Other investigators also reported a paucity of periodontal pathogens such as *P. gingivalis* and spirochetes around healthy implants inserted in fully edentulous subjects, even after 5 years in function (Mombelli & Mericske-Stern 1990). However, both *P. gingivalis* and *A. actinomycetemcomitans* were detected in peri-implantitis cases occurring 5 years or more after loading in edentulous subjects (Leonhardt *et al*. 1999).

Later publications using molecular techniques to identify periodontal pathogens in the peri-implant microbiota have indicated a higher prevalence of pathogens around implants in fully edentulous subjects than initially described (Lee *et al*. 1999b; Hultin *et al*. 2002; Quirynen *et al*. 2005a; Devides & Franco 2006). The implant microbiota in fully and partially edentulous subjects was examined using checkerboard DNA–DNA hybridization (Lee *et al*. 1999b). Periodontal pathogens including *P. gingivalis*, *T. forsythia*, and *A. actinomycetemcomitans* could be detected in samples from implants in the edentulous subjects, although less frequently than in samples from implants in partially dentate subjects. In addition, *P. gingivalis*, *Pr. intermedia*, *Pr. nigrescens*, *T. forsythia*, *A. actinomycetemcomitans*, *F. nucleatum*, *Tr. denticola*, *Pe. micros*, and *Streptococcus intermedius* were detected by checkerboard DNA–DNA hybridization in subgingival samples obtained from stable implants in edentulous subjects, although at levels below 10^6 cells (Hultin *et al*. 2002). The microbiota of 37 fully edentulous subjects restored with overdentures or fixed full prostheses for at least 10 years was also examined using checkerboard DNA–DNA hybridization. Pooled subgingival plaque samples were collected from the overdenture subjects and two implants in the canine area in the fixed denture group (Quirynen *et al*. 2005a). The detection frequencies of several periodontal pathogens were higher than previously reported: *A. actinomycetemcomitans* (35/37), *P. gingivalis* (33/37), and *T. forsythia* (10/37). The counts of most species were $<10^5$ cells. However, some subjects showed levels of key pathogens above 10^5 cells: *A. actinomycetemcomitans* (8/37), *P. gingivalis* (29/37), and *T. forsythia* (3/37). Other pathogens such as *Tr. denticola* and *Tr. socranskii* were rarely detected.

The prevalence of *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia* at implant sites in the mandible of fully edentulous subjects was also investigated using polymerase chain reaction (PCR) to detect the species (Devides & Franco 2006). The presence of these pathogens was evaluated before implant insertion, and at 4 and 6 months after restoration of the implants with immediately loaded fixed prostheses. Prior to implant placement, *A. actinomycetemcomitans* and *Pr. intermedia* were detected in 13.3% and 46.7% of subjects respectively, while *P. gingivalis* was not detected. The values for these species at 4 and 6 months after prosthesis insertion were: 60.0% and 73.3%; 46.7% and 53.3%; 46.7% and 53.3%, for *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia*, respectively. The data indicated a higher frequency of detection of periodontal pathogens around implants in fully edentulous subjects than had been described based on cultural techniques and latex agglutination assays, and also suggested an increased colonization of the fixtures over time. These data

were in accord with a study that compared checkerboard DNA–DNA hybridization and culture methods for the detection of 18 subgingival species in samples from teeth and implants from the same subjects (Leonhardt *et al*. 2003). The frequency of detection of all test species in implant samples was lower when culture rather than checkerboard DNA–DNA hybridization was employed. Molecular techniques have also been shown to be more sensitive than culture for the detection of periodontal pathogens in periodontally healthy subjects (Borrell & Papapanou 2005). The use of molecular techniques has demonstrated a greater prevalence of periodontal pathogens at implant sites in fully edentulous subjects than was previously recognized.

The pre- and post-implantation microbiota on implants and the dorsum of the tongue were examined in fully edentulous subjects using checkerboard DNA–DNA hybridization (Lee *et al*. 1999b). The results demonstrated that species such as *Streptococcus sanguinis*, *A. naeslundii*, *Capnocytophaga ochracea*, and *Campylobacter rectus* were infrequently found in peri-implant samples when not present on the dorsum of the tongue. The authors concluded that the tongue may be the source of bacteria initially colonizing implant fixtures and suggested that other soft tissue surfaces might also be reservoirs. The microbiota in the oral cavity of edentulous subjects without implants has been examined using checkerboard DNA–DNA hybridization (Socransky & Haffajee 2005). Periodontal pathogens were detected in samples of saliva and in samples from different intraoral surfaces, such as: dorsum, lateral and ventral surfaces of the tongue; floor of the mouth; hard palate; attached gingiva; buccal mucosa; vestibule and the surface of the dentures. These data suggested that the soft tissues of edentulous subjects harbor periodontal pathogens and are the likely source for colonization of implants after insertion in fully edentulous subjects.

The microbiota on implants in partially edentulous subjects

The literature comparing the microbiota around implants in edentulous subjects with the microbiota in partially edentulous subjects seemed to reinforce the role of the remaining dentition as a major source for colonization of implants by periodontal pathogens. Reported microbiological differences between samples from implants in partially and fully edentulous subjects included a higher percentage and frequency of detection of "black-pigmented *Bacteroides*" (Nakou *et al*. 1987; Apse *et al*. 1989; Hultin *et al*. 1998), fewer coccoid cells and significantly more motile rods and spirochetes (Quirynen & Listgarten 1990; Papaioannou *et al*. 1995), and a higher frequency of detection of *P. gingivalis* and *Pr. intermedia* on implant surfaces in partially edentulous subjects (George *et al*. 1994; Kalykakis *et al*. 1998).

Investigations comparing the peri-implant microbiota with the microbiota of neighboring teeth described several similarities in the composition of the two. For instance, counts of different morphotypes did not differ significantly between subgingival samples from implants and natural teeth in partially edentulous subjects (Quirynen & Listgarten 1990). Similarities in the subgingival microbiota of implants and natural teeth were also found using darkfield microscopy and the benzoyl-DL-arginine-naphthylamide (BANA) test, which detected the presence of trypsin-like enzymes produced primarily by the red complex species (Palmisano *et al*. 1991). The intraoral transmission of bacteria from teeth to implants was investigated in partially edentulous subjects using phase contrast microscopy (Quirynen *et al*. 1996). The results suggested that implants harbored more spirochetes and motile rods when teeth were present in the same jaw and when the pockets around teeth presented a pathogenic microbiota. The microbiota of implants that had been in function for 10 years in partially edentulous subjects was examined using DNA probes (Hultin *et al*. 2000). It was found that there were no significant differences between the microbiota around the natural teeth and fixtures and that the most common species isolated from both surfaces were *Tr. denticola*, *S. intermedius*, and *Pe. micros.* The microbiota of successfully osseointegrated implants in partially edentulous subjects was investigated using checkerboard DNA–DNA hybridization (Lee *et al*. 1999a). *S. intermedius*, *S. oralis*, *S. sanguinis*, *Streptococcus gordonii*, *Veillonella parvula*, *F. nucleatum*, and *Capnocytophaga gingivalis* were the dominant species in biofilms that formed on the fixtures. It was also demonstrated that the microbiota of healthy implants and clinically comparable crowned teeth present in the same subject were quite similar, suggesting that the major influence on the peri-implant microbiota was the microbiota on the remaining teeth.

The studies reporting similarities in the composition of the microbiota on teeth and implants were suggested but did not prove that teeth were the primary source of colonizing microorganisms for implant fixtures. Using pulsed field gel electrophoresis (PFGE), chromosomal DNA segmentation patterns of isolates of *P. gingivalis* and *Pr. intermedia* obtained from implants and natural teeth in the same subjects were compared (Sumida *et al*. 2002). The PFGE patterns of *P. gingivalis* strains isolated from the implant and tooth samples from the same subject were identical, while PFGE patterns differed among samples from different subjects. Similarly, the PFGE patterns of *Pr. intermedia* strains from teeth and implants were identical in two of three subjects examined. In another study using the same methodology, it was found that 75% of the *P gingivalis* isolates in samples from teeth and implants were the same in a subject, while 100% of the *Pr. intermedia* strains within a subject were a perfect match, clearly demonstrating

transmission from the natural teeth to the implant fixtures (Takanashi *et al*. 2004). Unfortunately, PFGE patterns were not examined for the same test species isolated from soft tissues. Although the remaining dentition seems to be the primary source of bacteria for the colonization of implant surfaces in partially edentulous subjects, the potential role of soft tissues surfaces and saliva as reservoirs for implant infection cannot be discarded.

The microbiota on implants in subjects with a history of periodontal disease

Since the remaining dentition has been implicated as a source of microorganisms that colonize implants, it might be surmised that higher levels of periodontal pathogens would colonize implants in subjects with a history of periodontal infection. The early colonization of dental implants in subjects who had been treated for aggressive periodontitis was examined in 22 subjects who were on a maintenance program for periods ranging from 12–240 months (De Boever & De Boever 2006). 68 non-submerged implants were microbiologically sampled at 10 days and 1, 3, and 6 months after implant installation. DNA probes were used to determine the levels of subgingival species such as *A. actinomycetemcomitans*, *P. gingivalis*, *Pr. intermedia*, *T. forsythia*, and *Tr. denticola*. The implants were colonized by all five periodontal pathogens as early as 10 days after implant insertion and an increase in the frequency of detection of most pathogens was observed over time. The number of implants with at least one periodontal pathogen increased from 36 to 66 implants after 6 months in the oral environment. However, some subjects presented with only low levels (10^3–10^4 cells) of these pathogens.

Other studies found that the composition of the microbiota on the implant fixtures in partially edentulous subjects was similar to the subgingival microbiota of the residual teeth, although lower levels of most species were detected on the implants. For example, subgingival plaque samples from teeth and implant fixtures in partially edentulous subjects previously treated for periodontal disease were evaluated for the presence of *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia* using cultural techniques, (Leonhardt *et al*. 1993). The prevalence of subjects positive for the test bacterial species at both teeth and fixtures was similar after 6 months of implant exposure. The composition of the subgingival microbiota around implants and teeth 1 and 2 years after implant loading was examined in 25 subjects who had previously been treated for moderate to severe chronic periodontitis (Sbordone *et al*. 1999). There was an increase in the percentage of motile rods on implants over time and also an increase in the frequency of detection of *A. actinomycetemcomitans* and *P. gingivalis*. Although periodontal pathogens were present at low levels on both teeth and implants (<1% of the total cultivable microbiota), *P. gingivalis* and *Capnocytophaga* spp. were the most frequent isolates around implants at both 1 and 2 years after loading.

Mombelli *et al*. (1995) also examined the colonization of implants placed in partially edentulous subjects previously treated for periodontal disease. Subgingival plaque samples were collected from the deepest residual periodontal pocket of each quadrant in 20 subjects prior to installation of single-stage implants or prior to exposure of two-stage implants in the oral cavity. After 3 and 6 months of exposure of the implant fixtures to the oral environment, the implants and the residual deepest pocket in each quadrant were also sampled. Darkfield microscopy demonstrated that, after 3 months, samples from implants presented a distribution of morphotypes similar to samples from the residual deepest pockets. Further, the composition of the implant microbiota did not change between 3 and 6 months. The frequency of detection of subgingival species identified by cultural methods on implants was similar to the frequency of detection in the deepest residual pocket samples. When *P. gingivalis*, *Pr. intermedia*, and *Fusobacterium* spp. were found in high proportions in baseline samples from the residual deep pockets, they were also found in elevated proportions in the 3-month implant samples. The findings supported the notion that the residual pockets acted as reservoirs for colonization of the implant surfaces. They also suggested that compared with implants in fully edentulous and periodontally healthy subjects, the prevalence of periodontal pathogens on implants was higher in partially dentate periodontitis subjects.

A prospective study was designed to follow the clinical and microbiological outcomes at implants placed in subjects with a history of generalized aggressive and chronic periodontitis (Mengel *et al*. 1996, 2001; Mengel & Flores-de-Jacoby 2005). Fifteen generalized aggressive periodontitis (GAP), 12 generalized chronic periodontitis, and 12 periodontally healthy subjects were monitored for 3 years. Microbiological samples were collected yearly from both implants and teeth and examined using darkfield microscopy and DNA probe analysis for the detection of *A. actinomycetemcomitans*, *P. gingivalis*, and *Pr. intermedia*. The subjects with disease were extensively treated over a period for several years. This reduced the numbers and complexity of the colonizing microbiota on the natural dentition. Thus, after implant placement the microbiota colonizing the implants in samples from the two disease categories and periodontal health were similar in composition and dominated by coccoid cells over a period of 3 years. The clinical results indicated a continuous loss of attachment at both teeth and implants in GAP subjects. These subjects also exhibited the greatest amount of bone loss at teeth and implants. A small subset of five

subjects with GAP was followed for up to 5 years. In these subjects, the microbiota around implants demonstrated a sharp increase in spirochetes, motile rods, filaments, and fusiforms from year 4 to year 5 (Fig. 10-5). Further, the levels of *P. gingivalis* and *Pr. intermedia* increased during the last 3 years of observation. These microbiological changes were preceded by a clear deterioration in the implant clinical parameters between years 3 and 4 (Fig. 10-6). The implant success rate for this subgroup was only 88.8%, compared to a 3-year success rate of 97.9% for the entire sample of 15 subjects.

The microbiota on implants and teeth from subjects with a previous history of periodontitis enrolled in a supportive maintenance program was also examined (Agerbaek *et al*. 2006). A total of 128 peri-implant samples and 1060 subgingival tooth samples were processed using checkerboard DNA–DNA hybridization. Overall, the proportions of the majority of the 40 test subgingival species were similar in implant and tooth samples; only the proportions of the *Actinomyces* spp. and the purple complex species (*V. parvula* and *Actinomyces odontolyticus*) were higher at tooth sites. Taken together, the data indicated that the microbiota colonizing implants in subjects with periodontitis was similar to that observed in the samples from periodontal pockets in the same individuals and harbored more pathogenic species than observed in fully or partially edentulous subjects with minimal or no periodontal disease.

The microbiota of peri-implantitis sites

Marked differences were found in the distribution of different morphotypes in the biofilms of successful implants (n = 10) in subjects with only healthy implants when compared with successful implants (control sites, n = 6) and peri-implantitis sites (test sites, n = 8) in subjects with peri-implantitis (Mombelli *et al*. 1987). Stable implants in healthy subjects were colonized primarily by coccoid cells, while fusiforms and motile rods were present at very low levels and spirochetes were absent. Spirochetes and fusiforms were detected in low proportions in samples from the healthy implants in peri-implantitis subjects. No significant differences could be found in the microbiotas of samples from healthy implants in subjects with or without peri-implantitis. The microbiota at peri-implantitis sites presented much higher levels of motile rods, spirochetes, and fusiforms, while coccoid cells accounted for only 50% of the microbiota (Fig. 10-8). Checkerboard DNA–DNA hybridization was employed to study the microbiota associated with peri-implantitis in 22 subjects with peri-implantitis sites, and eight control subjects with healthy implants (Salcetti *et al*. 1997). Forty subgingival taxa were examined and only four species were found to be positively associated with peri-implantitis versus healthy implants: *Pr. nigrescens*, *Pe. micros*, *F. nucleatum ss vincentii*, and *F. nucleatum ss nucleatum*. Although not statistically significant, there was a trend for a higher prevalence of *P. gingivalis*, *T. forsythia*, and *Tr. denticola* on implants present in subjects with failing implants compared to healthy implants from the control group. The healthy implants in the control subjects also displayed a tendency towards greater detection frequencies of streptococci, especially *S. gordonii* and *S. mitis*, as well as *Pr. intermedia*.

The presence of microorganisms in 18 samples of granulation tissue surgically removed from peri-implant infrabony pockets (>5 mm) from edentulous subjects was examined using cultural techniques

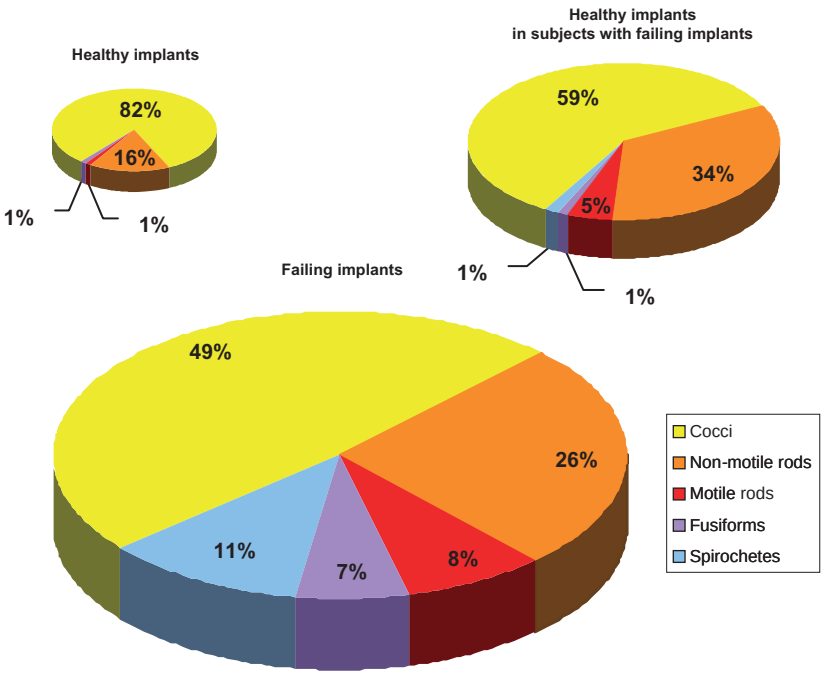

Fig. 10-8 Pie charts of the mean percentage of different morphotypes in the microbiota of samples from ten healthy implant sites in subjects with successful implants only, samples from six healthy implant sites and from eight peri-implantitis sites in subjects with peri-implantitis. The numbers correspond to the mean percentage of each morphotype within the microbiota. The areas of the pies have been adjusted to reflect mean total counts of each site category. Data adapted from Mombelli *et al*. (1987).

(Augthun & Conrads 1997). The species most frequently isolated were: "*Bacteroidaceae*" (16/18), *A. actinomycetemcomitans* (16/18 samples), *F. nucleatum* (4/18), *Capnocytophaga spp* (5/18), and *Eikenella corrodens* (3/18). The microbiota associated with peri-implantitis in 37 subjects with failing implants was compared with the microbiota in 51 subjects with healthy implants (Leonhardt *et al*. 2003). Microbiological samples were analyzed using cultural methods for the occurrence of *Pr. intermedia/nigrescens*, *A. actinomycetemcomitans*, *P. gingivalis*, enterics, yeast, and *Staphylococcus* spp. There were four groups of subjects. None of the test species were detected in the healthy edentulous subjects. In the healthy dentate patient group *Pr. intermedia/nigrescens* was detected in 26% of subjects but *A. actinomycetemcomitans* and *P. gingivalis* were detected in only one subject each. The edentulous peri-implantitis group exhibited *P. gingivalis*, *A. actinomycetemcomitans* and *Pr. intermedia/nigrescens* in 25%, 13%, and 38% of subjects respectively, while 31%, 3%, and 66% of dentate peri-implantitis subjects exhibited these species. *Staphylococcus epidermidis* was found in 17% of the dentate peri-implantitis subjects, enterics were found in 30% of the peri-implantitis group, but in only 8% of the healthy group ($p < 0.001$). *Candida albicans* was isolated in samples from 10% of the dentate peri-implantitis subjects.

The distribution of periodontal pathogens recovered from peri-implantitis sites and teeth with chronic or recurrent periodontitis was examined using microbial samples sent to the Microbiological Testing Laboratory at University of Pennsylvania by different dental practitioners (Listgarten & Lai 1999). Forty-one consecutive samples from subjects with failing implants, chronic periodontitis or recurrent periodontitis were examined using darkfield microscopy and cultural methods for the detection of: *A. actinomycetemcomitans*, *C. rectus*, *Pr. intermedia/nigrescens*, *E. corrodens*, *P. micros*, *Capnocytophaga*, *Fusobacterium* spp., *Staphylococcus aureus*, *Staphylococcus* spp., and yeast. *P. gingivalis* and *T. forsythia* were detected by indirect immunofluorescence. *T. forsythia* was the most frequently detected species and was found in 83% of samples from chronic periodontitis, 85% of recurrent periodontitis samples, and 59% of samples of peri-implantitis sites, although at low levels (1–3% of the total cultivable microbiota). Most bacterial species had a higher frequency of detection and were present in higher levels in samples from teeth than in samples from implants. On the other hand, enteric rods were more prevalent (10% of subjects) and present in higher proportions on implants and in recurrent periodontitis compared with the chronic periodontitis. Yeasts were more prevalent in chronic periodontitis samples than on failing implants and *S. aureus* and *Staphylococcus* spp. were detected infrequently.

Checkerboard DNA–DNA hybridization was employed to examine the levels of 12 microorganisms in subgingival samples obtained from five different categories of sites: (1) peri-implantitis sites in partially edentulous subjects (n = 14); (2) healthy implant sites from the same subjects with peri-implantitis (n = 17); (3) teeth from the same group with peri-implantitis (n = 17); (4) healthy implant sites from partially edentulous (n = 13) and fully edentulous subjects (n = 6) with only healthy implant sites; (5) teeth from subjects with healthy implant sites (n = 13) (Hultin *et al*. 2002). Periodontal pathogens, such as *P. gingivalis*, *Pr. intermedia*, *T. forsythia*, *A. actinomycetemcomitans*, and *Tr. denticola*, were present in samples from all categories of sites, however, species were recovered at levels above 10^6 cells only around failing fixtures. When peri-implantitis sites and healthy sites from the same subjects were compared, peri-implantitis sites had higher levels of *A. actinomycetemcomitans*, *F. nucleatum*, and *Tr. denticola* (Fig. 10-9). Further, *C. rectus* and *S. noxia* were only found around implants in subjects with

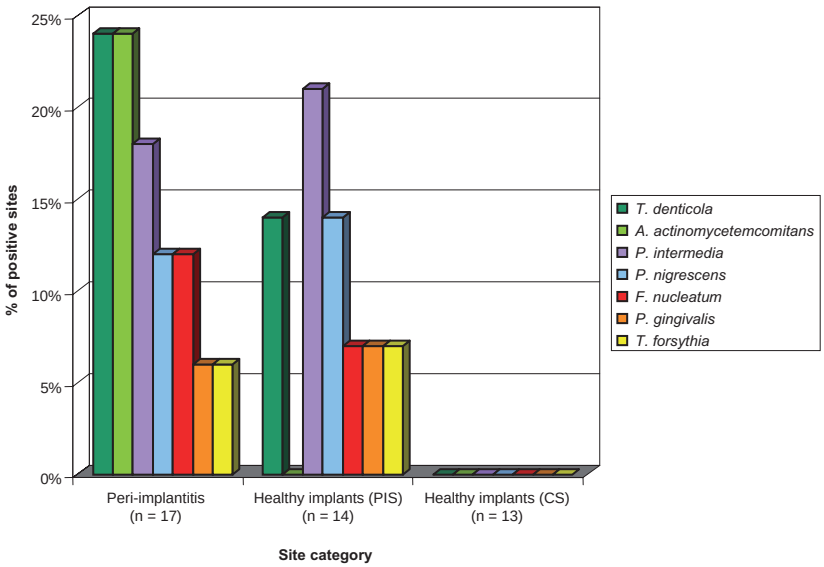

Fig. 10-9 Bar chart of the mean frequency of detection of seven subgingival species in different implant site categories: implants affected by peri-implantitis, healthy implants in subjects with peri-implantitis (PIS) and healthy implants in partially edentulous control subjects (CS). Data adapted from Hultin *et al.* (2002).

peri-implantitis. Using cultural methods, Botero *et al*. (2005) compared the microbiota associated with 16 implants with peri-implantitis in 11 subjects with the microbiota on 15 healthy implants in 8 subjects. All subjects were partially edentulous and the microbiota associated with the remaining teeth in subjects with peri-implantitis was also examined. *P. gingivalis* was detected only in peri-implantitis samples (43.7% of the samples), while peri-implant lesions harbored statistically significantly higher levels of enteric rods and *Pr. intermedia/nigrescens*.

For the most part, the literature on the microbiota of failing implants describes the presence of elevated levels of species previously associated with periodontal infections. Other microorganisms, not commonly implicated as etiological agents of periodontal diseases, have also been recovered from peri-implant lesions, including staphylococci, enteric rods, and yeast, although a causal relationship between these microorganisms and peri-implant infections is premature.

Summary

Although the microbiology of the dental implant in clinically healthy and diseased situations has been studied less intensively than the microbiology of the natural dentition, available data suggest the following:

1. The new "hard tissue" surface presented to the oral environment by the implant provides a surface for the attachment of salivary proteins, peptides, and other substances. These substances rapidly form a pellicle that is probably quite similar to the pellicle formed on natural teeth.
2. The pellicle provides receptors for the adhesins on specific species of oral bacteria that form the early colonizers of the implant. These species appear to be similar to those that colonize the teeth and include members of the genera *Streptococcus*, *Actinomyces*, and *Veillonella*.
3. The insertion of the implant appears to "set the clock back" for the development of the mature biofilm; i.e. for a number of years the microbial composition of biofilms on healthy implants may be similar to that observed on the surfaces of periodontally healthy teeth in the adolescent.
4. With time, varying from months to years, the implant microbiota becomes more complex. Pockets may develop around the implant, which harbor increased numbers and proportions of orange and red complex species in a fashion analogous to the increase in these species in deep periodontal pockets adjacent to natural teeth.
5. The development of peri-implantitis appears to be accompanied in large part by an increase in bacterial species that have been found to increase in periodontitis. These include periodontal pathogens, such as *P. gingivalis*, *T. forsythia*, and *A. actinomycetemcomitans*, as well as additional taxa including staphylococci and enteric rods.
6. The microbiota of implants in partially edentulous subjects who have had periodontitis appears to harbor more periodontal pathogens than the microbiota at implants in partially edentulous subjects without periodontitis and implants in fully edentulous subjects. The presence of these species appears to increase the long-term risk for peri-implantitis in subjects with a history of periodontitis.

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Part 4: Host–Parasite Interactions

Chapter 11

Pathogenesis of Periodontitis

Denis F. Kinane, Tord Berglundh, and Jan Lindhe

Introduction

Inflammatory and immune reactions to microbial plaque are the predominant features of gingivitis and periodontitis. The inflammatory reaction is visible both clinically and microscopically in the affected periodontium.

Inflammatory and immune processes operate in the gingival tissues to protect against local microbial attack and prevent microorganisms or their damaging products from spreading into or invading the tissues. These host defense reactions are, however, also considered potentially harmful to the host in that inflammation can damage surrounding cells and connective tissue structures. Furthermore, inflammatory and immune reactions that extend deep into the connective tissue beyond the cemento-enamel junction (CEJ) may include loss of connective tissue attachment to the tooth involved as well as loss of alveolar bone. These "defensive" processes could therefore paradoxically contribute to the tissue injury observed in gingivitis and periodontitis.

Whilst inflammatory and immune reactions within the periodontal tissues may appear similar to those seen elsewhere in the body, there are significant differences. To some extent this is a consequence of the anatomy of the periodontium, e.g. the permeable junctional epithelium that has remarkable cell and fluid dynamics, with its prime purpose to preserve epithelial continuity across the hard and soft tissue interface. Another important feature is that the "defensive processes" in the periodontal tissues occur in response to large numbers and varieties of microbes that reside on the tooth surface in a biofilm community, close to rather than within the gingiva.

Periodontal disease has sometimes been referred to as a "mixed bacterial infection" to denote that multiple microbial species contribute to the development of disease. Microbial species interact, and although some may not be overtly pathogenic they may still influence the disease process by aiding and assisting the pathogenic bacteria also contained within the microbial biofilm. Thus, purportedly 'commmensal' microbes may endorse the virulence potential of other microbes by providing specific growth conditions or defensive factors; this calls into question our definition of commensal and pathogen with respect to biofilm related diseases.

The microorganisms in the biofilm within periodontal pockets are in a continual state of flux; species, which are relevant at one stage of disease, may not be important at other disease phases. In other words, tissue destruction may result from combinations of bacterial factors, which vary over time. This contrasts with most other classical infectious diseases (e.g. tuberculosis, syphilis, gonorrhea) where the host contends with one organism and the diagnosis of the disease is indicated by the presence or absence of this particular pathogen.

The pathogenicity of microorganisms relates as much to the individual host's innate and/or inflammatory and/or immune capability, as to the virulence of the bacteria themselves. For example, periodontal tissue breakdown could result from microbial enzymes that directly digest the tissue but also, and more likely, from host responses

to these enzymes. Furthermore, tissue destructive responses might result from the host's inflammatory or immune reaction to normal physiological components of the bacteria such as the lipopolysaccharides found in the outer membrane of Gram-negative bacteria.

Epidemiological studies have shown that even within the same individual, the severity of periodontal tissue injury often varies from tooth to tooth and from one tooth surface to another. Thus, whilst many teeth within an individual mouth may exhibit advanced loss of connective tissue attachment and alveolar bone, other teeth or tooth surfaces (sites) may be almost unaffected and surrounded by a normal periodontium. Hence, a patient who is susceptible to, and is exhibiting, periodontal disease is not afflicted with a "homogeneous" condition (see Chapter 18). Each affected site in his/her mouth represents an "individualized" or "specific" microenvironment. In some sites, the inflammatory lesion may be contained within the gingiva (gingivitis) for prolonged periods of time without any apparent progression of the disease into deeper tissues. In other sites, active periodontal tissue destruction (periodontitis) may occur and may be a consequence of a variety of host and parasite factors.

However, it is not presently understood why in some patients the inflammatory lesions remain confined to the marginal portion of the gingival tissues, whilst in other susceptible subjects they progress to involve more apical portions of the periodontium and cause loss of connective tissue attachment and alveolar bone. The same arguments are true for individual sites within a susceptible individual. Clearly some imbalance of the host–parasite relationship is occurring in the destructive lesions. This imbalance may be unique to that site and to gingivitis- and periodontitis-susceptible individuals generally.

Clinically healthy gingiva

"*Clinically healthy gingiva*" is a term used to describe the level of gingival health that may be attained by patients who clean their teeth in a meticulous manner. The oral surface of clinically healthy gingiva consists of keratinized oral epithelium that is continuous with the junctional epithelium (Fig. 11-1a) that is attached to the tooth surface by hemidesmosomes. Supporting the oral and junctional epithelia is a network of connective tissue that includes prominent collagen fibers, which maintain the shape of the gingival tissues and assist the relatively weak hemidesmosomal attachment of the junctional epithelium to the tooth. Immediately inside the junctional epithelium there is a dentogingival plexus, containing large numbers of venules, which supplies the epithelium with various nutrients as well as defense cells (leukocytes) (Fig. 11-1b,c).

The clinically healthy gingiva consistently features a small infiltrate of inflammatory cells that involves both the junctional epithelium and the subjacent connective tissue (Page & Schroeder 1976). This inflammatory reaction occurs in response to the continuous presence of bacterial products in the crevice region (Fig. 11-2). The small inflammatory lesion also harbors lymphocytes and macrophages. Transudates and exudates of fluid that contains varying amounts of plasma proteins leave the vessels of the dentogingival plexus and arrive in the gingival crevice region as the gingival crevicular fluid (GCF) (Egelberg 1967; Cimasoni 1983). Among the leukocytes, neutrophils (polymorphonuclear (PMN) cells) predominate in the crevice region (sulcus) and appear to migrate continuously through the junctional epithelium into the crevice (Figs. 11-3, 11-4). The recruitment of leukocytes from the gingival tissue to the crevice is due to the chemoattractant actions of products derived from the biofilm as well as from factors release by the host.

Sites with *clinically healthy gingiva* appear to deal with continuous microbial challenges without progressing to clinical gingivitis (redness, swelling, bleeding on probing), probably because of several defensive factors that include:

- The intact barrier provided by the junctional epithelium
- The regular shedding of epithelial cells into the oral cavity
- The positive flow of fluid to the gingival crevice which may wash away unattached microorganisms and noxious products
- The presence in GCF of antibodies to microbial products
- The phagocytic function of neutrophils and macrophages
- The detrimental effect of complement on the microbiota.

The host–microbial interplay or balance, which constitutes the situation in clinically healthy gingiva, must clearly change if *gingivitis* is to follow. Gingivitis will follow if there is sufficient plaque accumulation and retention such that microbial products evoke a more substantive inflammatory response. Lesions characteristic of gingivitis occupy a larger volume than those present in clinically healthy gingiva and are accompanied by more pronounced loss of collagen (Fig. 11-4). The inflammatory reaction will also initiate and perpetuate immune responses to the oral microorganisms. Gingival lesions may persist for many years without concomitant loss of periodontal attachment, destruction of periodontal ligament or evidence of bone loss. Clearly certain individuals (and sites), however, go on to develop periodontitis from gingivitis lesions. It is well known that individuals with obvious defects of the inflammatory system, e.g. neutrophil depletion or dysfunction, may rapidly develop advanced periodontitis.

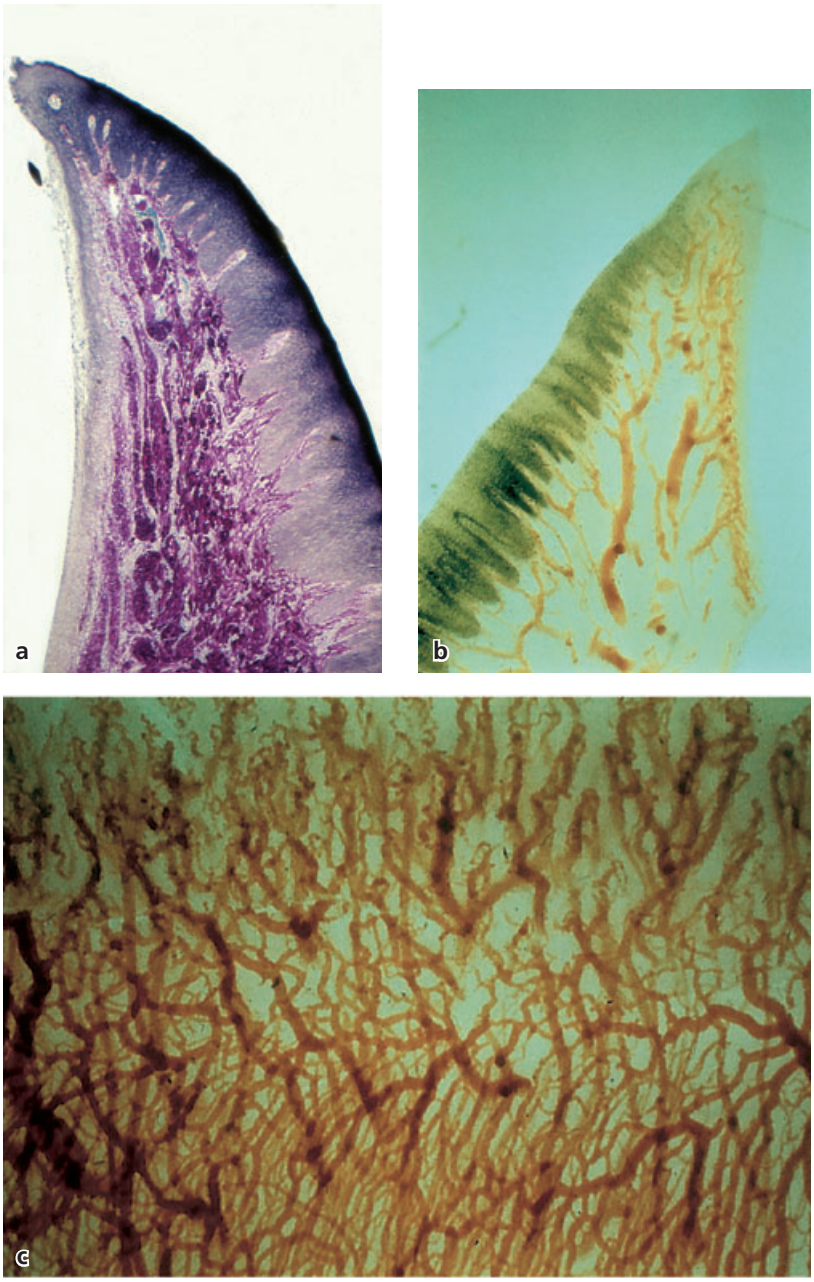

Fig. 11-1 (a) Buccal–lingual section of a normal beagle dog gingiva. The oral epithelium is continuous with a junctional epithelium, which is facing the enamel surface. (b) Micrograph of a buccal–lingual section of a normal (pristine) beagle dog gingiva illustrating the vasculature of the gingival unit. A thin vascular network is present beneath the junctional epithelium. (c) The thin vascular network (plexus) is shown in a mesial-distal section.

There is an accumulating body of evidence, which suggests that the host's immune response to periodontal pathogens may be quite different in subjects that become affected by advanced chronic periodontitis and those who will not progress beyond gingivitis.

Gingival inflammation

The classical phases of "acute" and "chronic" inflammation are not easily applied in periodontal disease, probably because in clinically healthy gingiva a small lesion similar to an acute inflammatory reaction is already present. Subsequently developing chronic inflammatory changes become superimposed so that both acute and chronic elements co-exist in most gingival lesions.

Histopathological features of gingivitis

The clinical symptoms of inflammation may appear subtle in the early stages of gingivitis but the underlying histopathological changes, albeit present in a small compartment of the gingival tissues, are quite marked. Alterations in the vascular network occur with many capillary beds being opened up. Exudation of GCF and proteins from the dentogingival plexus will increase and this will make the tissue edematous and swollen. Inflammatory cells leave the vasculature and accumulate in the connective tissue lateral to the junctional epithelium. The connective tissue infiltrate is at first mainly comprised of macrophages and lymphocytes. As the cellular infiltrate becomes enlarged, plasma cells dominate the lesion and collagen depletion becomes quite substantial.

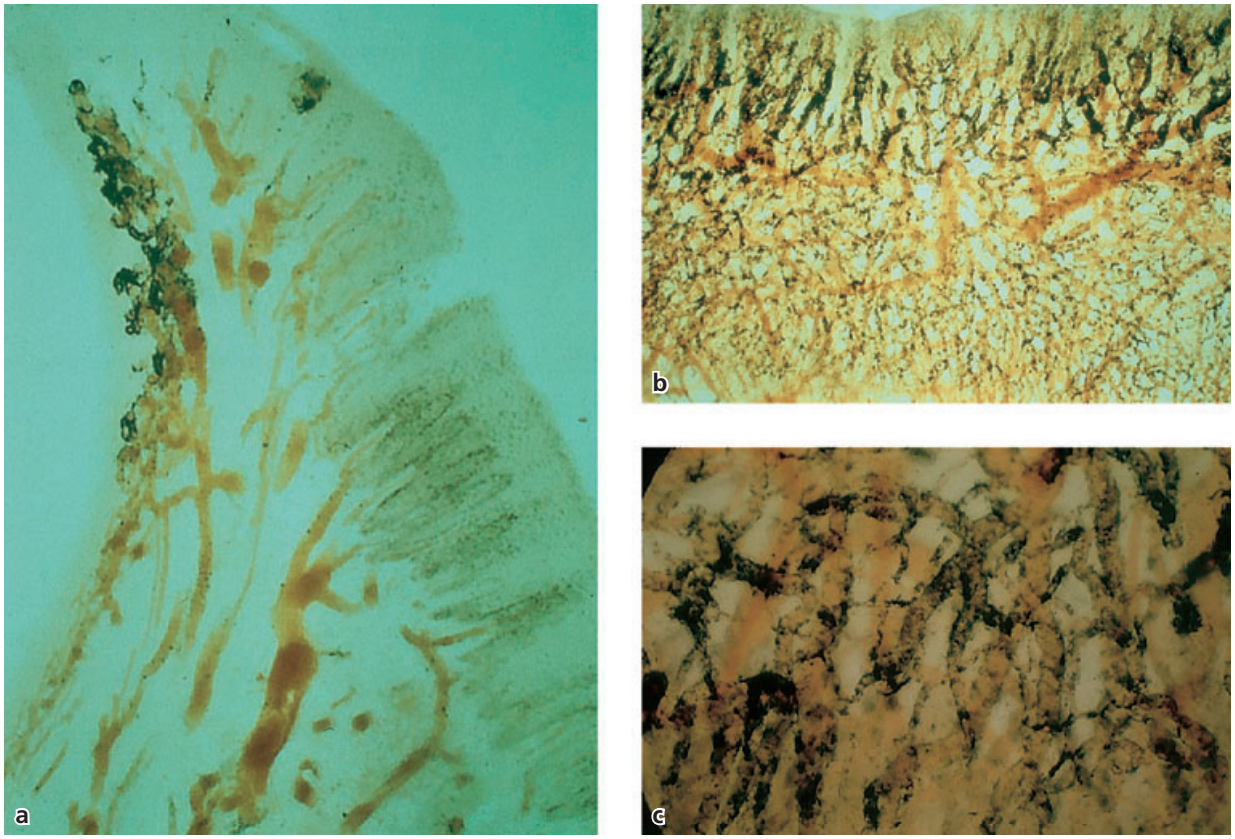

Fig. 11-2 (a) Microphotograph of a buccal–lingual section of a normal beagle dog gingiva. A filter paper strip has been introduced between the junctional epithelium and the tooth. An increased permeability of the gingival vessels has occurred, identified by the presence of carbon particles, which were injected intravenously prior to biopsy. The carbon particles have become trapped in the open endothelial junctions, and so-called vascular labelling has occurred. (b) A mesio-distal section of the same gingival unit as in (a). (c) Higher magnification of (b) (from Egelberg 1967).

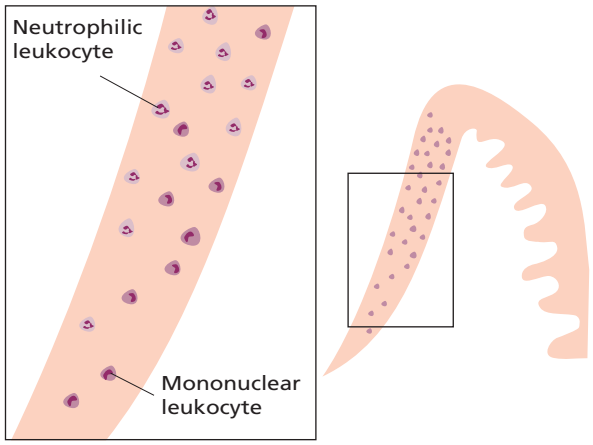

Fig. 11-3 Leukocytes in the junctional epithelium. Observe that the volume of leukocytes decreases in an apical direction and approaches 0 in the most apical portion. Within the junctional epithelium, the mononuclear leukocytes are located in more basal layers, while the neutrophilic granulocytes are present primarily in the superficial portions of the junctional epithelium.

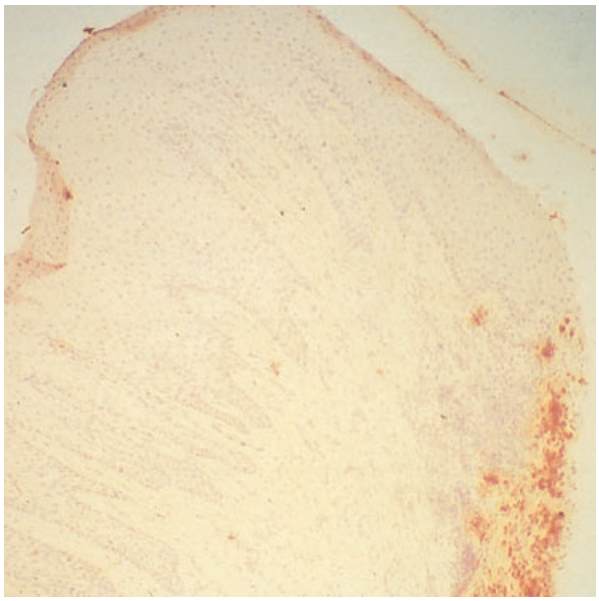

Fig. 11-4 Immunostained section showing neutrophils in the junctional epithelium of healthy gingiva.

In this context it is important to emphasize that the lesion in the gingiva is closely related to the presence and extension of the biofilm on the associated tooth surface. Thus, findings from analyses of human autopsy material (Waerhaug 1952) indicated that the distance between plaque and calculus on the tooth surface and the inflammatory lesion in the gingiva never exceeded 1–2 mm.

Different lesions in gingivitis/periodontitis

In 1976, Page and Schroeder divided the progressing lesion in the gingival/periodontal tissues into four phases: *initial, early, established*, and *advanced* stages or lesions. The descriptions of the initial and early lesion were intended to characterize the histopathology of clinically healthy gingiva and early stages of gingivitis, while the established lesion featured "chronic" gingivitis. The advanced lesion was considered to reflect the phase when gingivitis progressed to periodontitis and was a lesion that was consistently associated with attachment and bone loss. The evidence on which these descriptions were based was the prevailing information generated predominantly from animal biopsy material and some human adolescent samples.

Below we have used the terms initial, early, established, and advanced lesion to describe some features of the developing inflammatory process in the gingival and periodontal tissues. We have, however, not consistently adhered to the definitions and descriptions used in the original publication by Page and Schroeder.

The initial lesion

Inflammation soon develops as plaque is allowed to form on the gingival third of the tooth surface. Within 24 hours marked changes are evident in the dentogingival plexus as more blood is brought to the area. Dilation of the arterioles, capillaries, and venules of the vascular network becomes a prominent feature (Fig. 11-2). Hydrostatic pressure within the microcirculation increases and intercellular gaps form between adjacent endothelial cells in the capillaries. Thus, an increase in the permeability of the microvascular bed results, so that proteins and, subsequently, fluids may exude into the tissues (Fig. 11-5).

The flow of GCF increases. Noxious substances released from the biofilm are diluted both inside the gingival tissue and in the crevice. Furthermore, bacteria and their products may be flushed away from the crevice region and end up in the saliva. Plasma proteins are part of GCF and include defensive proteins such as antibodies, complement and protease inhibitors, and other macromolecules with numerous functions. Already during this initial phase of the host response, PMN cell migration is facilitated by the presence of various adhesion molecules (intercellular adhesion molecule-1 (ICAM-1), endothelial leukocyte adhesion molecule-1 (ELAM-1)), and other adhesions in the dentogingival vasculature. These molecules assist the binding of PMN cells to the venules and subsequently they help the cells to leave the blood vessel (Fig. 11-6). The PMNs migrate up a chemo-attractant gradient to the crevice and are further assisted in their movement (1) by other adhesion molecules uniquely present on the junctional epithelial cells (Moughal *et al*. 1992) and (2) by the presence of microbial chemotactic factors. Lymphocytes are retained in the connective tissues on contact with antigens, cytokines or adhesion molecules and are therefore not so readily lost through the junctional epithelium and into the oral cavity, as are PMNs. Most lymphocytes have the ability to produce CD44 (CD, cluster determinant) receptors on their surfaces, which permit the binding of the cell to the connective tissue framework.

Within 2–4 days of plaque build-up the cellular response described above is probably well established and is maintained by chemotactic substances originating from the plaque microbiota as well as from host cells and secretions (Fig. 11-7).

The early lesion

An ensuing and somewhat different gingival lesion will become present after several days of plaque accumulation (Fig. 11-8). The vessels in the dentogingival plexus remain dilated, but their numbers increase due to the opening up of previously inactive capillary beds. The increased size and enhanced numbers of vascular units are reflected in increased redness of the marginal gingiva that is a characteristic clinical symptom during this phase (Egelberg 1967; Lindhe & Rylander 1975).

Lymphocytes and PMNs are also the predominant leukocytes in the infiltrate at this stage of gingivitis and very few plasma cells are noted within the expanding lesion (Listgarten & Ellegaard 1973; Payne *et al*. 1975; Seymour *et al*. 1983; Brecx *et al*. 1987). Several fibroblasts within the lesion exhibit signs of degeneration. This probably occurs through apoptosis and serves to remove fibroblasts from the area, thus permitting more leukocyte infiltration (Page & Schroeder 1976; Takahashi *et al*. 1995). Similarly breakdown of collagen fibers occurs in the infiltrated area. This net loss of collagen fibers will provide space for the infiltrating cells.

The basal cells of the junctional and sulcular epithelium now proliferate. This represents an attempt by the body to enhance the "mechanical" barrier to plaque bacteria and their products. Epithelial rete pegs can be seen invading the coronal portion of the lesion in the connective tissue (Schroeder 1970; Schroeder *et al*. 1973). Tissue alterations during this phase also involve the loss of the coronal portion of the junctional epithelium. A niche forms between the

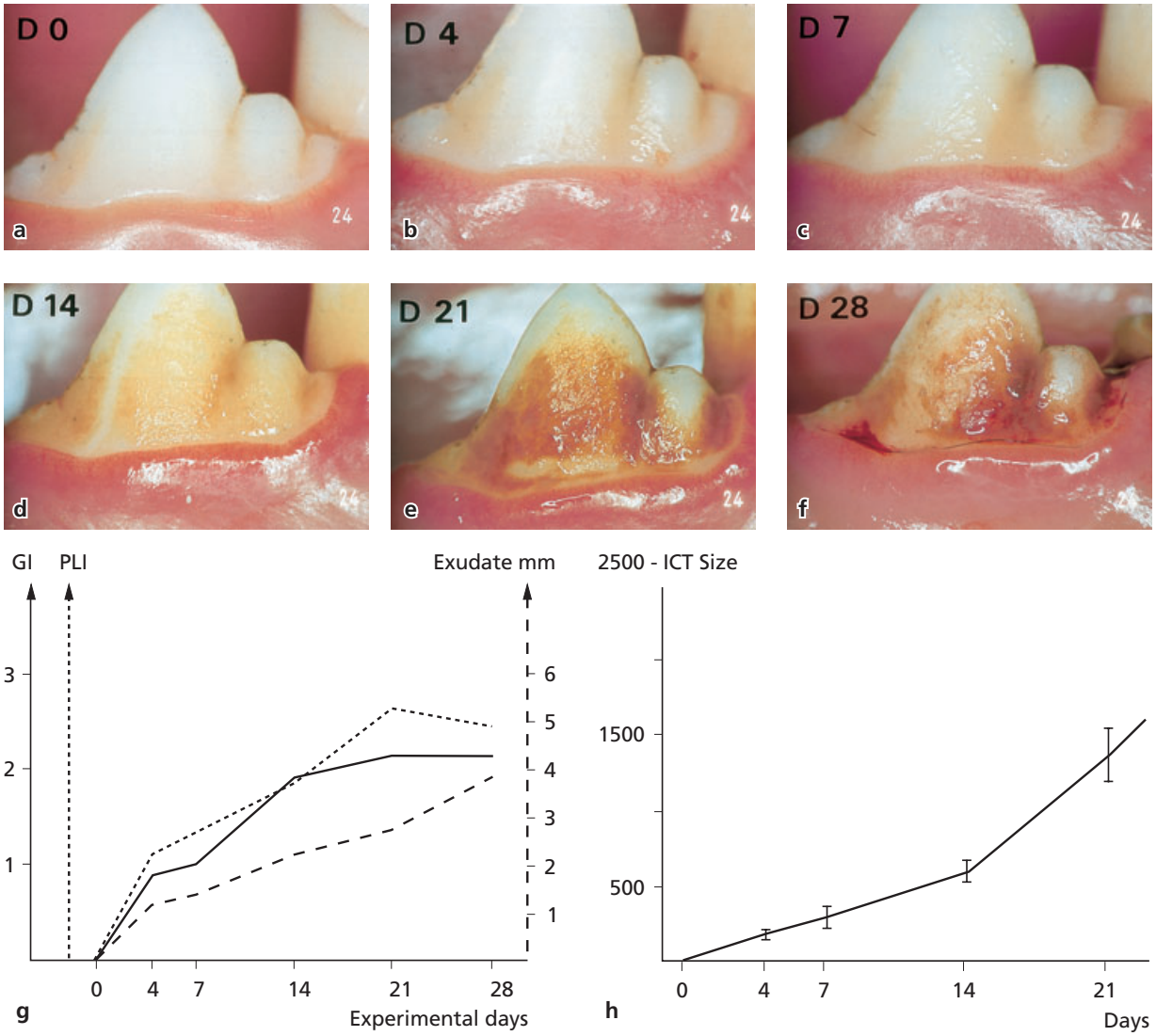

Fig. 11-5 Gingival alterations which occurred during a 28-day period of plaque accumulation and gingivitis development in beagles. (a) Normal gingiva. (b) Day 4. (c) Day 7. (d) Day 14. (e) Day 21. (f) Day 28 of undisturbed plaque accumulation. Note the gradually developing plaque on the tooth surfaces and the inflammatory changes in the gingiva. The vascular reaction is illustrated by a gradually increasing number of vessels in the gingival margin. (g) Gingival index (GI), plaque index (PLI) and gingival exudate alterations (exudate) that occurred during the experimental gingivitis period. (h) In gingival biopsy specimens obtained at various time intervals it can be seen that the inflammatory cell infiltrate (ICT) in the gingiva gradually increased in size.

epithelium and the enamel surface and a subgingival biofilm may now form.

This so-called early lesion may persist for long periods and the variability in time required to produce an established lesion may reflect variance in susceptibility between subjects.

The established lesion

As the exposure of plaque continues there is a further enhancement of the inflammatory response of the gingival tissue. The flow of GCF is increased. The connective tissue as well as the junctional epithelium is transmigrated by an increased number of leukocytes.

The lesion, as defined by Page and Schroeder (1976), is dominated by plasma cells. This conclusion was based mainly on data from animal experiments. Results from examinations of human biopsies, however, revealed that in young individuals lymphocytes occupied a somewhat larger proportion of the infiltrate than plasma cells (Brecx *et al*. 1988; Fransson *et al*. 1996). On the other hand, in old subjects, plasma cells were the dominant cell type in established gingivitis lesions (Fransson *et al*. 1996).

Collagen loss continues as the inflammatory cell infiltrate expands, resulting in collagen-depleted spaces extending deeper into the tissues, which then become available for infiltration and accumulation of leukocytes (Figs. 11-9, 11-10). During this time the dentogingival epithelium continues to proliferate and the rete pegs extend deeper into the connective tissue in an attempt to maintain epithelial integrity and a barrier to microbial entry. The junctional

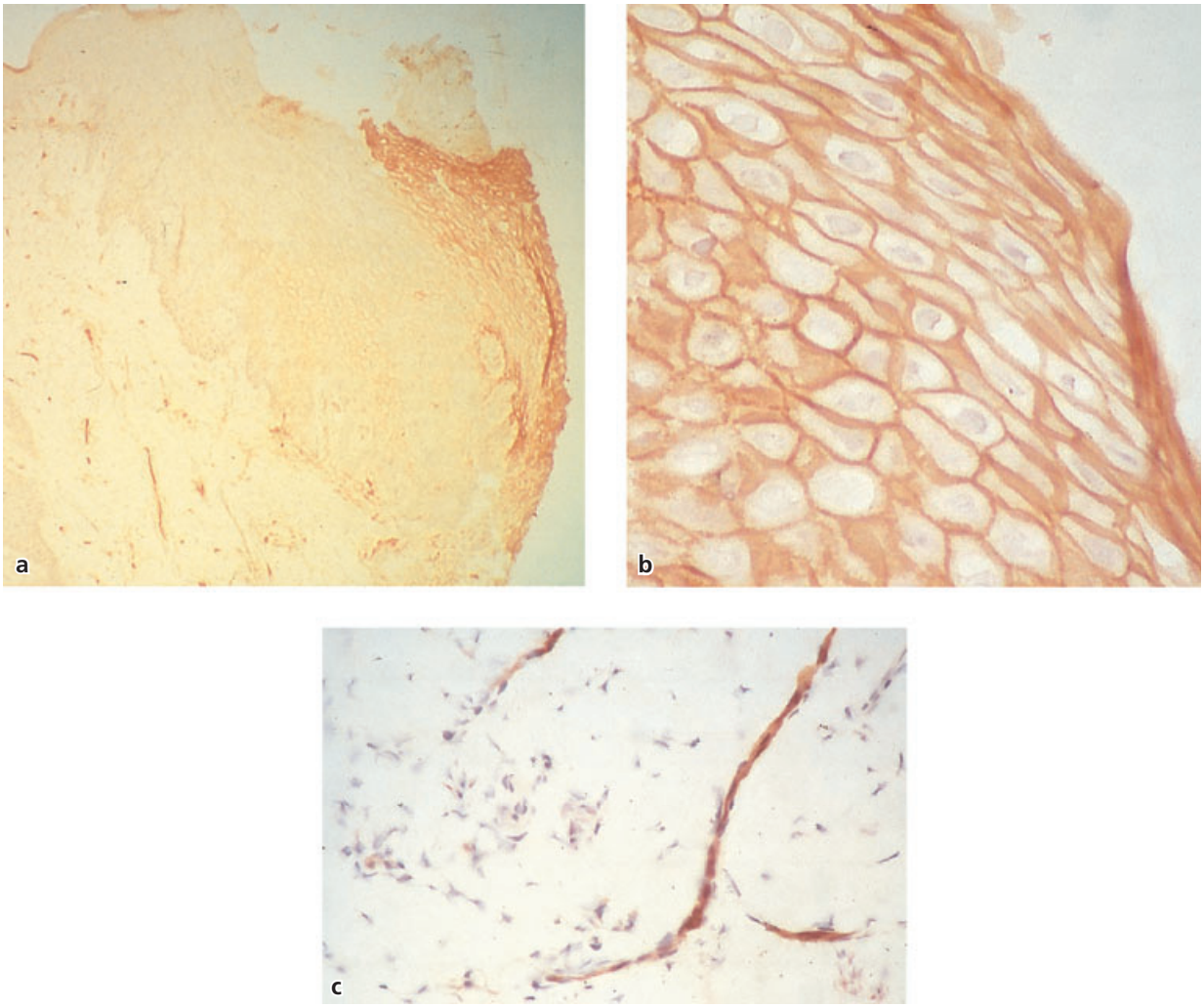

Fig. 11-6 (a) ICAM-1 immunohistochemical staining of a gingival biopsy sample during an experimental gingivitis study in humans after day 7. ICAM-1 positive blood vessels and junctional epithelium can be clearly seen. (b) Higher magnification of (a) showing the extensive junctional epithelium staining. (c) Higher magnification of (a) showing the ICAM-1 positive vessels within the connective tissue.

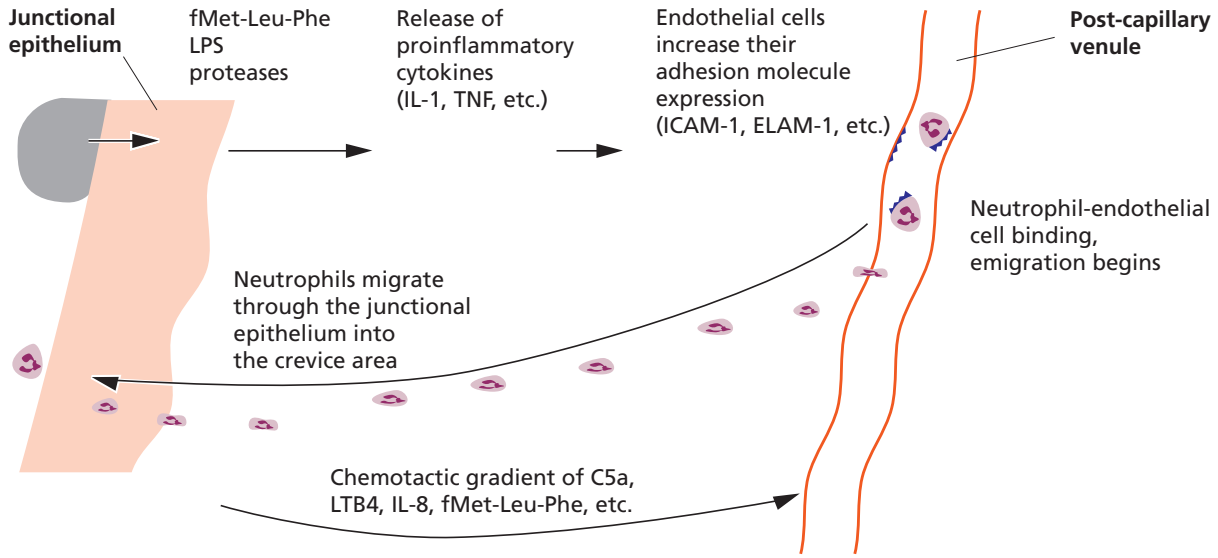

Fig. 11-7 Schematic illustration of the process whereby neutrophils are attracted into the junctional epithelium and crevice region.

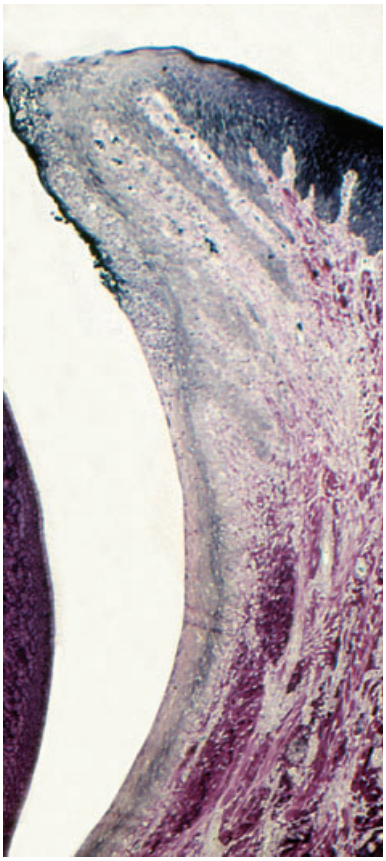

Fig. 11-8 Buccal–lingual section of beagle dog gingiva with an early lesion. Note the epithelial rete pegs in the coronal portion of the lesion.

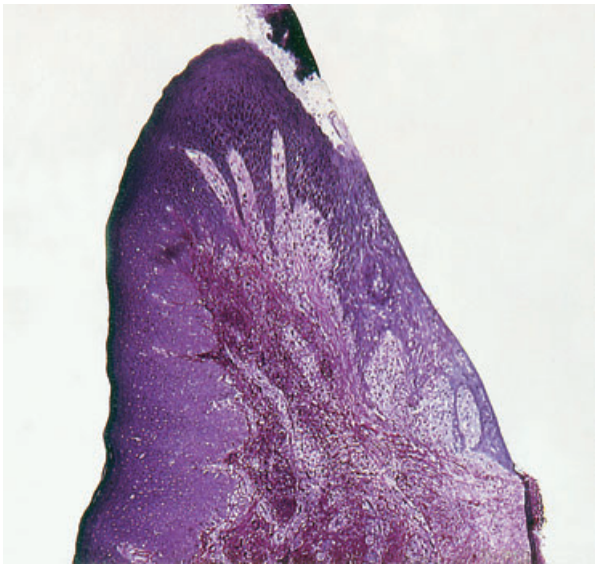

Fig. 11-9 Buccal–lingual section of beagle dog gingiva exhibiting an established lesion. The junctional epithelium is replaced by a pocket epithelium and rete pegs extend deep into the infiltrated connective tissue.

epithelium is substituted by a pocket epithelium that is not attached to the tooth surface. This allows for a further apical migration of the biofilm. The pocket epithelium harbors large numbers of leukocytes, predominantly PMNs. In comparison to the original

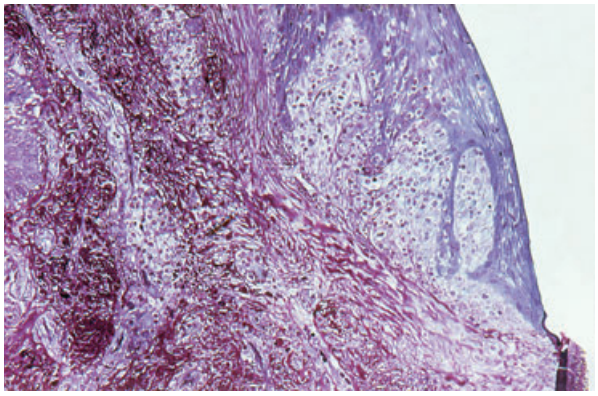

Fig. 11-10 Detail of Fig. 11-9. Note the large number of leukocytes in the inflammatory cell infiltrate and the pocket epithelium.

junctional epithelium, the pocket epithelium is more permeable to the passage of substances into and out of the underlying connective tissue. This pocket epithelium may be ulcerated in places. Figure 11-11 schematically illustrates the alterations which occur during the development of gingivitis and periodontitis.

Two types of established lesion appear to exist: one remains stable and does not progress for months or years (Lindhe *et al*. 1975; Page *et al*. 1975), while the second becomes more active and converts more rapidly to a progressive and destructive advanced lesion.

The advanced lesion

As the pocket deepens, the biofilm continues its apical downgrowth and flourishes in this anaerobic ecological niche. The gingival tissues offer reduced resistance to periodontal probing.

The inflammatory cell infiltrate extends further apically into the connective tissues. The advanced lesion has many of the characteristics of the established lesion but differs importantly in that loss of connective tissue attachment and alveolar bone occurs (Fig. 11-12). The damage to the collagen fibers is extensive. The pocket epithelium migrates apically from the cemento-enamel junction, and there are widespread manifestations of inflammation and immunopathological tissue damage. The lesion is no longer localized to the gingival tissues, but the inflammatory cell infiltrate extends laterally and apically into the connective tissue of the true attachment apparatus. It is generally accepted that plasma cells are the dominant cell type in the advanced lesion (Garant & Mulvihill 1972; Berglundh & Donati 2005).

In summary, in the progression from health to gingivitis and on to periodontitis there are many unknown factors related to timing. In addition, there is extensive subject and site variability in both exacerbating factors and innate susceptibility.

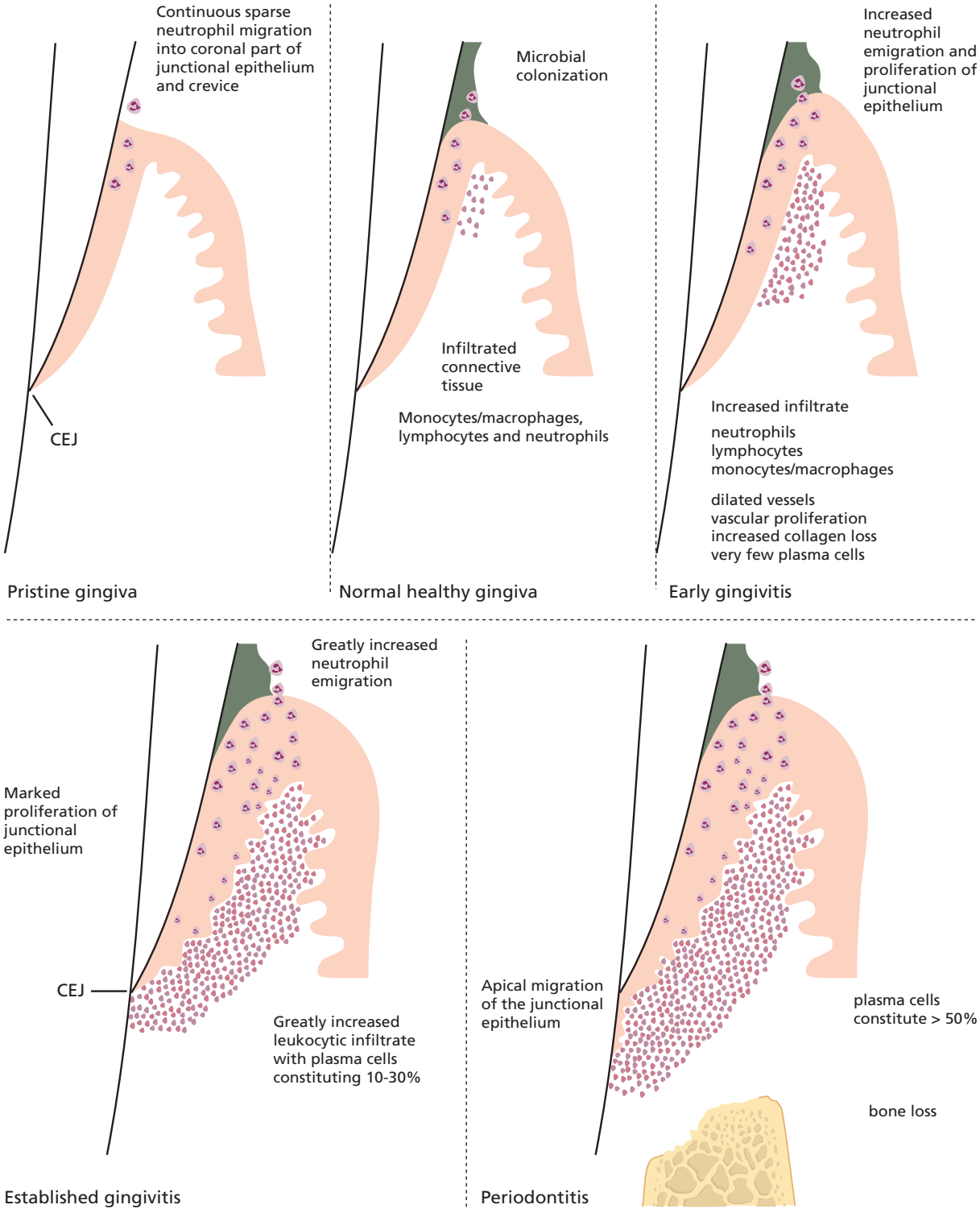

Fig. 11-11 Schematic illustration of the changes in the gingival tissues during the development of gingivitis and periodontitis. The most significant differences are in the extent and composition of the inflammatory infiltrate and the epithelial proliferation in gingivitis, and the apical migration of epithelium and bone loss seen in periodontitis lesions. CEJ: cemento-enamel junction.

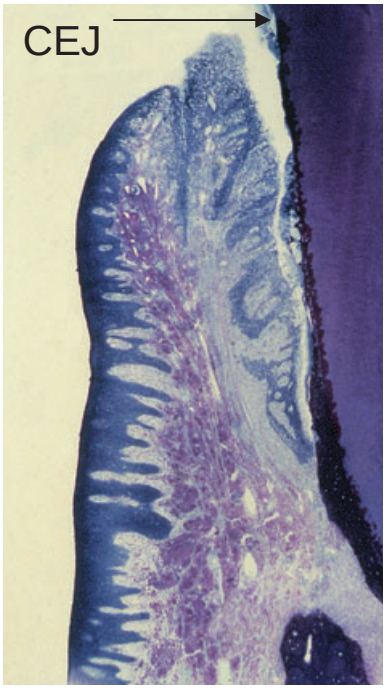

Fig. 11-12 Buccal–lingual section of a periodontitis (advanced) lesion in a beagle dog. Note the apical extension of the inflammatory cell infiltrate and the loss of connective tissue attachment and supporting bone. CEJ: cemento-enamel junction.

Host–parasite interactions

Microbial virulence factors

Periodontal disease is initiated and sustained by factors (substances) produced by the subgingival microbiota (the biofilm). Some of these substances can directly injure host cells and tissues. Other microbial constituents may activate inflammatory or cellular and humoral immune systems that cause damage to the periodontal tissues. It is the latter pathway which accounts for most injury to the periodontal tissues.

Microbial invasion

The invasion of the dentogingival epithelium by spirochetes was conclusively documented by Listgarten (1965) who studied the histopathology of lesions of necrotizing ulcerative gingivitis (ANUG). Although there have been numerous reports of microbial invasion in other forms of gingivitis and periodontitis, the significance of these observations is unclear. Even if bacteria can be found in the tissues, it is not known whether this represents true invasion (i.e. microbial colonization and proliferation within the tissues) or displacement or translocation of bacteria from the biofilm into the soft tissues. In conclusion, it is not known yet whether microbial invasion presents an important challenge to the host or represents an artifact.

Enzymes

Microorganisms produce a variety of soluble enzymes that may digest extracellular host proteins and other molecules and thereby produce nutrients for bacterial growth. In addition to enzymes, bacteria also release numerous, harmful metabolic waste products, such as ammonia, indole, hydrogen sulfide, and butyric acid.

Amongst the enzymes released by bacteria in the biofilm, *proteases* (proteinases) are capable of digesting collagen, elastin, fibronectin, fibrin, and various other components of the intercellular matrix of both epithelial and connective tissues. One protease that has attracted much attention is the Arg1-protease produced by *Porphyromonas gingivalis* for which high potency is claimed. This protease, in addition, has the capability to induce a strong humoral immune response (Aduse-Opoku *et al*. 1995). Another protease, leukotoxin, was a focus of interest for many years, but as yet no *in vivo* evidence exists for its claimed role in periodontal tissue destruction (Haubek *et al*. 1995). This leukotoxin has been studied in both America and Europe but it appears that the strains of *Aggregatibacter actinomycetemcomitans* that produce the protease differed (Haubek *et al*. 1995). It seems that the more virulent form, which produces leukotoxin in excess and thus has great capacity to kill leukocytes, is common in strains from America but virtually absent in strains from Europe, despite identical disease prevalence.

Endotoxin

*Lipopolysaccharide*s (LPSs) of Gram-negative microorganisms are capable of invoking both the inflammatory and immune responses as they interact with host cells. Many of the functions attributed to LPS are associated with their ability to stimulate the production of cytokines. LPS also has profound effects on blood coagulation and on the complement system. The properties of LPS, as well as of *lipoteichoic acids* (LTAs) of Gram-positive bacteria, are numerous and may be influenced by many other molecules that interact with these outer membrane structures. LPS and LTA are produced and released from microorganisms present in the subgingival biofilm and cause release of chemical mediators of inflammation to produce vascular permeability and encourage, through chemotactic actions, inflammatory cells to move into and accumulate in the gingival tissues. Furthermore, leukocytes are stimulated to release pro-inflammatory agents and cytokines.

Summary: Microbes are capable of producing a variety of substances which either directly or indirectly harm the host. The main detrimental effect may be the host's own innate, inflammatory, and immune response to the foreign molecules and antigens of the microbe.

Host defense processes

Host–parasite reactions can be divided into innate (non-specific) and adaptive (specific) responses. Innate reactions include the inflammatory response and do not involve immunological mechanisms. Adaptive reactions that include immunological responses tend to be very effective as the host response is specifically "tailored" to the offending pathogen(s).

Important aspects of host defense processes

Inflammatory processes

The host has an extensive repertoire of defensive responses to ward off invasion by pathogens. Such responses may either result in a rapid resolution of the lesion (e.g. a staphylococcal abscess which heals) or that no lesion at all develops in the affected tissue (e.g. smallpox infection in a successfully vaccinated host). An ineffective response may result in a chronic lesion that does not resolve (e.g. tuberculosis) or if excessively deployed, in a lesion in which the host responses contribute significantly to tissue destruction (e.g. rheumatoid arthritis or asthma).

In the classical description of inflammation, a tissue is presented that appears macroscopically red, swollen, hot, and painful, and with possible loss of function in specific sites. Redness and heat are due to vasodilatation and increased blood flow. Swelling is a result of increased vascular permeability and leakage of plasma proteins that create an osmotic potential that draws fluid into the inflamed tissues. Related to the vascular changes there is an accumulation of inflammatory cells infiltrating the lesion. Pain is rarely experienced in aggressive and chronic periodontal disease, but could theoretically occur due to stimulation of afferent nerves by chemical mediators of inflammation in necrotizing periodontal disease. Impairment of function is classically illustrated in arthritically swollen joints.

Molecules, cells, and processes

Proteinases (proteases)

Periodontal disease results in tissue degradation, and thus proteases, derived both from the host and from bacteria, are central to the disease processes. Proteinases (collagenase, elastase-like and trypsin-like, as well as serine and cysteine proteinases) cleave proteins by hydrolyzing peptide bonds and may be classified into two major classes, *endopeptidases* and *exopeptidases*, depending on the location of activity of the enzyme on its substrate. Efforts have been made to assess endopeptidase activity in gingival tissues and in GCF. A reduction of protease levels following treatment was obtained in several studies.

Proteinase inhibitors

Release of proteinases in the gingiva and the crevicular area promotes inflammatory reactions and contributes to connective tissue damage via several pathways. In contrast, *proteinase inhibitors* would dampen the inflammatory process. Among such inhibitors alpha-2 macroglobulin (A2-M) and alpha1 antitrypsin (A1-AT) must be recognized. In fact, gingival collagenase inhibition by A2-M has been demonstrated to occur in gingival tissues and polymorphonuclear leukocyte (PMN) collagenase is also inhibited by A1-AT.

Many host and microbial enzymes are likely to be present in the crevice at any one time. Realizing the potentially destructive features of such enzymes, consideration should be given to the source of these enzymes, their relative proportions and the inhibitory mechanisms available within the crevice. The main enzyme activity is host derived and specific and non-specific inhibitors are plentiful within the crevice and thus enzyme activity will be localized and short-lived.

Matrix metalloproteinases

The periodontium is structurally comprised of fibrous elements, including collagen, elastin, and glycoproteins (laminin, fibronectin, proteoglycans), minerals, lipids, water, and tissue-bound growth factors. In addition there exists a large variety of extracellular matrix components, including tropocollagen, proteoglycans, and other proteins (elastin, osteocalcin, osteopontin, bone sialoprotein, osteonectin, and tenascin). All of these matrix components are constantly in a state of turnover and thus there is much matrix enzyme activity in health, disease, and tissue repair and remodeling (Kinane 2001). Matrix metalloproteinases (MMPs) are responsible for remodeling and degradation of the matrix components.

One of the MMPs that has received much attention is the *neutrophil (PMN) collagenase* that is found in higher concentrations in inflamed gingival specimens than in clinically healthy gingiva. The increased presence of these MMP enzymes in diseased over healthy sites (Ohlsson *et al*. 1973), their increase during experimental gingivitis (Kowashi *et al*. 1979), and decrease after periodontal treatment (Haerian *et al*. 1995, 1996) suggest that MMPs from PMNs are involved in periodontal tissue breakdown.

The periodontal ligament is one of the most metabolically active tissues in the body, and collagen metabolism represents most of this activity. The biological reason for this activity probably relates to its ability to adapt to occlusal forces generated during function. An important feature of connective tissues in general and the periodontal ligament in particular, is the process of constant renewal of the extracellular matrix components involving MMP.

It is evident that the activity of MMPs and their inhibitors is associated with tissue turnover as well as with gingivitis, destructive periodontitis, and with the healing of the periodontal tissues following therapy.

Cytokines

Cytokines are soluble proteins, secreted by cells involved in both the innate and adaptive host response, and act as messenger molecules that transmit signals to other cells. They have numerous actions that include initiation and maintenance of immune and inflammatory responses and regulation of growth and differentiation of cells. Cytokines are numerous, many have overlapping functions, and they are interlinked to form an active network which controls the host response. Control of cytokine release and action is complex and involves inhibitors and receptors. Many cytokines are capable of acting back on the cell that produced them so as to stimulate (or downgrade) their own production and the production of other cytokines.

Interleukins are important members of the cytokine group and are primarily involved in communication between leukocytes and other cells, such as epithelial cells, endothelial cells, and fibroblasts engaged in the inflammatory process. In addition, *interleukin (IL)-1a*, *IL-1b*, and *tumor necrosis factor (TNF)-alpha* stimulate bone resorption and inhibit bone formation.

A series of more than 20 molecules has been identified, that act to recruit defense cells (PMNs, macrophages, lymphocytes) to areas where they are required. These chemotactic cytokines play an important role in cell-mediated immune responses.

Prostaglandins

Prostaglandins are derivatives of arachidonic acid and are important mediators of inflammation. Macrophages in particular, but also several other cells produce prostaglandins, particularly PGE_2 which is a potent vasodilator and inducer of cytokine production by various cells. PGE_2 acts on fibroblasts and osteoclasts to induce production of MMPs, which are of importance for tissue turnover and tissue destruction in gingivitis and periodontitis (see above).

Polymorphonuclear leukocytes

The PMN is the predominant leukocyte within the gingival crevice/pocket in both health and disease. PMNs are attracted from the circulation to the affected area via chemotactic stimuli elicited from, for example, microorganisms in the biofilm, and host-derived chemokines. *Elastase*, a serine protease, is contained in the primary granules of the PMN. Elastase may cause tissue breakdown and is present with increased activity at sites of gingival inflammation. *Lactoferrin* is contained in the secondary granules of the PMN, and is released during PMN migration and is associated with PMN activation. Differences in the relative amounts of elastase and lactoferrin were found in periodontal sites with varying degrees of inflammation. A greater proportion of lactoferrin to elastase was found in advanced periodontitis lesions than in gingivitis sites. This variation in the release of primary and secondary granule enzymes by PMNs may indicate alterations in PMN function in different disease environments (Fig. 11-13).

Bone destruction

Tissue destruction is one of the hallmarks of periodontitis and involves connective tissue structures and alveolar bone. Degradation of collagen and matrix components in the connective tissue is regulated by inflammatory processes in the periodontitis lesion and includes the production of various MMPs (see above).

Bone resorption is mediated by osteoclasts and takes place concomitant with the breakdown of the connective tissue attachment during disease progression. Thus, the mechanisms involved in bone resorption respond to signals from inflammatory cells in the lesion and initiate degradation of bone in order to maintain a "safety" distance to the periphery of the inflammatory cell infiltrate. Analyses of human autopsy material and biopsy specimens from animal experiments have demonstrated that the alveolar bone in periodontitis is separated from the inflammatory cell infiltrate by a 0.5–1 mm wide zone of a non-infiltrated connective tissue. This encapsulation of the lesion is an important feature of host defense mechanisms in periodontitis and bone resorption is thus required to re-establish dimensions of the connective tissue capsule following a phase of attachment loss during disease progression.

Osteoclasts are multinucleated cells that develop from osteoclast progenitor cells/macrophages and exhibit specific abilities to degrade organic and inorganic components of bone. As mentioned above, different mediators such as IL-1 beta, PGE_2 and TNF-alpha but also IL-6, IL-11 and IL-17 may act as activators on osteoclasts. Another and more important system in osteoclast activation includes the receptor activator of nuclear factor-kappa beta (RANK), the RANK ligand (RANKL) and osteoprotegrin (OPG). RANK is a receptor expressed by osteoclast progenitor cells. RANKL and OPG are cytokines that belong to the TNF family and are produced by osteoblasts and bone marrow stromal cells. While RANKL promotes activation of osteoclasts, OPG has the opposite effect. Thus, the binding of RANKL to the RANK will result in the differentiation of osteoclast progenitor cells into active osteoclasts, while OPG that binds to RANKL will inhibit the differentiation process (for review see Lerner 2006). Analyses of human biopsy specimens revealed that levels of RANKL were higher and levels of OPG were lower in sites with

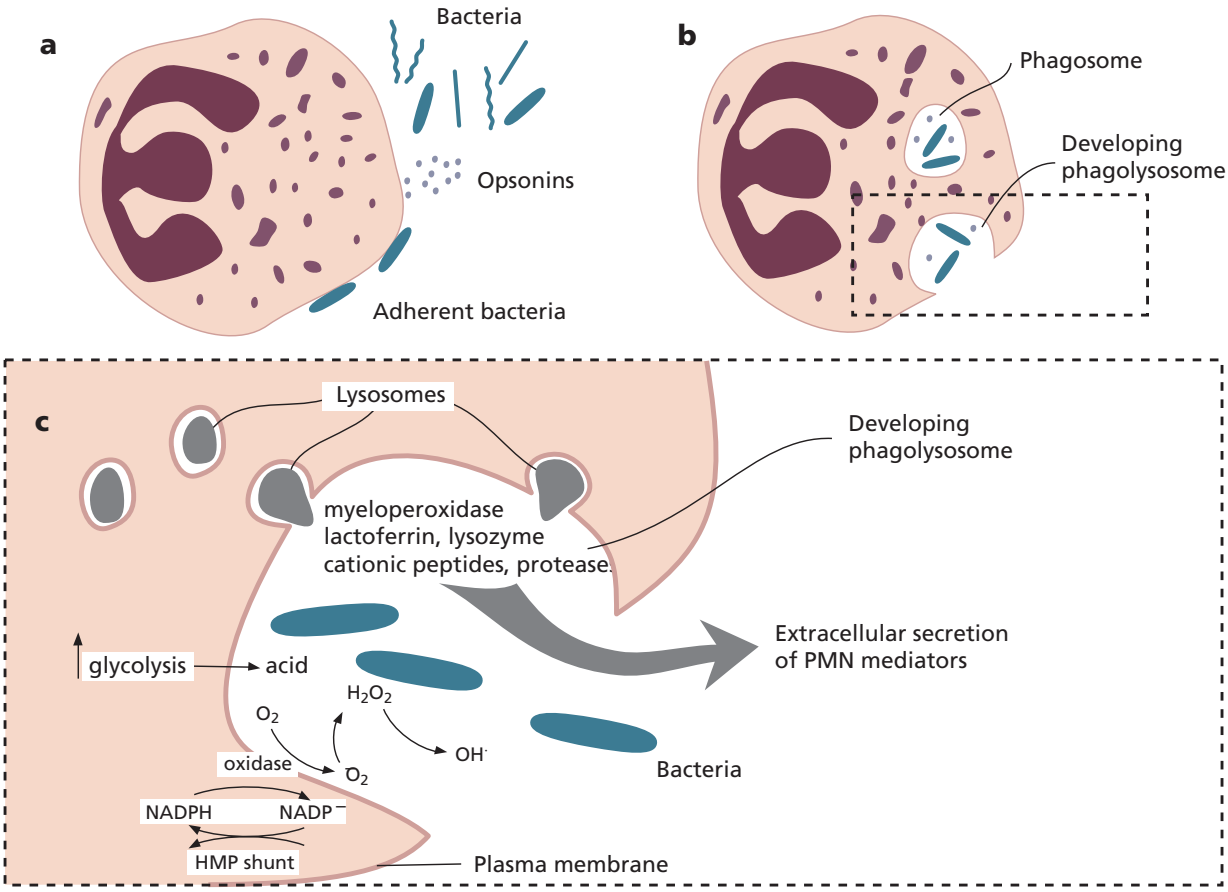

Fig. 11-13 Major events in the encounter between PMNs and invading microorganisms. (a) Once PMNs emigrate from the microcirculation, they migrate toward bacteria under the influence of chemotactic factors. Upon contact PMNs adhere to the organisms (many types of bacteria must be opsonized to facilitate PMN adherence and phagocytosis). (b) Coincident with adhesion, PMNs begin to phagocytose these organisms. This is accomplished as the plasma membrane flows around and then invaginates to internalize attached organisms which are now contained within phagosomes. Several bacteria can be phagocytosed simultaneously by the PMN. (c) As these events occur PMNs demonstrate dramatic metabolic alterations including: an elevation in glycolysis; a marked rise in oxygen consumption; and increased glucose utilization by the hexose monophosphate shunt. Glycolytic metabolism of glucose provides the energy required by phagocytosis and also results in a drop in intracellular pH due to the formation of lactate. The oxidative burst is largely the result of NADPH oxidase activity (an enzyme associated with the cell membrane), which oxidizes NADPH to NADP and results in the reduction of oxygen to various free radicals. These oxidants are released into the phagosome to kill bacteria. The hexose monophosphate shunt provides for the regeneration of NADPH. At the same time, lysosomes are mobilized toward the developing phagosome and fuse with the phagosome membrane, giving rise to a phagolysosome. Lysosomal antimicrobial compounds (myeloperoxidase, lysozyme, lactoferrin, cationic proteins, etc.) are discharged into the vacuole. The combination of oxidative and non-oxidative (acid pH, lysosomal agents) pathways explains how PMNs kill ingested organisms. Lysozyme and neutral proteases (particularly elastase) derived from lysosomes digest and dispose of the dead organisms. Before invagination is completed, biologically active products can be released from the phagosome into the external environment. These agents play a role in extracellular killing of microorganisms but also may adversely affect surrounding host cells and tissue structures.

periodontitis than in sites representing healthy gingiva (Crotti *et al*. 2003; Liu *et al*. 2003).

The RANK/RANKL/OPG system is also involved in bone degradation processes that are induced by pro-inflammatory cytokines such as PGE_2, TNF-alpha, IL-1 beta, IL-6, IL-11, and IL-17. In addition, the production of the RANKL is not confined to osteoblasts and bone marrow stromal cells. Thus, the contribution of RANKL by T cells and other cells in inflammation must be considered. The role of T cells, however, is unclear given that this cell not only produces RANKL but also inhibitors of RANKL, such as interferon (IFN)-gamma and IL-4 (Takayanagi 2005).

In summary, bone resorption is part of the encapsulation process of the inflammatory cell infiltrate in periodontitis. Osteoclasts develop from osteoclast progenitor cells or macrophages and are regulated by the RANK/RANKL/OPG system and/or pro-inflammatory cytokines.

The innate defense systems

Innate immune mechanisms operate without any previous contact with the disease-causing microorganism. These mechanisms include the *barrier function* of the oral epithelia and *vascular* and *cellular* aspects of the *inflammatory responses*.

The gingival crevice is the first region of the periodontium that comes into contact with microorganisms that attempt to attach and colonize the area. Several innate mechanisms serve to prevent such microbial colonization and include (1) the mechanical washing effect of the *saliva* and *GCF*, and (2) the detrimental effect on bacterial growth of *constituents* of these fluids (e.g. antibodies and proteases, complement, salivary lactoferrin, and other proteins).

The oral mucosa itself is not simply a barrier but has a chemical composition that may be harmful to bacteria. Furthermore, the cells of the epithelium can respond to the bacteria by (1) producing antimicrobial peptides, including beta-defensin etc., that kill the microbes, (2) releasing other molecules, such as IL-1 beta, capable of inducing or enhancing the local inflammatory reaction, and (3) releasing IL-8, a chemokine which attracts host defense cells such as neutrophils and macrophages to reduce the microbial insult. The epithelium can also respond by increasing the expression of surface molecules such as cell adhesion molecules that, in turn, may interact with proinflammatory cytokines and chemokines to assist the recruitment of leukocytes to the crevice.

Molecules in saliva, such as *lactoferrin*, may bind iron, change the local environment, and hence prevent microbial proliferation. In addition, lactoferrin is highly bactericidal. Molecules present in the GCF include *complement*, which can kill bacteria directly or together with antibodies, and can bring PMNs to the region (via chemotaxis) and hereby initiate and facilitate the process of phagocytosis.

The concept that epithelial and endothelial cells and fibroblasts are structural cells not involved in specific immune or inflammatory reactions has been disproved. Toll-like receptors are structures evolved to detect bacterial challenge and are present on all human cells, including epithelial and endothelial cells, and may bind microbial cell molecules, such as lipopolysaccharides, microbial fimbriae, and lipoteichoic acid. This suggests that even innate responses of the host may be tailored to particular bacteria. The host and its pathogens have developed together over millions of years and have learned to recognize, mimic, and utilize each other's systems in highly sophisticated ways.

Innate immune processes

The primary etiologic agent in the initiation of the gingivitis is the accumulation of the bacterial plaque biofilm in the gingival crevice. Irritation of the gingival tissues induces an "inflammatory response". The rapid inflammatory process that occurs in gingivitis is an early step in the initiation of the overall immune and inflammatory response, and is part of the *innate immune* system; i.e. it is part of the inherent biologic responses that require no prior experience. Inflammation is an extremely well coordinated process that comprises increased vascular permeability, migration of PMN leukocytes, monocytes, and lymphocytes into the affected tissues, and activation of cells to secrete inflammatory mediators that guide an amplifying cascade of biochemical and cellular events. Although inflammation was once considered a nonspecific arm of the immune response, the inflammatory response is actually a relatively specific event, which is carefully orchestrated through a wide-ranging repertoire of receptors and corresponding ligands.

The specific nature of inflammation allows rapid identification and a better tailored response to infection. For example, bacterial lipopolysaccharide (LPS), a common antigen of Gram-negative bacteria, is specifically recognized by host receptors such as soluble LPS binding protein, membrane-associated CD14 and toll-like receptors (TLRs). The interactions between LPS and these host proteins activate an intracellular cascade of events which leads to secretion of specific inflammatory mediators and antimicrobial proteins. These specific interactions may explain why the inflammatory response to Gram-positive bacteria is less pronounced than the inflammatory response to Gram-negative bacteria during *in vitro* and *in vivo* inflammatory assays. In addition, the discovery that there is a group of TLRs that can recognize a wide but restricted set of pathogen-associated molecular structures may explain how different bacteria induce different responses. In fact, even LPS from different bacteria may activate different TLRs, and induce a different response. These interactions enable the host to sample and sort its current environmental condition, to discriminate between pathogenic bacterial challenges, and to mount a selective and appropriate response. Recent data indicate that TLRs may respond to bacterial and non-bacterial challenges, such as oxidized low-density lipoprotein cholesterol. Thus the host may respond through inflammation to a range of challenges, from bacteria to cholesterol. However, the nature of the response differs and its character depends on the microbial triggering of specific receptors, the signal transduction pathways, and the way cells and tissues respond to these signals in terms of cytokine and defensive protein production.

During experimental gingivitis studies, individual variations in the rate of development of gingival inflammation have been noted (see Chapter 17) and the difference in gingivitis susceptibility is not simply due to plaque differences. Trombelli *et al.* (2004) have also shown that while all individuals will develop some degree of inflammation, there are interindividual differences in response to dental plaque. These differences may be explained by genetics or environment. Using the "twin study approach", Michalowicz *et al*. (2000), could not demonstrate an association between gingival inflammation and genetics, perhaps due to the cross-sectional approach of the study. However, their data support the major role of genetics in the development of periodontitis, in which

gingival inflammation is considered as a major part of the pathogenesis. In summary, all of the above studies are consistent with the hypothesis of genetically based host modulation of gingival inflammation.

Variation in microbial modulation of innate responses

Innate immunity represents the inherited resistance to microbial infection, which is detected by pattern-recognition receptors (PRRs). PRRs are strategically located at the interface between the mammalian host and the microbes, and have evolved to recognize conserved microbial motifs, known as microbe-associated molecular patterns (MAMPs). TLRs constitute an evolutionarily ancient PRR family, which plays a central role in the induction of innate immune and inflammatory responses. Not surprisingly, TLRs are expressed predominantly in cells which mediate first-line defense, such as neutrophils, monocytes/macrophages, and dendritic cells, as well as epithelial cells. Distinct members of the TLR family respond to different types of MAMPs, endowing the innate response with a relative specificity. The discovery of TLRs and the identification of their ligand repertoire have prompted the "bar code" hypothesis of innate recognition of microbes. According to this concept, TLRs read a "bar code" on microbes which is then decoded intracellularly to tailor the appropriate type of innate response. For instance, simultaneous activation of TLR5 and TLR4 would be interpreted as infection with a flagellated Gram-negative bacterium, whereas activation of TLR2 together with TLR5 would likely indicate the presence of a flagellated Gram-positive bacterium. However, this "bar code" detection system would not readily distinguish between pathogens and commensals, since they both share similar invariant structures (e.g., LTA, LPS, or flagellae). The immune system, however, generally elicits a vigorous inflammatory response against pathogens aimed at eliminating them, whereas it normally tolerates commensals.

The immune or adaptive defense system

In contrast to the innate host response, the adaptive response utilizes strategies of recognition, memory, and binding to support the effector systems in the elimination of challenging elements. Thus, the host response to factors released by microbial plaque in periodontal diseases involves a series of different effector mechanisms that are activated by the *innate* immune response. The effector mechanisms in this first line of defense may be insufficient to eliminate a given pathogen. The *adaptive* immune response, which is a second line of defense, is then activated. The adaptive response improves the host's ability to recognize the pathogen.

Immune memory and *clonal expansion* of immune cells are the hallmarks of adaptive immunity.

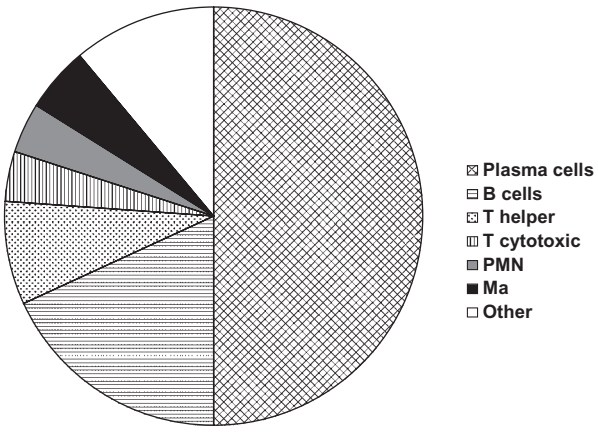

Fig. 11-14 Distribution of cell proportions in periodontitis lesions. Adapted from Berglundh & Donati (2005).

Although the effector mechanisms activated by the adaptive system appear to be similar to those of the innate system, the antimicrobial activities in adaptive immunity are specialized functions regulated by lymphocytes. This means that the defense mechanisms in the gingiva are synchronized by the communication through signals (cytokines) between specific groups of cells.

The cells involved in the adaptive response and which reside in the inflammatory lesion in sites with periodontitis have been described in several studies that included a histopathological analysis of the composition of the cell infiltrate. In a recent review on aspects of adaptive host response in periodontitis a meta-analysis was made with regard to the cell composition in periodontitis lesions (Berglundh & Donati 2005). Plasma cells represent about 50% of cells, while B cells comprise about 18%. The proportion of B cells is larger than that of all T cells. T helper cells occur in larger numbers than T cytotoxic cells. PMN cells and macrophages represent less than 5% of cells (Fig. 11-14). In the review it was further observed that lesions in aggressive and chronic forms of periodontitis exhibit similar features with respect to cellular composition. In both chronic and aggressive forms of periodontitis the proportions of plasma cells and B cells appear to be larger in lesions obtained from sites representing severe periodontitis than in lesions from areas with moderate or mild periodontitis.

The following outline provides an overview of T cell and B cell characteristics and immunoregulatory mechanisms of adaptive host response in periodontitis (Fig. 11-15).

Antigen presentation

The biofilm is consistently challenging the host. The antigens produced include proteins from Gram-positive bacteria and LPSs (endotoxins) from Gram-negative microorganisms. Antigen-presenting cells (APCs) have a unique ability to internalize and process antigens. Langerhans cells, macrophages,

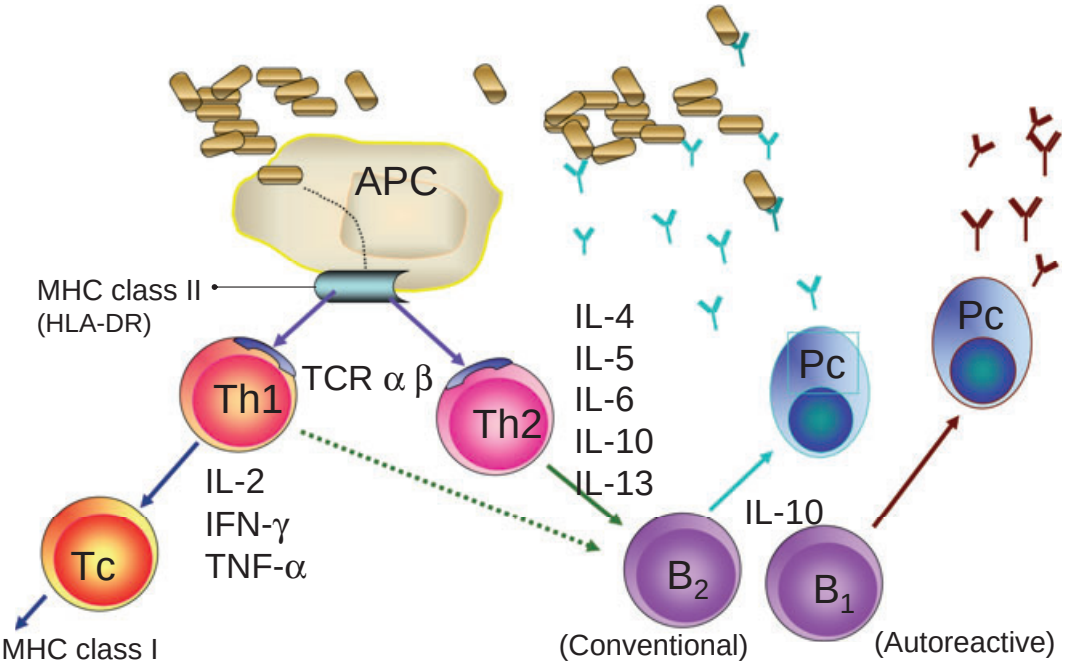

Fig. 11-15 Immune regulation in periodontal disease.

and dendritic cells are professional APCs and contribute to antigen recognition and early response mechanisms in host defense. B cells are considered to be important APCs in periodontitis and use the capacity of their memory systems in antigen presentation within the adaptive host response. The processed antigen (e.g. a peptide) inside the APC binds to an important carrying molecule. This molecule, termed *class-II* molecule of the major histocompatibility complex (MHC), transports the peptide to the cell surface. The peptide will thus, together with the MHC class-II molecule, become identifiable (i.e. presented) to T cells.

T cell receptors

The presentation of the processed antigen involves interactions with receptors on the T cells: T cell receptors (TCRs). It is in this context important to realize that the resulting immune response from this presentation varies with the build up of the TCR. The TCR is comprised of two glycoprotein chains, mainly alpha and beta (Fig. 11-15). The external portion of these alpha and beta chains contains a variable segment, which has many features in common with the antigen-binding site at immunoglobulins. This means that the composition of the variable segment in the alpha or the beta chain determines the type of immune reaction that will occur.

It is well known that the composition, or expression, of the variable chains of TCRs (TCR alpha/beta phenotype or genes) is of importance in several autoimmune diseases (Bröker *et al*. 1993) and also in periodontal disease (Nakajima *et al*. 1996; Yamazaki *et al*. 1997; Geatch *et al*. 1997; Berglundh *et al*. 1998). The results reported on TCRs in periodontitis have consistently revealed that the TCR repertoire of T cells in the local periodontitis lesions differs from that of T cells in peripheral blood. In other words, factors present at the local site, i.e. antigens released from microorganisms in the subgingival biofilm, may influence the expression of TCRs in the periodontitis lesion (Mathur *et al*. 1995). This fact also explains the differences observed in the distribution of TCRs in gingival tissues before and after periodontal therapy (Berglundh *et al*. 1999) as well as between adult subjects with advanced chronic periodontitis and children with aggressive periodontitis (Berglundh *et al*. 2001).

T cell dependent (mediated) processes

Cytokines produced by T helper (Th) cells regulate most functions within the adaptive defense system in the periodontal tissues. Th cells occur as Th-1 and Th-2 cells. Both Th-1 and Th-2 cells express the CD4 marker but are distinguished from each other by their cytokine production (cytokine profiles) (Fig. 11-15). Th-1 cells produce *IL-2*, *IFN-gamma*, and *TNF-alpha.* These cytokines have several functions and may activate other T cells, including the so-called cytotoxic T cells (Tc).

Tc cells express the CD8 marker and serve as guards against microorganisms that are capable of invading host cells, i.e. viruses and invasive bacteria. In the infected host cells, the antigen (e.g. a peptide) produced by the intracellularly located pathogen binds to MHC class-I molecules, which carry the peptide to the surface of the infected host cell. The Tc cell has the ability to recognize this alteration in the MHC class-I molecules and exerts its host defense action by destroying the membrane of the infected

cell and by activating its nucleases. This cell-mediated host response orchestrated by the Tc cell also includes activation of macrophages.

It is well established that CD8-positive cells are found in smaller numbers in gingivitis/periodontitis lesions than CD4-positive cells (Yamazaki *et al*. 1995; Berglundh *et al*. 2002a; Berglundh & Donati 2005). It may therefore be anticipated that viruses and other invasive microorganisms do not constitute a major part of the antigens in peridodontitis.

B cell regulation processes

The large amounts of soluble and accessible antigens occurring in the periodontal environment require the involvement of host defense systems different from those involved in cell-mediated immunity. Specific antibodies (immunoglobulins), occurring in fluids such as plasma or GCF, have the ability to bind to antigens. This type of host defense is called *humoral immune response*. In the process through which the antigen becomes bound to the antibody, certain effector systems, e.g. *complement*, are activated. The activation of the complement system, in turn, mediates PMN and macrophage migration to the site and phagocytosis is initiated. The process in which the antibody contributes to the elimination of antigens by enhancing phagocytosis is termed *opsonization.*

Antibodies are produced by plasma cells that represent the final stage in B cell proliferation. The activation and differentiation of B cells require the presence of certain cytokines, IL-4, IL-5, and IL-6, that are mainly produced by Th-2 cells (Gemmell & Seymour 1998). Since plasma cells and B cells constitute a major part of the leukocytes in advanced periodontitis lesions, it is reasonable to assume that Th-2 functions may dominate over those dependent on Th-1. In early studies it was indeed suggested that the immunoregulatory mechanisms in the advanced periodontitis lesions involve Th-2 cells to a larger extent than Th-1 cells (Seymour *et al*. 1993, 1996). Several later studies have, however, failed to confirm this observation (Yamazaki *et al*. 1994, 1997; Fujihashi *et al*. 1996; Prabhu *et al*. 1996; Yamamoto *et al*. 1997). Berglundh *et al*. (2002a) reported that the connective tissue lesions in advanced periodontitis contained similar proportions of cells expressing cytokine profiles characteristic for Th-1 (IFN-gamma and IL-2) and Th-2 (IL-4 and IL-6) cells. Current data thus suggest that chronic periodontitis lesions are regulated by a combined Th-1 and Th-2 function.

The immunoglobulins produced by plasma cells in the gingival lesions are mainly directed towards antigens present in the subgingival biofilm. Data have been presented, however, which indicate that antibodies directed against host tissue components, i.e. *autoantibodies*, may also occur in the gingival lesion (Hirsch *et al*. 1988, 1989; Jonsson *et al*. 1991). *Auto-reactive B cells*, also referred to as *B-1 cells*, are associated with the production of auto-antibodies. Large amounts of B-1 cells are present in the peripheral blood of patients with autoimmune disease, such as rheumatoid arthritis and Sjögren's syndrome (Youinou *et al*. 1988). The presence of circulating auto-reactive B cells in periodontitis patients has also been described. Thus, Afar *et al*. (1992) and Berglundh *et al*. (1998, 2002b) reported that B-1 cells occur in large numbers in the peripheral blood of patients with advanced chronic periodontitis. The gingival lesion in patients with such advanced periodontitis also contains a substantial number of B cells out of which about 30% exhibit auto-reactive characteristics (Sugawara *et al*. 1992; Berglundh *et al*. 2002b).

In this context it should be recognized that clinically successful, non-surgical periodontal therapy (i.e. resolution of gingivitis and reduction of sites with deep pockets) failed to alter the proportion of B-1 cells in peripheral blood (Berglundh *et al*. 1999). It was suggested that the elevated levels of B-1 cells in peripheral blood may not entirely reflect a response to microorganisms in the subgingival biofilm. Rather, it appears that the effector systems in the humoral immune response in periodontitis may also include production of antibodies directed to the periodontal tissues of the host.

In the humoral immune response the function, i.e. the avidity (binding strength to the antigen) of the antibody most also be considered. Thus, some but not all antibodies have a strong ability to opsonize bacteria and thereby prevent bacterial colonization. Account must also given to issues such as (1) whether antibody levels in the GCF or in serum or both are of importance for the protection of the host, (2) whether local levels of antibodies are merely a reflection of serum levels, or (3) whether significant antibody production by plasma cells present in the gingiva is taking place. In addition, there is evidence that the subclass of immunoglobulin produced has a bearing on aspects of its function such as complement fixation and opsonization. Thus, in aggressive periodontitis there seems to be a preponderance of IgG2 production over IgG1. This means that the functionally less effective IgG2 may play a role in rendering such patients more susceptible to periodontal tissue destruction (Wilson *et al*. 1995). Several studies suggest that assessments of the titer and avidity (the binding strength) of a patient's antibody to various microorganisms in the subgingival biofilm may be useful in the differential diagnosis and classification of periodontal diseases (Mooney *et al*. 1993).

IgG has four subclasses and IgA has two subclasses. Antibodies of different subclasses have different properties. Thus, IgG2 antibodies are effective against carbohydrate antigens (LPS) whereas the other subclasses are mainly directed against proteins. Kinane *et al*. (1997) studied the immunoglobulin subclasses (IgG1–4 and IgA1–2) produced by plasma cells in the gingival lesion of periodontitis patients (Fig. 11-16). The proportions of plasma cells producing IgG and IgA subclasses were similar to the

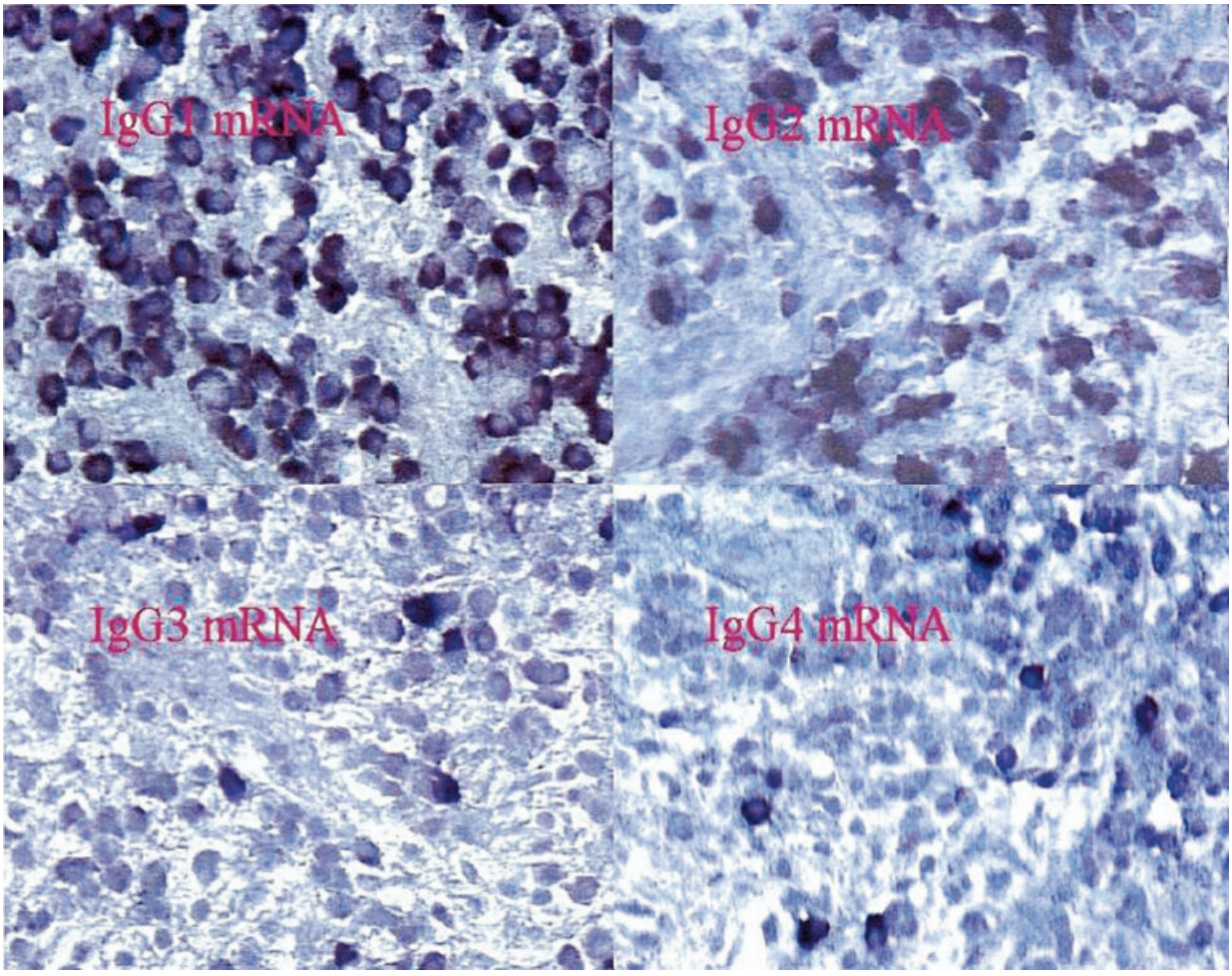

Fig. 11-16 Plasma cells within the periodontal gingiva. The mRNA for immunoglobulin production is noted in abundance within the plasma cell cytoplasms indicating that gingival plasma cells have the ability to produce antibodies locally (Kinane *et al*. 1997).

proportions of these immunoglobulin subclasses in serum. IgG1-producing plasma cells were predominant (mean 63%) in the gingival lesions; 23% of all IgG-producing plasma cells produced IgG2 antibodies, while IgG3- and IgG4-producing cells were present in much smaller numbers (3% and 10% respectively).

The protective role of the immune responses

Recruitment of leukocytes into areas of injury or infection is essential for an effective host defense. The constant migration of T cells and other leukocytes to tissues throughout the body allows the immune system to protect the host from a variety of antigenic challenges.

Leukocyte migration into tissues is particularly prominent during inflammatory responses and results from the cytokine-induced expression of adhesion molecules on the surface of vascular endothelial cells (Kinane *et al*. 1991) (Fig. 11-7). Endothelial leukocyte adhesion molecule-1 (ELAM-1) and intercellular adhesion molecule-1 (ICAM-1) are crucial for cellular trafficking (Fig. 11-6). The changes in vascular adhesion molecule expression and numbers of infiltrating leukocytes during a 21-day experimental gingivitis episode were investigated by Moughal *et al*. (1992). ELAM-1 and ICAM-1 positive vessels as well as PMNs and T cells were identified within gingival biopsy specimens taken on days 0, 7, 14, and 21. Vascular endothelium expressed ELAM-1 and ICAM-1 both in clinically "healthy" tissue (day 0) and in experimentally inflamed tissue (days 7–21). Positive vessels were found mainly in the connective tissue subjacent to the junctional epithelium where the highest numbers of T cells and neutrophils were also seen. A gradient of ICAM-1 was found to exist in the junctional epithelium, with the strongest staining in the marginal (crevicular) portion. This observation, together with the vascular expression of ELAM-1 and ICAM-1 in both clinically "healthy" and inflamed tissue, suggests that the function of the adhesion molecules is crucial and that these molecules direct leukocyte migration towards the gingival crevice (Fig. 11-7). The importance of these mechanisms is highlighted by the rapid progress of periodontitis that is found in patients with insufficient levels of ELAM-1

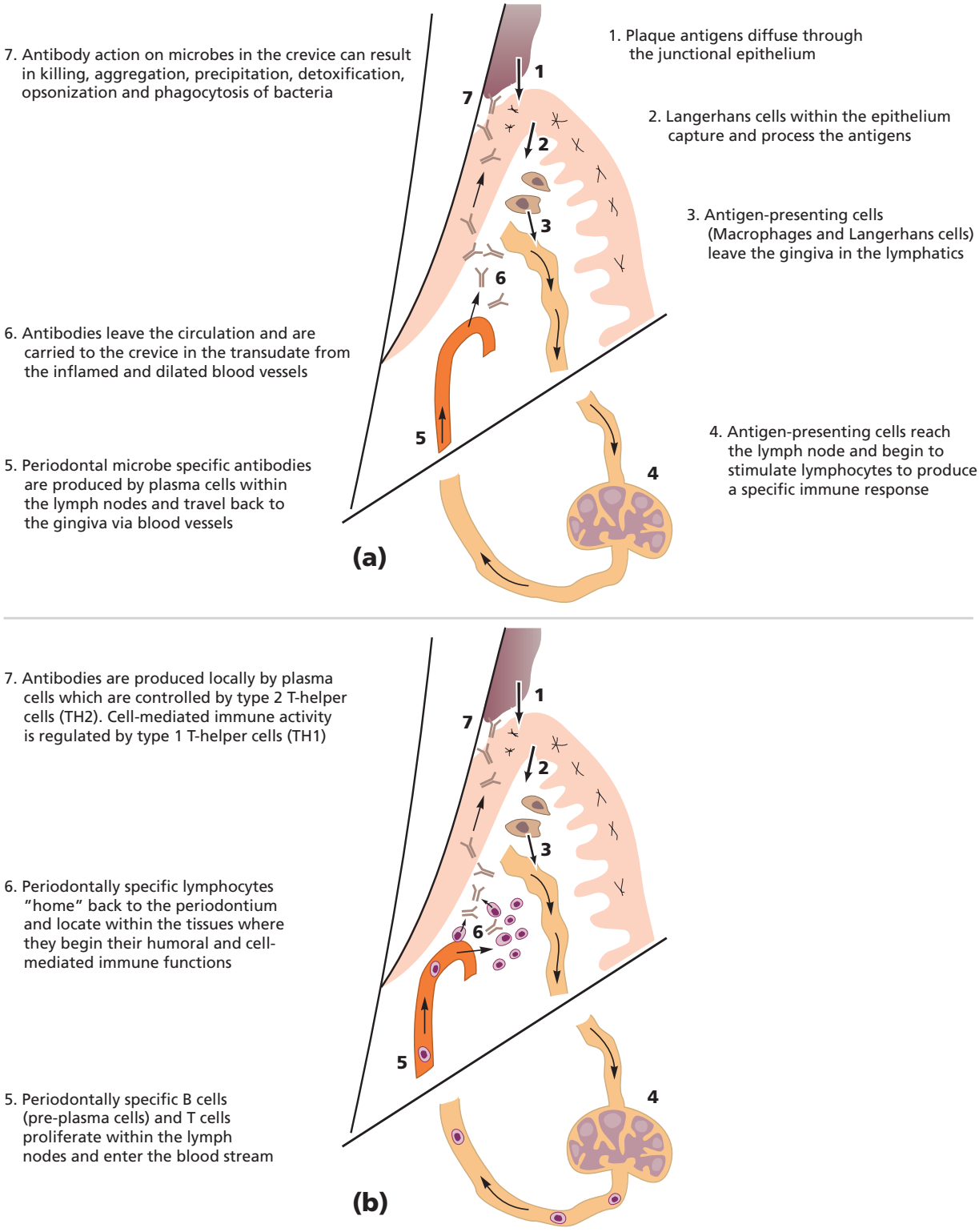

Fig. 11-17 (a) Schematic illustration of the systemic humoral immune response to microbial antigens within the gingival crevice region. (b) Schematic illustration of the local cellular immune response within the gingival crevice region and how this is invoked by microbial antigens and the mechanism by which pertinent periodontal immune cells traffic to the periodontium.

and ICAM-1, i.e. subjects suffering from *leukocyte adhesion deficiency syndrome* (LAD).

Specific antibody responses

P. gingivalis and *A. actinomycetemcomitans* are considered to be important pathogens in various forms of periodontal disease. Several studies have demonstrated that the antibody titers to these two organisms are increased in patients with periodontitis compared with subjects without disease (Kinane *et al.* 1993, 1999; Mooney & Kinane 1994).

Furthermore, Naito *et al.* (1987) and Aukhil *et al.* (1988) demonstrated that the serum titer to

P. gingivalis was *reduced* in subjects with advanced periodontitis following successful treatment. In this regard a study by Mooney *et al*. (1995) must be recognized. They reported on specific antibody titer and avidity to *P. gingivalis* and *A. actinomycetemcomitans* in chronic periodontitis patients before and after periodontal therapy. The authors observed that *IgG avidities* (the binding strength of the antibodies) to *P. gingivalis* increased significantly and specific *IgA levels* more than doubled as a result of treatment. Interestingly, only patients who had high levels of antibody before treatment showed a significant increase in antibody avidity. In addition, patients who originally had high levels of IgG and IgA to *P. gingivalis* also had better treatment outcomes, in terms of a reduced number of deep pockets and sites which bled on probing, than patients with initially lower titers.

Antibody levels are probably dependent on a number of factors including previous exposure to the subgingival microbiota and the host's ability to respond to particular antigens. The effect of treatment on antibody level and avidity may be the result of an inoculation (transient bacteremia) effect that occurs during scaling and root planing. The reduction in the amount of bacteria, i.e. the antigen load, which occurs after subgingival scaling and root planing, may allow the activation of B cells (clones) that produce antibodies with high avidity.

The findings described above suggest that periodontal therapy affects the magnitude and quality of the humoral immune response to periodontal pathogens, that this effect is dependent on initial serostatus, and that, thus, initial serostatus may have a bearing on treatment outcome.

In conclusion, the humoral immune response, especially IgG and IgA, is considered to have a protective role in the pathogenesis of periodontal disease but the precise mechanisms are still unknown. Periodontal therapy may improve the magnitude and quality of the humoral immune response through a process of immunization.

Homing – recruitment of cells to the periodontium

As explained previously, the recruitment of leukocytes into areas of injury or infection (homing) is essential for an effective host defense and the constant migration of leukocytes into the inflamed periodontal tissues results from the cytokine-induced expression of adhesion molecules on the surface of vascular endothelial cells. It has been suggested that antigen-presenting cells set up humoral immune response functions within peripheral lymph nodes (Fig. 11-17). Evidence exists, however, that homing of cells involved in both humoral and cellular immune responses is pronounced in diseased periodontal tissues. Recently Zitzmann *et al*. (2005a,b) reported on the specific "homing receptor" MadCAM-1 in periodontitis lesions. It is also possible that local proliferation of such leukocytes may occur in periodontitis. In an experimental gingivitis study in subjects who were treated for severe chronic periodontitis, Zitzmann *et al*. (2005b) reported that the presence of a residual inflammatory infiltrate influenced the reactions to *de novo* plaque formation. Thus, the increase of (1) the size of the gingival lesion, (2) the proportions of T and B cells, and (3) the expression of vascular adhesion molecules (including MadCAM-1) that occurred during the 21-day plaque formation period was more pronounced in sites that contained residual inflammatory infiltrates than in sites with no or only small remaining lesions. In other words, the large number of T cells and B cells that occur in the periodontitis lesion may be attracted to the diseased site through selective homing which is enhanced by local T and B cell presence.

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Chapter 12

Modifying Factors

Richard Palmer and Mena Soory

Diabetes, pregnancy, and tobacco smoking have profound and far-reaching effects on the host, including effects on the:

1. Physiological response
2. Vascular system
3. Inflammatory response
4. Immune system
5. Tissue repair.

They therefore have the potential to modify the:

1. Susceptibility to disease
2. Plaque microbiota
3. Clinical presentation of periodontal disease
4. Disease progression
5. Response to treatment.

Diabetes and smoking were cited as risk factors for periodontitis in Chapter 7 and the epidemiological evidence for their association with periodontitis was dealt with. Both factors are particularly important because they may affect the individual over a great many years, usually decades, and challenge the host to varying degrees. In contrast, pregnancy is of relatively short duration (although possibly with multiple episodes) but should be considered in relation to other hormonal changes which occur at puberty, menopause, and in women on hormonal contraceptives.

These three modifying factors are extremely important in many other disease processes, for example cardiovascular disease, which also affects people to varying degrees. Much of this variation in susceptibility is probably due to genetic interactions, and there is increasing evidence of important associations with many genetic polymorphisms. There will undoubtedly be emerging genetic evidence to link periodontal disease susceptibility to modifying factors considered in this chapter.

Diabetes mellitus

Diabetes mellitus (DM) is a complex disease with varying degrees of systemic and oral complications, depending on the extent of metabolic control, presence of infection, and underlying demographic variables. This has led to conflicting results in epidemiologic studies, with regard to periodontal disease presentation in diabetic patients and their response to treatment. This section deals with diabetes and its implications on the host response to bacterial plaque, in the context of clinical and laboratory data pertaining to periodontal disease.

Type 1 and type 2 diabetes mellitus

DM is categorized as type 1 and type 2 DM. Type 1 DM develops due to impaired production of insulin, while type 2 DM is caused by deficient utilization of insulin. Type 1 DM results from destruction of the insulin-producing β cells of the pancreas. This can occur when genetically predisposed individuals succumb to an inducing event such as a viral infection or other factors that trigger a destructive autoimmune response (Szopa *et al*. 1993). Approximately

10–20% of all diabetics are insulin-dependent or type 1. They usually have a rapid onset of symptoms associated with a deficiency or total lack of insulin and the condition may be difficult to control. Nearly 90% are diagnosed before the age of 21 years.

Type 2 DM results from insulin resistance, which also contributes to cardiovascular and other metabolic disturbances (Murphy & Nolan 2000). However, insulin production may decrease later in the disease process and require supplementation (Slavkin 1997), in addition to controlling diet or using oral hypoglycemic agents. The onset of symptoms in type 2 DM is more gradual and less severe, usually presenting after the age of 40 years.

Clinical symptoms

The typical signs and symptoms of diabetes are polyuria, polydipsia, polyphagia, pruritus, weakness, and fatigue. These features are more pronounced in type 1 than in type 2 DM, and are a result of hyperglycemia. The complications of DM include retinopathy, nephropathy, neuropathy, macrovascular disease, and impaired wound healing (Lalla *et al*. 2000; Soory 2000a). The treatment of DM is aimed at reducing blood glucose levels to prevent such complications.

There is conclusive evidence of the importance of glycemic control in the prevention of diabetic complications. Patients regularly use blood glucose monitors to provide effective feedback for adjustment of insulin dosage to meet individual requirements (Mealey 1998). Recent studies have shown significant improvement in reducing complications associated with type 2 DM with controlled blood glucose levels (UKPDS 1998a,b). In these studies of over 5000 type 2 DM patients, the risk of retinopathy and nephropathy was reduced by 25% with effective glycemic control, using sulfonylureas, metformin or insulin. The risk of developing hypoglycemia needs to be monitored in these patients on intensive treatment regimes, particularly those on insulin.

Oral and periodontal effects

Poorly controlled diabetic subjects may complain of diminished salivary flow and burning mouth or tongue. Diabetic subjects on oral hypoglycemic agents may suffer from xerostomia, which could predispose to opportunistic infections with *Candida albicans*. Candidiasis has been reported in patients with poorly controlled DM (Ueta *et al*. 1993), associated with suppressed oxygen free radical release by polymorphonuclear cells (PMNs) and reduced phagocytosis.

There is good evidence to support the concept that there is an association between poorly controlled diabetes mellitus and periodontitis (Fig. 12-1). Any differences in periodontal health between type 1 and type 2 DM patients may relate to differences in management of glycemic control, age, duration of disease, utilization of dental care, periodontal disease susceptibility, and habits such as smoking. Type 1 DM patients have an increased risk of developing periodontal disease with age, and with the severity and duration of their diabetes.

Periodontal attachment loss has been found to occur more frequently in moderate and poorly controlled diabetic patients, of both type 1 and type 2 DM, than in those under good control (Westfelt *et al*. 1996). In addition, diabetics with more advanced systemic complications present with a greater frequency and severity of periodontal disease (Karjalainen *et al*. 1994). Conversely, initial phase periodontal treatment comprising motivation and debridement of periodontal pockets in type 2 diabetic patients resulted in improved metabolic control of diabetes (Stewart *et al*. 2001). A recent study by Kiran *et al*. (2005) confirmed these findings. In a study population of patients with type 2 DM and glycosylated hemoglobin values of 6–8%, initial phase periodontal treatment resulted in a significant improvement in glycaemic control. Total cholesterol, triglyceride, and low density lipoprotein levels also decreased in the test group and increased in the control group. These

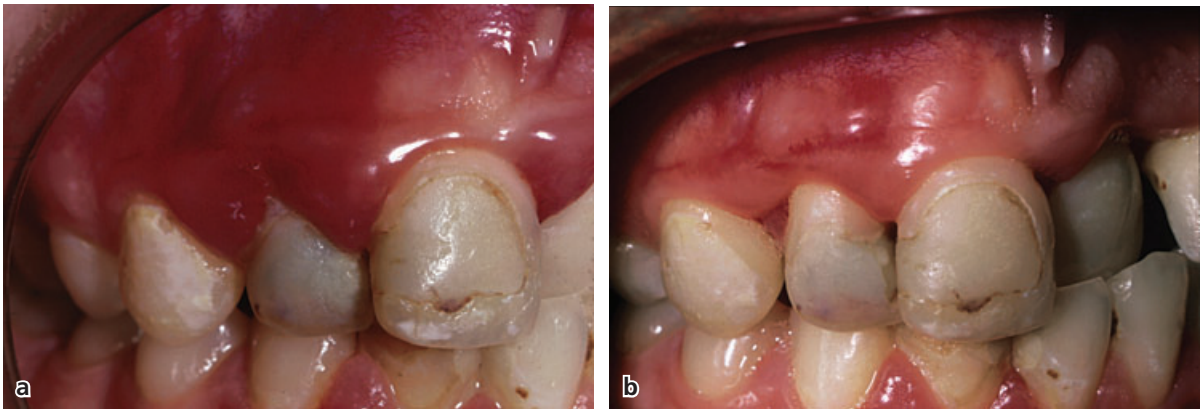

Fig. 12-1 Poorly controlled type 1 diabetes mellitus in a young female aged 19 years. (a) Very inflamed and swollen gingival tissues. Early attachment loss was present. (b) The same patient after responding to a course of non-surgical periodontal treatment and improved oral hygiene.

findings demonstrate that the status of periodontal disease control can contribute to metabolic control of DM (Faria-Almeida *et al*. 2006). The release of cytokines such as tumor necrosis factor (TNF)-α have implications on glucose and lipid metabolism (Cutler & Iacopino 2005) relevant to DM (Iacopino 2001) and cardiovascular disease. There are similar potential interactions between other systemic conditions and oral diseases (Pihlstrom *et al*. 2005; Kinane *et al*. 2006; Meurman & Hamalainen 2006). Insulin resistance can develop in response to chronic bacterial infection seen in periodontal disease, resulting in worse metabolic control in diabetic patients (Grossi *et al*. 1996). There is evidence to support the hypothesis that adequate control of severe inflammatory periodontal disease could alleviate symptoms of co-existing systemic diseases in susceptible individuals. In a population of Pima Indians with type 2 DM and severe periodontal disease, the risk of cardiorenal mortality and diabetic nephropathy was three times greater than amongst those with mild or moderate disease (Saremi *et al*. 2005).

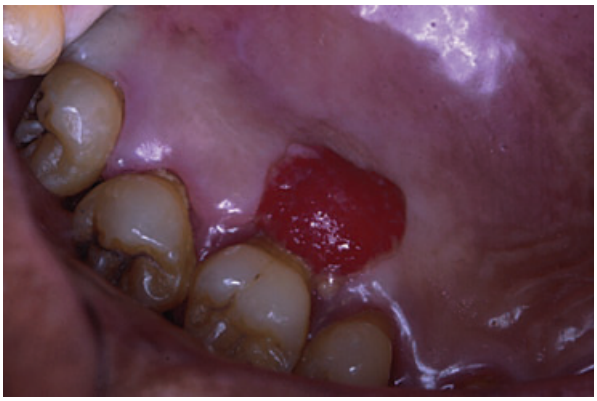

Fig. 12-2 A localized palatal periodontal abscess associated with a periodontal pocket in a 42-year-old poorly controlled diabetic patient.

Probably the most classic description of the undiagnosed or poorly controlled diabetic is the patient presenting with multiple periodontal abscesses, leading to rapid destruction of periodontal support (Figs. 12-2, 12-3). Harrison *et al*. (1983) reported a case of deep neck infection of the submental, sublingual, and submandibular spaces, secondary to periodontal abscesses involving the mandibular incisors, in a poorly controlled diabetic patient. In a population study Ueta *et al*. (1993) demonstrated that DM was a predisposing factor for periodontal and periapical abscess formation due to suppression of neutrophil function. The effects on the host response, and in particular neutrophil function, may account for this finding.

Association of periodontal infection and diabetic control

The presence of acute infection can predispose to insulin resistance (Atkinson & Maclaren 1990). This can occur independently of a diabetic state and persist for up to 3 weeks after resolution of the infection (Yki-Jarvinen *et al*. 1989). In a longitudinal study of subjects with type 2 DM, it was demonstrated that subjects with severe periodontal disease demonstrated significantly worse control of their diabetic condition than those with minimal periodontal

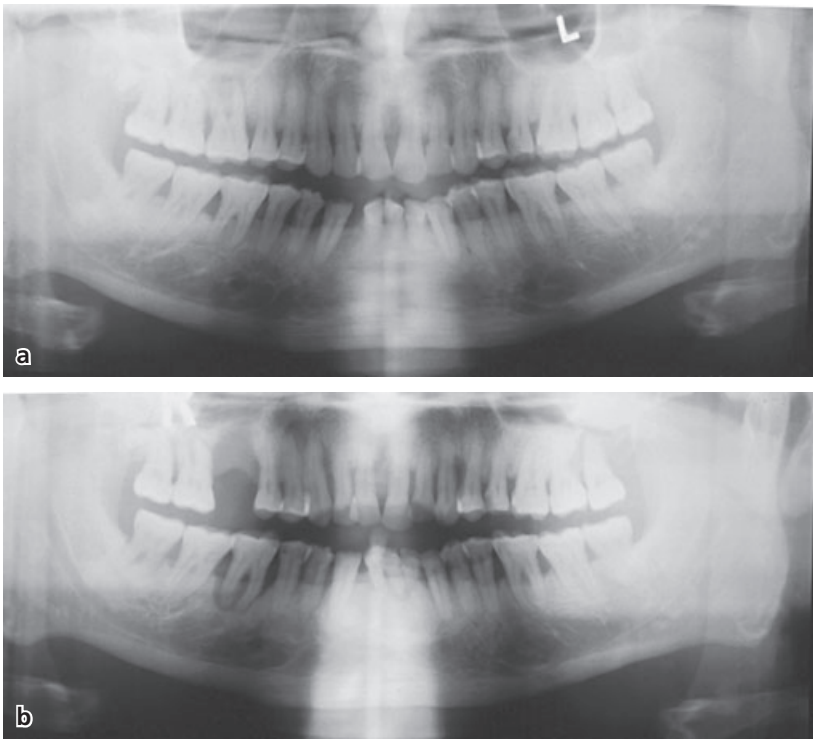

Fig. 12-3 Radiographs of a 50-year-old male who developed type 2 diabetes mellitus in the period between the two radiographs which were taken 3 years apart. There has been rapid bone loss and tooth loss associated with recurrent multiple periodontal abscesses.

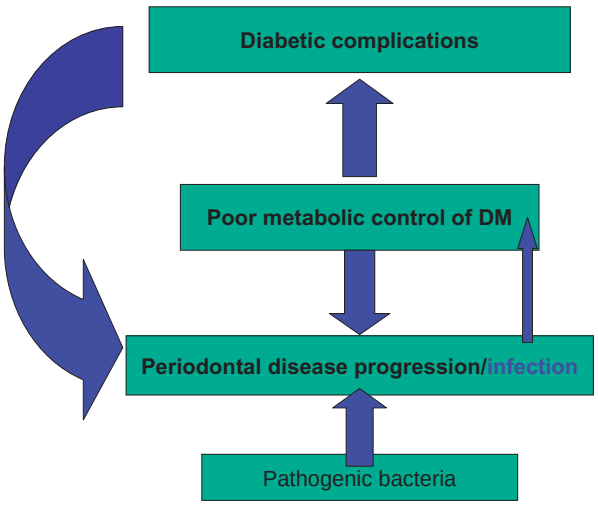

Fig. 12-4 Diabetes control and periodontal disease progression.

involvement (Taylor *et al*. 1996) (Fig. 12-4). The incidence of proteinuria and cardiovascular complications, as a result of uncontrolled diabetes, was found to be significantly greater in diabetics with severe periodontal disease than those with gingivitis or early periodontal disease (Thorstensson *et al*. 1996). Some studies have shown that stabilization of the periodontal condition with mechanical therapy, in combination with systemic tetracycline, improves the diabetic condition in such patients (Grossi *et al*. 1997b). Reduced insulin dosage in type 1 diabetics following periodontal treatment has also been reported (Sastrowijoto *et al*. 1990). However, other studies have not shown improvement in diabetic control following non-surgical periodontal treatment (Aldridge *et al*. 1995). These effects of periodontal therapy may be more pronounced in poorly controlled diabetic patients with severe periodontal disease.

Significant inflammatory lesions in severe periodontal disease could contribute to exacerbation of diabetes. Markers of inflammation common to diabetes and periodontal disease are an indication of disease control (Soory 2002, 2004).

Modification of the host–bacteria relationship in diabetes

Effects on microbiota

Hyperglycemia in uncontrolled diabetics has implications on the host response (Gugliucci 2000) and affects the regional microbiota. This can potentially influence the development of periodontal disease and caries in poorly controlled type 1 and type 2 DM patients. *Capnocytophaga* species have been isolated as the predominant cultivable organisms from periodontal lesions in type 1 diabetics, averaging 24% of the cultivable flora (Mashimo *et al*. 1983). A similar distribution of the predominant putative pathogens, *Prevotella intermedia*, *Campylobacter rectus*, *Porphyromonas gingivalis*, and *Aggregatibacter actinomycetemcomitans* (formerly known as *Actinobacillus actinomycetemcomitans*), to those associated with chronic adult periodontal disease was detected in periodontal lesions of type 2 diabetics (Zambon *et al*. 1988), with potential for disease activity during poor metabolic control. In an insulin-dependent diabetic population with a large proportion of poorly controlled diabetics, Seppala and Ainamo (1996) showed significantly increased percentages of spirochetes and motile rods and decreased levels of cocci in periodontal lesions, compared with well controlled patients.

Effects on the host response

Diabetes mellitus has far-reaching effects on the host response (Fig. 12-5).

Polymorphonuclear leukocytes

Reduced PMN function (Marhoffer *et al*. 1992) and defective chemotaxis in uncontrolled diabetics can contribute to impaired host defenses and progression of infection (Ueta *et al*. 1993). Crevicular fluid collagenase activity, originating from PMNs, was found to be increased in diabetic patients and this could be inhibited *in vitro* by tetracycline through its enzyme inhibitory effects (Sorsa *et al*. 1992). The PMN enzymes beta-glucuronidase (Oliver *et al*. 1993) and elastase, in association with diabetic angiopathy (Piwowar *et al*. 2000), have been detected at significantly higher levels in poorly controlled diabetic patients.

Cytokines, monocytes, and macrophages

Diabetic patients with periodontitis have significantly higher levels of interleukin (IL)-1β and prostaglandin E_2 (PGE_2) in crevicular fluid compared to non-diabetic controls with a similar degree of periodontal disease (Salvi *et al*. 1997). In addition, the release of these cytokines (IL-1β, PGE_2, TNF-α) by monocytes has been shown to be significantly greater in diabetics than in non-diabetic controls. Chronic hyperglycemia results in non-enzymatic glycosylation of numerous proteins, leading to the accumulation of advanced glycation end products (AGE), which play a central role in diabetic complications (Brownlee 1994). Increased binding of AGEs to macrophages and monocytes (Brownlee 1994) can result in a destructive cell phenotype with increased sensitivity to stimuli, resulting in excessive release of cytokines. Altered macrophage phenotype due to cell surface binding with AGE, prevents the development of macrophages associated with repair. This could contribute to delayed wound healing seen in diabetic patients (Iacopino 1995).

Connective tissue

A hyperglycemic environment, due to decreased production or utilization of insulin, can reduce growth,

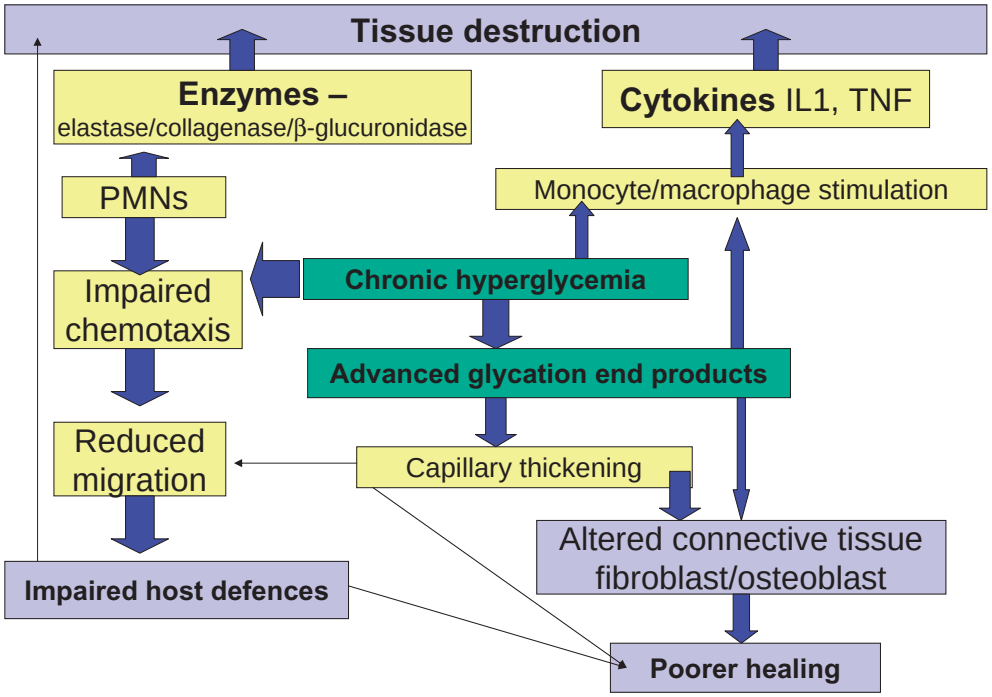

Fig. 12-5 Effects of diabetes mellitus on the host response.

proliferation, and matrix synthesis by gingival and periodontal ligament fibroblasts and osteoblasts. The formation of AGE results in reactive oxygen species, which are damaging to cellular function in gingival tissues, due to oxidative stress (Schmidt *et al*. 1996). The accumulation of AGE in tissues alters the function of several intercellular matrix components, including vascular wall collagen, resulting in deleterious complications (Ulrich & Cerami 2001). This has adverse effects on cell–matrix interactions and vascular integrity, potentially affecting periodontal disease presentation and treatment responses in uncontrolled diabetics. Vascular changes, such as thickening of the capillary basement membrane in a hyperglycemic environment, can impair oxygen diffusion, metabolic waste elimination, PMN migration, and diffusion of antibodies. Binding of AGE to vascular endothelial cells can trigger responses that induce coagulation, leading to vasoconstriction and microthrombus formation (Esposito *et al*. 1992), resulting in impaired perfusion of tissues. Recent work using a cell culture model has demonstrated that glucose, AGE, and nicotine inhibit the synthesis of steroid markers of wound healing (Rahman & Soory 2006). This inhibition was overcome by the antioxidant glutathione and insulin-like growth factor (IGF), which also functions as an antioxidant. These findings can be extrapolated to the 'in vivo' situation, demonstrating the relevance of oxidative stress-induced mechanisms in periodontal disease and DM, with therapeutic implications of medications with antioxidant effects (Soory & Tilakaratne 2003). These findings may be extrapolated to healing responses in the uncontrolled diabetic smoker with periodontal disease (Graves *et al*. 2006).

Effects on healing and treatment response

Wound healing is impaired due to the cumulative effects on cellular functions as described above. In summary, these factors include:

1. Decreased synthesis of collagen by fibroblasts
2. Increased degradation by collagenase
3. Glycosylation of existing collagen at wound margins
4. Defective remodeling and rapid degradation of newly synthesized, poorly cross-linked collagen.

Periodontal treatment

The treatment of well controlled DM patients would be similar to that of non-diabetic patients for most routine dental procedures. The short-term non-surgical treatment response of stable diabetics has been found to be similar to that of non-diabetic controls, with similar trends in improved probing depths, attachment gain, and altered subgingival microbiota (Christgau *et al*. 1998). Well controlled diabetics with regular supportive therapy have been shown to maintain treatment results 5 years after a combination of non-surgical and surgical treatment (Westfelt *et al*. 1996). However, a less favorable treatment outcome may occur in long-term maintenance therapy of poorly controlled diabetics, who may

succumb to more rapid recurrence of initially deep pockets (Tervonen & Karjalainen 1997).

Puberty, pregnancy, and the menopause

The hormonal variations experienced by women during physiological and non-physiological conditions (such as hormone replacement therapy and use of hormonal contraceptives) result in significant changes in the periodontium, particularly in the presence of pre-existing, plaque-induced gingival inflammation. The implications of these changes on the tissues of the periodontium have been reviewed comprehensively (Mascarenhas *et al*. 2003; Guncu *et al*. 2005). Periods of hormonal flux are known to occur during puberty, menstruation, pregnancy, and the menopause. Changes in hormone levels occur when the anterior pituitary secretes follicle-stimulating hormone (FSH) and luteinizing hormone (LH), resulting in the maturation of the ovary and cyclical production of estrogen and progesterone.

The gingiva is a target tissue for the actions of steroid hormones. Clinical changes in the tissues of the periodontium have been identified during periods of hormonal fluctuation. The effects of estrogen and progesterone on the periodontium have received significant research attention. The main potential effects of these hormones on the periodontal tissues can be summarized as:

- Estrogen affects salivary peroxidases, which are active against a variety of microorganisms (Kimura *et al*. 1983), by changing the redox potential.
- Estrogen has stimulatory effects on the metabolism of collagen and angiogenesis (Sultan *et al*. 1986).
- Estrogen can trigger autocrine or paracrine polypeptide growth factor signaling pathways, whose effects may be partially mediated by the estrogen receptor itself (Chau *et al*. 1998).
- Estrogen and progesterone can modulate vascular responses and connective tissue turnover in the periodontium, associated with interaction with inflammatory mediators (Soory 2000b).

The interaction of estrogen and progesterone with inflammatory mediators may help to explain the increased levels of inflammation seen during periods of hormonal fluctuation. For example, when cultured human gingival fibroblasts were incubated with progesterone concentrations common in late pregnancy, there was a 50% reduction in the formation of the inflammatory mediator IL-6, compared with control values (Lapp *et al*. 1995). IL-6 induces the synthesis of tissue inhibitor of metalloproteinases (TIMP) in fibroblasts (Lotz & Guerne 1991), reduces the levels of TNF and enhances the formation of acute phase proteins (Le & Vilcek 1989). A progesterone-induced reduction in IL-6 levels could result in less TIMP, more proteolytic enzyme activity, and higher levels of TNF at the affected sites, due to less inhibition, resulting in inflammation and obvious clinical manifestations.

Puberty and menstruation

During puberty, there are raised levels of testosterone in males and estradiol in females. Several studies have demonstrated an increase in gingival inflammation in children of circumpubertal age, with no change in plaque levels (Sutcliffe 1972). In a longitudinal study, Mombelli *et al*. (1989) reported that the mean papillary bleeding scores and percentage of interdental bleeding sites correlated with the development of secondary sexual characteristics at puberty, while other studies did not find a significant correlation between the onset of puberty and gingival changes in parapubescent women (Tiainen *et al*. 1992). These discrepancies may be attributed to factors such as the oral hygiene status of the population and study design.

The prevalence of certain periodontal pathogens reported during puberty may have a direct association with the hormones present and their utilization by selected pathogens. For example *Prevotella intermedia* is able to substitute progesterone and estrogen for menadione (vitamin K) as an essential nutrient (Kornman & Loesche 1979). An association between pubertal gingivitis, *P. intermedia* and serum levels of testosterone, estrogen, and progesterone has been reported in a longitudinal study (Nakagawa *et al*. 1994).

Pre-existing plaque-induced gingivitis may be an important factor in detecting hormone-induced changes during the menstrual cycle. Holm-Pedersen and Loe (1967) demonstrated that women with gingivitis experienced increased inflammation with an associated increase in crevicular fluid exudate during menstruation compared with healthy controls. Most female patients are not aware of any changes in their gingivae during the menstrual cycle (Amar & Chung 1994), while a few experience enlarged hemorrhagic gingivae in the days preceding menstrual flow. This has been associated with more gingivitis, increased crevicular fluid flow, and tooth mobility (Grant *et al*. 1988). Early studies demonstrated similar findings during the menstrual cycle in a population with pre-existing gingivitis, in response to fluctuations in the levels of estrogen and progesterone (Lindhe & Attstrom 1967).

Pregnancy

During pregnancy, the increased levels of sex steroid hormones are maintained from the luteal phase which results in implantation of the embryo, until parturition. Pregnant women, near or at term, produce large quantities of estradiol (20 mg/day), estriol (80 mg/day), and progesterone (300 mg/day).

Gingival inflammation initiated by plaque, and exacerbated by these hormonal changes in the second and third trimester of pregnancy, is referred to as pregnancy gingivitis. Parameters, such as gingival probing depths (Hugoson 1970; Miyazaki *et al*. 1991), bleeding on probing (Miyazaki *et al*. 1991), and crevicular fluid flow (Hugoson 1970), were found to be increased. These inflammatory features can be minimized by maintaining good plaque control.

According to early reports, the prevalence of pregnancy gingivitis ranges from 35% (Hasson 1966) to 100% (Lundgren *et al*. 1973). In a study of 130 pregnant women, Machuca *et al*. (1999) demonstrated gingivitis in 68% of the population, ranging from 46% in technical executives to 88% in manual workers. Cross-sectional studies examining pregnant and postpartum women have shown that pregnancy is associated with significantly more gingivitis than at postpartum, despite similar plaque scores (Silness & Loe 1963). Further observations were made by Hugoson (1970) in a longitudinal study of 26 women during and following pregnancy, which also demonstrated that the severity of gingival inflammation correlated with the gestational hormone levels during pregnancy (Fig. 12-6). A more recent study of a rural population of Sri Lankan women (Tilakaratne *et al*. 2000a) showed increased gingivitis of varying degrees of significance amongst all the pregnant women investigated, compared with matched non-pregnant controls. There was a progressive increase in inflammation with advancing pregnancy which was more significant in the second and third trimesters of pregnancy, despite the plaque levels remaining unchanged. At the third month after parturition, the level of gingival inflammation was similar to that observed in the first trimester of pregnancy. This suggests a direct correlation between gingivitis and sustained, raised levels of gestational hormones during pregnancy, with regression during the postpartum period. In investigations by Cohen *et al*. (1969) and Tilakaratne *et al*. (2000a), the values for loss of attachment remained unchanged during pregnancy and 3 months postpartum.

Effects on the microbiota

There is an increase in the selective growth of periodontal pathogens such as *P. intermedia* in subgingival plaque during the onset of pregnancy gingivitis at the third to fourth month of pregnancy. The gestational hormones act as growth factors, by satisfying the naphthoquinone requirement for bacteria (Di Placido *et al*. 1998). These findings were also confirmed by Muramatsu and Takaesu (1994) who showed that from the third to fifth month of pregnancy, the number of gingival sites which bled on probing corresponded with the percentage increase in *P. intermedia*. During pregnancy, progesterone is less actively catabolized to its inactive products, resulting in higher levels of the active hormone (Ojanotko-Harri *et al*. 1991). A 55-fold increase in the proportion of *P. intermedia* has been demonstrated in pregnant women compared with non-pregnant controls (Jensen *et al*. 1981), implying a role for gestational hormones in causing a change in microbial ecology in the gingival pocket. Although an overall association has been demonstrated, a cause and effect relationship may be less clear.

Effects on the tissues and host response

The increase in severity of gingivitis during pregnancy has been partly attributed to the increased circulatory levels of progesterone and its effects on the capillary vessels (Lundgren *et al*. 1973). Elevated progesterone levels in pregnancy enhance capillary permeability and dilatation, resulting in increased gingival exudate. The effects of progesterone in stimulating prostaglandin synthesis can account for some of the vascular changes (Miyagi *et al*. 1993).

The elevated levels of estrogen and progesterone in pregnancy affect the degree of keratinization of the

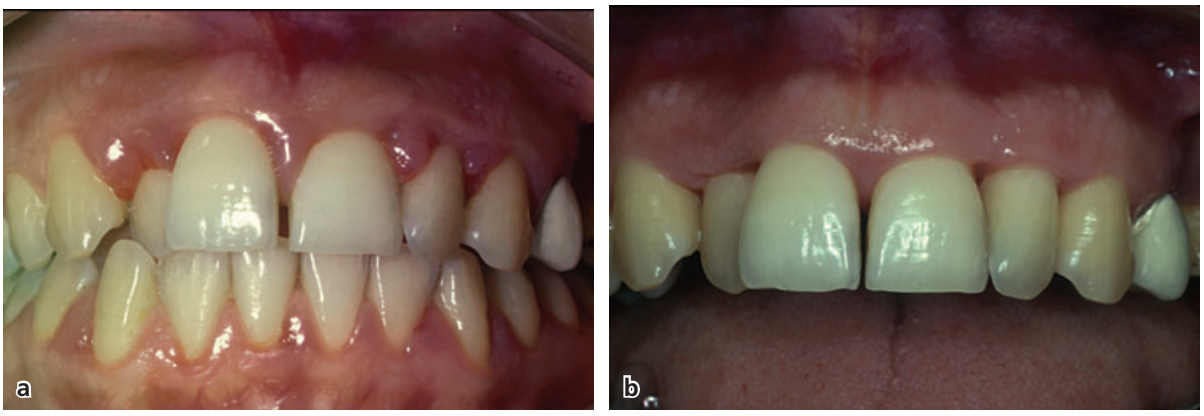

Fig. 12-6 Gingivitis associated with pregnancy. (a) A patient in the last trimester of pregnancy with very inflamed edematous gingival tissue which tended to bleed with the slightest provocation. (b) The improvement in gingival health 6 months after birth of the baby and an intensive course of non-surgical periodontal treatment.

gingival epithelium and alter the connective tissue ground substance. The decreased keratinization of the gingivae, together with an increase in epithelial glycogen, are thought to result in decreased effectiveness of the epithelial barrier in pregnant women (Abraham-Inpijn *et al*. 1996). Hormonal factors that affect the epithelium and increase vascular permeability can contribute to an exaggerated response to bacterial plaque during pregnancy. The influence of gestational hormones on the immune system can contribute further to the initiation and progression of pregnancy gingivitis. High levels of progesterone and estrogen associated with pregnancy (and the use of some oral contraceptives) have been shown to suppress the immune response to plaque (Sooriyamoorthy & Gower 1989). Neutrophil chemotaxis and phagocytosis, along with antibody and T cell responses, have been reported to be depressed in response to high levels of gestational hormones (Raber-Durlacher *et al*. 1993).

Pregnancy granuloma or epulis

A pedunculated, fibrogranulomatous lesion can sometimes develop during pregnancy and is referred to as a pregnancy granuloma or epulis. A combination of the vascular response induced by progesterone and the matrix stimulatory effects of estradiol contributes to the development of pregnancy granulomas, usually at sites with pre-existing gingivitis (Fig. 12-7). The vascular effects result in a bright red, hyperemic, and edematous presentation. The lesions often occur in the anterior papillae of the maxillary teeth and usually do not exceed 2 cm in diameter. They can bleed when traumatized and their removal is best deferred until after parturition, when there is often considerable regression in their size (Wang *et al*. 1997). Surgical removal of the granuloma during pregnancy can result in recurrence due to a combination of poor plaque control and hormone-mediated growth of the lesion. Careful oral hygiene and debridement during pregnancy are important in preventing its occurrence (Wang *et al*. 1997).

Periodontal treatment during pregnancy

Pregnant women need to be educated on the consequences of pregnancy on gingival tissues and thoroughly motivated in plaque control measures, with professional treatment as required. They are likely to be more comfortable to receive dental treatment during the second trimester than in the first or third trimester of pregnancy, although emergency treatment is permissible at any stage during pregnancy (Amar & Chung 1994). Since most medications cross the placental barrier and organogenesis occurs mainly in the first trimester, pregnant women are best treated in the second trimester, to avoid the occurrence of developmental defects. Any form of medication during pregnancy must only be used if the gravity of the condition being treated outweighs the consequences. Amongst the antibiotics, tetracycline, vancomycin, and streptomycin can contribute to staining of teeth and ototoxic and nephrotoxic effects during the fourth to ninth months of pregnancy; erythromycin, penicillins, and cephalosporins are relatively safer, but any medication must only be administered in consultation with the patient's obstetrician (Lynch *et al*. 1991).

Menopause and osteoporosis

During menopause there is a decline in hormonal levels due to decreased ovarian function. This is characterized by tissue changes such as desquamation of gingival epithelium (Fig. 12-8) and osteoporosis (Fig. 12-9) which may be attributed to hormone deficiency. It has been demonstrated that women with early onset of menopause have a higher incidence of osteoporosis and significantly lower bone mineral density (Kritz-Silverstein & Barrett-Connor 1993).

A third of women over age 60 are affected by postmenopausal osteoporosis (Baxter 1987). The changes involved are a reduction in bone density, affecting its mass and strength without significantly affecting its chemical composition. An alteration in the calcium–phosphate equilibrium due to deficient

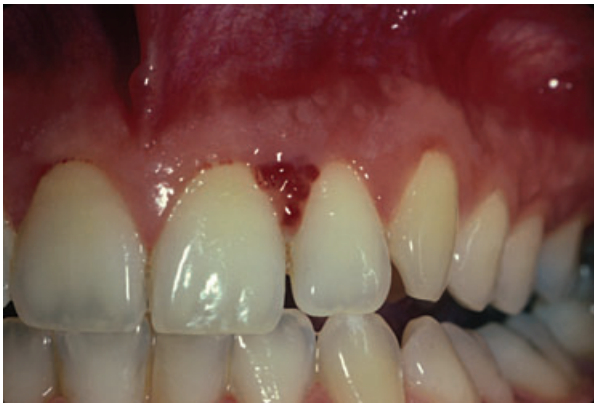

Fig. 12-7 Multi-lobulated appearance of an early pregnancy epulis, demonstrating vascular elements and tissue oedema.

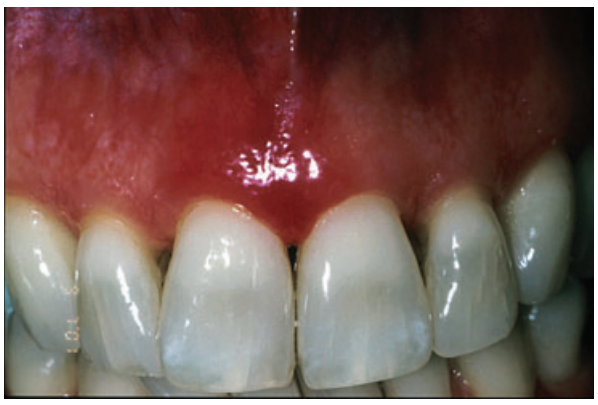

Fig. 12-8 Clinical appearance of anterior maxillary gingiva with pronounced desquamation in a woman during menopause.

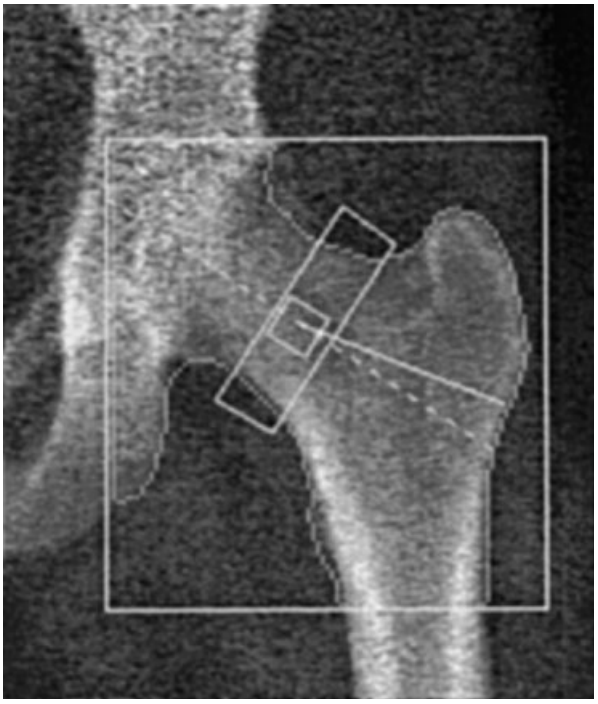

Fig. 12-9 A DEXA scan used to measure mineral bone density in the hip. This technique is not routinely applied to the jaws.

absorption of dietary calcium and increased excretion due to diminished estrogen levels can account for some of the bone changes seen in postmenopausal women (Shapiro *et al*. 1985), usually involving the mandible more than the maxilla.

Estrogen replacement therapy has been shown to prevent osteoporosis and maintain bone mineral content at several sites throughout the skeleton (Moore *et al*. 1990), with a 5% increase in bone mineral content in the region of the head compared to those taking placebo (Gotfredsen *et al*. 1986). The influence of estrogen on bone mineral density has been demonstrated in these studies, but a cause and effect relationship with periodontal disease is less clear.

A 2-year follow-up study of 42 171 postmenopausal women (Grodstein *et al*. 1996) showed that the risk of tooth loss was significantly lower amongst hormone users. These findings reinforce those of Paganini-Hill (1995), who showed a 36% decrease in tooth loss in estrogen users compared with non-users. There is evidence to suggest that use of estrogen is necessary to protect against bone loss (Grady *et al*. 1992). Although osteoporosis in postmenopausal women may not be the cause of periodontal disease, it may affect the severity of pre-existing disease. The circulating levels of estrogen have been shown to have an influence on alveolar bone density in postmenopausal women (Payne *et al*. 1997).

Effect of smoking on osteoporosis

A negative association between smoking and bone density has been demonstrated by Krall and Dawson-Hughes (1991). Smokers can differ from non-smokers in weight, caffeine intake, age at menopause, and alcohol consumption (Lindquist & Bengtsson 1979; Rigotti 1989); all these factors can potentially confound an association between smoking and bone density. A study on female twins by Hopper and Seeman (1994) showed that in the 20 pairs who varied most, by 20 or more pack years, the differences in bone density within pairs were 9.3% at the lumbar spine, 5.8% at the femoral neck, and 6.5% at the femoral shaft. This study also demonstrated increased serum levels of FSH and LH in smokers, implying reduced circulating levels of estrogen, leading to increased bone resorption. Other investigators have demonstrated the effects of smoking on the synthesis and degradation of estrogen (Jensen *et al*. 1985). The study by Jensen *et al*. (1985) investigated 136 postmenopausal women who were treated with three different doses of estrogen–progesterone or placebo. They showed reduced levels of estrogen in smokers (range of 1–30 cigarettes/day in the previous 6 months, mean 12.4), compared with non-smokers (not smoked in the previous 3 months). There was also a significant inverse correlation between the number of cigarettes smoked per day and the serum levels of estrogen, suggestive of increased hepatic metabolism of estrogen in postmenopausal smokers, resulting in lower serum levels of these hormones.

Treatment of osteoporosis

In osteoporotic patients, the rate of bone loss during the early postmenopausal period increases to 3–4% per year. Estrogen replacement therapy, which slows bone turnover, results in increased bone density in the trabecular spaces during remodeling (Frost 1989). The increased skeletal bone mass which occurs in response to estrogen replacement therapy is apparent in the first 2 years of treatment and maintained with continuation of treatment (Kimmel *et al*. 1994). The effects of estrogen in regaining bone mass to premenopausal levels and in preventing/reversing postmenopausal osteoporotic changes in the long bones and spine have been demonstrated in several studies (Armamento-Villareal *et al*. 1992; Takahashi *et al*. 1994).

There is some controversy with regard to the benefits of hormone replacement due to the risk factors involved. Fractures due to osteoporosis and heart disease in postmenopausal women can be reduced by 50% with estrogen replacement therapy. However, hormone replacement with estrogen alone exposes such patients to the risk of endometrial cancer. Long-term hormone replacement therapy has been shown to correlate with an increased risk of breast cancer. Modern formulations utilize combined therapy with a suitable dose of progesterone in combination with estrogen in order to minimize some of these risk factors (Whitehead & Lobo 1988).

Hormonal contraceptives

Contraceptives utilize synthetic gestational hormones (estrogen and progesterone), to reduce the likelihood of ovulation/implantation (Guyton 1987). Less dramatic but similar effects to pregnancy are sometimes observed in the gingivae of hormonal contraceptive users. The most common oral manifestation of elevated levels of ovarian hormones is an increase in gingival inflammation with an accompanying increase in gingival exudate (Mariotti 1994).

There are reported systemic risk factors associated with long-term use of hormonal contraceptives. The correlation between hormonal contraceptive use and significant cardiovascular disease associated with arterial and venous thromboembolic episodes has been reviewed by Westhoff (1996). Estrogen is responsible for both arterial and venous effects, while progesterone effects arterial changes. Women using oral contraceptives show elevated plasma levels of several clotting factors, related to the dose of estrogen. Raised levels of factors VIIc and XIIc are significant, since they increase the likelihood of coagulation and in men these factors have a strong positive correlation with ischemic heart disease. However, the relative risk is dependent on the contraceptive formulation used and there may not be a consistent biological plausibility to explain this association (Davis 2000).

There are several different formulations of hormonal contraceptives (Davis 2000) including:

1. Combined oral contraceptives containing artificial analogues of estrogen and progesterone
2. Progesterone-based mini-pill
3. Slow release progesterone implants placed subdermally that last up to 5 years (e.g. Norplant)
4. Depo Provera, a very effective progestin injection given by a doctor every 3 months.

Current combined oral contraceptives consist of low doses of estrogens (50 µg/day) and/or progestins (1.5 mg/day) (Mariotti 1994). The formulations used in the early periodontal studies contained higher concentrations of gestational hormones, e.g. 50 µg estrogen with 4 mg progestin (El-Ashiry *et al*. 1971), 100 µg estrogen with 5 mg progestin (Lindhe & Bjorn 1967). The results obtained in these studies would partly reflect the contraceptive preparation used. In one early study (Knight & Wade 1974) women who were on hormonal contraceptives for more than 1.5 years exhibited greater periodontal destruction compared to the control group of comparable age and oral hygiene. This could partly reflect higher dose of gestagens used in older contraceptive preparations. However, a recent study on a population of rural Sri Lankan women confirmed these findings (Tilakaratne *et al*. 2000b), showing significantly higher levels of gingivitis in contraceptive users (0.03 mg estradiol and 0.15 mg of a progestin), than non-users, despite similar plaque scores. There was also significant periodontal breakdown in those who used the progesterone injection (a depot preparation of 150 mg progesterone) 3-monthly for 2–4 years, compared with those who used it for less than 2 years. These findings may be attributed to the duration of use, and the effects of progesterone in promoting tissue catabolism, resulting in increased periodontal attachment loss. However, if low plaque levels are established and maintained for the duration of use, these effects could be minimized.

Effect on tissue response

Both estrogen and progesterone are known to cause increased gingival exudate, associated with inflammatory edema (Lindhe & Bjorn 1967). A 53% increase in crevicular fluid volume has been demonstrated in hormonal contraceptive users compared with controls. El-Ashiry *et al*. (1971) observed that the most pronounced effects on the gingiva occurred in the first 3 months of contraceptive treatment, but the dose of gestational hormones was higher in the older formulations compared with those used currently (Davis 2000), accounting for a more florid response in the tissues.

It has been suggested that the interaction of estrogen with progesterone results in the mediation of the effects characteristic of progesterone. Human gingiva has receptors for progesterone and estrogen (Vittek *et al*. 1982; Staffolani *et al*. 1989), providing evidence that gingiva is a target tissue for both gestational hormones. In *in vitro* studies of cultured gingival fibroblasts, estrogen enhanced the formation of anabolic androgen metabolites, while progesterone caused a diminished response. The combined effect of both gestational hormones on the yield of androgens was less pronounced than with estrogen alone, implying a more catabolic role for progesterone (Tilakaratne & Soory 1999).

Progesterone causes increased vascular permeability, resulting in the infiltration of polymorphonuclear leukocytes and raised levels of PGE_2 in the sulcular fluid (Miyagi *et al*. 1993). Increased capillary permeability may be induced by estrogen by stimulating the release of mediators such as bradykinin, prostaglandins, and histamine. However, the main effects of estrogen are in controlling blood flow. Hence the combination of estrogen and progesterone in the contraceptive pill can contribute to vascular changes in the gingivae. The resultant gingivitis can be minimized by establishing low plaque levels at the beginning of oral contraceptive therapy (Zachariasen 1993).

Tobacco smoking

Tobacco smoking is very common, with cigarettes being the main product smoked. In the European Union, an average of 29% of the adult population smoke, ranging from 17.5% in Sweden to 45% in Greece (http://www.ash.org.uk). The figure is higher

for men (35%) than for women (24%). Most smokers start the habit as teenagers, with the highest prevalence in the 20–24-year-old age group. Socioeconomic differences also exist with higher smoking in the lower socioeconomic groups. These data are similar for the US population (Garfinkel 1997; http://www.cdc.gov/tobacco/) where an estimated 44.5 million adults smoke. Reported smoking rates for third world countries are even higher. Smoking is associated with a wide spectrum of disease including stroke, coronary artery disease, peripheral artery disease, gastric ulcer, and cancers of the mouth, larynx, esophagus, pancreas, bladder, and uterine cervix. It is also a major cause of chronic obstructive pulmonary disease and a risk factor for low birth weight babies. Approximately 50% of regular smokers are killed by their habit and smoking causes 30% of cancer deaths.

Cigarette smoke is a very complex mixture of substances with over 4000 known constituents. These include carbon monoxide, hydrogen cyanide, reactive oxidizing radicals, a high number of carcinogens, and the main psychoactive and addictive molecule – nicotine (Benowitz 1996). Many of these components could modify the host response in periodontitis. In most of the *in vitro* studies considered in the latter parts of this chapter the experimenters utilized simple models with nicotine alone. Tobacco smoke has a gaseous phase and solid phase which contains tar droplets. The tar and nicotine yields of cigarettes have been reduced due to physical characteristics of the filters. However, there has been little change in the tar and nicotine content of the actual tobacco and the dose an individual receives is largely dependent upon the way in which they smoke (Benowitz 1989). Inter-subject smoking variation includes: frequency of inhalation; depth of inhalation; length of the cigarette stub left; presence or absence of a filter; and the brand of cigarette (Benowitz 1988).

The patient's exposure to tobacco smoke can be measured in a number of ways, including interviewing the subject using simple questions or more sophisticated questionnaires and biochemical analyses (Scott *et al*. 2001). The latter tests include exhaled carbon monoxide in the breath, which is commonly measured in smoking cessation clinics, and cotinine (a metabolite of nicotine) in saliva, plasma/serum or urine (Wall *et al*. 1988). Cotinine measurements are more reliable in determining a subject's exposure to tobacco smoke because the half-life is 14–20 hours compared with the shorter half-life of nicotine which is 2–3 hours (Jarvis *et al*. 1988). The mean plasma and salivary cotinine concentrations of regular smokers are approximately 300 ng/ml and urine concentrations are about 1500 ng/ml. Non-smokers typically have plasma/saliva concentrations under 2 ng/ml, but this may be raised slightly due to environmental exposure (passive smoking).

Inhalation of tobacco smoke allows very rapid absorption of nicotine into the blood and transport to the brain, which is faster than an intravenous infusion. Nicotine in tobacco smoke from most cigarettes is not well absorbed through the oral mucosa because the nicotine is in an ionized form as a result of the pH (5.5). In contrast cigar and pipe smoke is more alkaline (pH 8.5), which allows good absorption of un-ionized nicotine through the buccal mucosa (Benowitz 1988). Nicotine is absorbed rapidly in the lung where the smoke is well buffered. The administration of nicotine causes a rise in the blood pressure, an increase in heart rate, an increase in respiratory rate, and decreased skin temperature due to peripheral vasoconstriction. However, at other body sites, such as skeletal muscle, nicotine produces vasodilatation.

These differing actions of nicotine have led to some controversy over its action in the periodontal tissues. Clarke and co-workers (1981) showed that the infusion of nicotine resulted in a transient decrease in gingival blood flow in a rabbit model. However, Baab and Öberg (1987) using laser Doppler flowmetry to monitor relative gingival flow in 12 young smokers, observed an immediate but transient increase in relative gingival blood flow during smoking, compared to the presmoking or resting measurements. The authors hypothesized that the steep rise in heart rate and blood pressure due to smoking could lead to an increase in the gingival circulation during smoking. These results were confirmed by Meekin *et al*. (2000) who showed that subjects who smoked only very occasionally experienced an increase in blood flow to the head, whereas regular smokers showed no change in blood flow, demonstrating tolerance in the regular smoker. The increase in blood flow to the gingival and forehead skin following an episode of smoking in 13 casual consumers of tobacco was confirmed by Mavropoulos *et al*. (2003) and Morozumi *et al*. (2004) showed that the gingival blood flow significantly increased at 3 days following quitting, providing important information on the recovery of gingival tissue following quitting smoking.

Periodontal disease in smokers

Pindborg (1947) was one of the first investigators to study the relationship between smoking and periodontal disease. He discovered a higher prevalence of acute necrotizing ulcerative gingivitis, a finding that was confirmed in many subsequent studies of this condition (Fig. 12-10) (Pindborg 1949; Kowolik & Nisbet 1983; Johnson & Engel 1986). Early studies showed that smokers had higher levels of periodontitis but they also had poorer levels of oral hygiene (Brandzaeg & Jamison 1984) and higher levels of calculus (Fig. 12-11) (Alexander 1970; Sheiham 1971). Later studies which took account of oral hygiene status and employed more sophisticated statistical analyses showed that smokers had more disease regardless of oral hygiene (Ismail *et al*. 1983; Bergstrom 1989; Bergstrom & Preber 1994).

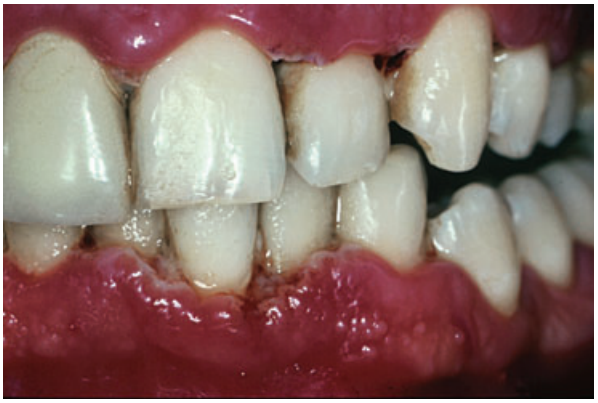

Fig. 12-10 The typical appearance of necrotizing ulcerative gingivitis in a heavy smoker with poor oral hygiene.

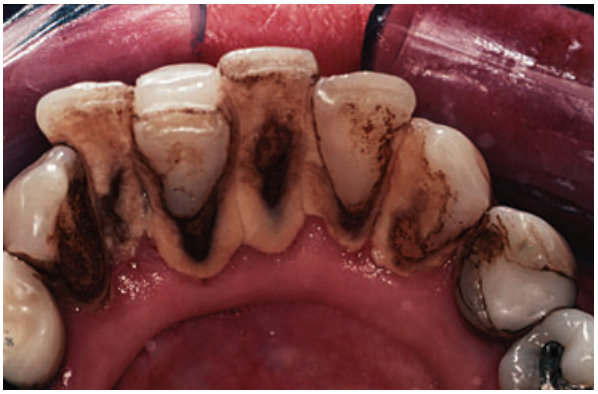

Fig. 12-11 The lingual aspects of the lower incisors showing gross supragingival calculus formation and relatively little gingival inflammation in a female patient who has smoked 20 cigarettes per day for over 20 years.

A large number of studies have established that in comparing smokers and non-smokers with periodontitis, smokers have:

1. Deeper probing depths and a larger number of deep pockets (Feldman *et al*. 1983; Bergstrom & Eliassson 1987a; Bergstrom *et al*. 2000a)
2. More attachment loss including more gingival recession (Grossi *et al*. 1994; Linden & Mullally 1994; Haffajee & Socransky 2001a)
3. More alveolar bone loss (Bergstrom & Floderus Myhred 1983; Bergstrom & Eliasson 1987b; Feldman *et al*. 1987; Bergstrom *et al*. 1991, 2000b; Grossi *et al*. 1995)
4. More tooth loss (Osterberg & Mellstrom 1986; Krall *et al*. 1997)
5. Less gingivitis and less bleeding on probing (Feldman *et al*. 1983; Preber & Bergstrom 1985; Bergstrom & Preber 1986; Haffajee & Socransky 2001a)
6. More teeth with furcation involvement (Mullally & Linden 1996).

The finding of less gingival bleeding on probing is associated with less inflamed marginal tissue and lower bleeding scores when probing the depth of the pockets. The typical clinical appearance of the smoker 's gingival tissue is shown in Fig. 12-12, which demonstrates relatively low levels of marginal inflammation and a tendency to a more fibrotic appearance with little edema. Despite the clinical appearance of the gingival tissue, the patient has deep pockets,

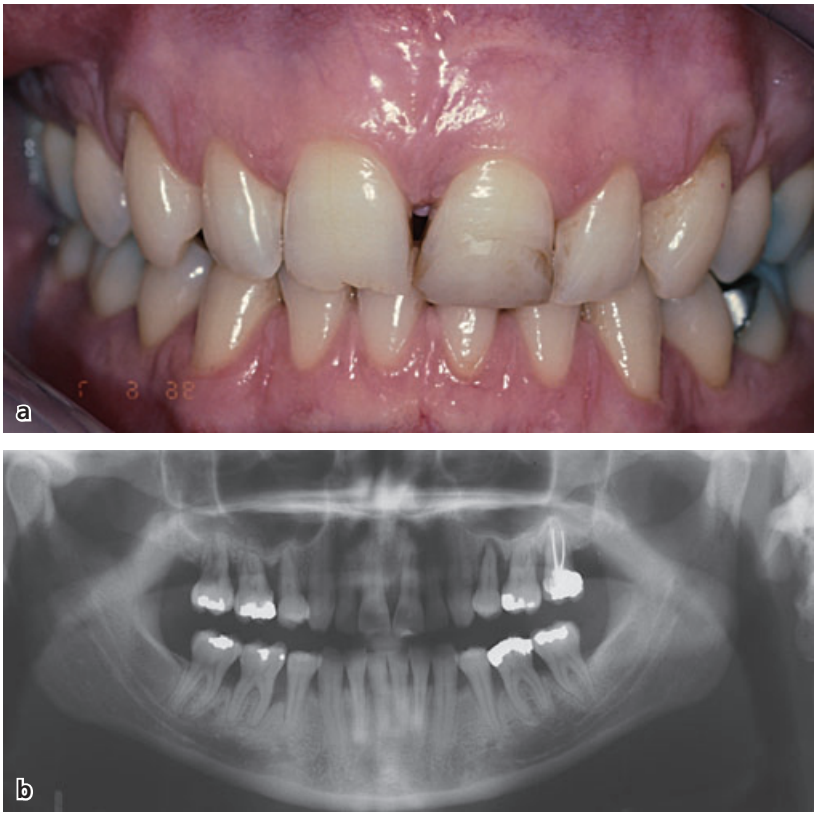

Fig. 12-12 A 30-year-old female smoker with advanced periodontitis. (a) The clinical appearance shows marginal gingiva with little signs of inflammation. Probing depths greater than 6 mm were present at most interproximal sites, but with little bleeding on probing. (b) Generalized advanced bone loss in this patient.

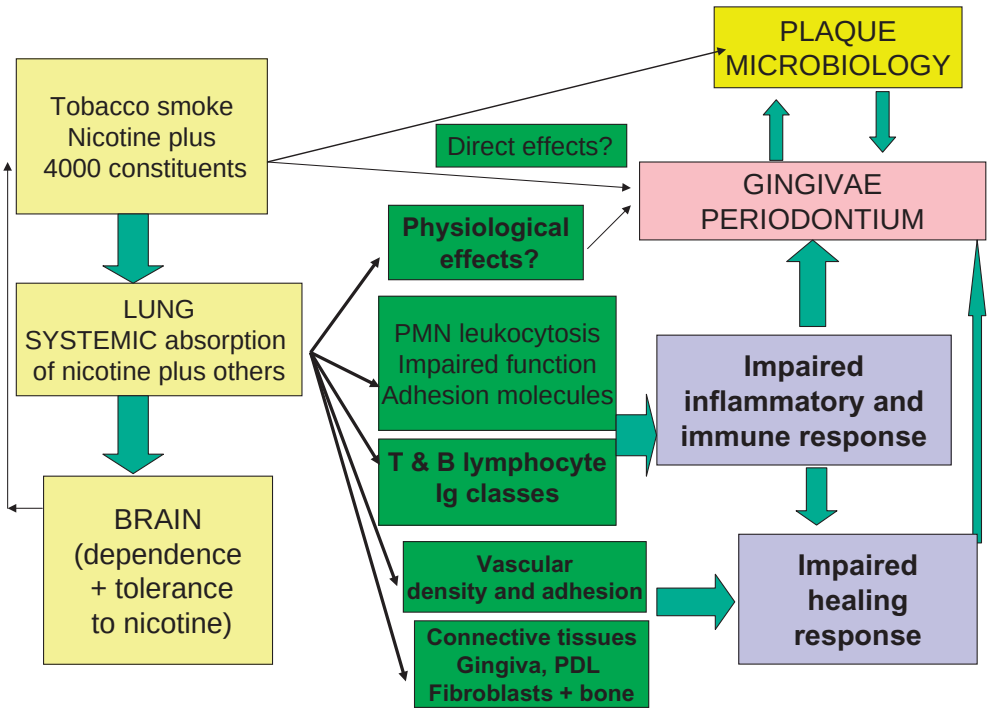

Fig. 12-13 Effects of tobacco smoking on the host response.

advanced attachment loss, and bone loss, as shown in Fig. 12-12b.

Modification of the host–bacteria relationship in smoking

There are several theories as to why smokers have more periodontal disease than non-smokers, involving both bacterial aspects and the host response (Barbour *et al*. 1997; Palmer *et al*. 2005). The potential interactions are illustrated in Fig. 12-13.

Effects on plaque bacteria

Smokers may have higher levels of plaque than non-smokers, which may be accounted for by poorer levels of oral hygiene rather than higher rates of supragingival plaque growth (Bergstrom 1981; Bergstrom & Preber 1986). Several studies have shown that smokers harbor more microbial species which are associated with periodontitis than non-smokers, including *P. gingivalis*, *A. actinomycetemcomitans*, *Tanerella forsythia (Bacteroides forsythus)* (Zambon *et al*. 1996), *P. intermedia*, *Peptostreptococcus micros*, *Fusobacterium nucleatum*, *Campylobacter rectus* (van Winkelhoff *et al*. 2001), *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* (Kamma *et al*. 1999). Smokers may have a higher proportion of sites harboring these putative periodontal pathogens, in particular the palatal aspects of the maxillary teeth and the upper and lower incisor regions (Haffajee & Socransky 2001a,b). In contrast several studies have failed to show differences in the bacterial species between smokers and non-smokers (Preber *et al*. 1992; Darby *et al*. 2000; Bostrom *et al*. 2001; van der Velden *et al*. 2003). Microbiological studies differ in their methodology, ability to identify and quantify putative pathogens, and the number of subjects included. Changes in the pocket environment secondary to the effect of smoking on the host tissues could result in a different microflora in smokers.

Effects on the host response

The relationship between plaque accumulation and development of inflammation in smokers has been studied in classical experimental gingivitis studies (Bergstrom & Preber 1986). They demonstrated that there is no difference in plaque accumulation when comparing smokers and non-smokers. However, the development of inflammation was very much retarded in the smoking group with less sites exhibiting redness or bleeding on probing. They also showed lower amounts of gingival crevicular fluid (GCF) during the development of gingivitis. Smoking may result in lower resting GCF flow rate (Persson *et al*. 1999) and an episode of smoking may produce a transient increase in GCF flow rate (McLaughlin *et al*. 1993). The reduced bleeding has previously been proposed to be caused by nicotine-induced vasoconstriction, but as previously described in this chapter, more recent evidence has failed to show a reduction in blood flow to the gingiva following smoking a cigarette in regular smokers (Meekin *et al*. 2000). The reduced bleeding on the other hand is probably due to long-term effects on the inflammatory lesion. Histological comparisons of the lesions from smokers and non-smokers have shown fewer blood vessels in

the inflammatory lesions of smokers (Rezavandi *et al*. 2001). It is pertinent to note that gingival bleeding on probing has been shown to increase within 4–6 weeks of quitting smoking (Nair *et al*. 2003), and this parallels reported recovery of reduced serum ICAM levels (Palmer *et al*. 2002).

Smoking has a profound effect on the immune and inflammatory system (reviewed by Barbour *et al*. 1997; Palmer *et al*. 2005). Smokers have an increased number of leukocytes in the systemic circulation (Sorenson *et al*. 2004), but fewer cells may migrate into the gingival crevice/pocket (Eichel & Shahrik 1969). Smoking is associated with chronic obstructive pulmonary disease (Barnes 2000) and many of the mechanisms indicated are paralleled in findings related to periodontal disease. It is thought that the main cell type responsible for destruction of lung parenchyma is the neutrophil, which is delayed in its transit through the pulmonary vasculature (McNee *et al*. 1989), where it is stimulated to release proteases including elastase, cathepsins, and matrix metalloproteases (Barnes 2000). These destructive molecules are balanced by inhibitors such as α-1-antitrypsin and tissue inhibitors of matrix metalloproteases.

Studies *in vitro* have shown a direct inhibition of neutrophil and monocyte–macrophage defensive functions by high concentrations of nicotine that may be achieved in patients using smokeless tobacco (Pabst *et al*. 1995). MacFarlane and co-workers (1992) examined patients with refractory periodontitis and found a high proportion of smokers in this diagnostic group. These investigators demonstrated abnormal PMN phagocytosis associated with a high level of cigarette smoking.

The PMN is a fundamental defense cell in the periodontal tissue. There is a constant traffic of PMNs from the gingival vasculature through the connective tissue and junctional epithelium into the gingival sulcus/pocket. This is described in some detail in Chapter 11. The PMN is the first line of defense and is chemotactically attracted to bacterial challenge at the dentogingival junction. The PMN contains a powerful battery of enzymes including elastase and other collagenases that have been implicated in tissue destruction in periodontitis and pulmonary disease. Eichel and Shahrik (1969) suggested decreased PMN migration into the oral cavity of smokers. Subsequently, PMNs harvested from the gingival sulcus of smokers were shown to have reduced phagocytic capacity compared to PMNs from non-smokers (Kenney *et al*. 1977). Neutrophil defects have been associated with an increased susceptibility to periodontitis, including cyclic neutropenia where there is a reduction in the number of neutrophils, and conditions such as leukocyte adhesion deficiency (LAD 1 and LAD 2), which may be responsible for cases of generalized prepubertal periodontitis as described by Page *et al*. (1983). It is proposed that smoking causes alterations to PMN function which could be considered to be minor variations of these more profound defects.

The normal passage of the PMN from the microvasculature to the periodontal tissues involves a classic series of events including capture, rolling on the endothelium, firm adhesion to the endothelium, and transmigration through the vessel wall into the connective tissue (Ley 1996). This involves a complex interaction between receptors and ligands on the leukocyte surface and endothelium including selectins, ICAM-1 and LFA1 (CD18, CD11b) (Crawford & Watanabe 1994; Gemmel *et al*. 1994). Defects in the functional ligands for the selectins have been implicated in LAD 2 and mutations in the gene encoding CD18 resulting in absence of the β 2 integrins with LAD 1. Subjects with LAD are susceptible to serious and life-threatening infections and have tremendous destruction of the periodontal tissues, often leading to total tooth loss in the deciduous dentition. These serious and rare conditions illustrate the overwhelming importance of the adhesion molecules and suggest that minor defects in them may also give rise to more subtle conditions that could lead to increased susceptibility to periodontal destruction. In this respect, it has been shown that smokers are affected by upregulation of molecules such as ICAM-1 on the endothelium and they have higher levels of circulating soluble ICAM-1 which could interfere with the normal receptor ligand binding and function of the leukocyte in the defense of the periodontal tissue (Koundouros *et al*. 1996; Palmer *et al*. 1999; Scott *et al*. 2000a). A potential destructive mechanism is the release of elastase from neutrophils following binding of ICAM with CD18 (Mac 1 and LFA 1) (Barnett *et al*. 1996). Lower levels of elastase detected in the gingival fluid of smokers compared to non-smokers, may indicate more elastase release within the tissues (Alavi *et al*. 1995), and this is especially important considering the effects of smoking on protease inhibitors.

Tobacco smoking has a chronic effect on the elevated levels of soluble ICAM (sICAM) and there is evidence that the subject may return to more normal levels after quitting smoking (Scott *et al*. 2000b; Palmer *et al*. 2002). These molecules can be detected in the serum and in the GCF. It has also been shown that cotinine is present in the GCF in about the same concentration as it appears in serum, but the levels of sICAM are much lower in smokers despite very much higher serum levels than non-smokers (Fraser *et al*. 2001). Many other molecules have been studied in the GCF of smokers with many reporting reduced levels compared to non-smokers. Alavi *et al*. (1995) showed significantly lower concentrations of elastase and elastase complexed with α1-antitrypsin in smokers GCF. Although Bostrom *et al*. (1999) showed higher levels of TNF-α in GCF in smokers, they reported no differences in levels of IL-6 (Bostrom *et al*. 2000). Rawlinson *et al*. (2003) found levels of IL-1beta and IL-1ra to be significantly lower in GCF from diseased sites in smokers compared to non-

smokers, and Petropoulos *et al*. (2004) showed that the concentration of IL-1alpha in GCF of smokers was approximately half that found in non-smokers.

PMN-related periodontal tissue destruction may also be related to suppression or exacerbation of the respiratory burst and generation of reactive oxygen species. For example Gustafsson *et al*. (2000) have shown that the priming capacity of TNF-α, measured as generation of oxygen radicals from stimulated neutrophils, is higher in neutrophils from smokers, compared to neutrophils from non-smokers. Thus, inappropriate activation of periodontal neutrophils is thought to contribute to the degradation of gingival tissues and the progression of inflammatory periodontal disease (Deas *et al*. 2003).

The effects of smoking on lymphocyte function and antibody production are very complex, with the various components having the potential to cause immunosuppression or stimulation. It is likely that the particulate phase of cigarette smoke confers immunosuppressive properties. Acute or chronic exposure to hydrocarbons may stimulate or inhibit the immune response, the net effect being dependent upon the dose and duration of the exposure to components of tobacco smoke. The leukocytosis observed in smokers results in increased numbers of circulating T and B lymphocytes (reviewed in Sopori & Kozak 1998). Studies that have examined T cell subsets report different findings of either reduced, increased or no change in the number of CD4 T cells (Loos *et al*. 2004). Smoking appears to affect both B and T cell function, inducing functional unresponsiveness in T cells.

It has been reported that serum IgG levels in smokers may be reduced (Quinn *et al*. 1998) with depression of IgG2, particularly in some racial groups (Quinn *et al*. 1996; Graswinkel *et al*. 2004). Reported levels of serum IgA and IgM classes are variable and IgE may be elevated (Burrows *et al*. 1981).

The clinical change in the tissues of smokers was described above. It is not surprising that histological evaluation of smokers' tissues has shown that there is a decrease in the vascularity of the tissues (Rezavandi *et al*. 2001). This is a chronic effect due to smoking and may also be associated with alterations in the expression of adhesion molecules within the endothelium. The effect of tobacco smoking on the expression of adhesion molecules on leukocytes, within the inflammatory lesion, in the junctional epithelium and cells of the pocket epithelium could have important implications on the progession of periodontitis in smokers. The effect of smoking on macrovasular disease is well documented (Powell 1998) and its effects on microvascular disease could also be of importance in periodontal disease and in healing.

Effects on healing and treatment response

The healing potential of tissues has important implications in any chronic inflammatory lesion and in repair following treatment. Smoking has been identified as an important cause of impaired healing in orthopedic surgery, plastic surgery, dental implant surgery (Bain & Moy 1993), and in all aspects of periodontal treatment including non-surgical treatment, basic periodontal surgery, regenerative periodontal surgery, and mucogingival plastic periodontal surgery (Preber & Bergstrom 1986; Miller 1987; Tonetti *et al*. 1995; Grossi *et al*. 1996, 1997a; Kaldahl *et al*. 1996; Bostrom *et al*. 1998; Tonetti 1998; Kinane & Chestnutt 2000; Heasman *et al*. 2006).

In non-surgical treatment, smoking is associated with poorer reductions in probing depth and gains in clinical attachment. In most studies smokers have a lower level of bleeding at baseline, and following treatment bleeding scores are reduced in smokers in a similar manner to those in non-smokers. The poorer reductions in probing depths and gains in attachment level amount to a mean of approximately 0.5 mm. Much of this may be due to less recession of the marginal tissues in smokers as there is less edema and more fibrosis in the gingiva. The same may be true for the deeper tissues of the periodontium where there is less of an inflammatory infiltrate and vascularity at the depth of the pocket. These differences in the tissues between smokers and non-smokers in the untreated state may largely account for the differences in response to non-surgical treatment. It has been proposed that these differences may be manifest by differences in probe penetration in smokers and non-smokers, particularly in deep pockets (Biddle *et al*. 2001).

The poor response of smokers to non-surgical treatment may also apply to those treated with adjunctive antibiotics (Kinane & Radvar 1997; Palmer *et al*. 1999). Response to non-surgical treatment may be seen merely as resolution of inflammation and improvement of the epithelial attachment together with some formation of collagen. However, the response following periodontal surgery is more complex and involves an initial inflammatory reaction followed by organization of the clot, and formation of granulation tissue consisting of capillary buds and fibroblasts laying down collagen. The surgical flaps have to revascularize and the epithelial attachment has to reform on the surface. In regenerative surgery there also has to be formation of a connective tissue attachment and cementogenesis. Tobacco smoke and nicotine undoubtedly affect the microvasculature, the fibroblasts and connective tissue matrix, the bone and also the root surface itself. It has been shown in *in vitro* studies that fibroblasts are affected by nicotine in that they demonstrate reduced proliferation, reduced migration and matrix production, and poor attachment to surfaces (Raulin *et al*. 1988; Tipton & Dabbous 1995; James *et al*. 1999; Tanur *et al*. 2000). The root surfaces in smokers are additionally contaminated by products of smoking such as nicotine, cotinine, acrolein, and acetaldehyde, and these molecules may affect the attachment of cells (Raulin

et al. 1988; Cattaneo *et al*. 2000; Gamal & Bayomy 2002; Poggi *et al*. 2002). Smoking has a direct effect on bone and is an established risk factor in osteoporosis. It has also been proposed that it may have a direct affect on bone loss in periodontitis (Bergstrom *et al*. 1991) and it undoubtedly delays healing of bone in fracture wound repair. It is not surprising therefore that tobacco smoking has been implicated in poorer responses to periodontal surgical treatment.

Smoking cessation

All patients should be assessed for smoking status and given advice to quit the habit. About 70% of people who smoke would like to quit and should be assisted. They should be referred to specialist cessation services if the treating practitioner does not feel confident in this area. They can be advised about nicotine replacement therapy. People's success with quitting is considerably improved using nicotine replacement therapy and drugs such as buproprion hydrochloride. Former smokers more closely resemble non-smokers in their periodontal health status and response to treatment, but the time required to revert to this status has not been defined. In one of the few papers that have attempted to combine a quit smoking and periodontal treatment interventional study, Preshaw *et al*. (2005) showed a more favorable periodontal treatment outcome in those subjects that managed to quit using well established quit smoking strategies including counseling, nicotine replacement therapy and bupropion. From the original group of 49 subjects there were only 11 continuous quitters at 12 months. It would be of great interest to determine what changes in periodontal status would have occurred with just the quit smoking intervention, and more randomized controlled clinical trials are required in this area.

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Chapter 13

Susceptibility

Bruno G. Loos, Ubele van der Velden, and Marja L. Laine

Introduction

Periodontitis is a chronic infectious disease of the supporting tissues of the teeth. Due to the bacterial infection, the periodontal tissues become inflamed and are slowly destroyed by the action of the inflammatory process. If left untreated, the teeth lose their ligamentous support to the alveolar bone, become mobile, and are eventually lost.

Periodontitis is considered to be a complex disease. Common features of complex human diseases (for example Alzheimer's disease, Crohn's disease, and cardiovascular diseases) are that these conditions present mostly with a relatively mild phenotype, and are slowly progressive and chronic in nature (Tabor *et al*. 2002). Furthermore, these types of disease are of relatively late onset (mostly adult onset) and relatively common. The pathophysiology of complex diseases is characterized by various biological pathways, leading to similar clinical phenomena. Importantly, complex diseases are associated with variations in multiple genes, each having a small overall contribution and relative risk for the disease process. Complex diseases are typically polygenic, i.e. multiple genes play each a limited role (low penetrance genes); the disease genes in complex diseases are therefore considered disease-modifying genes (Hart *et al*. 2000b). Analogous to other complex diseases, we estimate that for periodontitis, at least 10 and as many as 20 disease-modifying genes may be involved. However, it is important to realize that the number and type of disease-modifying genes for the same condition may not be equal for different forms of periodontitis and different ethnic populations; they are also influenced by environmental factors (gene–environment interactions).

Disease-modifying genes contrast to major disease genes. Aberrant allelic forms (see Box 13-1) of major genes are responsible for disease expression according to Mendel's laws (Hart *et al*. 2000b). For example, the fatal inherited disease cystic fibrosis is caused by a recessive mutation in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene (Brennan & Geddes 2002). This gene encodes for a protein that functions as a plasma membrane chloride channel in epithelial tissues, in particular in lung epithelium. If a person is homozygous for the *rare* disease allele (*R*-allele), then he/she will develop cystic fibrosis. On the other hand, individuals will not develop the disease if they are homozygous for the *normal (N)* allele (so called *wild type*) or when they are heterozygous, i.e. they have both the dominant *N*-allele and the recessive *R*-allele.

A genetic component in the etiology of periodontal disease was proposed as early as 1935 (reviewed in Loevy 1976). From the late 1990s a substantial increase in papers on putative genetic risk factors for susceptibility to and severity of periodontitis has appeared in the periodontal literature (Michalowicz *et al*. 1991; Hart 1994; Hart & Kornman 1997; Hart *et al*. 1997, 2000b; Page 1999; Page & Sturdivant 2002). The presence of genetic risk factors directly increases

Box 13-1 Human genes, polymorphisms and other definitions

Each normal human being has 23 pairs of chromosomes (the diploid human genome), 22 pairs of *autosomal* chromosomes and 1 pair of sex chromosomes (XX for females and XY for males) (Fig. 13-1). From each pair, one chromosome is inherited from the father and one from the mother. Chromosomes show differences in size and have characteristic lateral series of bands (G-banding); therefore each chromosome can be identified by its characteristic size and banding pattern.

Each chromosome contains a long duplex of deoxyribonucleic acid (DNA). DNA consists of chemically linked sequences of nucleotides; these are the "building blocks" of the DNA and always contain a nitrogenous base. Four nitrogenous bases exist: adenine (A), guanine (G), cytosine (C), and thymine (T). The bases are linked to a sugar (2-deoxyribose), where a phosphate group is also added. The *haploid* human genome (i.e. one copy of 22 autosomal chromosomes and one sex chromosome) consist of 3.3×10^9 nucleotides (also written as 3.3×10^9 base pairs (bp)). In the chromosomes, DNA is arranged in a double helix model: two polynucleotide chains in the duplex are associated together by hydrogen bonding between the nitrogenous bases. These reactions are described as base pairing and they are complementary: G pairs only with C, and A pairs only with T. Therefore, if one chain of DNA is sequenced, the complementary chain of the duplex can be deduced.

DNA contains the genetic code and a given specific sequence of nucleotides encodes for the sequence of amino acids that constitutes the corresponding protein (Fig. 13-2). The genetic code is read in groups of three nucleotides; each trinucleotide sequence (triplet) is called a codon. Written in the conventional direction from left to right, the nucleotide sequence of the DNA strand, a gene can be deciphered. A gene consists of two parts (Fig. 13-2): (1) a *coding region*, i.e. a reading frame starting at nucleotide position +1, containing a multitude of triplets that codes for a sequence of amino acids to form a protein; and (2) a *promoter region*, i.e. a sequence of nucleotides upstream (left) of the coding region starting with nucleotide position –1 read from right to left, that is not organized in a series of triplets but contains stretches of nucleotides that are essential for the regulation of the transcription of the coding region. Within the coding region intermittent areas of non-coding DNA exist; these regions are called introns. The true coding areas within the coding region are called exons (Fig. 13-2). From the recent results of the human genome project, it is estimated that about 25 000 human genes exist.

Variant forms (polymorphisms) of a gene that can occupy a specific chromosal site *(locus)* are called *alleles.* Two or more alleles for a given locus may exist in nature throughout evolution, but may develop at any time. A *polymorphic* locus is one whose alleles are such that the most common, *normal* variant (*N*-allele) among them occurs with <99% frequency in the population. Thus, if a locus is for example *bi-allelic*, the *rarer* allele (designated *R*-allele) must occur with a frequency >1% in the population. In this way, when different alleles of a given gene co-exist in the human population, we speak about *genetic polymorphisms*.

Polymorphisms arise as a result of gene mutations. All organisms undergo spontaneous mutations as a result of normal cellular function or random interactions with the environment. An alteration that changes only a single base pair is called a point mutation. Not all point mutations are repaired and can therefore be transmitted by inheritance through generations. The most common class of point mutations is the *transition*, comprising the substitution of a G-C (guanine–cytosine) pair with an A-T (adenine–thymine) pair or vice versa. The variation at the site harboring such changes has recently been termed a "single nucleotide polymorphism" (SNP) (Schork *et al*. 2000).

The SNP may have no effects or may have some important biological effects. For example, if a transition has taken place within the coding region of a gene, it may result in an amino acid substitution and therefore an altered protein structure, which may then alter its function. Or, when such mutations have taken place in the promoter region of the gene, it may alter gene regulation, for example resulting in (completely) inhibited or reduced gene expression or, alternatively, result in over-expression of the gene, perhaps with biological consequences. SNPs occur more frequently than any other type of genetic polymorphism; the frequency of SNPs across the human genome is estimated at every 0.3–1 kilobases (Kb).

Other SNPs result from *insertions* or *deletions*. The simple form of this polymorphism is where a single nucleotide pair may be deleted or may be inserted with the same potential effects as described above for the *transition*. Another common type of insertion/deletion polymorphism is the existence of variable numbers of repeated bases or nucleotide patterns in a genetic region. Repeated base patterns can consist of several hundreds of base pairs, known as "variable number of tandem repeats" (VNTRs or *mini-satellites*). Also common are *micro-satellites*, which consist of two, three or four nucleotide repeats, on a variable number of occasions.

(*Continued*)

Box 13-1 *Continued*

Micro-satellites are also referred to as *simple tandem repeats* (STRs). Such repeats are considered highly polymorphic and often result in many alleles or gene variants due to the existence of many different repeat sizes within the population. The STRs may occur every 3–10 Kb genome wide.

Genetic polymorphisms are very useful in studies of population genetics. After genotyping individuals and assessing genotype frequencies among groups of interest, one can also calculate the frequency of the *N*-allele and the *R*-allele among the groups or populations under study. Frequencies of genotypes and alleles may differ between a diseased and a healthy group. Subsequently, when a given allele is identified to be associated with disease, functional studies can be started to investigate the possible role of that gene in the etiology and pathogenesis of the disease.

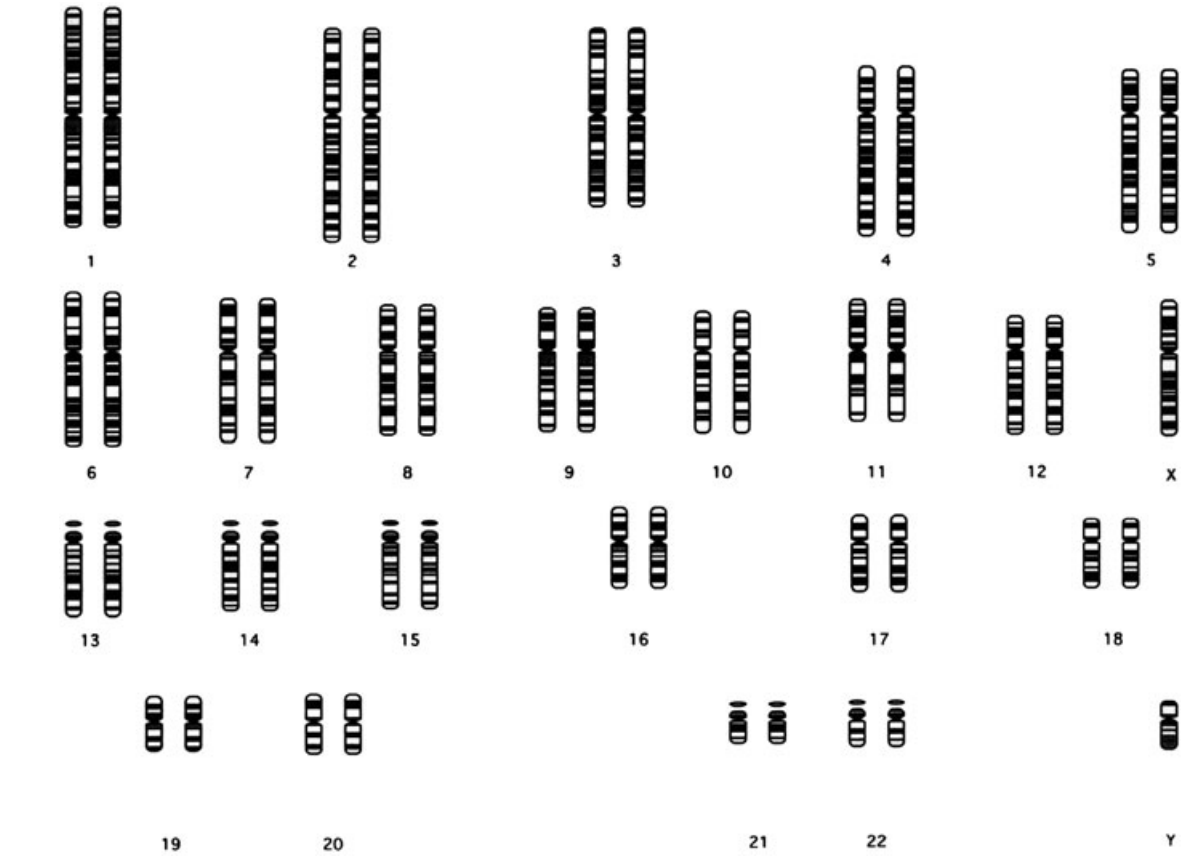

Fig. 13-1 Schematic drawing of 23 pairs of chromosomes (the diploid human genome). Twenty-two pairs of autosomal chromosomes and one pair of sex chromosomes are present. In this case the genome of a male is shown (one X and one Y chromosome). In the case of a female, two X chromosomes would have been present. G-banding generates a characteristic lateral series of bands in each member of the chromosome set. Adapted from Hart *et al.* (2000a).

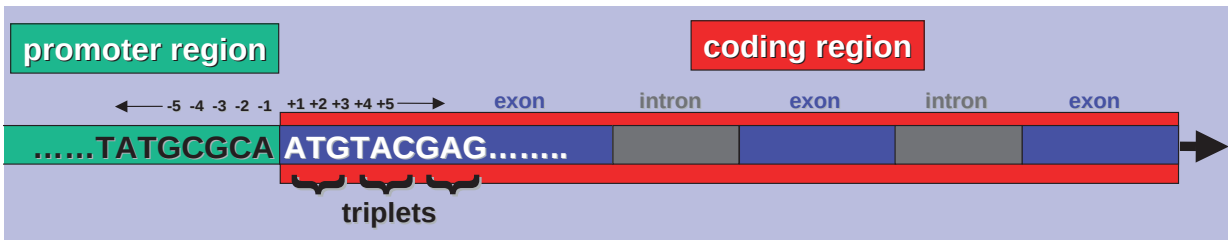

Fig. 13-2 Schematic representation of a gene. The gene consists of a promoter and a coding region. Within the coding region, intermittent areas of non-coding DNA exist (intron). Exons contain triplets of nucleotides (codons) that code for a specific amino acid. The number and length of exons and introns within the coding region is variable per gene. Nucleotides are numbered throughout the whole coding region starting with number 1 for the first nucleotide. The nucleotides in the promoter region are also numbered, starting with –1.

the probability of periodontal disease developing, and, if they are absent, this possibility is reduced. Genetic risk factors are part of the causal chain, or expose the host to the causal chain. Notably, it may be possible that an allele, which is originally defined as *R*-allele, is associated with absence of disease; in such cases, the *R*-allele could be considered protective.

Evidence for the role of genetics in periodontitis

In the past it was thought that periodontitis would eventually develop in subjects with a longstanding history of poor oral hygiene and gingivitis. However, during the last decades the concept of high-risk groups was introduced. This concept arose on the basis of the results from epidemiologic studies as well as from longitudinal clinical studies and has been one of the factors that supported the development of the theory that periodontitis may have a genetic background.

A study from 1966 is one of the earliest studies from which it could be deduced that certain individuals are more at risk for periodontitis than others (Trott & Cross 1966). In this study the principal reasons for tooth extractions in over 1800 subjects were investigated. The figures showed that in each age category the percentage of teeth lost due to periodontal disease is always higher than the percentages of patients who lost teeth due to periodontal disease. This means that relatively many teeth are lost in relatively few patients. This phenomenon could be confirmed in a 28 year longitudinal study of an American population. It was found that in a group of subjects who had a full dentition at a mean age of 28 years, 28 years later 22% of the subjects were responsible for 77% of all teeth lost (Burt *et al*. 1990). The same phenomenon was found in two longitudinal studies evaluating the effect of periodontal therapy in periodontitis patients over more than 15 years (Hirschfeld & Wasserman 1978; McFall 1982). These studies showed that 20% of the patient populations accounted for about 75% of all lost teeth. The concept of high risk for the development of periodontitis was further confirmed in longitudinal studies investigating the natural history of periodontal disease. In a Sri Lankan population without dental care and absence of oral hygiene, investigators (Löe *et al*. 1986) were able to identify three subpopulations: a group with no progression (11%), a group with moderate progression (81%), and a group with rapid progression of periodontal breakdown (8%). In a recent study the initiation and progression of periodontal breakdown was studied in a population deprived from regular dental care in a remote village on Western Java (van der Velden *et al*. 2006). The authors found that 20% of the subjects developed severe breakdown whereas the remaining population developed minor to moderate breakdown.

The phenomenon that a relatively small proportion of the population is at risk for developing severe forms of periodontitis may suggest that not everybody is equally susceptible to periodontitis. The microbial causation of inflammatory periodontal diseases is well established (Löe *et al*. 1965; Socransky & Haffajee 1992). In addition the prevalence and proportions of periodontal pathogens are higher in periodontitis patients compared to healthy controls (Griffen *et al*. 1998; van Winkelhoff *et al*. 2002). However if periodontitis is simply and solely caused by one or more specific periodontal pathogens, the disease should develop in the majority of subjects infected by these organisms. In contrast, periodontal pathogens show a relatively high prevalence in subjects with gingivitis or minor periodontitis. For example, it was found in a large group of subjects with gingivitis or minor periodontitis (mean age 52 years) that there was a prevalence of 38% for *Aggregatibacter actinomycetemcomitans*, 32% for *Porphyromonas gingivalis*, and 42% for *Prevotella intermedia* (Wolff *et al*. 1993). Therefore the existence of high-risk groups cannot be explained by the microbiology alone. There are, however, other factors that may play a major role in the development of periodontitis, i.e. the inflammatory and immune response both locally and systemically. These factors include systemic diseases, such as diabetes, and environmental factors, such as smoking and possible stress (Kinane *et al*. 2006). It is likely that the effectiveness of an individual's immune response influences the extent of periodontal destruction, which can be regarded as the susceptiblity of a subject to periodontitis.

Heritability of aggressive periodontitis (early onset periodontitis)

Some time ago it was recognized that siblings of patients with juvenile periodontitis (JP) frequently also suffer from periodontitis. This was mainly based on case reports of one or a few families ascertained on the basis of one subject (the proband) with JP. In an American study on 77 siblings of 39 probands with localized (L) or generalized (G) JP, it was shown that almost 50% of the siblings also suffered from JP (Boughman *et al*. 1992). In 11 families a co-occurrence of LJP and GJP was present. As an epidemiological survey in the US showed that the prevalence of JP varies between 0.16 and 2.49% (Löe & Brown 1991), the high prevalence of JP in these families suggests a genetic background for the disease.

The largest JP family study included 227 probands with aggressive periodontitis (Marazita *et al*. 1994). There were 26 GJP individuals whose earlier records were consistent with LJP, i.e. demonstrating progression from the localized to a more generalized form. Furthermore, there were 16 families with co-occurrence of LJP and GJP, confirming the findings of Boughman *et al*. (1992). Out of the 227 probands, 104 had at least one first-degree relative clinically

examined. Now it was possible to carry out a segregation analysis on 100 families (four families each had two probands). Segregation analysis is a formal method of studying families with a disease to assess the likelihood that the condition is inherited as a genetic trait. The family members included 527 subjects: 60 with LJP, 72 with GJP, 254 unaffected subjects, and 141 subjects with an unknown periodontal condition. The group of unaffected subjects included edentulous subjects, subjects with adult periodontitis, and periodontally healthy subjects. The majority of the families were of African American origin. The authors concluded that the most likely mode of inheritance was autosomal dominant in both African American and Caucasian kindred, with penetrance of 70% in African Americans and 73% in Caucasians.

Heritability of chronic periodontitis (adult periodontitis)

Very few investigations exist with regard to family studies of probands with chronic (adult) periodontitis or younger subjects with minor periodontitis. In an early study of nuclear families, path models were used to investigate the relative influences of genetic and environmental factors in a large Hawaiian population in the age range of 14 to over 60 years (Chung *et al*. 1977). They concluded that the data failed to detect significant heritability, and common family environment proved to be a major determinant in the variation of periodontal health. In a periodontal study of families in the US published in 1993, 75 families consisting of 178 subjects largely <40 years of age were investigated (Beaty *et al*. 1993). To determine familiar aggregation, standard familial correlations were computed, i.e. father–mother, parent–offspring, sibling–sibling, etc. The results showed a statistically significant family effect for mean plaque index, but not for mean gingival index and mean attachment loss. Both the gingival index and attachment loss showed a stronger correlation between mothers and offspring compared to fathers and offspring. Yet another study analyzed the periodontal condition in an untreated population in Guatemala consisting of 109 siblings from 40 nuclear families with an age range of 35–60 years (Dowsett *et al*. 2002). They failed to show a familial clustering for periodontal disease.

The effect of sibling relationship on the periodontal condition was investigated in an epidemiologic study of a group of young Indonesians deprived of regular dental care (van der Velden *et al*. 1993). The study population included 23 family units consisting of three or more siblings. In all, 78 subjects aged 15–25 years were studied. The results of the analysis showed a significant sibling relationship effect for plaque, calculus, and loss of attachment but not for pocket depth. In order to study familial aspects of chronic (adult) periodontitis in a Dutch population, 24 families were selected at the Academic Center for Dentistry, Amsterdam (Petit *et al*. 1994), each consisting of a proband with chronic (adult) periodontitis, a spouse and one to three children. The mean age of the probands was 39 years, with a range from 30–50 years. In total 49 children were investigated with an age range of 3 months to 15 years. The results showed that none of the children under the age of 5 years was affected by periodontitis, whereas in the group of 5–15 years, 21% had at least 1 pocket ≥5 mm in conjunction with loss of attachment. In the group of 10–15 years this was 45%. This contrasts with the results of a cross-sectional epidemiological study carried out in the city of Amsterdam; it was shown that the prevalence of pockets ≥5 mm in conjunction with loss of attachment in 15-year-old adolescents is about 5% (van der Velden *et al*. 1989). Thus, and on the basis of the Petit *et al*. (1994) study, it can be suggested that chronic (adult) periodontitis may aggregate in families.

A gene mutation with major effect on human disease and its association with periodontitis

This chapter focuses mainly on putative genetic risk factors that have been identified by the candidate gene approach, i.e. investigators have plausible arguments of a conceptual, biologic, and epidemiologic nature to investigate the association of the selected genetic polymorphism(s) with periodontitis. Nevertheless, by linkage analysis in specific families with several generations available and having among them one or more proband(s) with a strong disease phenotype, new disease genes may still be identified. Before the candidate genes and their respective genetic polymorphisms are explored in their association with periodontitis, we first discuss the discovery of a major disease gene associated with prepubertal periodontitis and Papillon-Lefèvre syndrome (PLS).

Periodontitis is recognized as a component of many single gene syndromes (Kinane & Hart 2003). Many of these disorders are characterized either by immune or structural deficiencies; of these syndromic disorders, PLS is relatively unique, in that periodontitis forms a significant component of the disease along with hyperkeratosis of the palms of the hands and soles of the feet.

The gene mutated in PLS was mapped to a specific band on the long arm of chromosome 11 (Fischer *et al*. 1997; Laass *et al*. 1997; Hart *et al*. 1998). Subsequently, this location was refined and a candidate gene within this region was identified that encoded for the lysosomal protease cathepsin C: the *CTSC* gene (Toomes *et al*. 1999). Cathepsin C is a proteinase, which is found in neutrophils and lymphocytes as well as in epithelial cells. Toomes *et al*. (1999) elucidated its genomic organization, demonstrated mutations in the *CTSC* gene in eight families, and showed that these mutations result in an almost complete loss of function of the enzyme. This was immediately con-

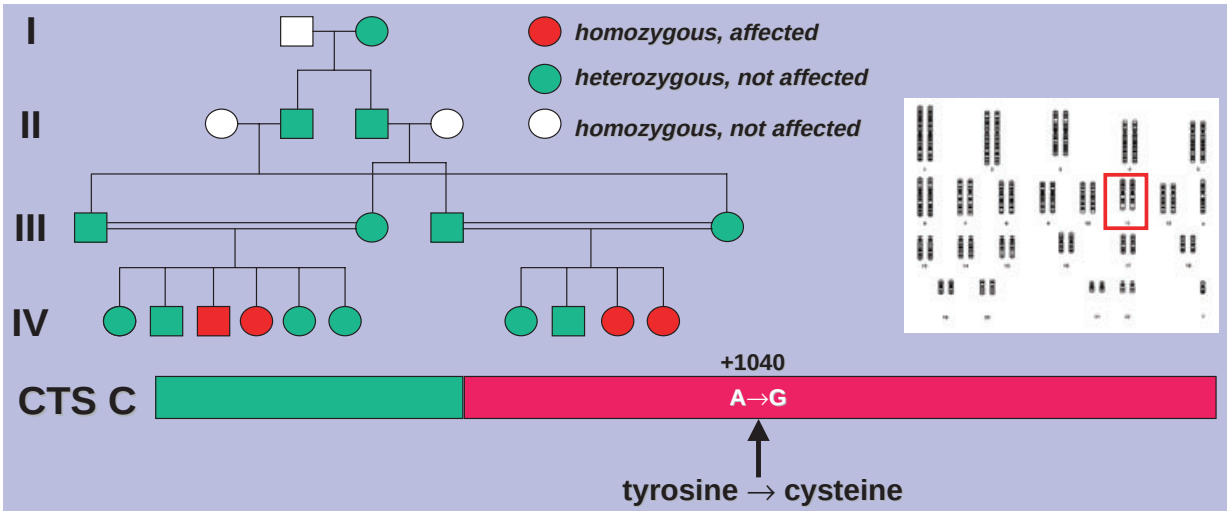

Fig. 13-3 Through an internal marriage event in a family of Jordanian descent, Hart and co-workers have identified and localized a gene on chromosome 11 that is responsible for a severe form of prepubertal periodontitis (Hart *et al*. 2000a). Starting with four affected children from generation IV of two families, a disease causing *R*-allele of the cathepsin C (CTS C) gene was discovered. Cathepsin C is a proteinase which is found in neutrophils and lymphocytes as well as epithelial cells. Affected children, but not their brothers and sisters, were homozygous for an A to G transition polymorphism at gene position +1040. This resulted in a substitution of the amino acid tyrosine by a cysteine. This polymorphism was shown to be functional as there was a decreased cathepsin C activity (Hart *et al*. 2000a). However, the mechanism by which an altered function of cathepsin C plays a role in the pathogenesis of the prepubertal form of periodontitis is unknown.

firmed (Hart *et al*. 1999) and Hart and co-workers demonstrated similar mutations in other families. To date more than 40 mutations have been reported in the *CTSC* gene (Selvaraju *et al*. 2003; de Haar *et al*. 2004; Noack *et al*. 2004). Furthermore, interesting data from analyses in a single family with four different *CTSC* mutations were reported (Hewitt *et al*. 2004) and the investigators proposed that minimal cathepsin C activity (~13%) was necessary to prevent the clinical features of PLS. However, the exact mechanism by which an altered function of cathepsin C plays a role in the pathogenesis of the prepubertal form of periodontitis is unknown.

CTSC mutations have also been identified in families with prepubertal periodontitis suggesting that this condition is allelic to PLS (Hart *et al*. 2000a) (Fig. 13-3). However, these mutations are not different to those observed in classical PLS and, notably, all cases of prepubertal periodontitis do not have mutations in *CTSC*. This suggests that prepubertal periodontitis is a genetically heterogeneous condition with some cases representing a variant of PLS (Hewitt *et al*. 2004). There has also been speculation that polymorphic functional variants of *CTSC* may be involved in the more common type of aggressive periodontitis. However, given that carriers of a mutant copy of the gene are phenotypically unaffected and that very little cathepsin C activity appears to be necessary in order to prevent the disease, this seems an unlikely hypothesis. Indeed, evidence against this hypothesis was provided (Hewitt *et al*. 2004); it was shown that there was no difference in cathepsin C activity between 30 cases of aggressive periodontitis and controls.

Disease-modifying genes in relation to periodontitis

Periodontitis develops in a limited subset of humans. About 10–15% of the population will develop severe forms of destructive periodontal disease. The disease is importantly influenced by the microorganisms in the subgingival biofilm, by acquired systemic diseases that reduce or hamper an "optimal" host response, and by environmental factors. Specific bacteria in the microbial biofilm and smoking are accepted as true rather than putative risk factors. On top of the above risk factors are disease-modifying genes, which contribute to susceptibility and severity of periodontitis. For these disease-modifying genes, Mendelian principles do not apply (Hart 1996; Hart *et al*. 2000b), because both heterozygous and homozygous subjects for a given disease-modifying gene may not necessarily develop the disease; other genetic risk factors (gene–gene interactions) and/or environmental risk factors (gene–environmental interactions) also need to be present simultaneously (definition of complex disease).

Currently, very little is known about which genes may be involved in periodontitis as disease-modifying genes. Table 13-1 summarizes the candidate gene polymorphisms investigated in relation to periodontitis. It is clear from this summary that, as the immune system plays a crucial role in the pathogenesis of periodontitis, researchers have concentrated on the identification of genetic polymorphisms in several aspects of host immunity.

Below we summarize the epidemiological findings in various studies of candidate genes as risk

Table 13-1 Summary of candidate genes, and the corresponding encoded proteins, for which gene polymorphisms have been investigated as putative risk factors for periodontitis

Gene	Coded protein
ACE	Angiotensin-converting enzyme
CARD15 (NOD2)	Caspase recruitment domain-15
CCR5	Chemokine receptor-5
CD14	CD-14
ER2	Estrogen receptor-2
ET1	Endothelin-1
FBR	Fibrinogen
FcγRIIa	Fc γ receptor IIa
FcγRIIb	Fc γ receptor IIb
FcγRIIIa	Fc γ receptor IIIa
FcγRIIIb	Fc γ receptor IIIb
FPR1	*N*-formylpeptide receptor-1
IFNGR1	Interferon γ receptor-1
IL1A	Interleukin-1α
IL1B	Interleukin-1β
IL1RN	Interleukin-1 receptor antagonist
IL2	Interleukin-2
IL4	Interleukin-4
IL6	Interleukin-6
IL10	Interleukin-10
LTA	Lymphotoxin-α
MMP1	Matrix metalloproteinase-1
MMP3	Matrix metalloproteinase-3
MMP9	Matrix metalloproteinase-9
MPO	Myeloperoxidase
NAT2	*N*-acetyltransferase-2
PAI1	Plasminogen-activator-inhibitor-1
RAGE	Receptor for advanced glycation end products
TGFB	Transforming growth factor-β
TIMP2	Tissue inhibitor of matrix metalloproteinase
TLR2	Toll-like receptor-2
TLR4	Toll-like receptor-4
TNFA	Tumor necrosis factor-α
TNFR2	Tumor necrosis factor receptor-2
VDR	Vitamin D receptor

factors (Loos *et al*. 2005). We have grouped some candidate genes together and possible mechanisms of action are given in boxes, i.e. which arguments have been used and which hypotheses have been proposed to study the various modifying genes in relation to periodontitis.

IL-1 and TNF-α gene polymorphisms

In Box 13-2, several arguments have been summarized to justify why the genes encoding for interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α) appear to be good candidates for genetic studies in relation to periodontitis.

Epidemiological findings for gene polymorphisms in the *IL1* gene cluster

The genes *IL1A*, *IL1B*, and *IL1RN* encoding for the proteins IL-1α, IL-1β, and IL-RA respectively, are located in close proximity in the *IL1* gene cluster on chromosome 2. Kornman *et al*. (1997) reported first on polymorphisms for the *IL1* genes in relation to periodontitis. This study reports on an *IL1* composite genotype (see below), however no data are presented for the carriage rates of the individual *IL1 R*-alleles (*IL1A*, *IL1B*, *IL1RN*). To date, the following *IL1* genetic polymorphisms have been studied in relation to periodontitis: *IL1A* –889 (in linkage with +4845), *IL1B* –511 (in linkage with –31), *IL1B* +3954 (also mentioned in the literature as +3953) and *IL1RN* VNTR (in linkage with +2018).

It has become clear that among the different studies with exclusively Caucasian subjects, considerable variation is seen for the carriage rates of the *IL1 R*-alleles. For example for the polymorphic *IL1A* –889 (+4845), the carriage rate for the *R*-allele varies from 34–64% for patients and 35–60% for controls. None of the studies involving Caucasians and non-Caucasians have found a significant association between periodontitis and/or disease severity and *IL1A* –889 (+4845) as single risk factor, except when combined with other *IL1* polymorphisms. The carriage rate of the *IL1A* –889 (+4845) *R*-allele in Chileans was comparable to that reported by other reports (Quappe *et al*. 2004), while the carriage rate among Japanese people appears lower (Tai *et al*. 2002). The latter finding demonstrates an important issue, that is that carriage rate of genetic polymorphisms may vary among different ethnic populations. Therefore, possible positive associations between a genetic polymorphism and disease within one population may not necessarily be extrapolated to other populations.

Three studies have reported carriage rates for the *IL1B* –511 (–31) *R*-allele, and to date this genetic polymorphism has not been associated with periodontitis. The carriage of the *R*-allele was higher among Japanese people (67–78%) than among Caucasians (59%) (Gore *et al*. 1998; Tai *et al*. 2002; Soga *et al*. 2003).

The SNP *IL1B* +3954 (+3953) initially appeared promising as risk factor for periodontitis among Caucasians. However there are conflicting results. Galbraith *et al*. (1998) found an association between the *R*-allele and periodontitis and Gore *et al*. (1998) observed an association with the severity of periodontal destruction. Quappe *et al*. (2004) reported that the *N*-allele might indeed be protective for periodontitis in Chileans. By contrast, Parkhill *et al*. (2000) observed an over-representation of the *N*-allele among early onset periodontitis (EOP) patients, and they concluded that the *N*-allele, and in particular in smokers, is associated with periodontitis, rather than the *R*-allele. The latter observation was also shown in a family linkage analysis, which included both families of African American and Caucasian heritage, therefore implying a role in the disease process for the *N*-allele (Diehl *et al*. 1999). Among Japanese subjects, the carriage rate of the *IL1B* +3954 (+3953) is

Box 13-2 Why are genes encoding for IL-1 and TNF good candidates as modifying disease genes for periodontitis?

There is evidence to suggest that IL-1 and TNF-α play important roles in the pathogenesis of periodontitis. IL-1α, IL-1β, and TNF-α are potent immunologic mediators with pro-inflammatory properties. Moreover, IL-1 and TNF-α have the capacity to stimulate bone resorption and they can regulate fibroblast cell proliferation, of both gingival and periodontal ligament origin. IL-1 and TNF-α levels are increased in the gingival crevicular fluid of periodontitis subjects and these cytokines are found in higher levels in inflamed periodontal tissues compared to healthy tissues.

Various studies have suggested that polymorphisms in the genes of the *IL1* cluster and in the *TNFA* gene, could predispose subjects to elevated IL-1 (decreased IL-1 receptor antagonist (RA)) and TNF-α protein levels. The majority of these cited studies suggest that the *R*-allele of a given polymorphism in the promoter region results in an upregulation of protein production. These studies have often been performed with isolated cells of healthy individuals or with cultured cell lines or cell constructs (transfected cells).

Inherent (most likely genetically determined) inter-individual differences have also been observed for IL-1 and TNF-α production by peripheral blood mononuclear cells or oral leukocytes, isolated from individuals with and without periodontitis. It is conceivable that these differences in IL-1 and TNF-α production and secretion play a role as risk factors, however insufficient evidence currently exists to conclude that this is a key phenomenon occurring in the pathophysiology of periodontitis. Nevertheless, the concept is attractive and may explain some of the epidemiologic findings of genetic polymorphisms associated with the susceptibility to and severity of periodontitis.

Some *IL1* and *TNFA R*-alleles have been suggested as potential genetic markers for other complex diseases. For example, *IL1* and *TNFA* gene polymorphisms have been associated with several inflammatory and infectious disease processes, including inflammatory bowel disease, Sjögren syndrome, rheumatoid arthritis, meningococcal disease, systemic lupus erythematosus, and psoriasis.

importantly low (<10%), and given this low carriage rate, no association with periodontitis can be expected. Clearly, large-scale studies in homogeneous populations are needed to further investigate the potential of the *IL1* +3954 (+3953) genotypes as risk factors for periodontitis.

Few studies have investigated polymorphisms in the *IL1RN* gene and again conflicting results are reported. In Caucasians the *R*-allele was not associated as single risk factor with periodontitis, however in combination with other *IL1* SNPs it was reported to have a possible relationship with periodontitis prevalence and severity (Laine *et al*. 2001; Meisel *et al*. 2002). In Japanese subjects the *IL1RN R*-allele was significantly associated with periodontitis (Tai *et al*. 2002). In contrast, Parkhill *et al*. (2000) observed the *IL1RN N*-allele in combination with the *IL1B* +3954 *N*-allele and smoking to be associated with early onset periodontitis (EOP).

Kornman *et al*. (1997) reported that the combined presence of the *R*-allele of the *IL1A* gene at nucleotide position −889 and the *R*-allele of the *IL1B* gene at nucleotide position +3954 (+3953) was associated with severity of periodontitis in non-smoking Caucasian patients. This combined carriage rate of the *R*-alleles was designated the *IL1* composite genotype (Kornman *et al*. 1997). Since that time a considerable number of studies investigating the *IL1* composite genotype in Caucasians and non-Caucasians has been published. An association between the *IL1* composite genotype and the severity of periodontal destruction has also been reported by two other cross-sectional studies (McDevitt *et al*. 2000; Papapanou *et al*. 2001). However, other studies have failed to corroborate that *IL1* composite genotype alone may behave as a risk factor for periodontitis severity (Gore *et al*. 1998; Ehmke *et al*. 1999; Cattabriga *et al*. 2001; Laine *et al*. 2001; Meisel *et al*. 2002, 2003, 2004). In contrast to the results of Kornman *et al*. (1997), Meisel *et al*. (2002, 2003, 2004) observed the *IL1* composite genotype to be associated with periodontitis in smokers. These conflicting results cast doubt on the utility of the *IL1* composite genotype as a putative risk factor for severity of periodontitis in Caucasians. Nevertheless, it has also been reported that patients with the *IL1* composite genotype more often harbored putative periodontal pathogens and have increased counts of these pathogens (Socransky *et al*. 2000). Interestingly, Laine *et al*. (2001) reported increased frequency of the *R*-alleles of the *IL1A*, *IL1B*, and *IL1RN* genes in non-smoking patients in whom *P. gingivalis* and *A. actinomycetemcomitans* could not be detected. These latter results suggest that *IL1* gene polymorphisms may play a role in the absence of other (putative) risk factors (Meisel *et al*. 2002, 2003, 2004).

Studies among Chinese Americans and African Americans have not resulted in interpretable findings, because the *IL1* composite genotype was hardly present in these ethnic populations (Armitage *et al*.

2000; Walker *et al*. 2000). In South American subjects the carriage rate of the *IL1* composite genotype (up to 25%) was somewhat lower than that reported for Europeans and North American study subjects (up to 48%) and no associations with periodontitis have been found.

Several longitudinal studies on *IL1* polymorphisms have been performed. From these studies it may be possible to assess whether a given genotype can be considered a true risk factor. For example, it was reported among periodontitis patients in maintenance over 5–14 years, that the *IL1* composite genotype increased the risk of tooth loss by 2.7-fold (McGuire & Nunn 1999). The *IL1* composite genotype in combination with heavy smoking increased the risk of tooth loss by 7.7-fold (McGuire & Nunn 1999). In an Australian study 295 gingivitis and moderate periodontitis subjects were followed for 5 years and the *IL1* composite genotype was determined (Cullinan *et al*. 2001); the investigators reported that among non-smoking subjects >50 years, those that were *IL1* composite genotype positive, had deeper probing depths than *IL1* composite genotype negative subjects. Furthermore, a significant interaction was found between carriage of the *IL1* composite genotype and age, smoking, and the presence of *P. gingivalis*, which suggests that the *IL1* composite genotype is a contributory but non-essential risk factor (Cullinan *et al*. 2001).

In summary, for the global population, polymorphisms in the *IL1* gene cluster cannot be regarded as (putative) risk factors for periodontitis or severity of periodontal destruction. For Caucasian patients with chronic periodontitis the role of the *IL1* composite genotype seems to hold some promise, however to date no clear evidence has emerged and there are currently too many conflicting and negative results. Large cohort studies of homogeneous composition should be initiated, in which all of the currently accepted non-genetic (putative) risk factors are included. Multi-variate analyses should be employed to estimate relative contributions of all factors.

Epidemiological findings for *TNFA* gene polymorphisms

The *TNFA* gene is located on chromosome 6 within the major histocompatibility complex (MHC) gene cluster. Several case–control studies in both Caucasians and non-Caucasians have investigated genetic polymorphisms in the *TNFA* gene as putative risk factors for periodontitis. SNPs in the gene encoding TNF-α are mainly studied in the promoter region at positions –1031, –863, –367, –308, –238 but also in the coding region in the first intron at position +489.

Similar to findings for genes of the *IL1* cluster, differences for the carriage rate of the *R*-alleles between Caucasians and other ethnic populations were apparent; at position –308 the *R*-allele carriage rate for Caucasians varied between 20% and 3%, while this was 2–3% for Japanese subjects. For the *TNFA* –238 the frequencies of *R*-alleles were comparable between both ethnic populations (<10%). The carriage rates of the *R*-alleles at positions –367 and –238 were <10%, making them less likely to be associated with periodontitis; indeed no associations have been found with periodontitis for these SNPs (Galbraith *et al*. 1998; Craandijk *et al*. 2002; Soga *et al*. 2003).

Among Japanese subjects, associations with periodontitis have been observed for the SNPs *TNFA* –1031 and –863 (Soga *et al*. 2003); these polymorphisms have not been tested in Caucasians. Among Caucasians, the only association of a *TNFA* polymorphism was observed at position –308 by Galbraith *et al*. (1998) and this was not corroborated by other studies with Caucasians in the study population. Among families with a high prevalence of EOP, the *TNFA* –308 gene polymorphisms have also been investigated, but were found not to be associated with EOP (Shapira *et al*. 2001). Another marker in the TNF-α gene was investigated in relation to susceptibility for aggressive periodontitis. This marker was based on a variable number of micro-satellite repeats, but was not found to be associated with generalized juvenile periodontitis (GJP) (Kinane *et al*. 1999).

Investigations into the severity of periodontitis in relation to any of the *TNFA R*-alleles did not reveal a positive association. The carriage of the *R*-allele at nucleotide positions –308 and –238 revealed no association between the percentage of teeth with ≥50% bone loss (Craandijk *et al*. 2002). Moreover, the carriage rates of the *R*-alleles at nucleotide positions –376, –308, –238, and +489 were not different between patients with moderate or severe periodontitis. Others reported also a lack of association of *TNFA* genetic polymorphisms with the severity of periodontitis (Kornman *et al*. 1997; Galbraith *et al*. 1998).

Based on the available literature to date, there is very limited data to support associations between any of the reported *TNFA* gene variations and periodontitis. *TNFA* –1031 and –863 may have promise, but they have only been tested in one study among Japanese subjects. More studies are needed to address *TNFA* polymorphisms and these studies should also involve investigations into other genetic polymorphisms in genes like *IL1*, for possible gene–gene interactions that may play a role in the complex pathogenesis of periodontitis.

FcγR gene polymorphisms

In Box 13-3, some background has been summarized to explain why the genes encoding for Fc gamma receptors (FcγR) seem good candidates for genetic studies in relation to periodontitis.

Several studies have investigated the *FcγRIIa* polymorphisms in relation to periodontitis in several populations. In Caucasians and African Americans, the carriage rate of the *R*-allele is relatively high: 63–77% (Colombo *et al*. 1998; Meisel *et al*. 2001; Fu *et al*.

Box 13-3 Why are genes encoding for FcγR good candidates as disease-modifying genes for periodontitis?

Leukocytes from both the myeloid and lymphoid lineages express receptors (FcγR) for the constant (Fc) region of immunoglobulin G molecules. Indeed, FcγR are found on a wide variety of immune cells in the periodontal tissues. FcγRs are likely to play a role in the pathogenesis of periodontitis, as a bridge between the cellular and humoral branches of the immune system. Microorganisms and bacterial antigens, opsonized with antibody, can be phagocytosed via FcγR on neutrophils or internalized via FcγR by a variety of antigen-presenting cells (APCs), including monocytes, macrophages and B cells. T cells and natural killer (NK) cells may become activated, when IgG-opsonized bacteria are bound to these cells via FcγR; a variety of cytokines and chemokines may also be released. When one or several of the FcγR-mediated leukocyte functions are compromised or exaggerated due to genetic polymorphisms in the FcγR genes, it is conceivable that the susceptibility to and/or severity of periodontitis is affected. This concept was proposed more than a decade ago.

The leukocyte *FcγR* genes are found on chromosome 1, and encode three main receptor classes: FcγRI (CD64), FcγRII (CD32), and FcγRIII (CD16). These classes are further subdivided into subclasses: FcγRIa and b, FcγRIIa, b, and c, and FcγRIIIa and b. FcγRIIa is found on all granulocytes, on APCs, platelets, endothelial cells, and a subset of T cells. FcγRIIIa is present on monocytes and macrophages, NK cells and a subset of T cells. The FcγRIIIb is the most abundantly expressed IgG receptor on neutrophils.

Structural and functional differences in FcγRIIa, IIIa and b have been described (Fig. 13-4). G to A transition polymorphisms in the FcγRIIa gene result in the substitution of histidine (H) for arginine (R) at amino acid position 131 of the receptor. FcγRIIa-H131 binds IgG2 immune complexes efficiently, whereas the FcγRIIa-R131 allotype cannot mediate this interaction. The G to T transition polymorphism in the FcγRIIIa gene, results in an amino acid 158-valine (V) substitution for 158-phenylalanine (F). The FcγRIIIa-V158 has a higher affinity for IgG1 and 3 than FcγRIIIa-F158. Moreover, FcγRIIIa-V158 can bind IgG4 while FcγRIIIa-F158 is unable to do so. A bi-allelic polymorphism in the FcγRIIIb gene underlies the FcγRIIIb-neutrophil antigen (NA) 1 or NA2 allotype. This is caused by four amino acid substitutions in the Fc-binding region resulting in differences in glycosylation. The NA2 type binds less efficiently human IgG1 and IgG3 immune complexes than FcγRIIIb-NA1.

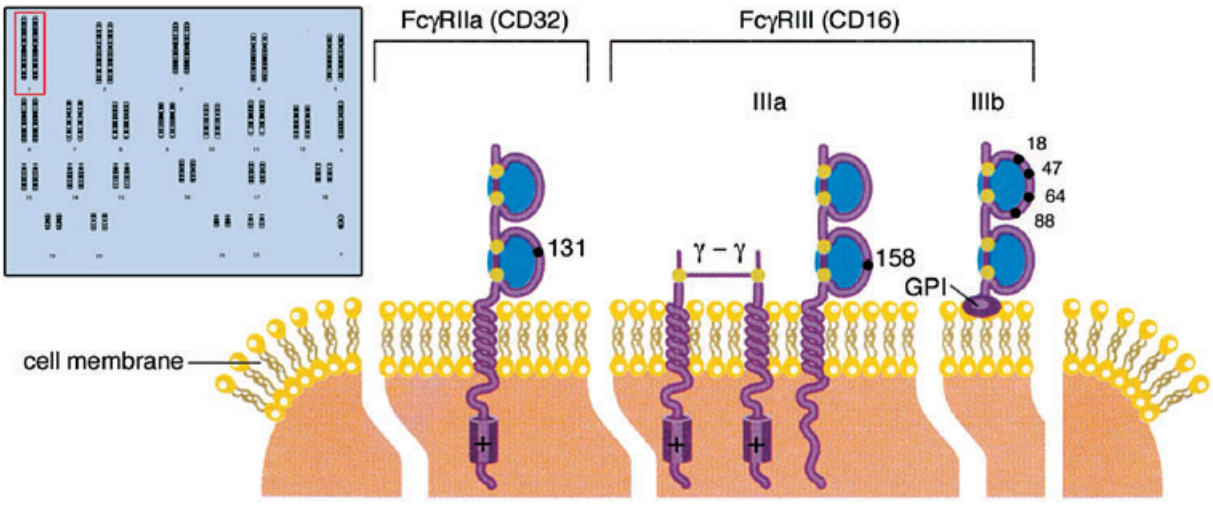

Fig. 13-4 Schematic drawing of three of the human Fc receptors for IgG. They have an extracellular part, a transmembrane region and a cytoplasmic tail (except FcγRIIIb, which is anchored in the outer leaflet of the cell membrane via a glycosyl-phosphatidyl-inositol (GPI) molecule). The extracellular part of leukocyte FcγR class II and III consists of two immunoglobulin-like domains. The + sign in the intracellular signaling motifs (cylinder) indicates the capacity of signaling to the cytoplasmic environment of the cell. The FcγRIIa-mediated effector functions can be established through the intracellular signaling motif (cylinder) within the cytoplasmic tail of the molecule. The FcγRIIIa is associated with a γ-chain homodimer, which serves as signaling subunit. The FcγRIIIb-mediated effector functions are transmitted through the GPI. The functional genetic polymorphisms are depicted as black dots (•) in the extracellular Ig-like domains. For the FcγRIIa at amino acid position 131, arginine (R) or histidine (H) is present. For the FcγRIIIa at amino acid position 158, valine (V) or phenylalanine (F) is present. The FcγRIIIb polymorphism is caused by four amino acid substitutions at positions 18, 47, 64, and 88 and results in glycosylation differences, affecting receptor affinity. The CD indication in parentheses indicates the numbering within the cluster of differentiation system of immunological markers (van der Pol & van de Winkel 1998).

2002; Loos *et al*. 2003; Yamamoto *et al*. 2004). In Japanese people the carriage rate is lower: 39–50%. In Japanese people and African Americans, the *FcγRIIa* polymorphisms are not associated with periodontitis or with the severity of the disease. However, in Caucasians some studies showed an association, with the *N*-allele rather than the expected *R*-allele (Loos *et al*. 2003; Yamamoto *et al*. 2004). A weak relationship with aggressive periodontitis was observed for the *FcγRIIa N*-allele (Loos *et al*. 2003). Moreover, periodontitis patients (aggressive and chronic periodontitis) homozygous for the *N*-allele (H/H131 genotype) have more periodontal bone loss than the other patients carrying one or two *R*-alleles. Homozygosity for the *N*-allele was significantly more prevalent in periodontitis (Yamamoto *et al*. 2004).

For the *FcγRIIIa* gene again a lower *R*-allele carriage rate is seen in Japanese than in Caucasian and African American subjects. The *FcγRIIIa N*-allele (V158) seems as a putative risk factor for periodontitis (Meisel *et al*. 2001; Loos *et al*. 2003). However, in Japan, both the *FcγRIIIa R*-allele (F158), as well as the *FcγRIIIa N*-allele, were proposed as risk factors. It is apparent that there are conflicting results and comparisons between the different studies are difficult as the prevalences of *FcγR* genotypes are different among subjects of different ethnic background.

In Japanese patients, the *FcγRIIIb R*-allele (NA2) was associated with generalized (G)-EOP (Kobayashi *et al*. 2000) and was found more often in adult patients with disease recurrence (Kobayashi *et al*. 1997). The carriage rate of the *FcγRIIIb R*-allele in Caucasians is relatively high (>75%) and to date no associations with periodontitis have been found.

The possibility that genes encoding for Fcγ receptors are associated with periodontitis in different ethnic groups seems promising. However, to date no clear and convincing data are present to definitively designate one or more of the *FcγR* gene polymorphisms as true risk factors for periodontitis. Further research is needed in larger groups of subjects from different global populations to confirm the current observations. Furthermore, functional studies among subjects with different FcγR genotypes need to be undertaken to investigate the corresponding phenotypes and unravel the role of the Fcγ receptors in the pathogenesis of periodontitis.

Gene polymorphisms in the innate immunity receptors

There are some good arguments why the genes encoding for proteins of the innate immune response are good candidate genes in relation to periodontitis (Box 13-4).

Two studies with Caucasian subjects investigated the *CD14* –260 polymorphism in chronic periodontitis, but did not find associations (Holla *et al*. 2002; Folwaczny *et al*. 2004a). However after stratification of the cohort according to gender, it was found that the *CD14* –260 *N*-allele was more prevalent among females with periodontitis (67%) than among healthy control subjects (44%) (Folwaczny *et al*. 2004a). In a Japanese study, again no association was found between the *CD14* –260 polymorphism and periodontitis (Yamazaki *et al*. 2003). Nevertheless, Holla *et al*. (2002) found among Caucasians a tendency for an increased frequency of the *CD14* –260 *R/R* genotype in patients with severe disease (19.2%) compared with the patients with moderate disease (8.3%). The *CD14* –260 *R/R* genotype was also associated with severe periodontitis in Dutch Caucasians; even stronger association was found after adjusting for age, gender, smoking, and presence of *P. gingivalis* and *A. actinomycetemcomitans* (Laine *et al*. 2005). Results for another polymorphism in the *CD14* gene have also been reported (Holla *et al*. 2002); a higher frequency of the *N*-allele and the *N/N* genotype of the *CD14* –1359 polymorphism was found in patients with severe periodontal disease than in patients with moderate periodontitis.

Two studies have attempted to associate *TLR* polymorphisms with periodontitis (Folwaczny *et al*. 2004b; Laine *et al*. 2005). However, despite the perceived importance of these functional *TLR* polymorphisms, no relation with periodontitis has been observed.

Although the polymorphisms of the *CARD15* (*NOD2*) gene are strongly associated with Crohn's disease (Hugot *et al*. 2001), to date they have not been associated with periodontitis (Folwaczny *et al*. 2004c; Laine *et al*. 2004).

Vitamin D receptor gene polymorphisms

Several arguments have been put forward for the vitamin D receptor (*VDR*) gene to be proposed as candidate gene in relation to periodontitis (see Box 13-5).

Several studies have identified a *VDR* polymorphisms in relation to periodontitis at positions *Taq-1*, *Bsm-1*, and *Fok-1* (Hennig *et al*. 1999; Tachi *et al*. 2001, 2003; Yoshihara *et al*. 2001; Sun *et al*. 2002; Taguchi *et al*. 2003; de Brito Junior *et al*. 2004). The studies on the *Taq-1* and *Bsm-1* SNPs of the *VDR* gene have found some associations with periodontitis, however not unconditionally. The carriage rate of the *R*-allele ranges between 12 and 66% across different ethnic populations, among Brazilians it was in the higher range (45–66%) and in Japanese the lower rate (5–12%). In the study by Hennig *et al*. (1999) the carriage rate of the *R*-allele ranged between 32 and 37%. Nevertheless, in five case–control studies an association of the *R*-allele with several forms of periodontitis have been observed (Hennig *et al*. 1999; Tachi *et al*. 2001; Yoshihara *et al*. 2001; Sun *et al*. 2002; de Brito Junior *et al*. 2004), while in one Japanese study an association with the *N*-allele has been found (Tachi *et al*. 2003). The apparent discrepancy cannot be explained, however it may relate to different

Box 13-4 Why are genes encoding for receptors of the innate immune response good candidates as disease-modifying genes for periodontitis?

The innate immune response is the first line of defense in infectious diseases. Without having to wait until an antigen-specific immune response is in full action (3–5 days), the host is challenged to detect the pathogen and to mount a rapid, immediate defensive response. The innate immune system recognizes pathogen-associated molecular patterns (PAMPs) that are expressed on microorganisms, but not on host cells. Extra- and intracellular receptors like CD14, CARD15, and toll-like receptors (TLRs) recognize PAMPs of Gram-positive and Gram-negative bacteria and mediate the production of cytokines necessary for further development of effective immune response (Fig. 13-5). Both TLR2 and TLR4 use CD14 as a co-receptor.

The *R*-allele in the promoter region of *CD14* at position –260 (–159) enhances the transcriptional activity of the gene. Individuals homozygous for the *R*-allele have increased serum levels of soluble (s) CD14 and an increased density of CD14 in monocytes. The *CD14* –260 SNP has previously been associated of increased risk with myocardial infarction and Crohn's disease. Furthermore, increased serum levels of sCD14 have been associated with periodontitis.

Two common co-segregating missense polymorphisms of *TLR4*, Asp299Gly and Thr399Ile, affect the extracellular domain of the TLR4 protein, leading to an attenuated efficacy of signaling and a reduced capacity to elicit inflammation. The *TLR4* Asp299Gly gene polymorphism has been correlated with hypo-responsiveness to inhaled LPS, sepsis, and infections caused by Gram-negative bacteria.

The 3020insC and 2104 C > T polymorphisms of the *CARD15 (NOD2)* gene lead to impaired activation of nuclear factor-kappa B, resulting in altered transcription of pro-inflammatory cytokine genes and reduced expression of these cytokines. These polymorphisms are strongly associated with Crohn's disease.

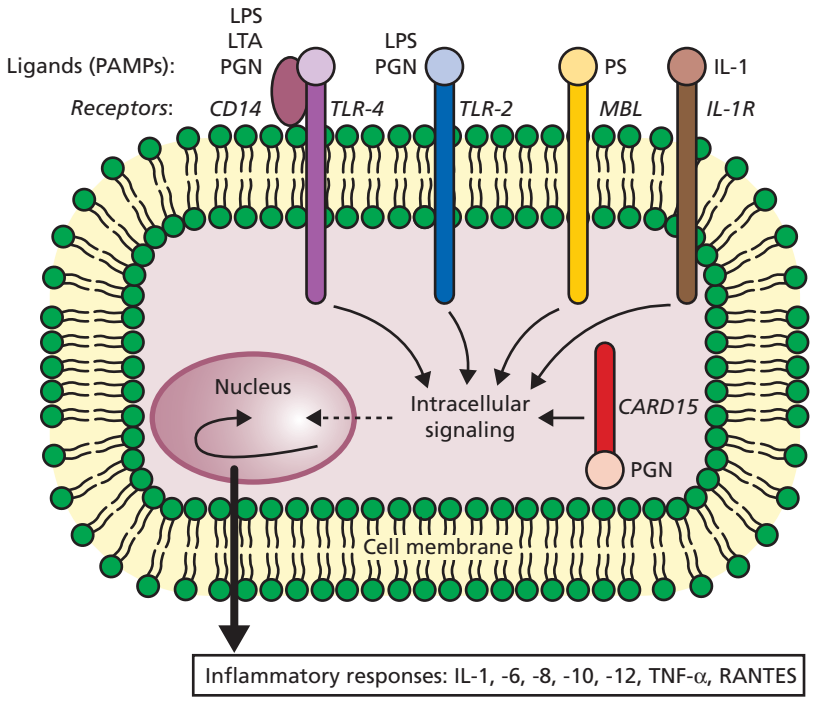

Fig. 13-5 Schematic drawing of a cell and the intracellular activation of the NF-kappa B pathway. The NF-kappa B pathway stimulates the nucleus to increase production of inflammatory mediators. Extra- and intracellular receptors, toll-like receptors 4 and 2 (TLR-4 and TLR-2), MBL, IL-1 receptor (IL-1R) and CARD15, recognize pathogen-associated molecular patterns (PAMPs) of Gram-positive and Gram-negative bacteria and mediate the production of cytokines necessary for further development of effective immune response. Both TLR-2 and TLR-4 use CD14 as a co-receptor. PAMPs are lipopolysaccharide (LPS), lipoteichoic acid (LTA), peptidoglygan (PGN), and polysaccharide (PS).

gene–environment interactions affecting different ethnic populations and/or it is related to differences in the type of periodontitis being investigated. Moreover, we cannot exclude that there is a lack of consistency in "case definition" for each disease type between studies.

The *VDR* gene is an interesting candidate gene for its association with periodontitis, because it affects both bone metabolism and immune functions. Moreover some encouraging results have been found for different ethnic populations. Further studies should be engaged to confirm the current preliminary data.

IL-10 gene polymorphisms

There are some interesting arguments why the gene encoding for interleukin-10 (IL-10) is a candidate gene for periodontitis (Box 13-6).

Box 13-5 Why is the gene encoding for vitamin D receptor a good candidate as a disease-modifying gene for periodontitis?

Alveolar bone destruction results from the periodontitis disease process. If left untreated, consequences of periodontitis are tooth mobility and eventually tooth exfoliation. Therefore, it is conceivable that mediators of bone metabolism play a role in the pathophysiology of periodontitis. With this is in mind investigators have identified genetic polymorphisms in genes coding for mediators in bone homeostasis, in particular the *VDR* gene. Bone homeostasis mediators are linked to factors affecting bone mineral density and have been related to disorders of bone metabolism, such as osteoporosis and osteoarthritis. Interestingly, genetic polymorphisms in the *VDR* gene have also been associated with infectious diseases, in particular tuberculosis. In addition to mediating bone homeostasis, vitamin D and its receptor play a role in phagocytosis by monocytes and affect monocyte differentiation.

Box 13-6 Why is the gene encoding for IL-10 a good candidate as a disease-modifying gene for periodontitis?

The gene encoding IL-10 is located on chromosome 1, in a cluster with closely related interleukin genes, including *IL19*, *IL20*, and *IL24*. IL-10 is produced by monocytes/macrophages and T cells and plays a role in the regulation of pro-inflammatory cytokines such as IL-1 and TNF-α. In particular, IL-10 is considered an anti-inflammatory cytokine, down-regulating the pro-inflammatory immune response of the monocyte/macrophage and stimulating the production of protective antibodies. However, it has also been suggested that IL-10 can stimulate the generation of auto-antibodies. As a matter of fact, auto-antibodies may play a role in periodontitis. Functional disturbance in the *IL10* gene due to genetic polymorphisms could be detrimental to host tissues and could be linked to periodontal disease susceptibility. The *IL10* SNPs have been associated with altered IL-10 production. *IL10* genetic polymorphisms have been associated with systemic lupus erythematosus and rheumatoid arthritis.

IL10 gene microsatellite markers have been investigated in relation to aggressive periodontitis (Kinane *et al*. 1999). However, no significant differences in frequencies of various *IL10* alleles between patients and periodontally healthy controls were observed. In Japanese patients either with G-EOP or with adult periodontitis (AP), as well as controls, three polymorphisms in the promoter region of the *IL10* gene were analyzed (Yamazaki *et al*. 2001). No significant differences for the carriage rates of the polymorphism in the *IL10* gene were seen between all patients and controls. Also no significant differences were observed for these latter haplotypes between AP and EOP.

The *IL10* –1087 polymorphism may be an interesting polymorphism for future studies among Caucasians. It has been shown in one study that the *N*-allele is more abundant in periodontitis in particular in non-smokers (Berglundh *et al*. 2003). These observations have led the authors to speculate that the *N*-allele prevalence in periodontitis patients may result in higher levels of auto-antibodies, which may lead to increased periodontal destruction (Berglundh *et al*. 2003). These observations were not corroborated by a Brazilian study (Scarel-Caminaga *et al*. 2004); the latter study observed a trend for increased carriage of the *IL10* –1087 *N*-allele among controls.

In summary, a limited number of studies have investigated genetic variations at three positions in the *IL10* promoter region, but to date *IL10* is not a strong candidate gene due to the mixed results in the various studies in the literature.

Miscellaneous gene polymorphisms

Table 13-2 lists various other candidate gene polymorphisms that have been studied in relation to periodontitis. These are not discussed as the other candidates above, since mainly negative results have been obtained and/or too few studies are published for a meaningful analysis. However, the table illustrates the variety of candidates and the difficulty in interpreting results; if some positive results are reported, these are often in subgroups or conditional. Clearly, further studies are needed employing larger patient numbers, which focus on candidate genes that have a proven role in the pathophysiology of periodontitis, where gene polymorphisms result in functional changes or are linked to other gene polymorphisms which in turn are strong markers of inflammatory and/or infectious diseases.

Disease-modifying genes in relation to implant failures and peri-implantitis

The success of implant dentistry is often reported as survival rate (i.e. the implant is functional and present in the mouth after a given observation period). Several longitudinal studies have reported survival rates of around 90–95% over periods of 5–10 years (Esposito *et al*. 1998; Berglundh *et al*. 2002; Roos-Jansaker *et al*. 2006). However, complications do

Table 13-2 Polymorphisms in miscellaneous genes studied in relation to periodontitis and reported association (adapted from Loos *et al*. 2005)

Polymorphism in gene	Number of studies	Associated with periodontitis reported respectively
ACE	1	– (+ [1])
CCR5	1	–
ER2	1	–
ET1	1	–
FBR	1	+ [2]
FcγRIIb	1	+
FPR1	1	– (+ [3])
IL2	1	– (+ [4])
IL4	4 and 1	– and +
IL6	1 and 2	+ and – (+ [5, 6])
INFGR1	1	– (+ [7])
LTA	1 and 1	+ and – (+ [8])
MMP1	2 and 1	– and – (+ [9])
MMP3	1	–
MMP9	1	–
MPO	1	– (+ [10])
NAT2	1 and 1	– (+ [11]) and + (+ [11])
PAI1	1	+
RAGE	1	+
TGFB	1 and 1	– and – (+ [12])
TIMP2	1	–
TNFR2	1	+

Symbols: – = association not found; + = association found.
[1] in combination with LTA.
[2] *R*-allele associated with higher serum fibrinogen.
[3] associated with LJP in African-Americans.
[4] *R*-allele associated with severity.
[5] *R*-allele protective.
[6] *R*-allele associated with higher serum levels of IL-6.
[7] *R*-allele in combination with smoking.
[8] *N*-allele protective in combination with *TNFA*-308.
[9] *R*-allele associated in non-smokers.
[10] *R*-allele protective for females.
[11] NAT2 slow phenotype associated with severity.
[12] *R*-allele possibly small effect in relation to severity.

occur; in the latter studies early implant loss has been reported to occur in 1–7% of the implants and late implant loss with a follow-up of 5–14 years can occur in 2–13% of the implants.

Previous studies have indicated that peri-implantitis and implant failures appear to cluster in subsets of individuals and that a patient who has lost one dental implant is at elevated risk of experiencing another implant loss (Weyant & Burt 1993; Hutton *et al*. 1995). These observations have led to the question of whether there is a common denominator for susceptibility to implant failures and/or complications. At this time, little is known about the genetic susceptibility and genetic polymorphisms involved in peri-implant complications; however, several scientific papers have appeared in the literature investigating this aspect. Table 13-3 summarizes the candidate genes studied in association with early or late implant failures and/or bone loss occurring around dental implants.

Table 13-3 Summary of candidate genes, and corresponding encoded proteins, for which gene polymorphisms have been investigated as markers for early or late implant failure and/or peri-implantitis

Gene	Coded protein
CTR	Calcitonin receptor
BMP4	Bone morphogenetic protein
IL1A	Interleukin-1α
IL1B	Interleukin-1β
IL1RN	Interleukin-1 receptor antagonist
IL2	Interleukin-2
IL6	Interleukin-6
MMP1	Matrix metalloproteinase-1
MMP9	Matrix metalloproteinase-9
TGFB1	Transforming growth factor-β
TNFA	Tumor necrosis factor-α

Early failures in implant dentistry

The IL-1 gene cluster polymorphisms in association with early failures

To date four studies have reported on the *IL1A* –889, *IL1B* –511, *IL1B* +3954, and *IL1RN* VNTR polymorphisms in early implant failures, either separately or in a combination (composite genotype; carriers of the *R*-allele in *IL1A* –889 and *IL1B* +3954). Homozygosity of the *IL1B* –511 *R*-allele has been reported to be associated with marginal bone loss around the dental implants in Japanese patients (Shimpuku *et al*. 2003). However, another study did not observed an association between the *IL1B* –511 *R*-allele homozygosity and early implant loss in white Brazilians (Campos *et al*. 2005). No other associations have been reported for *IL1* gene cluster polymorphisms and early implant failures/complications.

Miscellaneous gene polymorphisms in association with early failures

Polymorphisms in the *IL2*, *IL6*, *TNFA*, *TGFB1*, *MMP1*, and *MMP9* genes (Table 13-3) have been studied in white Brazilians, and *CTR* and *BMP4* gene polymorphisms in a Japanese population. One study reported that carriage of the *MMP1* –1607 *R*-allele is associated with early implant loss (Santos *et al*. 2004). All patients who lost at least one implant during the first year appeared to be carriers of the *R*-allele of *MMP1*, while 38% of those who did not lose implants were carriers of the *R*-allele of *MMP1*.

Bone morphogenetic protein (BMP) plays an important role in bone remodeling, and the *R*-allele of the *Alu*I polymorphism of the *BMP4* gene has been associated with marginal bone loss around implants in Japanese patients (Shimpuku *et al*. 2003).

Late failures in implant dentistry

The follow-up period of late implant failures in the available studies varied from 1–15 years and only genetic variation in the genes of the *IL1* cluster have been investigated. Two studies reported on the *IL1A* –889, *IL1B* –511, *IL1B* +3954, and *IL1RN* VNTR polymorphisms separately in association with late implant failures (Rogers *et al*. 2002; Laine *et al*. 2006). One study found an association between the carriage of the *IL1RN* VNTR *R*-allele and late implant failure, but not for the other *IL1* gene polymorphisms (Laine *et al*. 2006).

As has been studied in relation to periodontitis, the composite *IL1* genotype (carriage of the *R*-allele in *IL1A* –889 and *IL1B* +3954) has also been investigated in relation to late implant failures. Two out of five available studies found only a conditional association between the late implant failures and *IL1* composite genotype; the other studies reported negative findings. In the first positive study, 90 Caucasian patients were investigated for peri-implant bone loss at the time of re-examination (mean 5.6 years after prosthetic rehabilitation) (Feloutzis *et al*. 2003). Twenty-eight patients carrying the *IL1* composite genotype were stratified into non-smokers, former smokers, and heavy smokers. Heavy smokers were found to have more total and annual bone loss, when compared with non-smokers or former smokers. The other study also reported that the *IL1* composite genotype and smoking were significantly associated with peri-implant bone loss after 8 years in function (Gruica *et al*. 2004). However, the results from both studies need to be interpreted with care; the number of subjects in both studies after stratification for genotype carriage and heavy smoking was so low that the power of the studies is severely compromised (see below).

In summary, there are several studies that have shown an association between early or late dental implant failures in relation to genetic polymorphisms. However most of them still need to be confirmed in another study cohort, consisting of larger numbers of study subjects. For Caucasians who smoke, the *IL-1* composite genotype may be a possible marker for late implant failures; this was also a genetic marker possibly associated with periodontitis. It is important to emphasize that is difficult to compare and summarize the available literature due to the fact that there is diversity of definitions for the dental implant failure and peri-implant disease, as well as heterogeneity in study design and implant systems.

Conclusions and future developments

An important problem related to research in the heredity of periodontitis is that, whatever the cause of the disease is, the symptoms are the same; specifically, deepening of the periodontal pocket, loss of attachment, and alveolar bone loss. It is likely that overlapping clinical phenotypes exist between different forms of periodontitis. It is important that globally accepted definitions of "cases" of chronic, and localized and generalized aggressive forms of periodontitis are used in future studies, to allow valid comparisons to be made between gene polymorphism data from different parts of the world. In the majority of cases, it is likely that the development of periodontitis in an individual depends on the collective presence of a number of environmental risk factors in conjunction with a number of genetic risk factors at a given time point during life. The more genetic risk factors an individual has inherited, the greater the genetic predisposition and the higher the chance of early development of periodontitis. Whenever an individual has inherited a major disease gene mutation, we would expect early development of periodontitis. However to date, major disease gene mutations have not been identified, which result in the periodontitis phenotype in otherwise systemically healthy individuals. Since the children of patients with chronic periodontitis show a relatively high prevalence of incipient periodontitis, it is likely that some forms of early periodontitis share a common pathogenic pathway with that of chronic periodontitis in adults.

A multitude of polymorphisms in genes, most of which code aspects of the host immune response, have been explored. There are indications that some polymorphisms in the *IL1* gene cluster, the *FcγR* gene cluster and in the genes encoding the vitamin D receptor and IL-10, may be associated with periodontitis in certain ethnic groups. However, in general, even among studies with subjects of the same ethnic background, no consistent results have been obtained. Often, only by defining small subgroups of individuals or after stratification, researchers have found some significant associations, but the studies appear underpowered for proper interpretation. Moreover, carriage of specific combinations of alleles within a given locus (haplotype analysis) and among various genes (gene-gene interactions) have only been sparsely investigated. Therefore we conclude that until now no specific genetic risk factor for periodontitis has been identified.

In general, the genetic studies in relation to periodontitis are hampered by population heterogeneity and differences in patient selection and diagnostic criteria. At the same time, it is also possible that inconsistent results may reflect the underlying complexity and heterogeneity of genetic influence in periodontitis. The heterogeneity in periodontitis case definitions is still one of the major problems in the interpretation of the various studies available in the literature in relation to genetic risk factors for periodontitis.

Another problem encountered in the literature, is that many studies have investigated putative genetic risk factors without considering other, established

risk factors for periodontitis as co-variates. For example, most would agree that in periodontal research, age, gender, and smoking, should always be included in multivariate statistical analyses. Further, the vast majority of studies has not considered the infectious component (gene–environment interaction). We recommend strongly that, where possible, the bacterial microorganisms or appropriate surrogate measures of bacterial infection should be included as co-variates in the analyses.

Future studies applying the candidate gene approach could be guided by results from genome-wide searches or by results from gene expression signatures (Papapanou *et al*. 2004) or family linkage analyses (Diehl *et al*. 1999; Li *et al*. 2004). Furthermore, these types of studies need to be large scale, in consortium-based approaches, because single studies are greatly underpowered. It is estimated that meaningful results for the candidate gene approach may only be obtained with thousands of patients, since most associations refer to small odds ratios (range 1.1–1.50) (Ioannidis *et al*. 2003). Useful reviews and recommendations have been published on the topic of the candidate gene approach for complex diseases (Clayton & McKeigue 2001; Tabor *et al*. 2002; Colhoun *et al*. 2003; Ioannidis 2003).

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Part 5: Trauma from Occlusion

Chapter 14

Trauma from Occlusion: Periodontal Tissues

Jan Lindhe, Sture Nyman, and Ingvar Ericsson

Definition and terminology

Trauma from occlusion is a term used to describe pathologic alterations or adaptive changes which develop in the periodontium as a result of undue force produced by the masticatory muscles. *Trauma from occlusion* is only one of many terms that have been used to describe such alterations in the periodontium. Other terms often used are: *traumatizing occlusion*, *occlusal trauma*, *traumatogenic occlusion*, *periodontal traumatism*, *overload*, etc. In addition to producing damage in the periodontal tissues, excessive occlusal force may also cause injury in, for example, the temporomandibular joint, the masticatory muscles, and the pulp tissue. This chapter deals exclusively with the effects of *trauma from occlusion* on the periodontal tissues.

Trauma from occlusion was defined by Stillman (1917) as "a condition where injury results to the supporting structures of the teeth by the act of bringing the jaws into a closed position". The World Health Organization (WHO) in 1978 defined *trauma from occlusion* as "damage in the periodontium caused by stress on the teeth produced directly or indirectly by teeth of the opposing jaw". In "Glossary of Periodontic Terms" (American Academy of Periodontology 1986), *occlusal trauma* was defined as "an injury to the attachment apparatus as a result of excessive occlusal force".

Traumatizing forces may act on an individual tooth or on groups of teeth in premature contact relationship; they may occur in conjunction with parafunctions such as clenching and bruxism, or in conjunction with loss or migration of premolar and molar teeth with an accompanying, gradually developing spread of the anterior teeth of the maxilla, etc.

In the literature, the tissue injury associated with trauma from occlusion is often divided into *primary* and *secondary*. The *primary* form includes a tissue reaction (damage), which is elicited around a tooth with normal height of the periodontium, while the *secondary* form is related to situations in which occlusal forces cause injury in a periodontium of reduced height. The distinction between a *primary* and a *secondary* form of injury – *primary* and *secondary occlusal trauma* – serves no meaningful purpose, since the alterations which occur in the periodontium as a consequence of trauma from occlusion are similar and independent of the height of the target tissue, i.e. the periodontium. It is, however, important to understand that symptoms of trauma from occlusion may develop only in situations when the magnitude of the load elicited by occlusion is so high that the periodontium around the exposed tooth cannot properly withstand and distribute the resulting force with unaltered position and stability of the tooth involved. This means that in cases of severely reduced height of the periodontium even comparatively small forces may produce traumatic lesions or adaptive changes in the periodontium.

Trauma from occlusion and plaque-associated periodontal disease

Ever since Karolyi (1901) postulated that an interaction may exist between "*trauma from occlusion*" and "*alveolar pyrrohea*", different opinions have been presented in the literature regarding the validity of this claim. In the 1930s, Box (1935) and Stones (1938) reported experiments in sheep and monkeys, the result of which seemed to indicate that "trauma from occlusion is an etiologic factor in the production of that variety of periodontal disease in which there is

vertical pocket formation associated with one or a varying number of teeth" (Stones 1938). The experiments by Box and Stones, however, have been criticized because they lacked proper controls and because the experimental design of the studies did not justify the conclusions drawn.

The interaction between trauma from occlusion and plaque-associated periodontal disease in humans was frequently discussed in the period 1955–1970 in connection with "report of a case", "in my opinion" statements, etc. Even if such anecdotal data may have some value in clinical dentistry, it is obvious that conclusions drawn from research findings are much more pertinent. The research-based conclusions are not always indisputable but they invite the reader to a critique which anecdotal data do not. In this chapter, therefore, the presentation will be limited to findings collected from research endeavors involving: (1) human autopsy material, (2) clinical trials, and (3) animal experiments.

Analysis of human autopsy material

Results reported from carefully performed research efforts involving examinations of human autopsy material have been difficult to interpret. In the specimens examined (1) the histopathology of the lesions in the periodontium have been described, as well as (2) the presence and apical extension of microbial deposits at adjacent root surfaces, (3) the mobility of the teeth involved, and (4) "the occlusion" of the sites under scrutiny. It is obvious that assessments made in specimens from cadavers have a limited to questionable value when "cause–effect" relationships between occlusion, plaque, and periodontal lesions are to be described. It is not surprising, therefore, that *conclusions* drawn from this type of research can be controversial. This can best be illustrated if "Glickman's concept" is compared with "Waerhaug's concept" of what autopsy studies have revealed regarding trauma from occlusion and periodontal disease.

Glickman's concept

Glickman (1965, 1967) claimed that the pathway of the spread of a plaque-associated gingival lesion can be changed if forces of an abnormal magnitude are acting on teeth harboring subgingival plaque. This would imply that the character of the progressive tissue destruction of the periodontium at a "traumatized tooth" will be different from that characterizing a "non-traumatized" tooth. Instead of an even destruction of the periodontium and alveolar bone (suprabony pockets and horizontal bone loss), which, according to Glickman, occurs at sites with uncomplicated plaque-associated lesions, sites which are also exposed to abnormal occlusal force will develop angular bony defects and infrabony pockets.

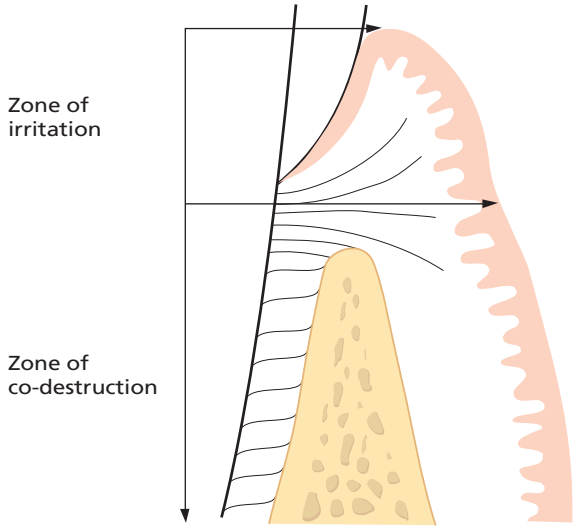


Fig. 14-1 Schematic drawing of the zone of irritation and the zone of co-destruction according to Glickman.

Since Glickman's concept regarding the effect of trauma from occlusion on the spread of the plaque-associated lesion is often cited, a more detailed presentation of his theory seems pertinent. The periodontal structures can be divided into two zones (Fig. 14-1):

1. The zone of irritation
2. The zone of co-destruction.

The *zone of irritation* includes the marginal and interdental gingiva. The soft tissue of this zone is bordered by hard tissue (the tooth) only on one side and is not affected by forces of occlusion. This means that gingival inflammation cannot be induced by trauma from occlusion but is the result of irritation from microbial plaque. The plaque-associated lesion at a "non-traumatized" tooth propagates in the apical direction by first involving the alveolar bone and only later the periodontal ligament area. The progression of this lesion results in an even (horizontal) bone destruction.

The *zone of co-destruction* includes the periodontal ligament, the root cementum, and the alveolar bone, and is coronally demarcated by the trans-septal (interdental) and the dento-alveolar collagen fiber bundles (Fig. 14-1). The tissue in this zone may become the seat of a lesion caused by trauma from occlusion.

The fiber bundles which separate the zone of co-destruction from the zone of irritation can be affected from two different directions:

1. From the inflammatory lesion maintained by plaque in the *zone of irritation*
2. From trauma-induced changes in the *zone of co-destruction*.

Through this exposure from two different directions the fiber bundles may become dissolved and/or

orientated in a direction parallel to the root surface. The spread of an inflammatory lesion from the *zone of irritation* directly down into the periodontal ligament (i.e. not via the interdental bone) may hereby be facilitated (Fig. 14-2). This alteration of the "normal" pathway of spread of the plaque-associated inflammatory lesion results in the development of angular bony defects. Glickman (1967) stated in a review paper that *trauma from occlusion* is an etiologic factor (co-destructive factor) of importance in situations where angular bony defects combined with infrabony pockets are found at one or several teeth (Fig. 14-3).

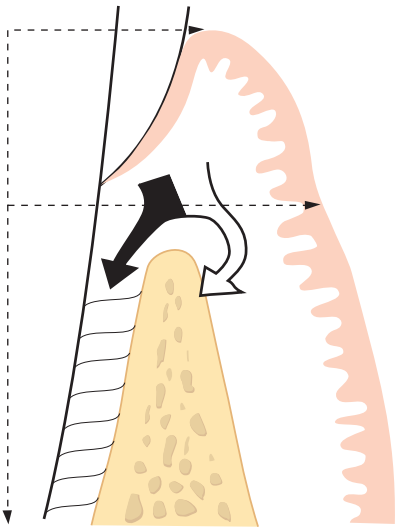


Fig. 14-2 The inflammatory lesion in the zone of irritation can, in teeth not subjected to trauma, propagate into the alveolar bone (open arrow), while in teeth also subjected to trauma from occlusion, the inflammatory infiltrate spreads directly into periodontal ligament (filled arrow).

Waerhaug's concept

Waerhaug (1979) examined autopsy specimens (Fig. 14-4) similar to Glickman's, but in addition measured the distance between the subgingival plaque and (1) the periphery of the associated inflammatory cell infiltrate in the gingiva, and (2) the surface of the adjacent alveolar bone. He concluded from his analysis that angular bony defects and infrabony pockets occur equally often at periodontal sites of teeth which are not affected by trauma from occlusion as in traumatized teeth. In other words, he refuted the hypothesis that trauma from occlusion played a role in the spread of a gingival lesion into the "zone of co-destruction". The loss of connective attachment and the resorption of bone around teeth are, according to Waerhaug, exclusively the result of inflammatory lesions associated with subgingival plaque. Waerhaug concluded that angular bony defects and infrabony pockets occur when the subgingival plaque of one tooth has reached a more apical level than the microbiota on the neighboring tooth, and when the volume of the alveolar bone surrounding the roots is comparatively large. Waerhaug's observations support findings presented by Prichard (1965) and Manson (1976) which imply that the pattern of loss of supporting structures is the result of an interplay between the form and volume of the alveolar bone and the apical extension of the microbial plaque on the adjacent root surfaces.

It is obvious, as stated above, that examinations of autopsy material have a limited value when determining "cause–effect" relationships with respect to trauma and progressive periodontitis. As a consequence, the conclusions drawn from this field of research have not been generally accepted. A number of authors tend to accept Glickman's conclusions that trauma from occlusion is an aggravating factor in

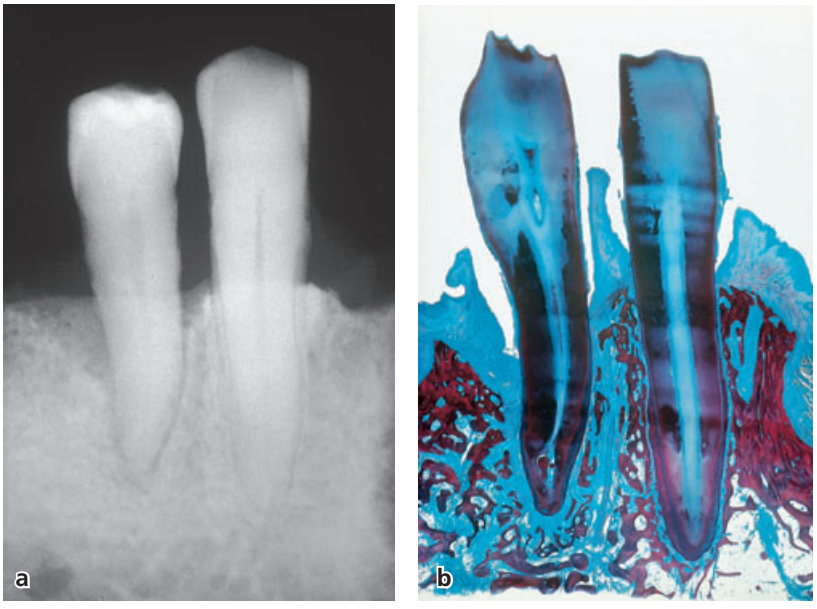


Fig. 14-3 (a) A radiograph of a mandibular premolar–canine region. Note the angular bony defect at the distal aspect of the premolar. (b) Histologic mesiodistal section of the specimen illustrated in (a). Note the infrabony pocket at the distal aspect of the premolar. From Glickman & Smulow (1965).

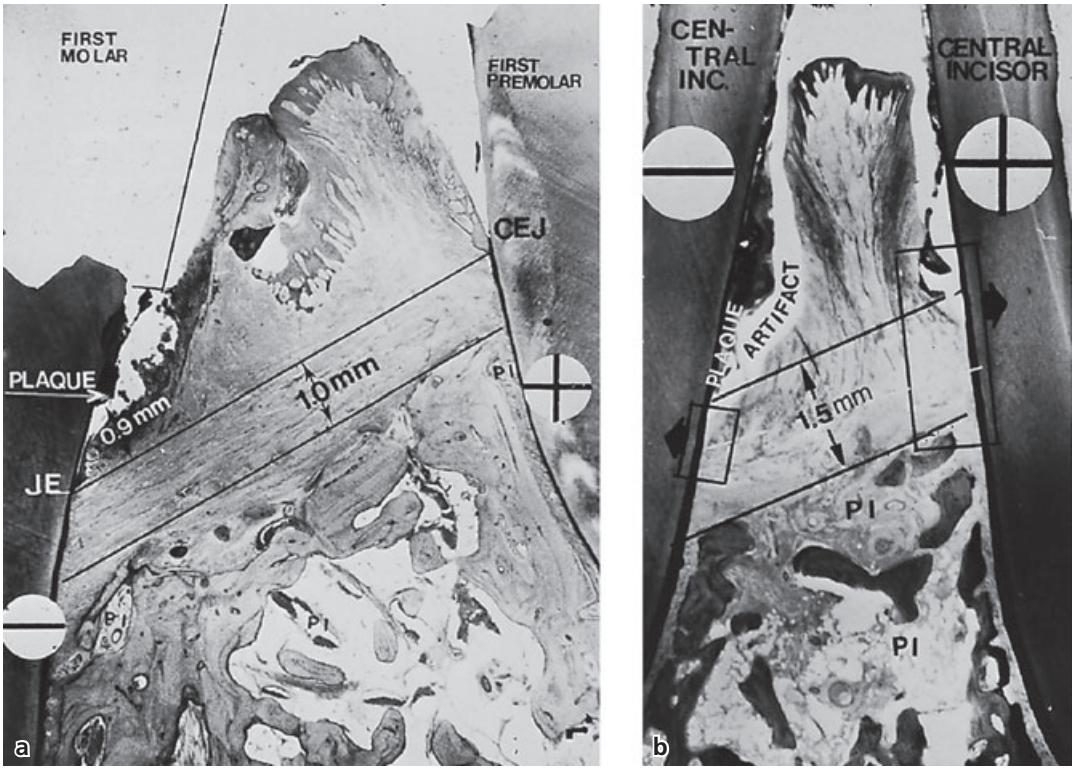


Fig. 14-4 Microphotographs illustrating two interproximal areas with angular bony defects. "–" denotes a tooth not subjected and "+" denotes a tooth subjected to trauma from occlusion. In categories "–" and "+" the distance between the apical cells of the junctional epithelium and the supporting alveolar bone is about 1–1.5 mm, and the distance between the apical extension of plaque and the apical cells of the junctional epithelium about 1 mm. Since the apical cells of the junctional epithelium and the subgingival plaque are located at different levels on the two adjacent teeth, the outline of the bone crest becomes oblique. A radiograph from such a site would disclose the presence of an angular bony defect at a non-traumatized ("–") tooth.

periodontal disease (e.g. Macapanpan & Weinmann 1954; Posselt & Emslie 1959; Glickman & Smulow 1962, 1965) while others accept Waerhaug's concept, i.e. that there is no relationship between occlusal trauma and the degree of periodontal tissue breakdown (e.g. Lovdahl *et al*. 1959; Belting & Gupta 1961; Baer *et al*. 1963; Waerhaug 1979).

Clinical trials

In addition to the presence of angular bony defects and infrabony pockets, *increased tooth mobility* is frequently listed as an important sign of occlusal trauma. For details regarding tooth mobility, see Chapter 51. Conflicting data have also been reported regarding the periodontal conditions of mobile teeth. In one clinical study by Rosling *et al*. (1976) patients with advanced periodontal disease associated with multiple angular bony defects and mobile teeth were exposed to antimicrobial therapy (i.e. subgingival scaling after flap elevation). Healing was evaluated by probing attachment level measurements and radiographic monitoring. The authors reported that "the infrabony pocket located at hypermobile teeth exhibited the same degree of healing as those adjacent to firm teeth". In another study, however, Fleszar *et al*. (1980) reported on the influence of tooth mobility on healing following periodontal therapy including both root debridement and occlusal adjustment. They concluded that "pockets of clinically mobile teeth do not respond as well to periodontal treatment as do those of firm teeth exhibiting the same disease severity".

A third study (Pihlstrom *et al*. 1986) studied the association between trauma from occlusion and periodontitis by assessing a series of clinical and radiographic features at maxillary first molars. Parameters included in this study were: probing depth, probing attachment level, tooth mobility, wear facets, plaque and calculus, bone height, widened periodontal space, etc. Pihlstrom and his associates concluded from their measurements and examinations that teeth with increased mobility and widened periodontal ligament space had, in fact, deeper pockets, more attachment loss, and less bone support than teeth without these symptoms.

Burgett *et al*. (1992) studied the effect of occlusal adjustment in the treatment of periodontitis. Fifty subjects with periodontitis were examined at baseline and subsequently treated for their periodontal condition with root debridement ± flap surgery. Twenty-two out of the 50 patients, in addition, received comprehensive occlusal therapy. Re-examinations performed 2 years later disclosed that probing attachment gain was on average about 0.5 mm larger in patients who received the combined treatment,

i.e. scaling and occlusal adjustment, than in patients in whom the occlusal adjustment was not included.

Nunn and Harrel (2001) and Harrel and Nunn (2001) examined the relationship between occlusal discrepancies and periodontitis in two studies. Their sample included about 90 subjects that had been referred for treatment of periodontal disease and who had at least two (≥1 year apart) complete periodontal records, including occlusal analysis. The patients were examined with respect to probing pocket depth (PPD), tooth mobility, and furcation involvement (at multirooted teeth). In addition, some occlusal contact relationships were studied such as (1) discrepancies in centric relation and centric occlusion, (2) premature occlusal contacts in protrusive movements (lateral and frontal) of the mandible in working and non-working quadrants. A treatment plan, including both periodontal and occlusal measures, was subsequently designed for each patient. About one third of the subjects decided to abstain from treatment, about 20 subjects accepted only a non-surgical approach of therapy (SRP), while about 50% of the patients accepted and received comprehensive treatment that included surgical pocket elimination (surgery) as well as occlusal adjustment (if indicated). Some teeth in the SRP group received occlusal therapy while other teeth with occlusal discrepancies were left untreated. It was observed that teeth with occlusal discrepancies had significantly deeper PPD values and higher mobility scores than teeth without occlusal "trauma" and also that teeth exposed to occlusal adjustment responded better (reduction in PPD) to non-surgical periodontal therapy than teeth with remaining occlusal discrepancies.

The findings in some of the clinical studies referred to above lend some support to the concept that trauma from occlusion (and increased tooth mobility) may have a detrimental effect on the periodontium. Neiderud *et al*. (1992), however, in a beagle dog study demonstrated that tissue alterations which occur at mobile teeth with clinically healthy gingivae (and normal height of the tissue attachment) may reduce the resistance offered by the periodontal tissues to probing. In other words, if the probing depth at two otherwise similar teeth – one non-mobile and one hypermobile – is recorded, the tip of the probe will penetrate 0.5 mm deeper at the mobile than at the non-mobile tooth. This finding must be taken into consideration when the above clinical data are interpreted.

Since neither analysis of autopsy material nor data from clinical trials can be used to properly determine the role trauma from occlusion may play in periodontal pathology, it is necessary to describe the contributions made by means of animal research in this particular field. Results from such experiments, describing the reactions of the normal and subsequently the diseased periodontium to occlusal forces, are presented below.

Animal experiments

Orthodontic type trauma

The reaction of the periodontal tissues to traumatic forces initiated by occlusion has been studied principally in animal experiments. In early experiments the reaction of the normal periodontium was studied following the application of forces which were inflicted on teeth in one direction only. Biopsy specimens, including tooth and periodontium, were harvested after varying experimental time intervals and prepared for histologic examinations. Analysis of the tissue sections (Häupl & Psansky 1938; Reitan 1951; Mühlemann & Herzog 1961; Ewen & Stahl 1962; Waerhaug & Hansen 1966; Karring *et al*. 1982) revealed the following: when a tooth is exposed to unilateral forces of a magnitude, frequency or duration that its periodontal tissues are unable to withstand and distribute while maintaining the stability of the tooth, certain well defined reactions develop in the periodontal ligament, eventually resulting in an adaptation of the periodontal structures to the altered functional demand. If the crown of a tooth is affected by such horizontally directed forces, the tooth tends to tilt (tip) in the direction of the force (Fig. 14-5). This tilting force results in the development of *pressure* and *tension zones* within the marginal and apical parts of the periodontium. The tissue reactions which develop in the *pressure zone* are characterized by increased vascularization, increased vascular permeability, vascular thrombosis, and disorganization of cells and collagen fiber bundles. If the magnitude of forces is within certain limits, allowing the maintenance of the vitality of the periodontal ligament cells,

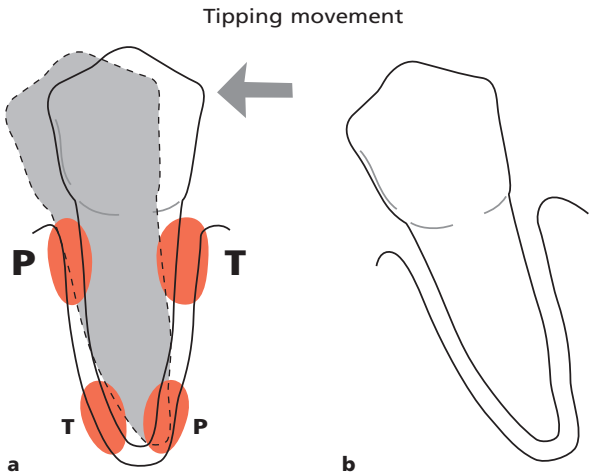


Fig. 14-5 (a) If the crown of a tooth is exposed to excessive, horizontally directed forces (arrow), pressure (P) and tension (T) zones will develop within the marginal and apical parts of the periodontium. The supra-alveolar connective tissue remains unaffected by force application. Within the pressure and tension zones tissue alterations take place which eventually allow the tooth to tilt in the direction of the force. (b) When the tooth is no longer subjected to the trauma, complete regeneration of the periodontal tissues takes place. There is no apical downgrowth of the dentogingival epithelium.

bone-resorbing osteoclasts soon appear on the bone surface of the alveolus in the *pressure zone*. A process of bone resorption is initiated. This phenomenon is called "*direct bone resorption*".

If the force applied is of higher magnitude, the result may be necrosis of the periodontal ligament tissue in the *pressure zone*, i.e. decomposition of cells, vessels, matrix, and fibers (*hyalinization*). "Direct bone resorption" therefore cannot occur. Instead, osteoclasts appear in marrow spaces within the adjacent bone tissue where the stress concentration is lower than in the periodontal ligament and a process of undermining or "*indirect bone resorption*" is initiated. Through this reaction the surrounding bone is resorbed until there is a breakthrough to the hyalinized tissue within the *pressure zone*. This breakthrough results in a reduction of the stress in this area, and cells from the neighboring bone or adjacent areas of the periodontal ligament can proliferate into the *pressure zone* and replace the previously hyalinized tissue, thereby re-establishing prerequisites for "direct bone resorption". Irrespective of whether the bone resorption is of a direct or an indirect nature the tooth moves (tilts) further in the direction of the force.

Concomitant with the tissue alterations in the *pressure zone*, apposition of bone occurs in the *tension zone* in order to maintain the normal width of the periodontal ligament in this area. Because of the tissue reactions in the *pressure* and *tension* zones the tooth becomes, temporarily, hypermobile. When the tooth has moved (tilted) to a position where the effect of the forces is nullified, healing of the periodontal tissues takes place in both the *pressure* and the *tension zones* and the tooth becomes stable in its new position. In orthodontic tilting (tipping) movements, neither gingival inflammation nor loss of connective tissue attachment will occur in a healthy periodontium and, as long as the tooth is not moved through the envelope of the alveolar process, there is no apical migration of the dentogingival epithelium. In other words, since the supraalveolar connective tissue is only bordered by hard tissue (the tooth) on one side (in the direction of the force), this structure remains unaffected by this type of force.

These tissue reactions do not differ fundamentally from those which occur as a consequence of *bodily tooth movement* in orthodontic therapy (Reitan 1951). The main difference is that the *pressure* and *tension zones*, depending on the direction of the force, are more extended in an apical–coronal direction along the root surface than in conjunction with tipping movement (Fig. 14-6). The supra-alveolar connective tissue is not affected by the force, either in conjunction with tipping or in conjunction with bodily movements of the tooth. Unilateral forces directed to the crown of teeth, therefore, will not induce inflammatory reactions in the gingiva or cause loss of connective tissue attachment.

Studies have demonstrated, however, that orthodontic forces producing bodily (or tipping) movement of teeth may result in gingival recession and loss of connective tissue attachment (Steiner *et al*. 1981; Wennström *et al*. 1987). This breakdown of the attachment apparatus occurred at sites with gingivitis when, in addition, the tooth was moved through the envelope of the alveolar process. At such sites bone dehiscence becomes established and, if the covering soft tissue is thin (in the direction of the movement of the tooth), recession (attachment loss) may occur.

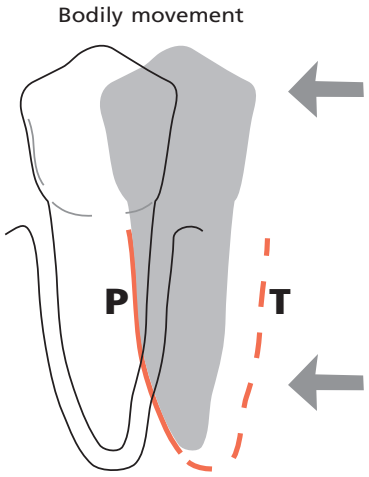


Fig. 14-6 When a tooth is exposed to forces which produce "bodily tooth movement", e.g. in orthodontic therapy, the pressure (P) and tension (T) zones, depending on the direction of the force, are extended over the entire tooth surface. The supra-alveolar connective tissue is not affected in conjunction either with tipping or with bodily movements of teeth. Forces of this kind, therefore, will not induce inflammatory reactions in the gingiva. No apical downgrowth of the dentogingival epithelium occurs.

Criticism has been directed, however, at experiments in which only unilateral trauma is exerted on teeth (Wentz *et al*. 1958). It has been suggested that in humans, unlike in the animal experiments described above, the occlusal forces act alternately in one and then in the opposite direction. Such forces have been termed *jiggling forces*.

Jiggling-type trauma

Healthy periodontium with normal height

Experiments have been reported in which traumatic forces were exerted on the crowns of the teeth, alternately in buccal and lingual or mesial and distal directions, and in which the teeth were not allowed to move away from the force (e.g. Wentz *et al*. 1958; Glickman & Smulow 1968; Svanberg & Lindhe 1973; Meitner 1975; Ericsson & Lindhe 1982). In conjunction with "*jiggling-type trauma*" no clearcut *pressure* and *tension zones* can be identified but rather there is a combination of pressure and tension on both sides of the jiggled tooth (Fig. 14-7).

The tissue reactions in the periodontal ligament provoked by the combined *pressure* and *tension* forces were found to be similar, however, to those reported

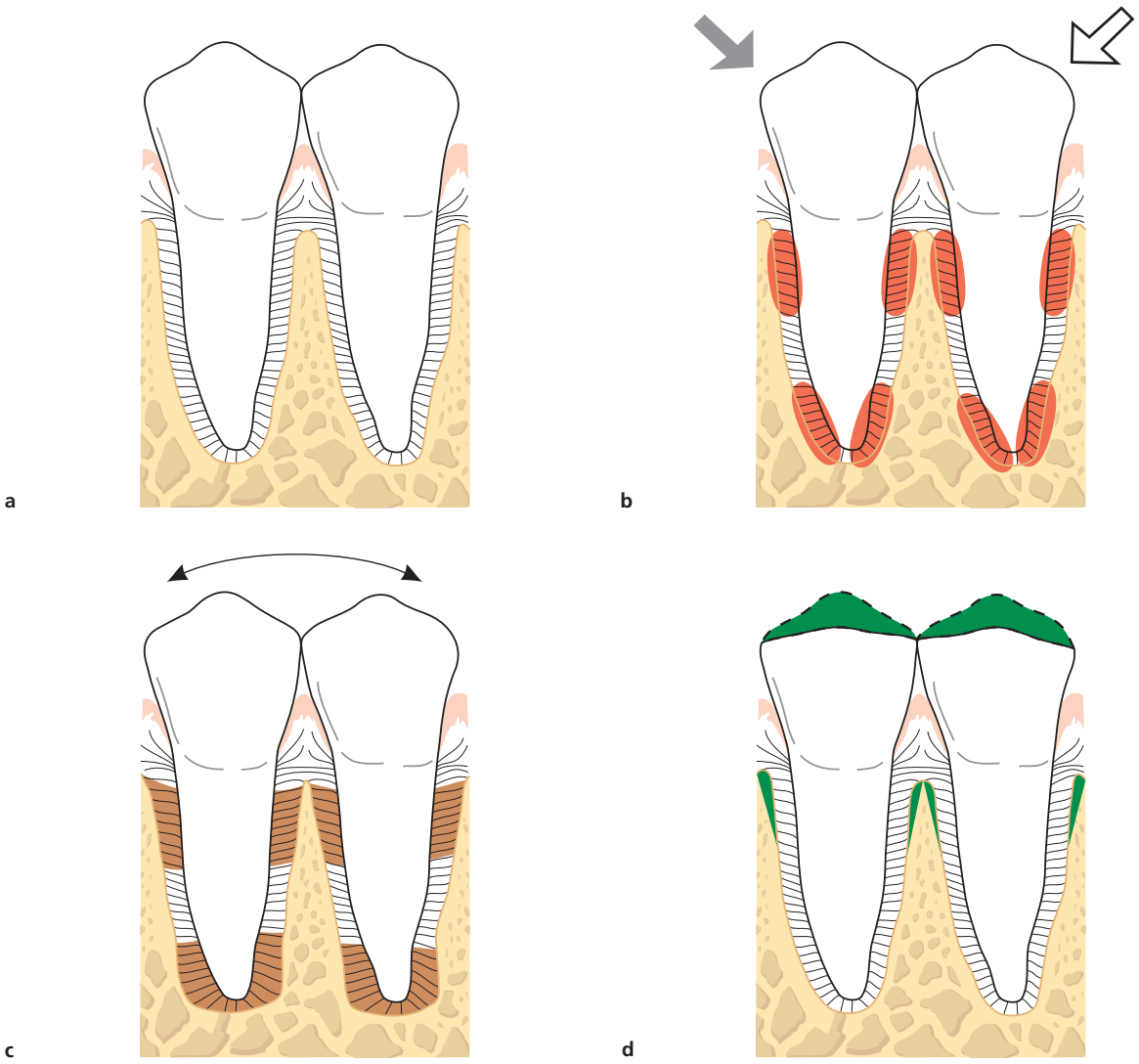


Fig. 14-7 Two mandibular premolars with normal periodontal tissues (a) are exposed to jiggling forces (b) as illustrated by the two arrows. The combined tension and pressure zones (encircled areas) are characterized by signs of acute inflammation including collagen resorption, bone resorption, and cementum resorption. As a result of bone resorption the periodontal ligament space gradually increases in size on both sides of the teeth as well as in the periapical region. (c) When the effect of the force applied has been compensated for by the increased width of the periodontal ligament space, the ligament tissue shows no sign of inflammation. The supra-alveolar connective tissue is not affected by the jiggling forces and there is no apical downgrowth of the dentogingival epithelium. (d) After occlusal adjustment the width of the periodontal ligament becomes normalized and the teeth are stabilized.

for the pressure zone at orthodontically moved teeth, with the one difference that the periodontal ligament space at jiggling gradually increased in width on both sides of the tooth. During the phase when the periodontal space gradually increased in width, (1) inflammatory changes were present in the ligament tissue, (2) active bone resorption occurred, and (3) the tooth displayed signs of gradually increasing (*progressive*) mobility. When the effect of the forces applied had been compensated for by the increased width of the periodontal ligament space, the ligament tissue showed no signs of increased vascularity or exudation. The tooth was hypermobile but the mobility was no longer *progressive* in character. Distinction should thus be made between *progressive* and *increased* tooth mobility.

In *jiggling-type trauma* experiments, performed on animals with a normal periodontium, the supra-alveolar connective tissue was not influenced by the occlusal forces, the reason being that this tissue compartment is bordered by hard tissue on one side only. This means that a gingiva which was uninflamed at the start of the experiment remained uninflamed, but also that an overt inflammatory lesion residing in the supra-alveolar connective tissue was not aggravated by the jiggling forces.

Healthy periodontium with reduced height

Progressive periodontal disease is characterized by gingival inflammation and a gradually developing loss of connective tissue attachment and alveolar bone. Treatment of periodontal disease, i.e. removal

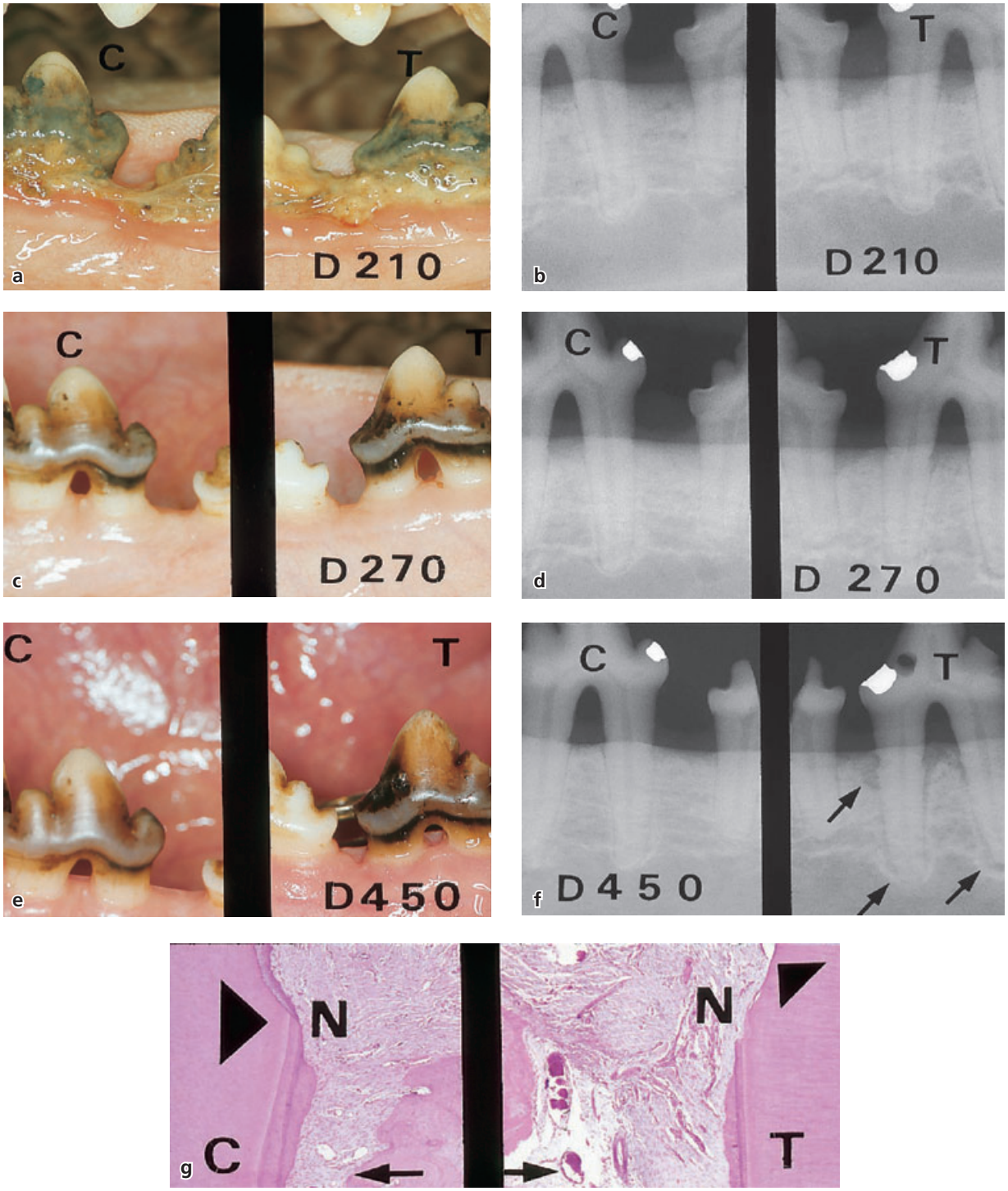


Fig. 14-8 (a) Dogs were allowed to accumulate plaque and calculus in the mandibular premolar regions over a 210-day period. (b) When around 40–50% of the periodontal tissue support had been lost the animals were treated by scaling, root planing, and pocket elimination. During surgery, a notch was prepared in the root at the level of the bone crest. (c, d) The dogs were subsequently placed on a plaque-control program and 2 months later (day 270) all experimental teeth (the lower fourth premolars; 4P and P4) were surrounded by a healthy periodontium with reduced height. (e) The mandibular left fourth premolar (T) was exposed to jiggling forces. (f) As a consequence, a widened periodontal ligament and increased tooth mobility resulted. (g) This increase in tooth mobility and the development of widened periodontal ligament space did not, however, result in apical downgrowth of the dentogingival epithelium. Arrowheads indicate the apical extension of the junctional epithelium which coincides with the apical border of the notch (N), prepared in the root surface prior to jiggling. C = control tooth; T = test tooth.

of plaque and calculus and elimination of pathologically deepened pockets, will result in the re-establishment of a healthy periodontium but with reduced height. The question is whether a healthy periodontium with reduced height has a capacity similar to that of the normal periodontium to adapt to traumatizing occlusal forces (secondary occlusal trauma).

This problem has also been examined in animal experiments (Ericsson & Lindhe 1977). Destructive periodontal disease was initiated in dogs by allowing the animals to accumulate plaque and calculus for a period of 6 months (Fig. 14-8). When around 50% of the periodontal tissue support had been lost (Fig. 14-8a,b), the progressive disease was subjected to treatment by scaling, root planing, and pocket elimination (Fig. 14-8c). During a subsequent 8-month period, the animals were enrolled in a careful plaque-control program. During this period certain premolars were exposed to traumatizing jiggling forces. The periodontal tissues in the combined *pressure* and *tension zones* reacted to the forces by vascular proliferation, exudation, and thrombosis, as well as by bone resorption. In radiographs, widened periodontal ligaments (Fig. 14-8d) could be found around the traumatized teeth, which displayed signs of *progressive* tooth mobility at clinical examination. The gradual increase in the width of the periodontal ligament and the resulting progressive increase in tooth mobility took place during a period of several weeks but eventually terminated. The active bone resorption ceased and the markedly widened periodontal ligament tissue regained its normal composition; healing had occurred (Fig. 14-8e). The teeth were hypermobile but surrounded by periodontal structures which had adapted to the altered functional demands.

During the entire experimental period the supra-alveolar connective tissue remained unaffected by the jiggling forces. There was no further loss of connective tissue attachment and no further downgrowth of dentogingival epithelium (Fig. 14-8e). The results from this study clearly reveal that within certain limits a healthy periodontium with reduced height has a capacity similar to that of a periodontium with normal height to adapt to altered functional demands (Fig. 14-9).

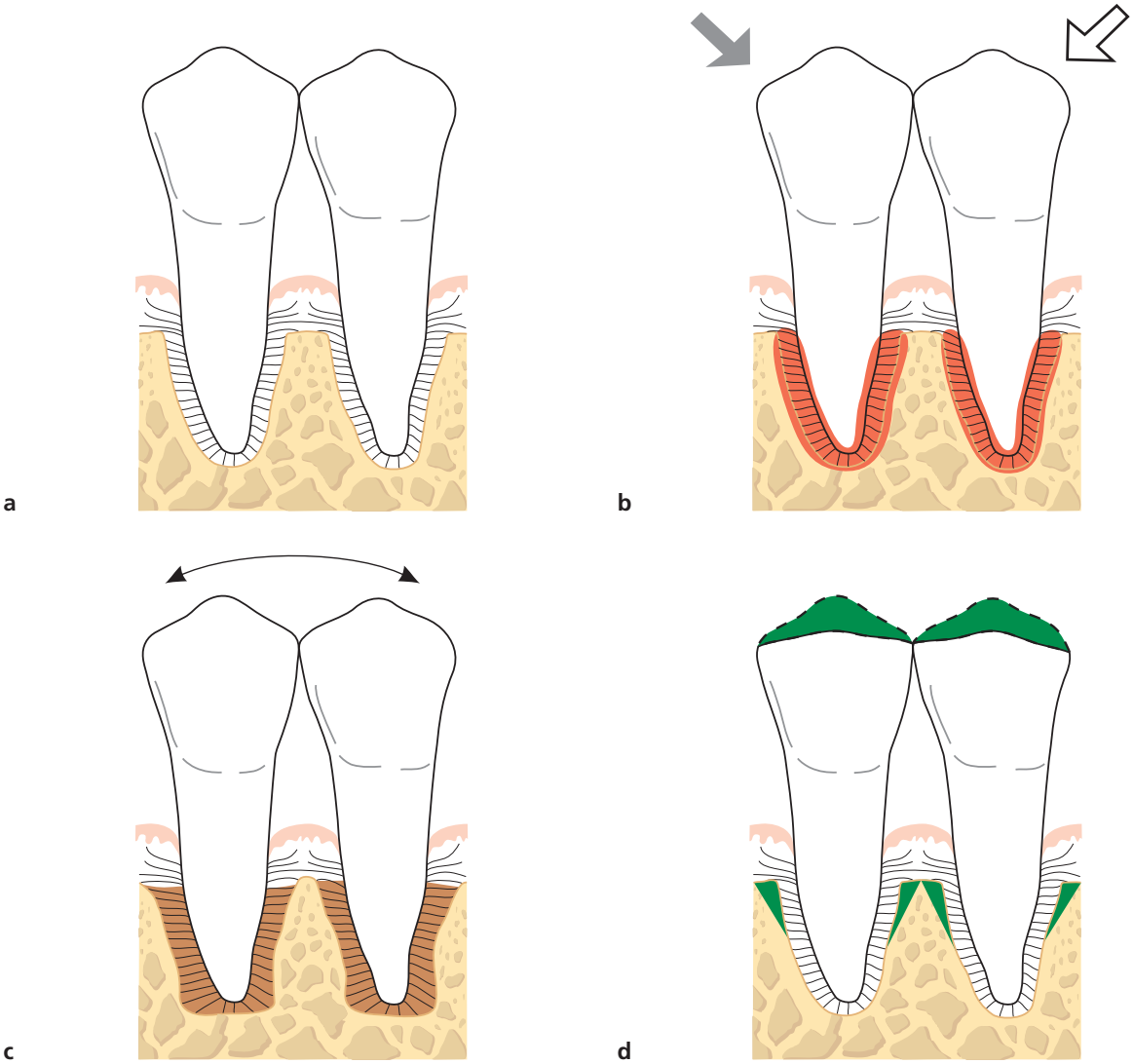


Fig. 14-9 (a) Two mandibular premolars are surrounded by a healthy periodontium with reduced height. (b) If such premolars are subjected to traumatizing forces of the jiggling type a series of alterations occurs in the periodontal ligament tissue. (c) These alterations result in a widened periodontal ligament space and in an increased tooth mobility but do not lead to further loss of connective tissue attachment. (d) After occlusal adjustment the width of the periodontal ligament is normalized and the teeth are stabilized.

Plaque-associated periodontal disease

Experiments carried out on humans and animals have demonstrated that *trauma from occlusion* cannot induce pathologic alterations in the supra-alveolar connective tissue, i.e. cannot produce inflammatory lesions in a normal gingiva or aggravate a gingival lesion associated with plaque and cannot induce loss of connective tissue attachment. The question remains if abnormal occlusal forces can influence the spread of the plaque-associated lesion and enhance the rate of tissue destruction in periodontal disease. This has been studied in animal experiments (Lindhe & Svanberg 1974; Meitner 1975; Nyman *et al*. 1978; Ericsson & Lindhe 1982; Polson & Zander 1983). In these experiments progressive and destructive periodontal disease was first initiated in dogs or monkeys by allowing the animals to accumulate plaque and calculus. Teeth thus involved in a progressive periodontal disease process were also subjected to trauma from occlusion.

"Traumatizing" jiggling forces (Lindhe & Svanberg 1974) were exerted on premolars and were found to induce certain tissue reactions in the combined *pressure/tension zones*. Within a few days of the onset of the jiggling forces, the periodontal ligament tissue in these zones displayed signs of inflammation, had increased numbers of vessels, showed increased vascular permeability and exudation, thrombosis, as well as retention of neutrophils and macrophages. On the adjacent bone surfaces there were a large number of osteoclasts. Since the teeth could not orthodontically move away from the jiggling forces, the periodontal ligament of both sides of the tooth gradually increased in width, the teeth became hypermobile (*progressive* tooth mobility) and angular bony defects could be detected in the radiographs. The forces were eventually nullified by the increased width of the periodontal ligament.

If the forces applied were of a magnitude to which the periodontal structures could adapt, the *progressive* increase of the tooth mobility terminated within a few weeks. The active bone resorption ceased but the angular bone destruction persisted as well as the increased tooth mobility. The periodontal ligament had an increased width but a normal tissue composition. Histologic examination of biopsy specimens revealed that this adaptation had occurred with no greater apical proliferation of the dentogingival epithelium than was caused by the plaque-associated lesion (Fig. 14-10) (Meitner 1975). This means that occlusal forces which allow adaptive alterations to develop in the *pressure/tension* zones of the periodon-

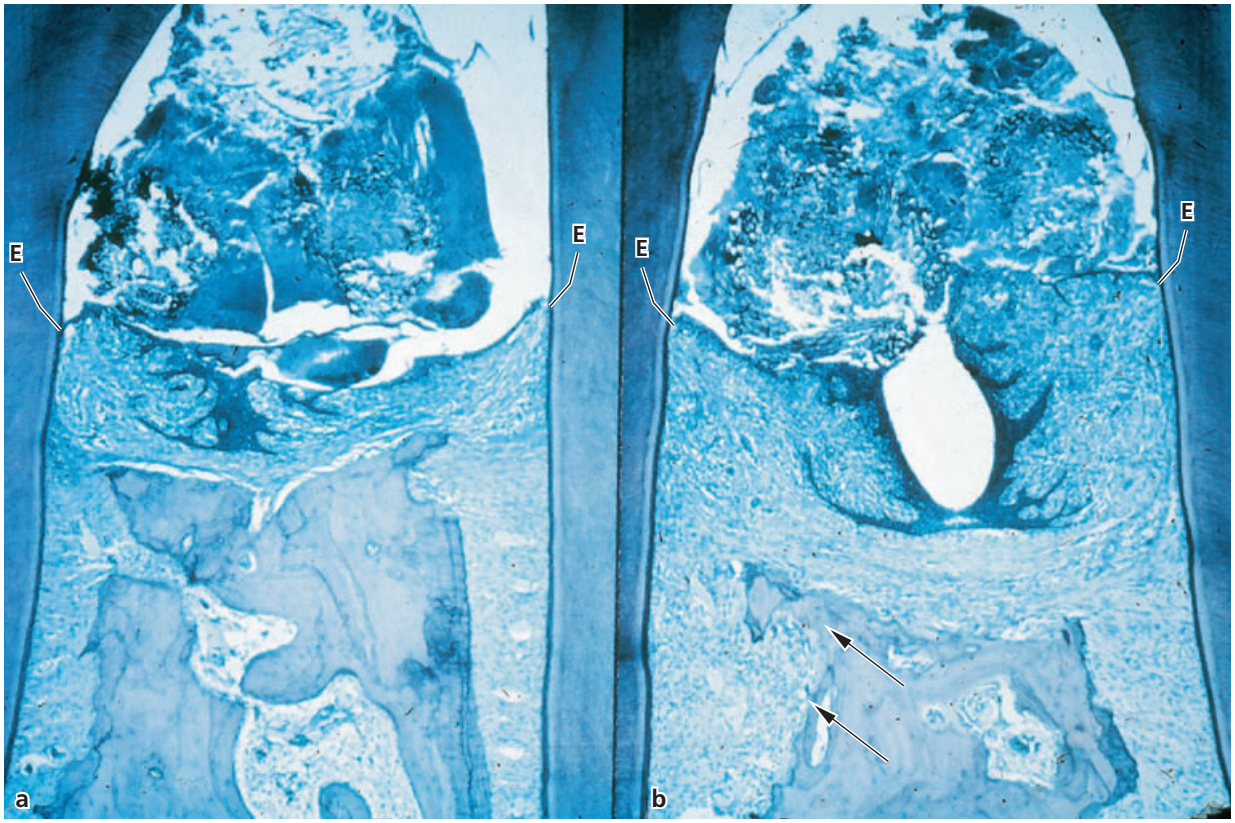


Fig. 14-10 (a) A composite photomicrograph illustrating the interdental space between two pairs of teeth. The teeth have been subjected to experimental, ligature-induced periodontitis and in (b) also to repetitive mechanical injury. In (b), there is considerable loss of alveolar bone and an angular widening of the periodontal ligament space (arrows). However, the apical downgrowth of the dentogingival epithelium in the two areas (a) and (b) is similar. E indicates the apical level of the dentogingival epithelium. Courtesy of Dr. S.W. Meitner.

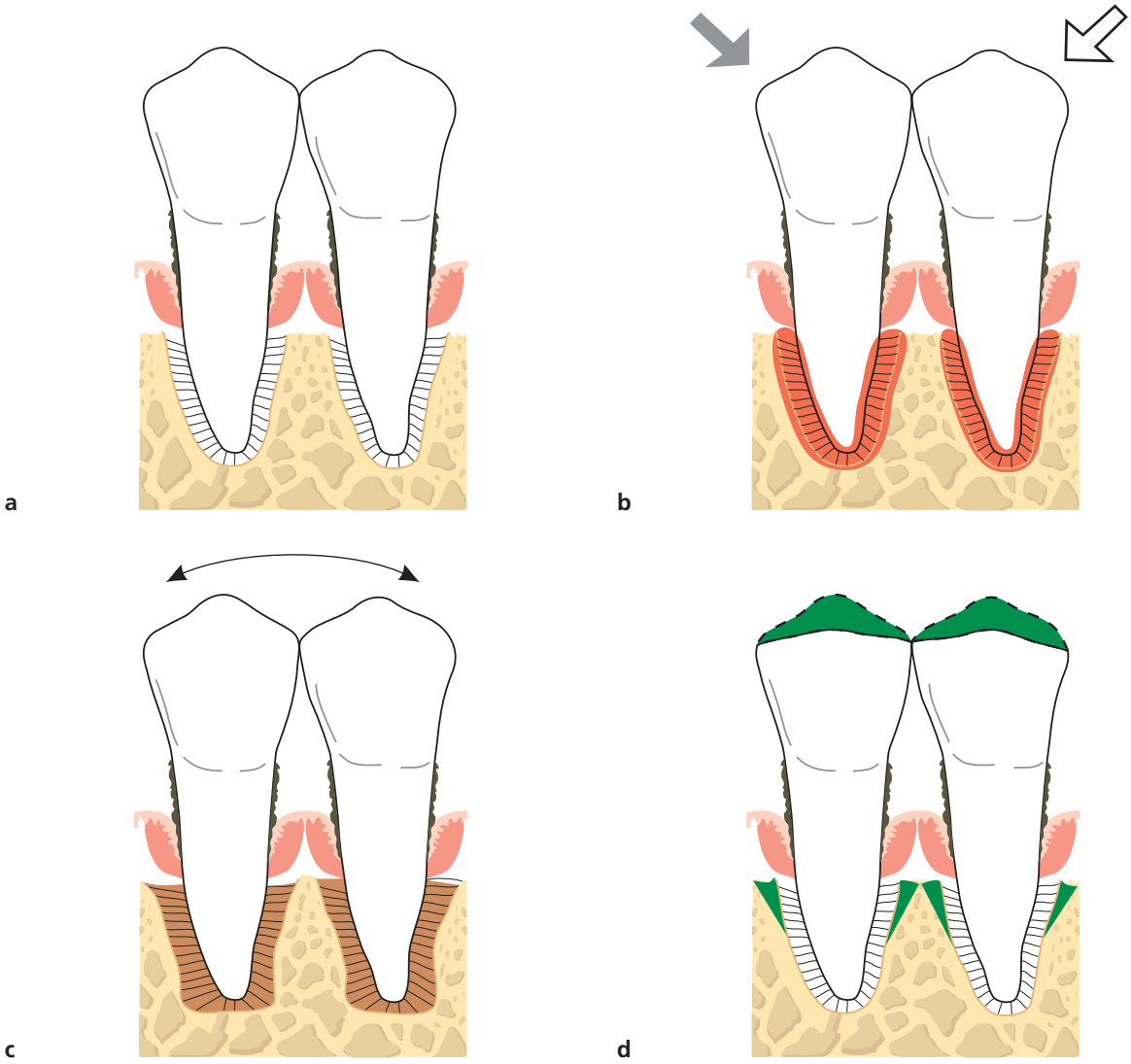


Fig. 14-11 (a) Two mandibular premolars with supra- and subgingival plaque, advanced bone loss and periodontal pockets of a suprabony character. Note the connective tissue infiltrate (shadowed areas) and the uninflamed connective tissue between the alveolar bone and the apical portion of the infiltrate. (b) If these teeth are subjected to traumatizing forces of the jiggling type, pathologic and adaptive alterations occur within the periodontal ligament space. (c) These tissue alterations, which include bone resorption, result in a widened periodontal ligament space and increased tooth mobility but no further loss of connective tissue attachment. (d) Occlusal adjustment results in a reduction of the width of the periodontal ligament and in less mobile teeth.

tal ligament will not aggravate a plaque-associated periodontal disease (Fig. 14-11).

If, however, the magnitude and direction of the jiggling forces were such that, during the course of the study (6 months), the tissues in the pressure/tension zones could not become adapted, the injury in the *zones of co-destruction* had a more permanent character. For several months the periodontal ligament in the pressure/tension zones displayed signs of inflammation (vascular proliferation, exudation, thrombosis, retention of neutrophils and macrophages, collagen destruction). Osteoclasts residing on the walls of the alveolus maintained the bone-resorptive process, which resulted in a gradual widening of the periodontal ligament in the pressure/tension zones (Fig. 14-12). As a consequence, the resulting angular bone destruction was continuous and the mobility of the teeth remained progressive. The plaque-associated lesion in the "zone of irritation" and the inflammatory lesion in the "zone of co-destruction" merged; the dentogingival epithelium proliferated in an apical direction and periodontal disease was aggravated (Figs. 14-13, 14-14) (Lindhe & Svanberg 1974).

Similar findings were reported from another experiment in the dog (Ericsson & Lindhe 1982) in which the effect was assessed of a *prolonged* period of jiggling force application on the rate of progression of plaque-associated, marginal periodontitis. Thus, in dogs with continuing periodontal disease, certain teeth were exposed to jiggling forces during a period of 10 months. Control teeth were not jiggled. Figure 14–15a illustrates the marked periodontal tissue breakdown around a tooth which was exposed to plaque infection combined with jiggling trauma for several months and Fig. 14-15b illustrates a

control tooth which was exposed to plaque infection only.

On the other hand, more short-term experiments in the monkey (Polson & Zander 1983), evaluating the effect of *trauma from occlusion* on teeth involved in an ongoing process of periodontitis, failed to support the findings by Lindhe and Svanberg (1974) and Ericsson and Lindhe (1982). Polson and Zander (1983) observed that trauma superimposed on periodontal lesions associated with angular bony defects (1) caused increased loss of alveolar bone but (2) failed to produce additional loss of connective tissue attachment.

Conclusions

Experiments carried out in humans as well as animals, have produced convincing evidence that neither unilateral forces nor jiggling forces, applied to teeth with a healthy periodontium, result in pocket formation or in loss of connective tissue attachment. *Trauma from occlusion cannot induce periodontal tissue breakdown*. Trauma from occlusion does, however, result in resorption of alveolar bone leading to an increased tooth mobility which can be of a transient or permanent character. This bone resorption with resulting increased tooth mobility should be regarded as a physiologic adaptation of the periodontal ligament and surrounding alveolar bone to the traumatizing forces, i.e. to altered functional demands.

In teeth with progressive, plaque-associated periodontal disease, trauma from occlusion may, under certain conditions, enhance the rate of progression of the disease, i.e. act as a co-factor in the destructive process. From a clinical point of view, this knowledge strengthens the demand for proper treatment of plaque associated with periodontal disease. This treatment will arrest the destruction of the periodontal tissues even if the occlusal trauma persists. Treatment directed towards the trauma alone, however, i.e. occlusal adjustment or splinting, may reduce the mobility of the traumatized teeth and result in some regrowth of bone, but it will not arrest the rate of further breakdown of the supporting apparatus caused by plaque. (For a detailed discussion of treatment of teeth exhibiting increased mobility, see Chapter 51.)

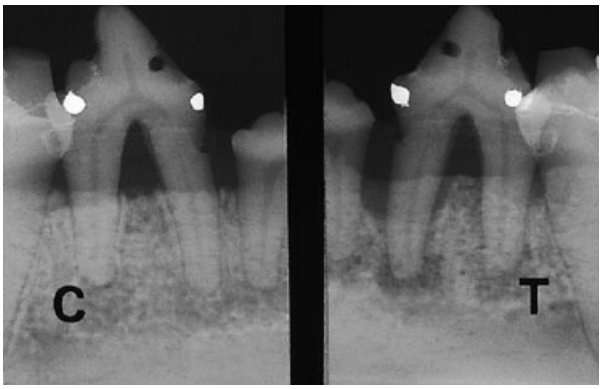


Fig. 14-12 Radiographic appearance of one test tooth (T) and one control tooth (C) at the termination of an experiment in which periodontitis was induced by ligature placement and plaque accumulation and in which trauma of the jiggling type was induced. Note angular bone loss particularly around the mesial root of the mandibular premolar (T) and the absence of such a defect at the mandibular premolar (C). From Lindhe & Svanberg (1974).

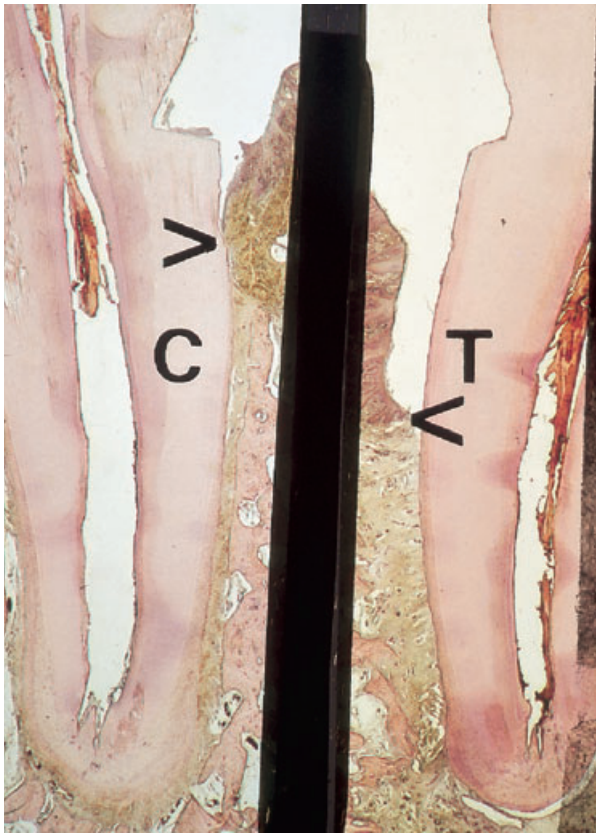


Fig. 14-13 Microphotographs from one control (C) and one test (T) tooth after 240 days of experimental periodontal tissue breakdown and 180 days of trauma from occlusion of the jiggling type (T). The arrowheads denote the apical position of the dentogingival epithelium. The attachment loss is more pronounced in T than in C. From Lindhe & Svanberg (1974).

Fig. 14-15 (a) Periodontal conditions around a tooth which has been exposed to trauma from occlusion (of the jiggling type) for 300 days in combination with plaque-associated experimental periodontitis. (b) Condition of a control tooth from the same dog in which experimental periodontitis but no jiggling trauma had been in operation. Note the difference between (a) and (b) regarding the degree of bone destruction and loss of connective tissue attachment. Note also in (a) the location of the subgingival plaque at the apex of the root. From Ericsson & Lindhe (1982).

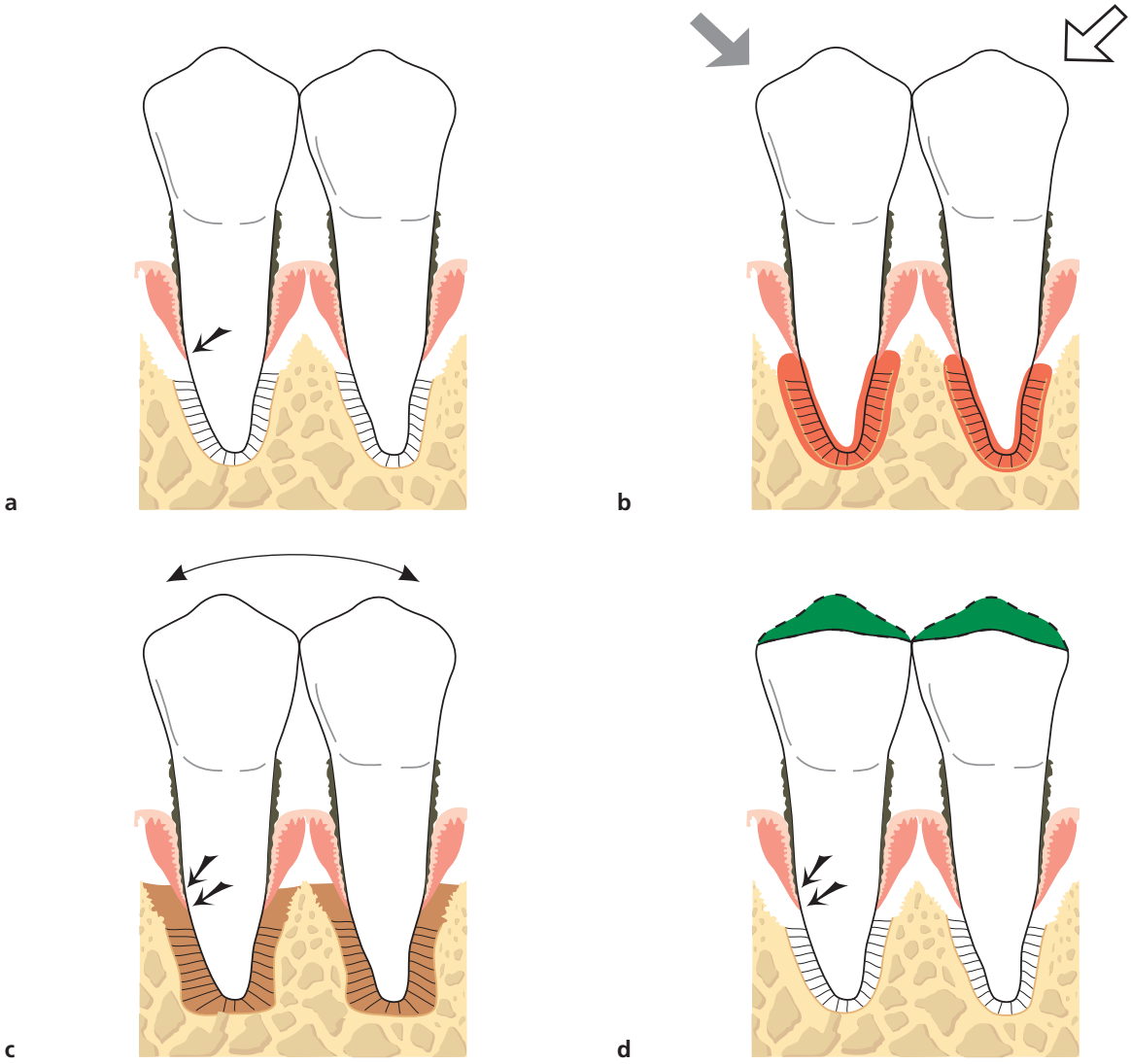
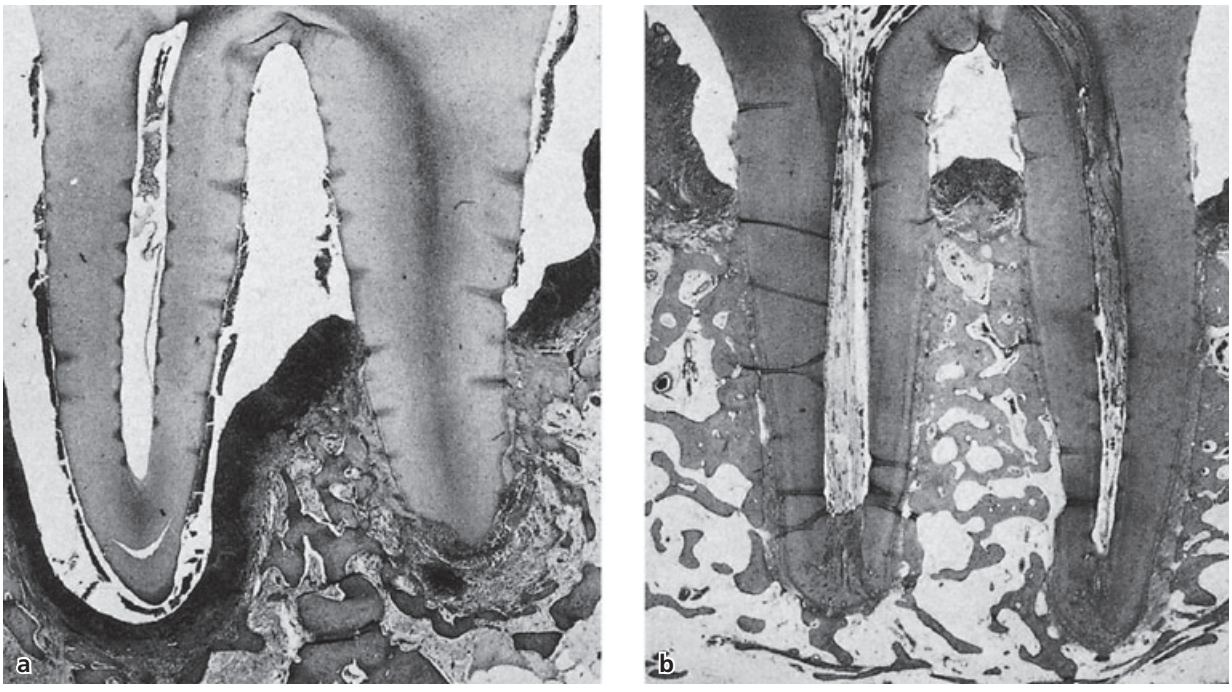


Fig. 14-14 (a) Illustration of a tooth where subgingival plaque has mediated the development of an infiltrated soft tissue (shadowed area) and an infrabony pocket. (b) When trauma from occlusion of the jiggling type is inflicted (arrows) on the crown of this tooth, the associated pathologic alterations occur within a zone of the periodontium which is also occupied by the inflammatory cell infiltrate (shadowed area). In this situation the increasing tooth mobility may also be associated with an enhanced loss of connective tissue attachment and further downgrowth of dentogingival epithelium; compare arrows in (c) and (d). Occlusal adjustment will result in a narrowing of the periodontal ligament, less tooth mobility, but no improvement of the attachment level (d) (Lindhe & Ericsson 1982).



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Chapter 15

Trauma from Occlusion: Peri-implant Tissues

Niklaus P. Lang and Tord Berglundh

Introduction

Enosseous osseointegrated oral implants have been suggested to serve as anchorage for orthodontic appliances where the existing dentition does not provide sufficient anchorage (see Chapter 58). Both clinical (Turley *et al*. 1988; Ödman *et al*. 1988, 1994; Haanaes *et al*. 1991) and experimental (Wehrbein & Diedrich 1993; Wehrbein *et al*. 1996) studies have demonstrated that osseointegrated implants were able to provide sufficient and stable anchorage for tooth movement during the period of orthodontic therapy, hereby eliminating the need of observing Newton's third law (1687) according to which an applied force can be divided into an *action* component and an equal and opposite *reaction* moment.

In long-term clinical studies of various two-stage submerged implant systems, however, implant loss has been attributed to *overloading or excessive loading*. In patients with edentulous (Adell *et al*. 1981; Lindquist *et al*. 1988) and partially edentulous jaws (Jemt *et al*. 1989; Quirynen *et al*. 1992) most of the losses of implants were considered to be the result of excessive occlusal loading. While it has been shown that early loading of oral implants may impede successful osseointegration (Sagara *et al*. 1993), the effect of excessive occlusal functional forces following successful osseointegration has not been documented so far. However, studies by Isidor (1996, 1997) have demonstrated that loading of implants through the creation of a massive supra-occlusion, leading to excessive, and most likely unphysiologic, laterally directed occlusal forces, established a high risk for the loss of osseointegration. Nevertheless, in one out of four experimental animals, even such excessive loading forces were unable to jeopardize the interfacial union of the alveolar bone with the implant surface.

The forces applied in the studies mentioned were characterized as being very high and of short duration. However, they could not be quantified. None of the experimental studies performed up to date allowed for the analysis of a direct relationship between changes in the stress and strain applied to oral implants which are encountered during functional loading and of the tissue reactions of the surrounding alveolar bone. Such information would appear to be of crucial importance for the evaluation of the etiology and pathogenesis of implant loss due to overload.

Orthodontic loading and alveolar bone

In order to evaluate the tissue reactions adjacent to oral implants following loading with well defined forces and to relate the strain values applied on the trabecular surface of the alveolar bone, an animal study was performed using finite element analysis (FEA) to determine the cellular activity (Melsen & Lang 2001).

In six adult monkeys, the lower first and the second premolars as well as the second molars were removed. After 6 months, two specially designed screw implants were inserted in the region of the lower left second premolar and second molar. After further 3 months, a square rod with three notches at different levels was inserted and tightened to the top of the implants. The notches served as reference for the measurements of the implant displacement. A flat disk was placed between the implant and the rod. To this disk two extensions were welded buccally and lingually in a way that a coil spring could be placed as close as possible to the estimated level of the center of resistance (Fig. 15-1). Immediately before buccal and lingual springs were inserted, the extensions were placed on the occlusal surface of the implants. Impressions of each segment were taken.

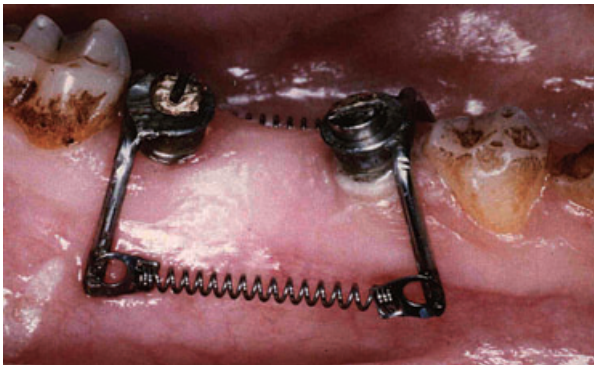

Fig. 15-1 Clinical picture demonstrating the Ni-Ti coil springs applied for a continuous loading through the centre of resistance. From Melsen & Lang (2001).

Subsequently, two measurements were performed with an electronic strain gauge-based measuring device. For anchorage of the device, a cast splint was fitted to the anterior segment of the dentition and each of the implant screws. One measurement was made between the notches close to the implant connection, and another between the notches close to the top of the square rod extensions. These were repeated after 11 weeks, i.e. at the termination of orthodontic loading period. The direction and magnitude of the displacement of the implant as a result of loading could thus be calculated in the sagittal plane.

Following the baseline recordings, springs extending from the anterior to the posterior implant were attached to the power arms buccally and lingually (Fig. 15-1). Forces applied to the implants varied from 100 cN to each implant to a total load of 300 cN per implant. One monkey served as control, i.e. the implants in this animal were not subjected to any loading.

At the end of the experiment, the monkeys were sacrificed. Subsequently, parallel horizontal tissue sections from the coronal to the apical end of the implants were cut and stained with fast green. A grid consisting of three concentric circular gridlines was projected on to the sections (Fig. 15-2). The circular grid lines were intersected by four equidistant radial lines starting at the center of the grid and coinciding with the central axis of the implants. The four radial lines divided the regions between the circles and into eight areas, two in the direction of the force (A: compression zone), two in the opposite direction (B: tension zone), and four lateral to the implants (C and D: shear zone) (Fig. 15-2).

At a magnification of ×160, the extent of resorption lacunae and the extent of osteoid covered surfaces as a fraction of the total surface of trabecular bone were assessed. Also, using morphometry, bone density was evaluated within each quadrant. Furthermore, to measure the amount of osseointegration, the proportion of direct bone-to-implant contact was calculated by projecting a grid consisting of 32 radial lines extending from the center of the implants on to the section to be analyzed (Fig. 15-3).

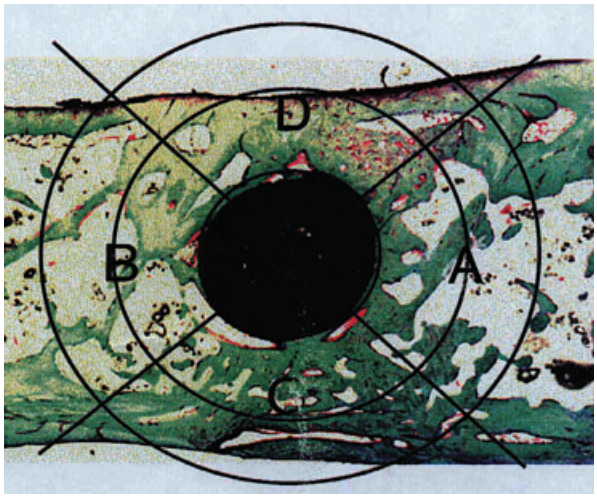

Fig. 15-2 Horizontal section of the implant with the projected grid used for the histomorphometrical evaluation of different regions surrounding the implant. Region A is submitted to compression, region B to tension, and regions C and D to shearing forces. From Melsen & Lang (2001).

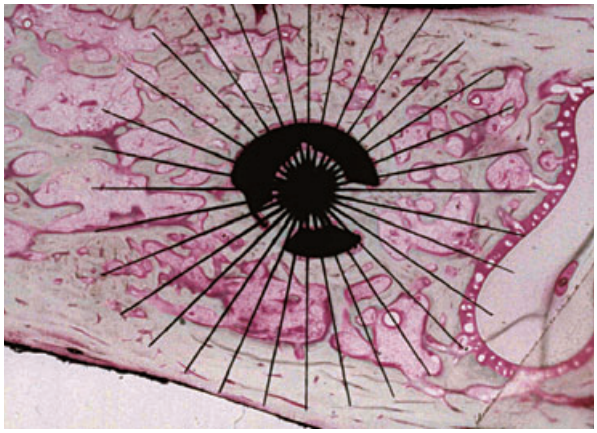

Fig. 15-3 Horizontal section of the implant on to which a grid with 32 radial lines was projected. The evaluation of the osseointegration included the determination of the percentage of direct bone-to-implant contact (magnification ×160). From Melsen & Lang (2001).

None of the implants had lost osseointegration after 11 weeks of orthodontic loading, but loading significantly influenced the turnover of the alveolar bone in the vicinity of the implants. Bone apposition was most frequently found when the calculated strain varied between 3400 and 6600 microstrain. On the other hand, when the strain exceeded 6700 microstrain, the remodeling of the bone resulted in a net loss of bone.

Clearly, the study supported the theory that apposition of bone around an oral implant is the biological response to a mechanical stress below a certain threshold, whereas loss of marginal bone or complete loss of osseointegration may be the result of mechanical stress beyond this threshold. Hence, occlusal forces would have to exeed the physiologic range substantially before occlusal contacts could jeopardize the tissue integrity of an implant.

Several other studies where orthodontic forces have been applied confirmed the apposition or increase in bone density rather than loss of bone surrounding an oral implant (Roberts *et al*. 1984; Wehrbein & Diedrich 1993; Asikainen *et al*. 1997; Akin-Nergiz *et al*. 1998).

Bone reactions to functional loading

A recent study addressed the reaction of peri-implant bone after longstanding functional loading compared to non-loaded controls (Berglundh *et al*. 2005).

After extractions of all mandibular premolars, four AstraTech® implants were placed in one side, and four Brånemark System® fixtures were installed in the contralateral side of the mandible. Three months after abutment connection, fixed dental prostheses (FDPs) were fabricated in gold and cemented on the maxillary canines and premolars (Fig. 15-4). FDPs were also installed on three of the four mandibular implants in both sides. The fourth implant remained unloaded and served as a control (Fig. 15-5).

Radiographs were obtained from each site following implant installation, abutment connection, and FDP placement. All radiographs were repeated after 10 months of functional loading. At this time biopsies were obtained and analyzed histologically.

The radiographic analysis revealed that the largest amount of bone loss occurred following implant installation and abutment connection. This bone loss was more pronounced at Brånemark® than at Astra Tech® implants. However, bone loss as a result of functional loading was small and did not differ from the unloaded control sites (Fig. 15-6).

The histologic analysis showed that implants subjected to 10 months of functional loading had more direct bone-to-implant contact than their unloaded counterparts. This was observed for both implant systems (Fig. 15-7).

Based on radiographic and histologic results this study has demonstrated that *functional loading of implants may enhance osseointegration* (direct bone-to-implant contact) rather than induce marginal bone loss and, hence, such bone loss should not be attributed to loading of implants.

Whenever marginal bone loss is observed around implants in function, the most likely etiologic factor is bacterial in nature (see Chapters 10 and 24).

Excessive occlusal load on implants

The effect of *excessive occlusal load* following placement of titanium implants in the presence of healthy peri-implant mucosal tissues was evaluated in an experimental dog study (Heitz-Mayfield *et al*. 2004). In six Labrador dogs, two TPS (titanium plasma sprayed) implants and two SLA (sandblasted, large grit, acid etched) implants were placed on each side of the mandible (Fig. 15-8a). A total of 45 implants were evaluated. Following 6 months of healing (Fig. 15-8b), gold crowns were placed on implants on the test side of the mandible. The crowns were in supraocclusal contact with the opposing teeth in order to create excessive occlusal load (Fig. 15-8c). Implants on the control side were not loaded. Plaque control was performed throughout the experimental period. Clinical measurements and standardized radiographs (Fig. 15-8d) were obtained at baseline and 1, 3, and 8 months after loading. At 8 months, all implants were osseointegrated, the dogs were killed, and histologic analyses were performed.

The mean probing depth was 2.5 ± 0.3 and 2.6 ± 0.3 mm at unloaded and loaded implants, respectively. Radiographically, the mean distance from the

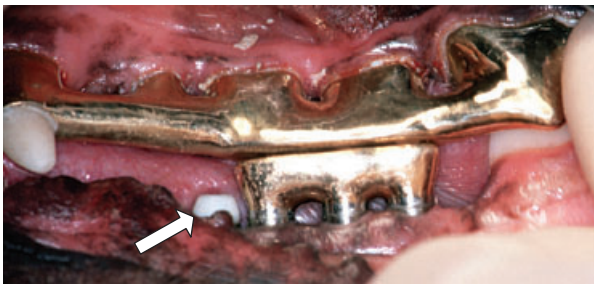

Fig. 15-4 Clinical documentation of the fixed dental prosthesis (FDP) supported by maxillary canines and premolars. In the mandible a FDP is installed on implants to provide masticatory function. The non-loaded control implant is mesial to the FDP (arrow). From Berglundh *et al.* (2005).

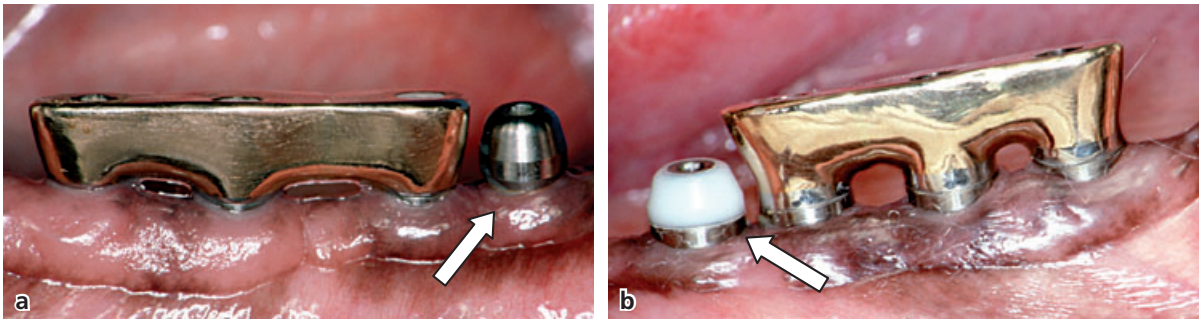

Fig. 15-5 FDPs fabricated of gold and installed on implants for functional loading. Unloaded implant as control (arrows). (a) Astra Tech® implants. (b) Brånemark System®. From Berglundh *et al.* (2005).

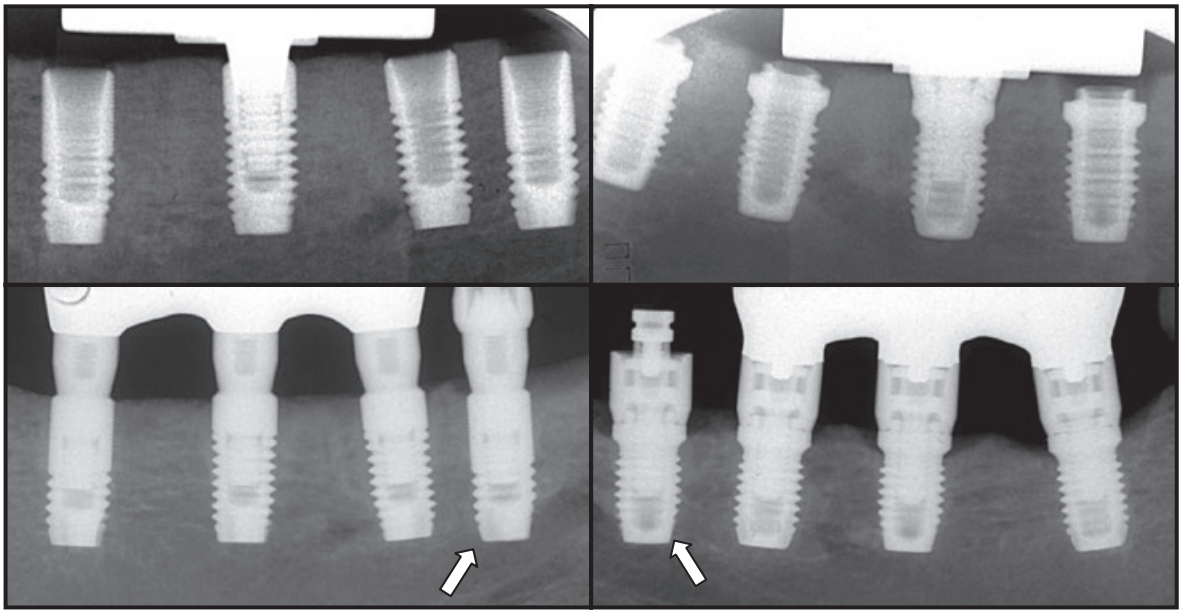

Fig. 15-6 Radiographs obtained from Astra Tech® (left side) and Brånemark® (right side) implants immediately after implant installation (top row) and following 10 months of functional loading (bottom row). Unloaded control implants are indicated with arrows. From Berglundh *et al.* (2005).

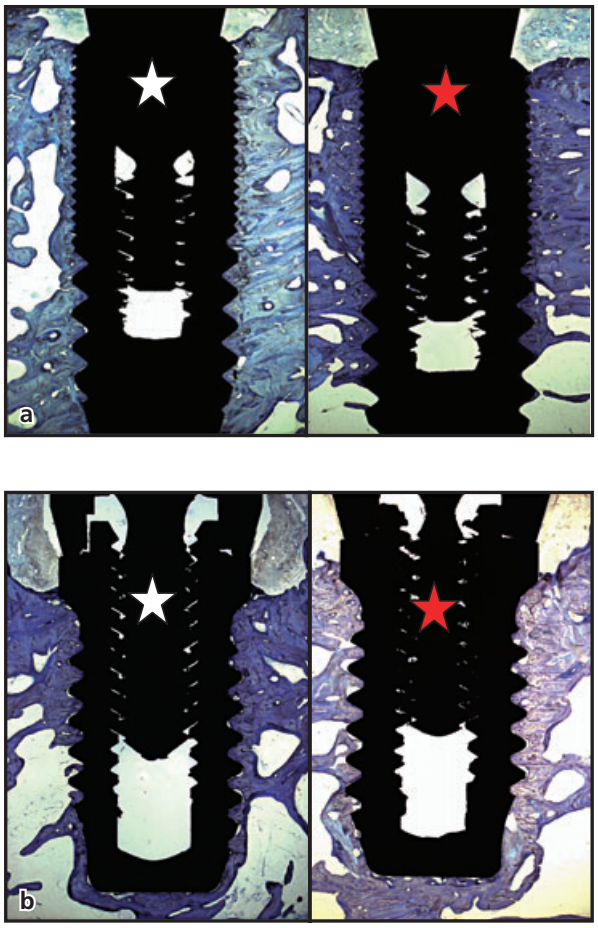

Fig. 15-7 (a) Non-loaded control. Astra Tech® implant after 10 months (white star) and functionally loaded Astra Tech® implant (red star) after 10 months. (b) Non-loaded control. Brånemark® implant after 10 months (white star) and functionally loaded Brånemark® implant (red star) after 10 months. From Berglundh *et al.* (2005).

implant shoulder to the marginal bone level was 3.6 ± 0.4 mm in the control group and 3.7 ± 0.2 mm in the test group. There were no statistically significant changes for any of the parameters from baseline to 8 months in the loaded and unloaded implants. Histologic evaluation (Fig. 15-9) showed a mean mineralized bone-to-implant contact of 73% in the control implants and 74% in the test implants, with no statistically significant difference between test and control implants.

Table 15-1 describes the level of osseointegration in relation to the total length of the implant after 8 months of excessive loading or non-loading. These values were generally slightly below those of the alveolar bone height (Table 15-2) for all sites and surfaces in both test and control implants. The differences varied between 1.1 and 3.7% and were not statistically significant. Likewise, there were no statistically significant differences between the excessively loaded and the unloaded implants in terms of peri-implant bone density either at the implant–bone interface or at a distance of 1 mm from the implant surface (Fig. 15-9) after 8 months.

Since none of the clinical, radiographic or histologic parameters yielded statistically significant differences between non-loaded and excessively loaded implants, the study clearly demonstrated that, in the presence of peri-implant mucosal health, a period of 8 months of *excessive occlusal load* on titanium implants *did not result in loss of osseointegration or marginal bone loss* when compared with non-loaded implants.

Static and cyclic loads on implants

While the study by Berglundh and co-workers (2005) addressed the possible influence of functional loading

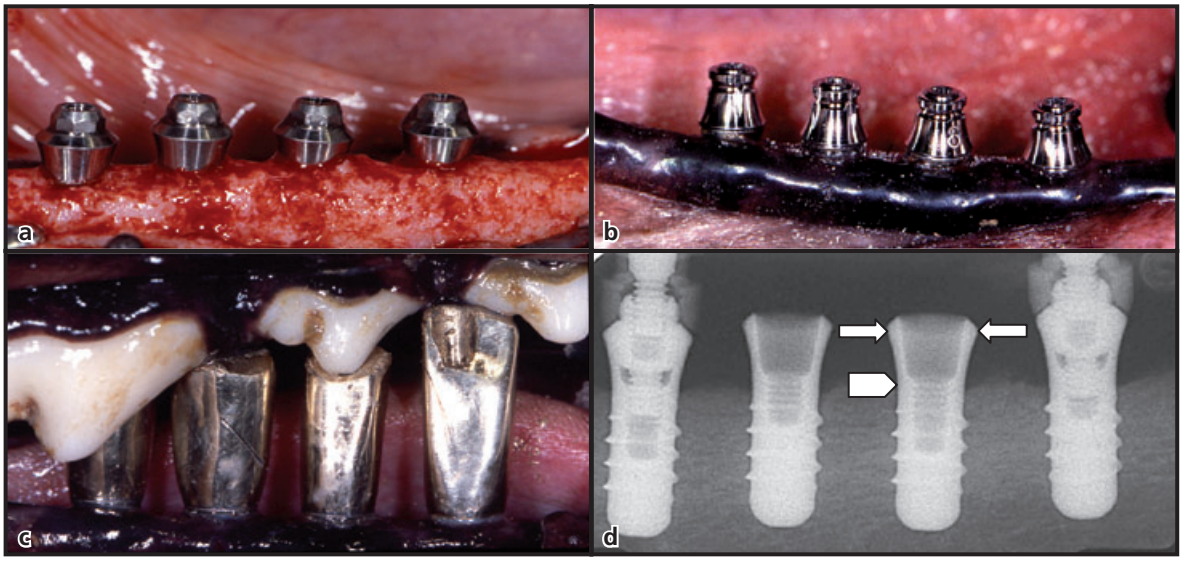

Fig. 15-8 (a) A clinical view of four ITI® implants at the time of placement in one side of the mandible. (b) A clinical view of the ITI® implants after 6 months of non-submerged healing. (c) A clinical view of the test side of the mandible in one dog. Note the four single gold crowns in supra-occlusal contact with the opposing teeth. (d) A standardized radiograph illustrating the level of the implant shoulder (arrows), and the first bone to implant contact visible in the radiograph (arrow head), at the mesial and distal surfaces of the implant. From Heitz-Mayfield *et al.* (2004).

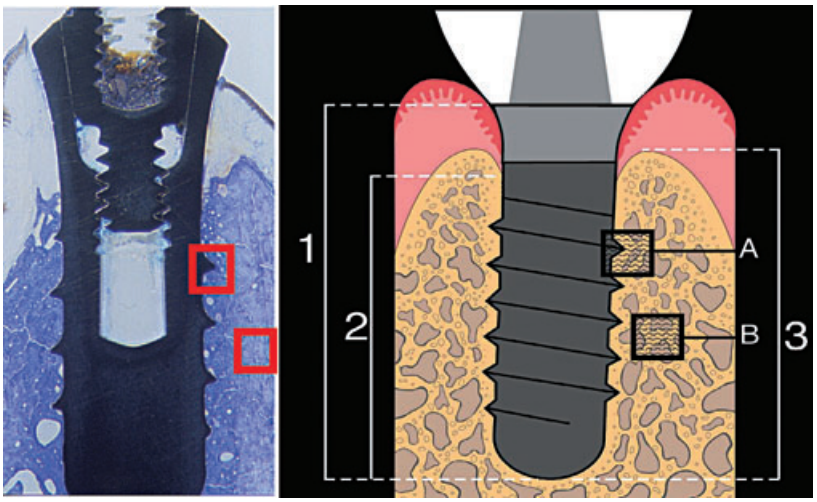

Fig. 15-9 A histologic and diagrammatic representation of the histomorphometric measurements: (1) Implant length = distance from the base of the implant to the implant shoulder. (2) The distance from the base of the implant to the most coronal point of bone-to-implant contact. (3) The distance from the base of the implant to the alveolar bone crest. (A) Percentage of mineralized bone density adjacent to the implant surface. (B) Percentage of mineralized bone density 1 mm distant from the implant surface. From Heitz-Mayfield *et al.* (2004).

Table 15-1 Buccal and lingual percentages of the level of osseointegration (bone-to-implant contact) in relation to the total length of the implant for control and test implants with a TPS or SLA surface after 8 months

	Buccal		Lingual	
	TPS	SLA	TPS	SLA
Control	57.9 (n = 12)	60.4 (n = 11)	67.5 (n = 12)	66.7 (n = 11)
Test	62.1 (n = 10)	59.2 (n = 12)	68 (n = 10)	68 (n = 12)

Table 15-2 Buccal and lingual percentages of alveolar bone height in relation to the total length of the implant for control and test implants with a TPS or SLA surface after 8 months

	Buccal		Lingual	
	TPS	SLA	TPS	SLA
Control	61.1 (n = 12)	63.8 (n = 11)	69.5 (n = 12)	68.7 (n = 11)
Test	64.7 (n = 10)	60.3 (n = 12)	71.4 (n = 10)	70.2 (n = 12)

on the marginal bone levels of implants applying a flat occlusal plane scheme and physiologic forces, many authors have studied the influence of loading forces exceeding physiologic functional conditions and impacting on the implants in a non-axial direction (Barbier & Schepers 1997; Gotfredsen *et al*. 2001a,b,c; Heitz-Mayfield *et al*. 2004).

The bone tissue reaction to axial versus non-axial load was evaluated using conventional three-unit FDPs in the mandible of beagle dogs for axial loading, while non-axial loading was provoked by installing a distal cantilever of two implants (Barbier & Scheppers 1977). Bone remodeling was modest at the implant sites supporting conventional FDPs, while the non-axial load induced by the cantilever FDP yielded a more pronounced bone response including a higher activity of osteoclasts in the peri-implant bone. However, bone levels were not affected. This was interpreted as an adaptive phenomenon within the peri-implant bone as a result of non-axial loading.

Bone reactions around osseointegrated implants to static load was addressed in three studies in dogs (Gotfredsen *et al*. 2001a,b,c). In the first study (Gotfredsen *et al*. 2001a), lateral static load was induced by an orthodontic expansion screw at eight ITI® TPS hollow-screw implants in each dog. After loading period of 24 weeks during which time the screws were activated every 4 weeks from 0.0, 0.2, 0.4, and 0.6 mm, histologic and histometric analysis revealed no marginal bone loss at loaded and unloaded implant sites. Peri-implant bone density and mineralized bone-to-implant contact was higher at the loaded than at unloaded implant sites. This, again, was interpreted that lateral static load resulted in an *adaptive remodeling of the peri-implant bone*.

In the second study (Gotfredsen *et al*. 2001b), two TPS and two turned ITI® hollow-screw implants were subjected to the 24-week loading period in each dog using orthodontic expansion screws. These were, again, activated with 0.6 mm every 4 weeks. The histologic and histometric analysis yielded higher marginal bone levels around TPS implants than around turned implants. Likewise, the peri-implant bone density and mineralized bone-to-implant contact was higher around the roughened TPS than the turned implants. Hence, it was concluded that surface roughness influences the bone reactions to the applied load. This, in turn would indicate that surface roughness may also be a determining factor in the remodeling process triggered by load at the bone-to-implant interface.

The third study (Gotfredsen *et al*. 2001c), addressed the dynamics of applying static load of various durations to ITI® implants in three beagle dogs. Maximal activation of static load was set at 24 weeks on to the implants of the right mandibular side resulting in a total period of load of 46 weeks at sacrifice. At 60 weeks maximal activation of static load was set onto the implants of the left mandibular side resulting in a total period of load of 10 weeks at sacrifice. Fluorochrome labeling was performed at weeks 62, 64, 66, and 68. The dogs were sacrificed at week 70. Similar distribution of bone markers, bone density, and bone-to-implant contact was observed at 10 and 46 weeks of static lateral loading. However, higher fluorochrome proportions were seen at 10 weeks compared to 46 weeks of lateral loading, suggesting higher adaptive activity at 10 weeks. Nevertheless, the structural adaptation appeared to be similar at the two observation periods.

In all three studies, larger bone-to-implant contact was identified at lateral static load application compared to non-loaded implants. Moreover, lateral static load failed to induce peri-implant bone loss or to enhance peri-implant bone loss. Hence, *lateral static load does not appear to be detrimental* to implants exhibiting peri-implant mucositis or peri-implantitis (Gotfredsen *et al*. 2001a,b,c).

In contrast to the findings of the studies presented are the results from a study in dogs (Hoshaw *et al*. 1994). In that study excessive cyclic axial forces had been applied to implants placed in the tibiae of ten animals. Bone loss was observed to occur around the neck of the Brånemark implants after 1 year and exposed to high cyclic (500 cycles/day) axial tension (10–300 N) for 5 consecutive days (Hoshaw *et al*. 1994). Similar results were reported for a rabbit model (Duyck *et al*. 2001) in which dynamic load to implants resulted in the establishment of marginal crater-like defects, while no effects on osseointegration could be identified at other parts of the implants.

Load and loss of osseointegration

It has been reported (Isidor 1996, 1997) that excessive occlusal load may, under certain circumstances, lead to loss of osseointegration along the entire length of the implant, hereby resulting in implant mobility. In this study, four monkeys received 18 self-tapping screw implants in the mandible after the first molars (n = 7), premolars (n = 8), and incisors (n = 3) had been extracted. Using an opposing maxillary splint in heavy supra-occlusal contacts, *excessive occlusal load*, predominantely in non-axial (lateral) direction was applied to eight implants. Furthermore, cotton ligatures for increased plaque retention were placed around another ten implants resulting first in mucositis and later in peri-implantitis (Lindhe *et al*. 1992; Lang *et al*. 1993). After 18 months of excessive occlusal loading, two of the eight implants were lost. Two implants out of ten revealed partial loss of osseointegration as a result of plaque-induced peri-implantitis (Fig. 15-10a). As for the remaining six implants subjected to excessive load, two implants yielded complete loss of osseointegration with a connective tissue capsule formed around the entire outline of the implants (Fig. 15-10b). Radiographically, the two implants showing complete loss of osseointegration and clinical mobility yielded a peri-implant

radiolucency after 18 months of excessive occlusal load. However, no loss of marginal bone height was evident. Also, another two excessively loaded implants (in one monkey) showed no loss of osseointegration whatsoever. Instead, an increase in bone density and the highest percentage of bone-to-implant contact area was seen at these implants in relation to the remaining implants. Neither did this monkey develop ligature induced peri-implantitis (at three implants). Two implants under excessive occlusal load revealed a reduced bone-to-implant contact.

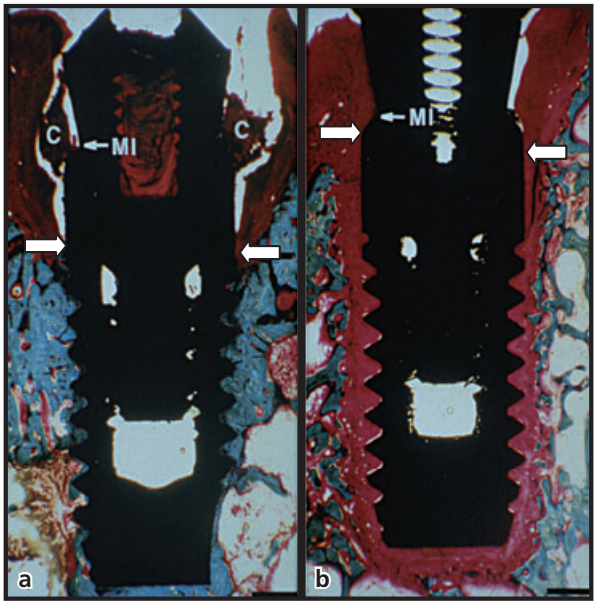

Fig. 15-10 (a) Osseointegrated implant with plaque accumulation. The marginal bone level is located apical to the margin of the implant. (b) Excessively loaded implant with complete loss of osseointegration. The marginal bone level is located near the margin of the implant. Narrow zone of fibrous tissue interposed between implant and bone. MI = margin of implant; white arrows = apical extent of epithelium; C = cotton ligature. (Courtesy of F. Isidor, Århus, Denmark, *Clinical Oral Implants Research* 8, 1–9.)

Thus, the study has demonstrated that excessive occlusal load can, indeed, result in loss of osseointegration characterized by a fibrous connective tissue capsule around the implant as opposed to the marginal bone loss encountered at implants with ligature induced peri-implantitis. It has to be realized, however, that the bone trabecular structure around the implant losing osseointegration as a result of excessive occlusal load (Fig. 15-10b) was much less dense than that of, for example, the implants subjected to experimental peri-implantitis (Fig. 15-10a). In that sense, the described study does not support the concept that occlusal overload may lead to implant losses. Rather, the study supports the fact that marginal bone loss at implants is associated with peri-implant disease.

Masticatory occlusal forces on implants

Closing and occlusal functional force distributions have been studied using one-dimensional (Lundgren *et al*. 1987, 1989; Falk *et al*. 1989, 1990) or three-dimensional piezo-electric force transducers (Meriscke-Stern *et al*. 1996, 2000; Meriscke-Stern 1997, 1998). Eight strain gauge transducers were mounted bilaterally in a maxillary complete denture to occlude with a mandibular implant-supported fixed cantilever prosthesis (Fig. 15-11a) (Lundgren *et al*. 1989).

The study demonstrated that closing and chewing forces *increased* distally along the cantilever beams when occluding with complete dentures. Moreover, on both the preferred and non-preferred chewing sides, significantly larger closing and chewing forces were measured over the cantilever segments than over the implant-supported area (Fig. 15-11b). Also, the distally increasing force distribution pattern could be altered to a distally *decreasing* force distribution pattern by infraoccluding the second cantilever unit by as little as 100 µm. Such slight reductions in

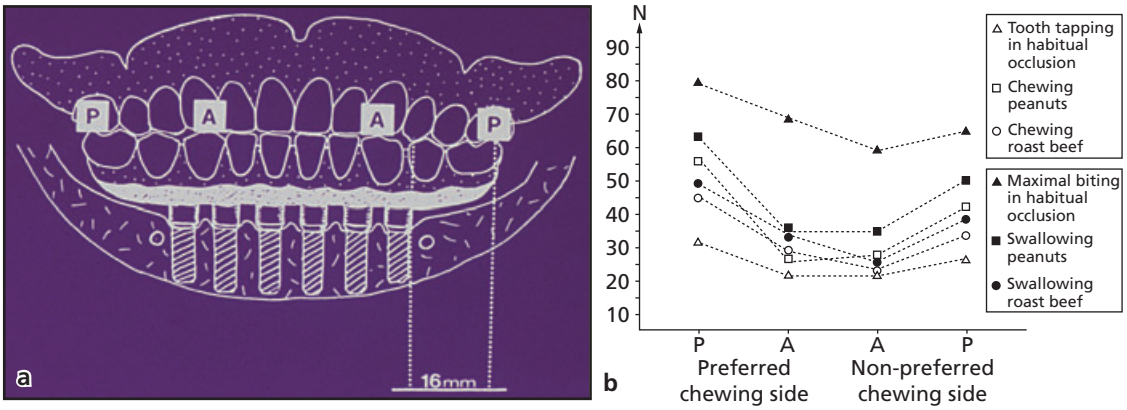

Fig. 15-11 (a) Eight strain gauge transducers placed into a maxillary complete removable prosthesis and occluding against an implant supported fixed mandibular dental prosthesis with cantilever beams of 16 mm. (b) Chewing forces amounting to a maximum biting force of 80 N on the preferred (right) chewing side and 64 N on the non-preferred (left chewing side). While masticating higher forces are applied to the cantilever beams than to the implant-supported part of the mandibular FDP. (Courtesy of D. Lundgren, Göteborg, Sweden, *International Journal of Oral and Maxillofacial Implants* **4**, 277–283.)

posterior occlusal contacts on cantilevers may have to be considered whenever the opposing masticatory unit is a complete removable dental prosthesis. However, maximal biting and chewing forces *decreased* distally along the cantilever beams when occluding with tooth-supported fixed dental prostheses (FDPs) (Fig. 15-12) (Lundgren *et al*. 1987).

From this series of experimental clinical studies it was concluded that forces directed to the implants *per se* are difficult to evaluate using the transducer methodology. Nevertheless, maximal closing forces were always substantially greater than chewing forces. In addition, each subject in the studies referred to developed a preferred chewing side that was associated with higher chewing forces than the non-preferred chewing side (Lundgren *et al*. 1987, 1989; Falk *et al*. 1989, 1990).

More recently, occlusal force distribution patterns have been studied for mandibular overdentures using three-dimensional piezo-electric transducers that were mounted on to two mandibular implants in the canine region designed to support either a ball-joint-retained or a bar-retained mandibular complete removable prosthesis. Rigid bars provided the best distribution of forces in a vertical direction on to the two mandibular implants (Mericske-Stern *et al*. 1996; Mericske-Stern 1998). Moreover, short distal bar extensions did not negatively influence the force pattern (Mericske-Stern 1997). When ball-joint anchors were used to retain the mandibular overdenture, rather low forces were measured on the implants, particularly in a vertical direction (Mericske-Stern 1998). Vertical forces amounted to 60–140 N, while horizontal forces were much smaller (15–60 N).

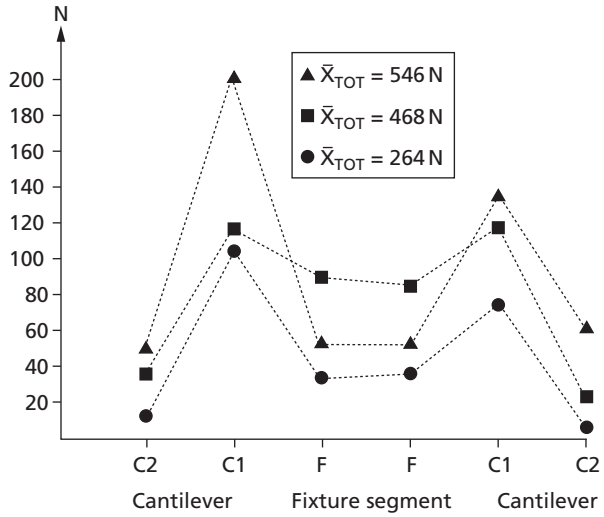

Fig. 15-12 Chewing force patterns in implant-supported fixed dental prosthesis with cantilever beams occluding against tooth-supported FDPs. (Courtesy of D. Lundgren, Göteborg, Sweden, *Journal of Prosthetic Dentistry* **58**, 197–203.)

Tooth–implant supported reconstructions

In reconstructing patients with inadequate masticatory function, oral implants are often used to increase the patient's chewing comfort (see Chapter 52) and provide additional chewing units in an edentulous posterior region. Occasionally, it may be contemplated to reconstruct a chewing side with a reconstruction supported by both a tooth and an implant (Fig. 15-13). In this way, problems of the location of the mental nerve in an area of a planned implant installation or lack of an adequate bone volume may be overcome.

Combined tooth–implant reconstructions have been associated with numerous clinical problems including root intrusion as a potential clinical hazard of non-rigid connection. Hence, it has been claimed that natural teeth should not be connected to implants beneath a fixed prosthesis. However, experimental studies have clearly established that no detrimental effects on the periodontium of abutment teeth could be demonstrated despite a different biomechanical condition mediated by a periodontal ligament as

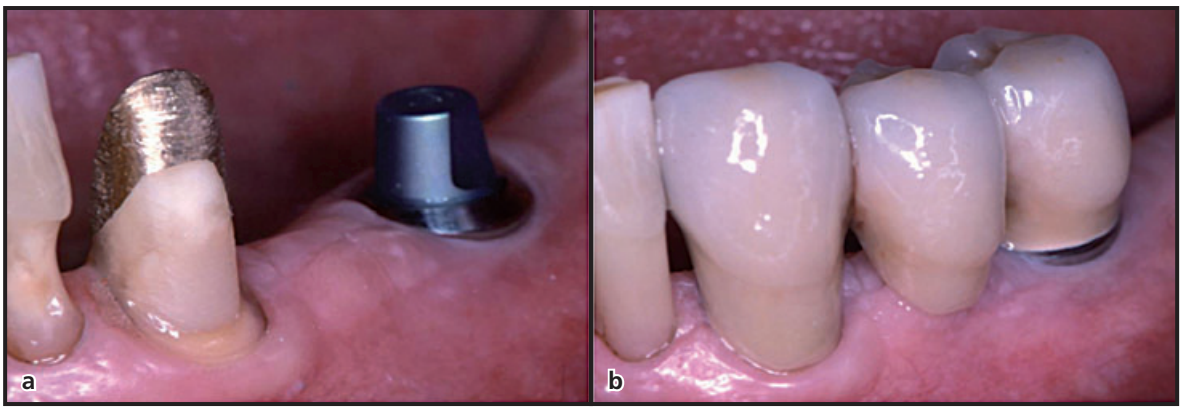

Fig. 15-13 Reconstruction of a chewing side in the left mandible using a fixed dental prosthesis. (a) Prepared abutment tooth 33 after having established adequate abutment height by the installation of a cast post and core prior to seating a three-unit FDP. (b) Tooth–implant-supported three-unit FDP, 10 years after placement.

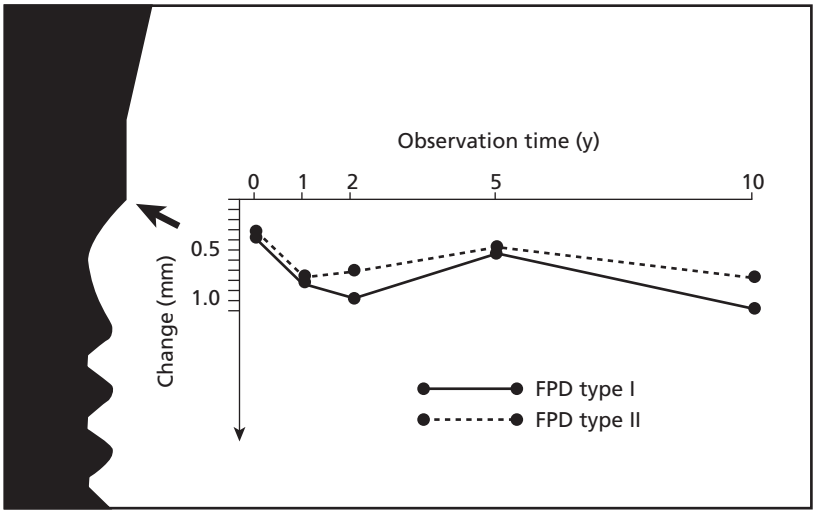

Fig. 15-14 Ten-year randomized controlled clinical trial of three-unit FDPs, either implant–implant (type I) or tooth–implant (type II) supported. No differences in the crestal bone levels after 1, 2, 5, and 10 years in function. (Courtesy of J. Gunne *et al*. *International Journal of Prosthodontics* **12**, 216–221.)

opposed to the ankylotic anchorage of an implant (Biancu *et al*. 1995).

In vivo measurements of vertical forces and bending moments during biting and chewing were carried out on ten three-unit prostheses in the posterior mandibles of five patients. Each patient had two prostheses, one supported by two implants and the other supported by one implant and one tooth. The results demonstrated no major difference in functional load magnitudes related to the support type. Obviously, functional loads were shared between the teeth and the implants (Gunne *et al*. 1997; Rangert *et al*. 1991, 1995). Further studies using finite element analysis yielded no increased risk of stress concentrations at the implant's neck (Gross & Laufer 1997; Laufer & Gross 1998).

Clinical studies reporting life table statistics in combined implant and tooth restorations do not show adverse effects of splinting teeth to implants. No increased risk of tooth intrusion were reported if the implant was rigidly connected to the tooth (Fugazzotto *et al*. 1999; Lindh *et al*. 2001; Naert *et al*. 2001a,b). The results of 843 consecutive patients treated in a private practice (Fugazzotto *et al*. 1999) with 1206 natural tooth–implant supported prostheses utilizing 3096 screw-fixed attachments showed that only 9 intrusion problems were noted after 3–14 years in function. All problems were associated with fractured or lost screws.

Probably the most relevant clinical study was a 10-year randomized controlled prospective study on 23 patients with residual mandibular anterior teeth (Gunne *et al*. 1999). Each patient received two three-unit FDPs either supported by two implants or, on the contralateral side, by one implant and one tooth, thus permitting intraindividual comparison. The distribution of the two types of FDPs in each jaw was randomized. Implant success rates, marginal bone changes, and mechanical complications were studied. The tooth–implant connection did not demonstrate any negative influences on the overall success rates for the 10-year period when compared to the implant–implant supported FDPs (Fig. 15-14). Hence, it was suggested that a prosthetic construction supported by both a tooth and an implant may be recommended as a predictable and reliable treatment alternative in the posterior mandible (Gunne *et al*. 1999).

Based on the evidence available today it can be stated that a combination of implant and tooth support for FDPs is acceptable (Belser *et al*. 2000). While a recent systematic review (Lang *et al*. 2004) indicated that tooth–implant reconstructions reveal a 5-year survival rate of 94.1%, comparing very well with the 5-year survival rate of implant–implant reconstructions of 95.0% (Pjetursson *et al*. 2004), the 10-year survival of tooth–implant reconstructions (77.8%) appears to be significantly lower than the 10-year survival of implant–implant reconstructions (86.7%). However, owing to the fact that the former 10-year survival rate was based on only 60 (I-T) FDPs and the latter on only 219 (I–I) FDPs, the reliability of such 10-year survival has to be questioned.

The biomechanical aspects of implant–tooth-supported fixed dental prostheses have been presented (Lundgren & Laurell 1994). As the implant is rigidly fixed within the alveolus, and the tooth is surrounded by a periodontal ligament that allows minute movement, rigid FDP designs have been advocated. The movement of the natural tooth abutment was found to affect the load-bearing capacity of the FDP, whenever a long-span FDP was constructed (e.g. a beam length of 24 mm or two premolar or molar pontics). Before occlusal load is applied, the FDP acts as a cantilever construction. Upon loading, an angular deflection of implant–crown unit of approximately 50 μm are noted. Together with bending of the long-span beam an apical deflection of the tooth of approximately 50 μm is allowed, hereby leading to a bilateral (tooth and implant) support of the FDP. If the tooth

and implant only support a short-span FDP (e.g. a beam length of 12 mm or one premolar pontic only), however, angular deflection of the implant–crown unit of approximately 50 μm and the bending of the short-span beam are insufficient to achieve a bilateral support of the bridge. The apical deflection of the tooth will not be reached and the implant will cope with the entire occlusal load applied to the FDP. As indicated above, there is no doubt that osseointegration will cope with such functional loads.

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Part 6: Periodontal Pathology

Chapter 16

Non-Plaque Induced Inflammatory Gingival Lesions

Palle Holmstrup

Gingival inflammation, clinically presenting as gingivitis, is not always due to accumulation of plaque on the tooth surface, and non-plaque induced inflammatory gingival reactions often present characteristic clinical features (Holmstrup 1999). They may occur due to several causes, such as specific bacterial, viral or fungal infection without an associated plaque-related gingival inflammatory reaction. Gingival lesions of genetic origin are seen in hereditary gingival fibromatosis, and several mucocutaneous disorders manifest as gingival inflammation. Typical examples of such disorders are lichen planus, pemphigoid, pemphigus vulgaris, and erythema multiforme. Allergic and traumatic lesions are other examples of non-plaque induced gingival inflammation. Dentists, and especially specialists in periodontology, are the key persons in the diagnostic unraveling and treatment of patients affected by such lesions.

This chapter focuses on those non-plaque induced inflammatory gingival lesions of the gingival tissues which are most relevant, either because they are common or because they are important examples for the understanding of the variety of tissue reactions that take place in the periodontium. For further information the reader is referred to oral medicine textbooks. The modifying factors of plaque-related gingivitis such as smoking, sexual hormones, and metabolic anomalies (diabetes) are dealt with in Chapter 12.

Gingival diseases of specific bacterial origin

Infective gingivitis and stomatitis may occur on rare occasions in both immunocompromised and non-immunocompromised individuals, when non-plaque-related pathogens overwhelm innate host resistance (Rivera-Hidalgo & Stanford 1999). The lesions may be due to bacteria and may not be accompanied by lesions elsewhere in the body. Typical examples of such lesions are due to infections with *Neisseria gonorrhoeae* (Scully 1995; Siegel 1996), *Treponema pallidum* (Scully 1995; Ramirez-Amador *et al*. 1996; Siegel 1996; Rivera-Hidalgo & Stanford 1999), streptococci, *Mycobacterium chelonae* (Pedersen & Reibel 1989) or other organisms (Blake & Trott 1959; Littner *et al*. 1982). The gingival lesions manifest as fiery red edematous painful ulcerations, as asymptomatic chancres or mucous patches, or as atypical non-ulcerated, highly inflamed gingivitis. Biopsy supplemented by microbiologic examination reveals the background of the lesions.

Gingival diseases of viral origin

Herpes virus infections

Several viral infections are known to cause gingivitis (Scully *et al*. 1998b). The most important are the herpes viruses: herpes simplex viruses type 1 and 2 and varicella-zoster virus. These viruses usually enter the human body in childhood and may give rise to oral mucosal disease followed by periods of latency and sometimes reactivation. Herpes simplex virus type 1 (HSV-1) usually causes oral manifestations, whereas herpes simplex virus type 2 (HSV-2) is mainly involved in anogenital infections and only occasionally is involved in oral infection (Scully 1989).

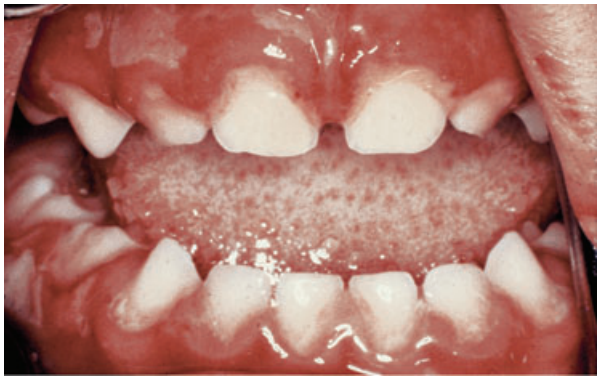

Fig. 16-1 Herpetic gingivostomatitis in a 3-year-old child. Erythematous swelling of attached gingiva with serofibrinous exudate along the gingival margin.

Primary herpetic gingivostomatitis

Herpes simplex infections are among the most common viral infections. Herpes simplex is a DNA virus with low infectiousness, which after entering the oral mucosal epithelium, penetrates a neural ending and, by retrograde transport through the smooth endoplasmatic reticulum (200–300 mm/day), travels to the trigeminal ganglion where it can remain latent for years. The virus has also been isolated in extraneural locations such as the gingiva (Amit *et al*. 1992). Sometimes herpes simplex viruses may also play a role in recurring erythema multiforme. It is presently unknown whether the virus plays a role in other oral diseases, but herpes simplex virus has been found in gingivitis (Ehrlich *et al*. 1983), acute necrotizing gingivitis (Contreras *et al*. 1997), and periodontitis (Parra & Slots 1996).

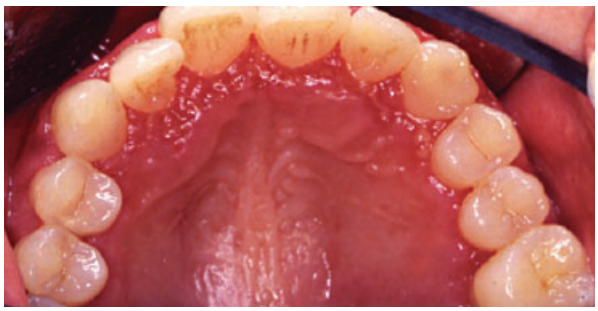

Fig. 16-2 Herpetic gingivostomatitis affecting palatal gingiva. Numerous vesicles and small ulcerations.

When a baby is infected, sometimes from the parent's recurrent herpes labialis, it is often wrongly diagnosed as "teething". With increased hygiene in the industrialized society, more and more primary infections occur at higher ages, i.e. during adolescence or even adulthood. It is estimated in the US that there are about half a million cases per year (Overall 1982). The primary herpetic infection may run an asymptomatic course in early childhood, but may also give rise to severe gingivostomatitis, which usually occurs before adolescence (Fig. 16-1). This manifestation includes painful severe gingivitis with redness, ulcerations with serofibrinous exudate and edema accompanied by stomatitis (Figs. 16-2 and 16-3). The incubation period is 1 week. A characteristic feature is the formation of vesicles, which rupture, coalesce, and leave fibrin-coated ulcers (Scully *et al*. 1991; Miller & Redding 1992). Fever and lymphadenopathy are other classic features. Healing occurs spontaneously without scarring in 10–14 days (Fig. 16-4). During this period pain can render eating difficult.

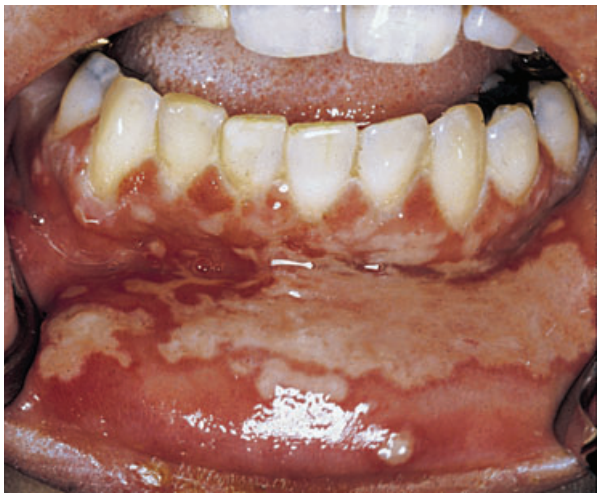

Fig. 16-3 Herpetic gingivostomatitis in a 38-year-old woman. Widespread ulceration of lower lip mucosa and gingiva.

The virus remains latent in the ganglion cell, probably through integration of its DNA in that of the chromosomal DNA (Overall 1982). Reactivation of the virus resulting in recurrent infections occurs in 20–40% of individuals with the primary infection (Greenberg 1996) and usually presents in the form of herpes labialis, but recurrent intraoral herpes infections are also seen. Recurrent infections occur in general more than once per year, usually at the same location on the vermilion border and/or the skin adjacent to it, where neural endings are known to be clustering. A large variety of factors trigger reactivation of latent virus. These are trauma, ultraviolet light

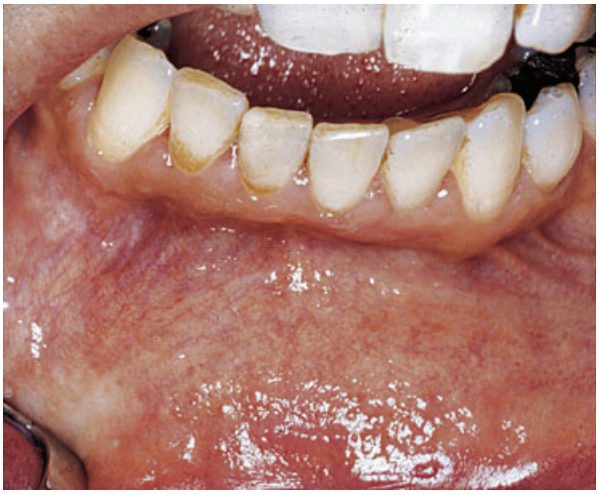

Fig. 16-4 Same patient as shown in Fig. 16-3, 4 weeks later. Healing without loss of tissue or scar formation.

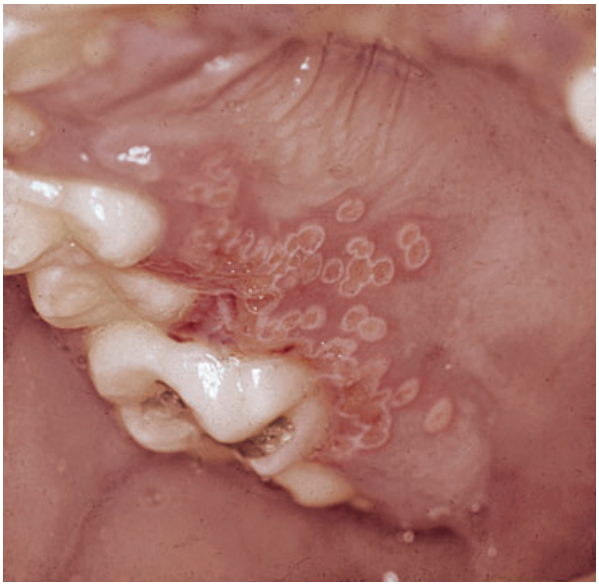

Fig. 16-5 Recurrent intraoral herpes infection. Ruptured vesicles of right palatal gingiva and mucosa.

exposure, fever, menstruation and others (Scully *et al*. 1998b).

While recurrences at the vermilion border are well recognized, recurrent intraoral herpes lesions often remain undiagnosed because they are considered aphthous ulcerations (Lennette & Magoffin 1973; Sciubba 2003), irrespective of the fact that aphthous ulcers do not affect keratinized mucosa. Recurrent intraoral herpes typically presents a less dramatic course than does the primary infection. A characteristic manifestation is a cluster of small painful ulcers in the attached gingiva and hard palate (Yura *et al*. 1986) (Fig. 16-5). The diagnosis can be made on the basis of the patient history and clinical findings supported by isolation of HSV from lesions. A reliable isolation of virus is best obtained from intact vesicular lesions, for instance by aspiration of the vesicle fluid with a small syringe. Isolation and growth of herpes viruses are elaborate because of their fragility. The virus must be transferred to a special cell line in the laboratory within 24 hours, or stored at –70°C. The herpes virus is detected within 5 days, and while a positive viral culture can be taken as evidence of viral infection, a negative result does not rule out such an infection. Laboratory diagnosis may also involve examination of a blood sample for increased antibody titer against herpes virus. However, this is most relevant in cases of primary infection, because the antibody titer remains elevated for the rest of the lifetime. The histopathologic features of cytologic smears from the gingival lesions are not specific, but the presence of giant cells and intranuclear inclusion bodies may indicate intracellular activity of virus (Burns 1980).

Immunodeficient patients, such as HIV-infected individuals, are at increased risk of acquiring the infection (Holmstrup & Westergaard 1998). In the immunocompromised patient the recurrence of herpes infection, either gingival or elsewhere, may be severe and even life-threatening.

The treatment of herpetic gingivostomatitis includes careful plaque removal to limit bacterial superinfection of the ulcerations, which delays their healing. In severe cases, including patients with immunodeficiency, the systemic use of antiviral drugs such as aciclovir, valaciclovir or famciclovir is recommended (O'Brien & Campoli-Richards 1989; Mindel 1991; Arduino & Porter 2006). Resistance to aciclovir, especially among immunodeficient patients on long-term therapy, is a growing concern (Westheim *et al*. 1987) and explains why other antiviral drugs may be relevant. Prophylactic antiviral treatment before dental treatment has been recommended for patients at risk of experiencing a recurrence as well as to minimize transmission of the disease (Miller *et al*. 2004).

Herpes zoster

Varicella-zoster virus causes varicella (chicken pox) as the primary self-limiting infection. It occurs mainly in children and later reactivation of the virus in adults causes herpes zoster (shingles). Both manifestations can involve the gingiva (Straus *et al*. 1988; Scully 1995). Chicken pox is associated with fever, malaise, and a skin rash. The intraoral lesions are small ulcers usually on the tongue, palate, and gingiva (Miller 1996; Scully *et al*. 1998b). The virus remains latent in the dorsal root ganglion from where it can be reactivated years after the primary infection (Rentier *et al*. 1996). Later reactivation results in herpes zoster, with unilateral lesions following the infected nerve (Miller 1996). The reactivation normally affects the thoracic ganglia in elderly or immunocompromised patients. Reactivation of virus from the trigeminal ganglion occurs in 20% of reported cases (Hudson & Vickers 1971). If the second or third branch of the trigeminal nerve is involved, skin lesions may be associated

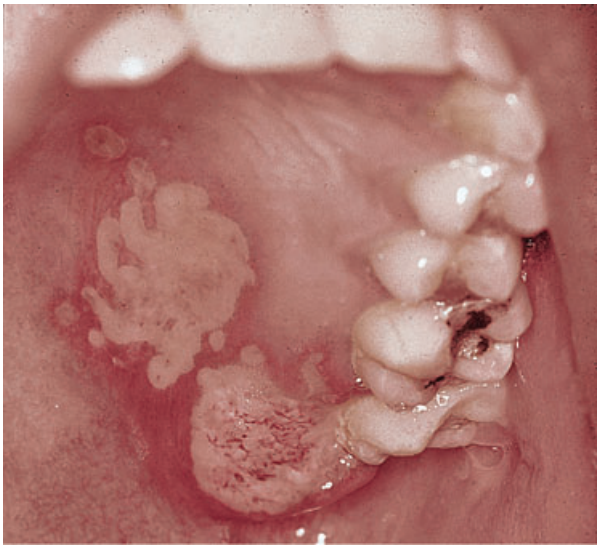

Fig. 16-6 Herpes zoster of left palatal gingiva and mucosa. Irregular fibrin coated ulcerations with severe pain.

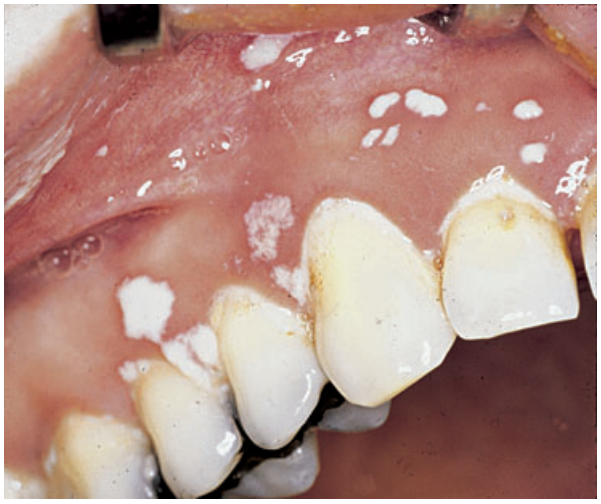

Fig. 16-7 Pseudomembranous candidosis of maxillary gingiva and mucosa in HIV-seropositive patient. The lesions can be scraped off, leaving a slightly bleeding surface.

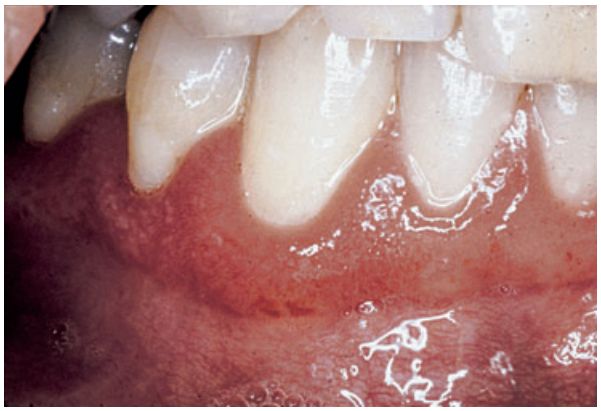

Fig. 16-8 Erythematous candidosis of attached mandibular gingiva of HIV-seropositive patient. The mucogingival junction is invisible.

with intraoral lesions, or intraoral lesions may occur alone (Eisenberg 1978), for instance affecting the palatal gingiva (Fig. 16-6). Initial symptoms are pain and paresthesia, which may be present before lesions occur (Greenberg 1996). The associated pain is usually severe. The lesions, which often involve the gingiva, initiate as vesicles. They soon rupture to leave fibrin-coated ulcers, which often coalesce to irregular forms (Millar & Traulis 1994) (Fig. 16-6). In immunocompromised patients, including HIV-infected individuals, the infection can result in severe tissue destruction with tooth exfoliation and necrosis of alveolar bone and high morbidity (Melbye *et al*. 1987; Schwartz *et al*. 1989). The diagnosis is usually obvious due to the unilateral occurrence of lesions associated with severe pain. Healing of the lesions usually takes place in 1–2 weeks.

Treatment consists of soft or liquid diet, rest, atraumatic removal of plaque, and diluted chlorhexidine rinses. This may be supplemented by antiviral drug therapy.

Gingival diseases of fungal origin

Fungal infection of the oral mucosa includes a range of diseases such as aspergillosis, blastomycosis, candidosis, coccidioidomycosis, cryptococcosis, histoplasmosis, mucormycosis, and paracoccidioidomycosis infections (Scully *et al*. 1998b), but some of the infections are very uncommon and not all of them manifest as gingivitis. The present chapter focuses on candidosis and histoplasmosis, both of which may cause gingival infection.

Candidosis

Various *Candida* species are recovered from the mouth of humans including *C. albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis*, *C. parapsilosis*, and *C. guillermondii* (Cannon *et al*. 1995). *C. albicans* is by far the most common. It is a normal commensal of the oral cavity but also an opportunistic pathogen. The prevalence of oral carriage of *C. albicans* in healthy adults ranges from 3–48% (Scully *et al*. 1995), the large variation being due to differences in examined populations and the procedures used. The proportion of *C. albicans* in the total oral yeast population can reach about 50–80% (Wright *et al*. 1985), and by far the most common fungal infection of the oral mucosa is candidosis mainly caused by the organism *C. albicans* (Scully *et al*. 1998b); the proteinase-positive strains of *C. albicans* are associated with disease (Negi *et al*. 1984; Odds 1985) and invasion of keratinized epithelia such as that of the gingiva. Invasion and increased desquamation is due to the hyaluronidase production. Infection by *C. albicans* usually occurs as a consequence of reduced host defense systems (Holmstrup & Johnson 1997), including immunodeficiency (Holmstrup & Samaranayake 1990) (Figs. 16-7 to 16-9), reduced saliva secretion, smoking, and

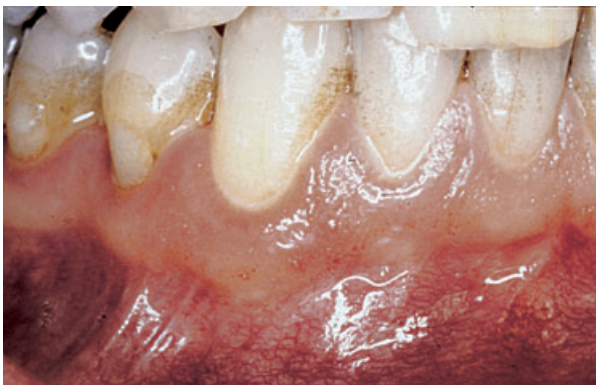

Fig. 16-9 Same patient as shown in Fig. 16-8 after topical antimycotic therapy. The mucogingival junction is visible.

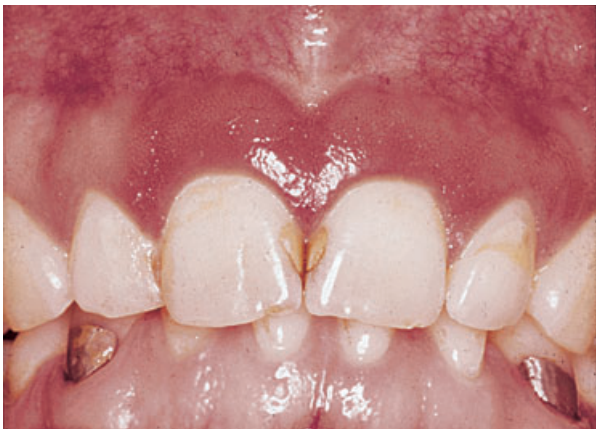

Fig. 16-10 Chronic erythematous candidosis of maxillary attached gingiva of the incisor region.

treatment with corticosteroids, but may be due to a wide range of predisposing factors. The occurrence of oral candidosis may act as a predictor of immune and virologic failure in HIV-infected patients treated with antiviral drugs (Miziara & Weber 2006). Disturbances in the oral microbial flora, such as after therapy with broad-spectrum antibiotics, may also lead to oral candidosis. The predisposing factors are, however, often difficult to identify. Based on their site, infections may be defined as superficial or systemic. Candidal infection of the oral mucosa is usually a superficial infection, but systemic infections are not uncommon in debilitated patients.

In otherwise healthy individuals, oral candidosis rarely manifests in the gingiva. This is surprising, considering the fact that *C. albicans* is frequently isolated from the subgingival flora of patients with severe periodontitis (Slots *et al*. 1988). The most common clinical characteristic of gingival candidal infections is redness of the attached gingiva, often associated with a granular surface (Fig. 16-10).

Various types of oral mucosal manifestations are pseudomembranous candidosis (also known as thrush in neonates), erythematous candidosis, plaque-type candidosis, and nodular candidosis (Holmstrup & Axéll 1990). Pseudomembranous candidosis shows whitish patches (Fig. 16-7), which can be wiped off the mucosa with an instrument or gauze leaving a slightly bleeding surface. The pseudomembranous type usually has no major symptoms. Erythematous lesions can be found anywhere in the oral mucosa (Fig. 16-10). The intensely red lesions are usually associated with pain, which is sometimes severe. The plaque type of oral candidosis is a whitish plaque, which cannot be removed. There are usually no symptoms and the lesion is clinically indistinguishable from oral leukoplakia. Nodular candidal lesions are infrequent in the gingiva; they are characterized by slightly elevated nodules of white or reddish color (Holmstrup & Axéll 1990).

A diagnosis of candidal infection can be accomplished on the basis of culture, smear, and biopsy. A culture on Nickersons medium at room temperature is easily handled in the dental premises. Microscopic examination of smears from suspected lesions is another easy diagnostic procedure, either performed as direct examination by phase contrast microscopy or as light microscopic examination of periodic-acid-Schiff-stained or Gram-stained smears. Mycelium-forming cells in the form of hyphae or pseudohyphae and blastospores are seen in great numbers among masses of desquamated cells. Since oral carriage of *C. albicans* is common among healthy individuals, positive culture and smear does not necessarily imply candidal infection (Rindum *et al*. 1994). Quantitative assessment of the mycological findings and the presence of clinical changes compatible with the above types of lesions are necessary to obtain a reliable diagnosis, which can also be obtained on the basis of identification of hyphae or pseudohyphae in biopsy specimens from the lesions.

Topical treatment involves application of antifungals, such as nystatin, amphotericin B or miconazole. Nystatin may be used as an oral suspension. Since it is not absorbed it can be used in pregnant or lactating women. Miconazole exists as an oral gel. It should not be given during pregnancy and it can interact with anticoagulants and phenytoin. The treatment of the severe or generalized forms also involves systemic antifungals such as fluconazole.

Linear gingival erythema

Linear gingival erythema (LGE) is regarded as a gingival manifestation of immunosuppression characterized by a distinct linear erythematous band limited to the free gingiva (Consensus Report 1999) (Fig. 16-11). It is characterized by a disproportion of inflammatory intensity for the amount of plaque present. There is no evidence of pocketing or attachment loss. A further characteristic of this type of lesion is that it does not respond well to improved oral hygiene or to scaling (EC Clearinghouse on Oral Problems 1993) and it is now a requirement for the diagnosis to be considered that the lesion persists after removal of

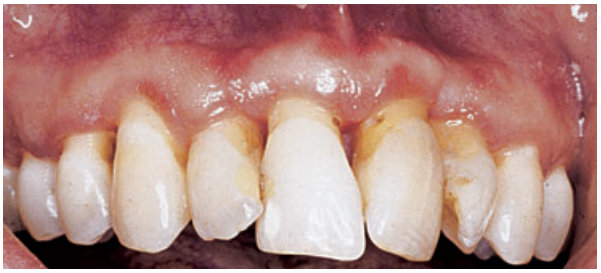

Fig. 16-11 Linear gingival erythema of maxillary gingiva. Red banding along the gingival margin, which does not respond to conventional therapy.

plaque in the initial visit (Umadevi *et al*. 2006). The extent of gingival banding measured by number of affected sites has been shown to depend on tobacco usage (Swango *et al*. 1991). While 15% of affected sites were originally reported to bleed on probing and 11% exhibited spontaneous bleeding (Winkler *et al*. 1988), a key feature of LGE is now considered to be lack of bleeding on probing (Robinson *et al*. 1994).

Some studies of various groups of HIV-infected patients have revealed prevalences of gingivitis with band-shaped patterns in 0.5–49% (Klein *et al*. 1991; Swango *et al*. 1991; Barr *et al*. 1992; Laskaris *et al*. 1992; Masouredis *et al*. 1992; Riley *et al*. 1992; Ceballos-Salobrena *et al*. 1996; Robinson *et al*. 1996). These prevalence values reflect some of the problems with non-standardized diagnosis and selection of study groups. A few studies of unbiased groups of patients have indicated that gingivitis with band-shaped or punctate marginal erythema may be relatively rare in HIV-infected patients, and probably a clinical finding which is no more frequent than in the general population (Drinkard *et al*. 1991; Friedman *et al*. 1991).

It is interesting to note that, whereas there was no HIV-related preponderance of red banding, diffuse and punctate erythema was significantly more prevalent in HIV-infected than in non-HIV-infected individuals in a British study (Robinson *et al*. 1996). Red gingival banding as a clinical feature alone was, therefore, not strongly associated with HIV infection.

There are indications that candidal infection is the background of some cases of gingival inflammation including LGE (Winkler *et al*. 1988; Robinson *et al*. 1994), but studies have revealed a microflora comprising both *C. albicans*, and a number of periopathogenic bacteria consistent with those seen in conventional periodontitis, i.e. *Porphyromonas gingivalis*, *Prevotella intermedia*, *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum*, and *Campylobacter rectus* (Murray *et al*. 1988, 1989, 1991). By DNA probe detection, the percentage of positive sites in HIV-associated gingivitis as compared with matched gingivitis sites of HIV-seronegative patients for *A. actinomycetemcomitans* was 23% and 7% respectively, for *P. gingivalis* 52% and 17%, *Pr. intermedia* 63% and 29%, and for *C. rectus* 50% and 14% (Murray *et al*. 1988, 1989, 1991). *C. albicans* has been isolated by culture in about 50% of HIV-associated gingivitis sites, in 26% of unaffected sites of HIV-seropositive patients and in 3% of healthy sites of HIV-seronegative patients. The frequent isolation and the pathogenic role of *C. albicans* may be related to the high levels of the yeasts in saliva and oral mucosa of HIV-infected patients (Tylenda *et al*. 1989).

An interesting histopathologic study of biopsy specimens from the banding zone has revealed no inflammatory infiltrate but an increased number of blood vessels, which explains the red color of the lesions (Glick *et al*. 1990). The incomplete inflammatory reaction of the host tissue may be the background of the lack of response to conventional treatment.

A number of diseases present clinical features resembling those of LGE and which do not resolve after improved oral hygiene and debridement. Examples are (1) oral lichen planus, which is frequently associated with an inflammatory red band of the attached gingiva (Holmstrup *et al*. 1990) and so is sometimes mucous membrane pemphigoid (Pindborg 1992), or (2) erythematous lesions associated with renal insufficiency because of the salivary ammonia production associated with the high levels of urea.

There is little information about treatment based on controlled studies of this type of condition. Conventional therapy plus rinsing with 0.12% chlorhexidine gluconate twice daily has shown significant improvement after 3 months (Grassi *et al*. 1989). It was mentioned above that some cases of LGE might be related to the presence of *Candida* strains; clinical observations suggest that improvement is frequently dependent on successful eradication of intraoral *Candida* strains (Winkler *et al*. 1988). Consequently, attempts to identify the presence of fungal infection either by culture or smear is recommended, followed by antimycotic therapy in *Candida*-positive cases.

Histoplasmosis

Histoplasmosis is a granulomatous disease caused by *Histoplasma capsulatum*, a soil saprophyte found mainly in feces from birds and cats. The infection occurs in the north-eastern, south-eastern, mid Atlantic and central states of the US. It is also found in Central and South America, India, East Asia, and Australia. Histoplasmosis is the most frequent systemic mycosis in the US. It is mediated by airborne spores from the mycelial form of the organism (Rajah & Essa 1993). In the normal host, the course of the infection is subclinical (Anaissie *et al*. 1986). The clinical manifestations include acute and chronic pulmonary histoplasmosis and a disseminated form, mainly occurring in immunocompromised patients (Cobb *et al*. 1989). Oral lesions have been seen in 30% of patients with pulmonary histoplasmosis and in 66% of patients with the disseminated form (Weed & Parkhill 1948; Loh *et al*. 1989). The oral lesions may

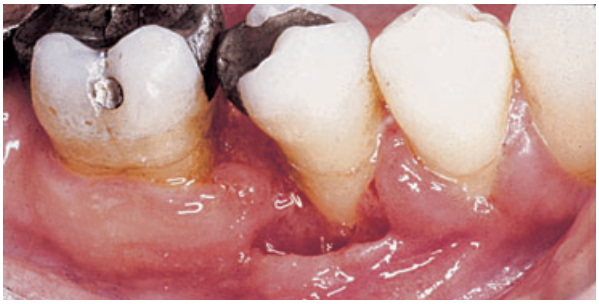

Fig. 16-12 Gingival histoplasmosis with loss of periodontal tissue around second premolar.

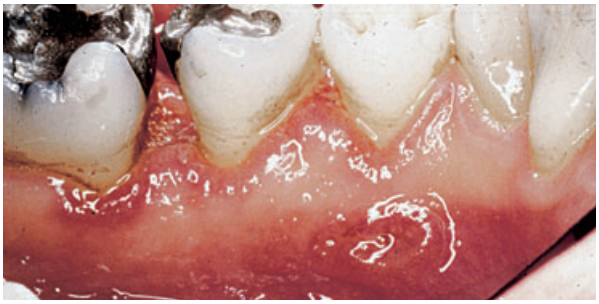

Fig. 16-13 Same patient as shown in Fig. 16-12. Lingual aspect with ulceration in the deeper part of crater-like lesion.

affect any area of the oral mucosa (Chinn *et al*. 1995), including the gingiva, which appears to be one of the most frequent sites affected (Hernandez *et al*. 2004). The lesions are initially nodular or papillary and later may become ulcerative, with loss of gingival tissue, and painful (Figs. 16-12 and 16-13). They are sometimes granulomatous and the clinical appearance may resemble a malignant tumor (Boutros *et al*. 1995). The diagnosis is based on clinical appearance and histopathology and/or culture, and the treatment consists of systemic antifungal therapy.

Gingival lesions of genetic origin

Hereditary gingival fibromatosis

Gingival hyperplasia (synonymous with gingival overgrowth, gingival fibromatosis) may occur as a side effect to systemic medications, including phenytoin, cyclosporine, and nifedipine (Coletta & Graner 2006). These lesions are to some extent plaque-dependent and they are reviewed in Chapter 17. Gingival hyperplasia may also be of genetic origin. Such lesions are known as hereditary gingival fibromatosis (HGF), which is an uncommon condition characterized by diffuse gingival enlargement, sometimes covering major parts of, or the total, tooth surfaces. The lesions develop irrespective of effective plaque removal.

HGF may be an isolated disease entity or part of a syndrome (Gorlin *et al*. 1990), associated with other clinical manifestations, such as hypertrichosis (Horning *et al*. 1985; Cuestas-Carneiro & Bornancini

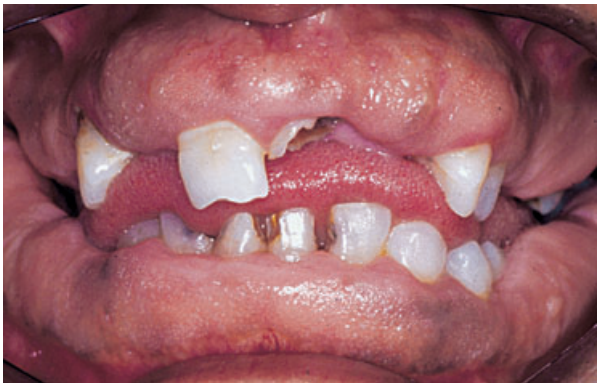

Fig. 16-14 Hereditary gingival fibromatosis. Facial aspect with partial coverage of teeth.

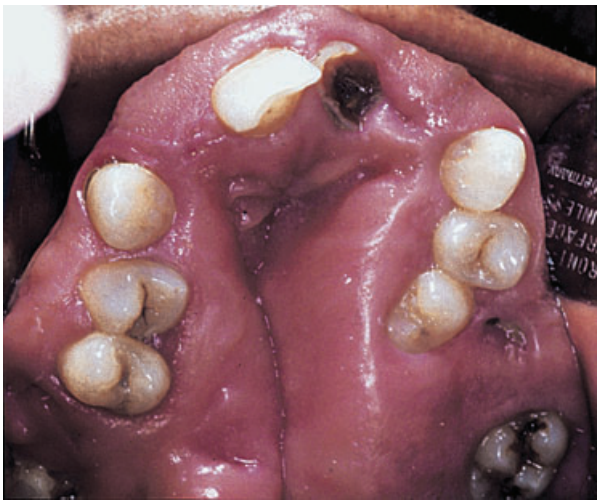

Fig. 16-15 Same patient as shown in Fig. 16-14. The maxillary gingival fibromatosis is severe and has resulted in total disfiguration of the dental arch.

1988), learning difficulties (Araiche & Brode 1959), epilepsy (Ramon *et al*. 1967), hearing loss (Hartsfield *et al*. 1985), growth retardation (Bhowmick *et al*. 2001), and abnormalities of extremities (Nevin *et al*. 1971; Skrinjaric & Basic 1989). Most cases are related to an autosomal dominant mode of inheritance, but cases have been described with an autosomal recessive background (Emerson 1965; Jorgensen & Cocker 1974; Singer *et al*. 1993). The most common syndrome of HGF includes hypertrichosis, epilepsy and learning difficulties; the two latter features, however, are not present in all cases (Gorlin *et al*. 1990).

Typically, HGF presents as large masses of firm, dense, resilient, insensitive fibrous tissue that cover the alveolar ridges and extend over the teeth, resulting in extensive pseudopockets. The color may be normal or erythematous if inflamed (Figs. 16-14 and 16-15). Depending on extension of the gingival enlargement, patients complain of functional and esthetic problems. The enlargement may result in protrusion of the lips, and they may chew on a considerable hyperplasia of tissue covering the teeth. HGF is seldom present at birth but may be noted at

an early age. If the enlargement is present before tooth eruption, the dense fibrous tissue may interfere with or prevent eruption (Shafer *et al*. 1983).

Studies have suggested that an important pathogenic mechanism may be enhanced production of transforming growth factor (TGF-beta 1) reducing the proteolytic activities of HGF fibroblasts, which again favor the accumulation of extracellular matrix (Coletta *et al*. 1999). A locus for autosomal dominant HGF has previously been mapped to a region on chromosome 2 (Hart *et al*. 1998; Xiao *et al*. 2000), although at least two genetically distinct loci seem to be responsible for this type of HGF (Hart *et al*. 2000); a novel locus for maternally inherited human gingival fibromatosis has recently been reported at human chromosome 11p15 (Zhu *et al*. 2006).

The histologic features of HGF include moderate hyperplasia of a slightly hyperkeratotic epithelium with extended rete pegs. The underlying stroma is almost entirely made up of dense collagen bundles with only a few fibroblasts. Local accumulation of inflammatory cells may be present (Shafer *et al*. 1983). Histologic examination may facilitate the differential diagnosis from other genetically determined gingival enlargements such as Fabry disease, which is characterized by telangiectasia.

Treatment of HGF is surgical removal, often in a series of gingivectomies, but relapses are not uncommon. If the volume of the overgrowth is extensive, a repositioned flap to avoid exposure of connective tissue by gingivectomy may better achieve elimination of pseudopockets.

Gingival diseases of systemic origin

Mucocutaneous disorders

Various mucocutaneous disorders present with gingival manifestations, sometimes in the form of desquamative lesions or ulceration of the gingiva. The most important of these diseases are lichen planus, pemphigoid, pemphigus vulgaris, erythema multiforme, and lupus erythematosus.

Lichen planus

Lichen planus is the most common mucocutaneous disease manifesting on the gingiva. The disease may affect skin and oral as well as other mucous membranes in some patients while others may present with either skin or oral mucosal involvement alone. Oral involvement alone is common and concomitant skin lesions in patients with oral lesions have been found in 5–44% of cases (Andreasen 1968; Axéll & Rundquist 1987). The disease may be associated with severe discomfort; it has been shown to possess a premalignant potential, although this is still a controversial issue (Holmstrup 1992), so it is important to diagnose and treat cases and to have regular oral examinations as follow-up (Holmstrup *et al*. 1988; Mattson *et al*. 2002; Mignogna *et al*. 2006).

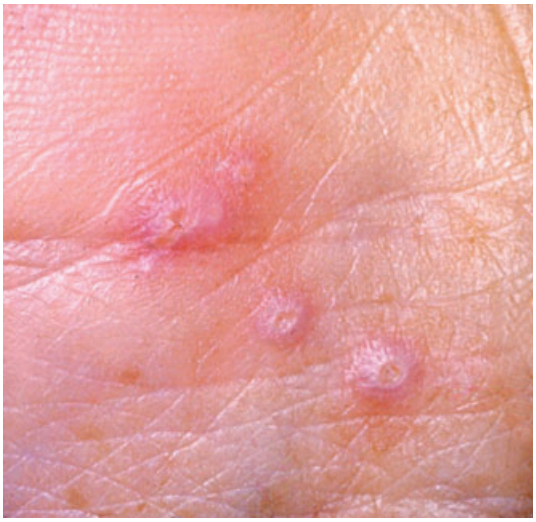

Fig. 16-16 Skin lesions of lichen planus. Papules with delicate white striations.

The prevalence of oral lichen planus (OLP) in various populations has been found to be 0.1–4% (Scully *et al*. 1998a). The disease may afflict patients at any age although it is seldom observed in childhood (Scully *et al*. 1994). Skin lesions are characterized by papules with white striae (Wickham striae) (Fig. 16-16). Itching is a common symptom, and the most frequent locations are the flexor aspects of the arms, the thighs and the neck. In the vast majority of cases the skin lesions disappear spontaneously after a few months, which is in sharp contrast with the oral lesions, which usually remain for years (Thorn *et al*. 1988).

A variety of clinical appearances is characteristic of OLP. These include:

- Papular (Fig. 16-17)
- Reticular (Figs. 16-18 and 16-19)
- Plaque-like (Fig. 16-20)
- Atrophic (Figs. 16-21 to 16-25)
- Ulcerative (Figs 16-22 and 16-27)
- Bullous (Fig. 16-29).

Simultaneous presence of more than one type of lesion is common (Thorn *et al*. 1988). The most characteristic clinical manifestations of the disease and the basis of the clinical diagnosis are white papules (Fig. 16-17) and white striations (Figs 16-18, 16-19, 16-26 and 16-27), which often form reticular patterns (Thorn *et al*. 1988), usually of bilateral occurrence (Ingafou *et al*. 2006). Sometimes atrophic and ulcerative lesions are referred to as erosive (Rees 1989). Papular, reticular, and plaque-type lesions usually do not give rise to significant symptoms, whereas atrophic and ulcerative lesions are associated with moderate to severe pain, especially in relation to oral hygiene procedures and eating. OLP frequently persists for many years (Thorn *et al*. 1988). Any area of the oral mucosa may be affected by OLP, but the

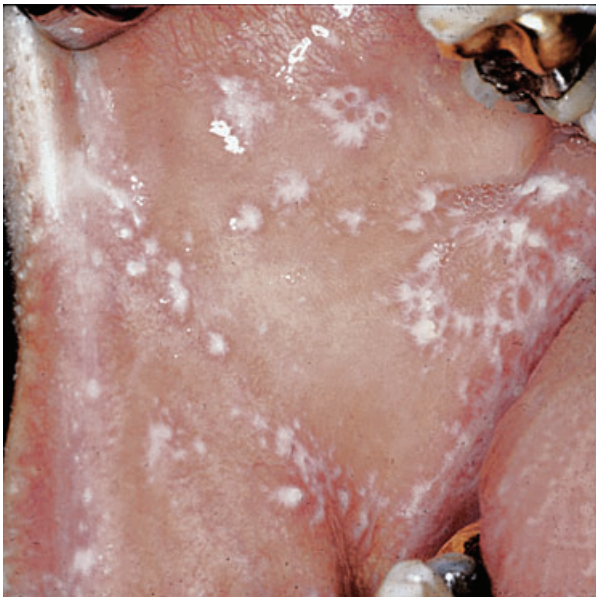

Fig. 16-17 Oral lichen planus. Papular lesion of right buccal mucosa.

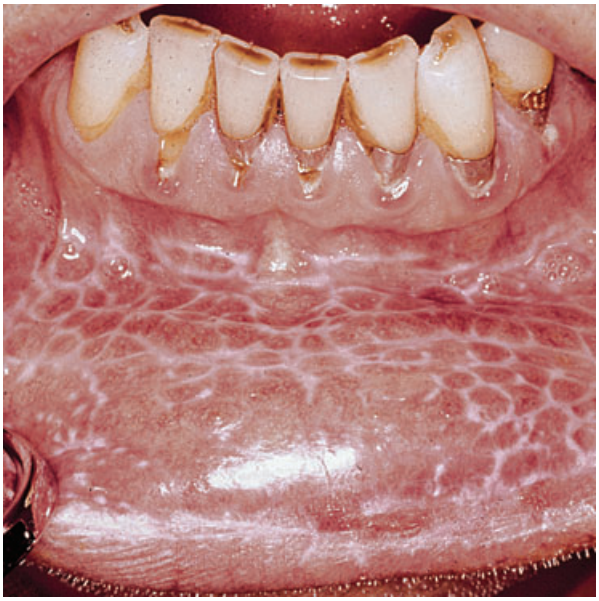

Fig. 16-18 Oral lichen planus. Reticular lesion of lower lip mucosa. The white striations are denoted Wickham striae.

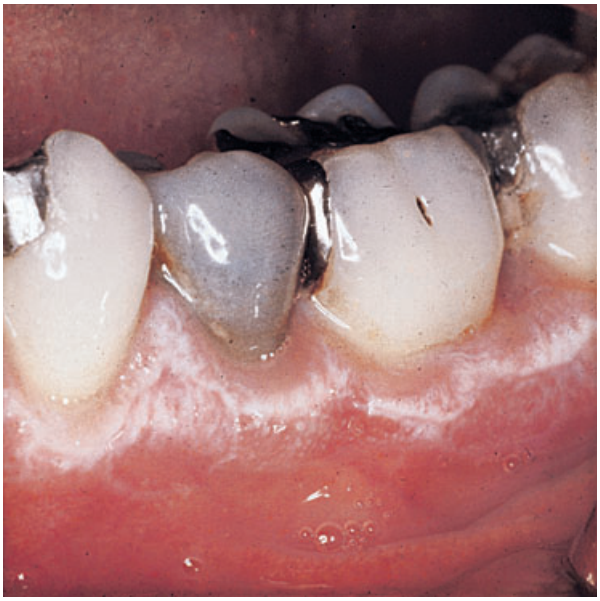

Fig. 16-19 Oral lichen planus. Reticular lesions of gingiva in lower left premolar and molar region.

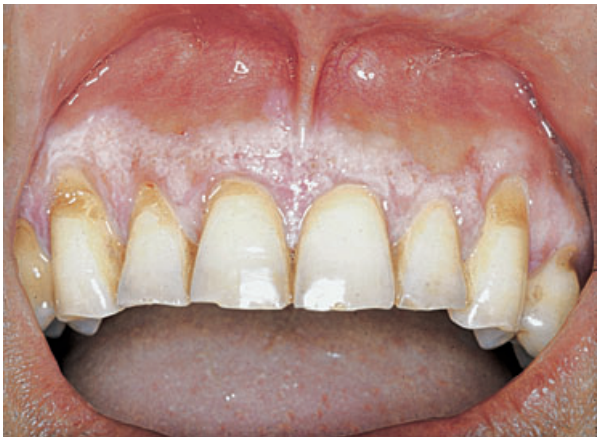

Fig. 16-20 Oral lichen planus. Plaque-type lesion of maxillary gingiva.

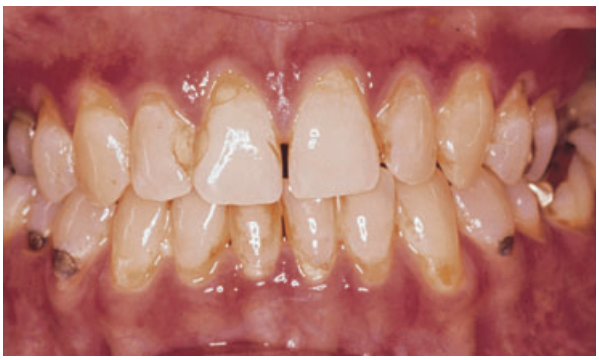

Fig. 16-21 Oral lichen planus. Atrophic lesions of facial maxillary and mandibular gingiva. Such lesions were previously termed desquamative gingivitis.

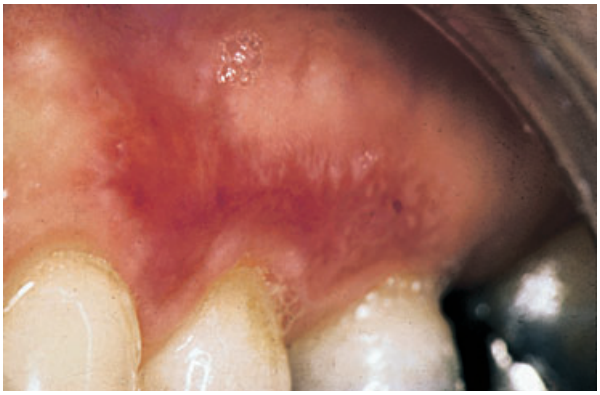

Fig. 16-22 Oral lichen planus. Atrophic and ulcerative lesion of maxillary gingiva. Note that the margin of the gingiva has a normal color in the upper incisor region, which distinguishes the lesions from plaque-induced gingivitis.

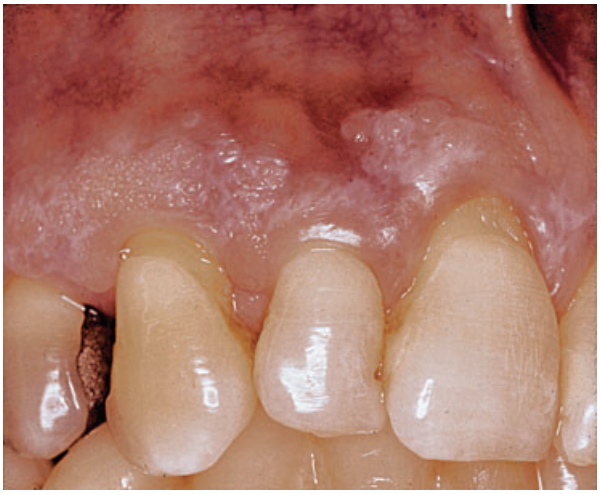

Fig. 16-23 Oral lichen planus. Atrophic and reticular lesion of maxillary gingiva. Several types of lesions are often present simultaneously.

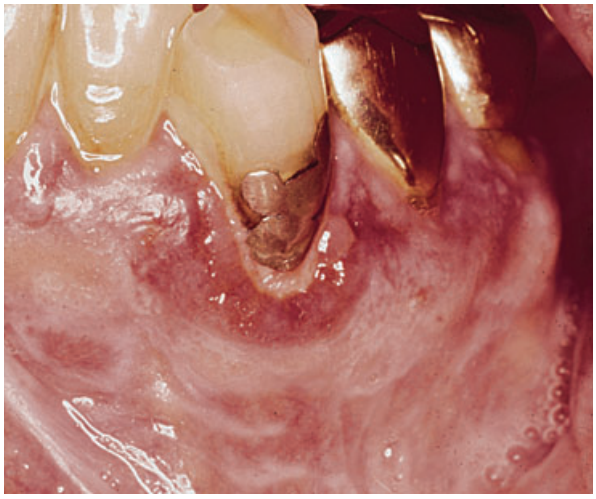

Fig. 16-24 Oral lichen planus. Atrophic and reticular lesion of lower left canine region. Plaque accumulation results in exacerbation of oral lichen planus, and atrophic lesions compromise oral hygiene procedures. This may lead to a vicious circle that the dentist can help in breaking.

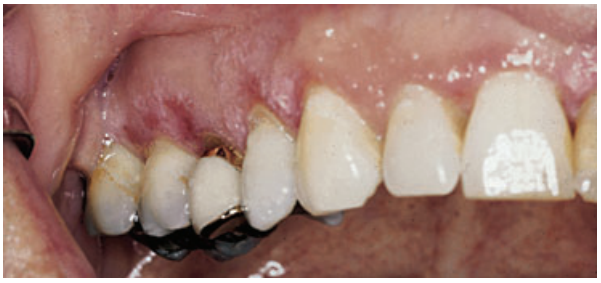

Fig. 16-25 Oral lichen planus. Atrophic and reticular lesion of right maxillary gingiva in a patient using an electric toothbrush, which is traumatic to the marginal gingiva. The physical trauma results in exacerbation of the lesion with atrophic characteristics and pain.

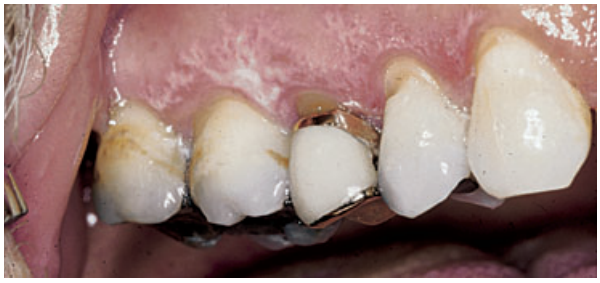

Fig. 16-26 Same patient as shown in Fig. 16-25 after modified toothbrushing procedure with no traumatic action on marginal gingiva.

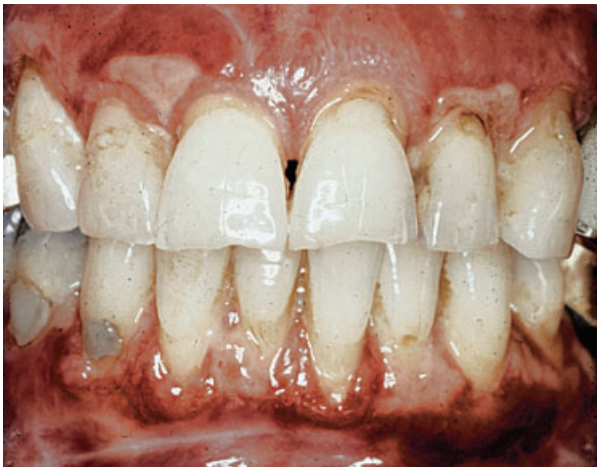

Fig. 16-27 Oral lichen planus. Atrophic and ulcerative/reticular lesions of maxillary and mandibular incisor region. The patient, a 48-year-old woman, suffers from severe discomfort from food, beverages, and toothbrushing.

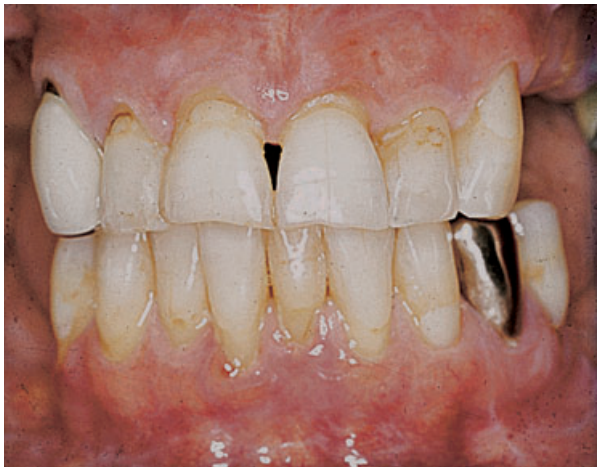

Fig. 16-28 Same patient as shown in Fig. 16-27 after periodontal treatment and extraction of teeth with deep pockets. An individual oral hygiene program, which ensured gentle, meticulous plaque removal has been used by the patient for 3 months. The atrophic/ulcerative lesions are now healed and there are no more symptoms.

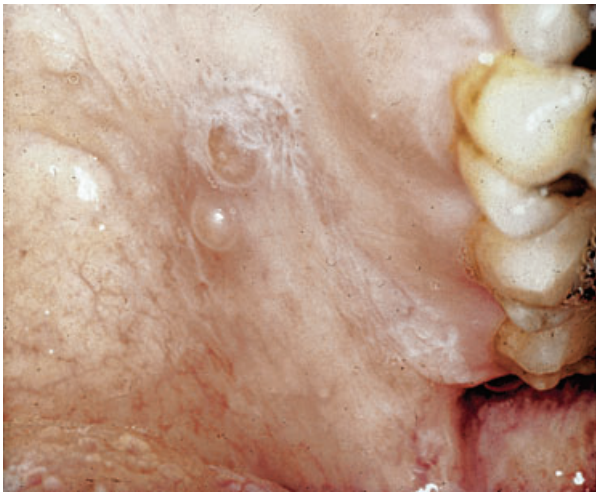

Fig. 16-29 Oral lichen planus. Bullous/reticular lesion of left palatal mucosa.

lesions often change in clinical type and extension over the years. Such changes may imply the development of plaque-type lesions, which are clinically indistinguishable from oral leukoplakia. This may give rise to a diagnostic problem if other lesions more characteristic of OLP have disappeared (Thorn *et al*. 1988).

A characteristic histopathologic feature in OLP is a subepithelial, band-like accumulation of lymphocytes and macrophages characteristic of a type IV hypersensitivity reaction (Eversole *et al*. 1994). The epithelium shows hyperortho- or hyperparakeratinization and basal cell disruption with transmigration of lymphocytes into the basal and parabasal cell layers (Eversole 1995). The infiltrating lymphocytes have been identified as CD4+ and CD8+ cells (Buchner 1984; Walsh *et al*. 1990; Eversole *et al*. 1994). Other characteristic features are Civatte bodies, which are dyskeratotic basal cells. Common immunohistochemical findings of OLP lesions are fibrin in the basement membrane zone, but deposits of IgM, C3, C4, and C5 may also be found. None of these findings are specific to OLP (Schiødt *et al*. 1981; Kilpi *et al*. 1988; Eversole *et al*. 1994).

The subepithelial inflammatory reaction in OLP lesions is presumably due to an as yet unidentified antigen in the junctional zone between epithelium and connective tissue or to components of basal epithelial cells (Holmstrup & Dabelsteen 1979; Walsh *et al*. 1990; Sugerman *et al*. 1994). A lichen planus specific antigen in the stratum spinosum of skin lesions has been described (Camisa *et al*. 1986), but this antigen does not appear to play a significant role in oral lesions since it is rarely identified there. It is still an open question whether OLP is a group of etiologically diverse diseases with common clinical and histopathologic features or a disease entity characterized by a type IV hypersensitivity reaction to an antigen in the basement membrane area. The clinical diagnosis is based on the presence of papular or reticular lesions. The diagnosis may be supported by histopathologic findings of hyperkeratosis, degenerative changes of basal cells, and subepithelial inflammation dominated by lymphocytes and macrophages (Holmstrup 1999).

The uncertain background of OLP results in several borderline cases of so-called oral lichenoid lesions (OLL) for which a final diagnosis is difficult to establish (Thornhill *et al*. 2006). The most common OLLs are probably lesions in contact with dental restorations (Holmstrup 1991) (see later in this chapter). Other types of OLL are associated with various types of medications including antimalarials, quinine, quinidine, non-steroidal anti-inflammatory drugs, thiazides, diuretics, gold salts, penicillamine, beta-blockers, and others (Scully *et al*. 1998a). Graft-versus-host reactions are also characterized by a lichenoid appearance (Fujii *et al*. 1988) and a group of OLLs is associated with systemic diseases, including liver disease (Fortune & Buchanan 1993; Bagan *et al*. 1994; Carrozzo *et al*. 1996). This appears to be particularly evident in Southern Europe and Japan where hepatitis C has been found in 20–60% of OLL cases (Bagan *et al*. 1994; Gandolfo *et al*. 1994; Nagao *et al*. 1995).

Several follow-up studies have demonstrated that OLP is associated with increased development of oral cancer, the frequency of cancer development being in the range of 0.5–2% (Holmstrup *et al*. 1988; Mattson *et al*.2002; Mignogna *et al*. 2006; Ingafou *et al*. 2006).

The most important part of the therapeutic regimen is an atraumatic meticulous plaque control, which results in significant improvement in many patients (Holmstrup *et al*. 1990) (Figs. 16-25 to 16-28). Individual oral hygiene procedures with the purpose of effective plaque removal without traumatic influence on the gingival tissue should be established for all patients with symptoms. In cases of persistent pain, typically associated with atrophic and ulcerative affections, antifungal treatment may be necessary if the lesions contain yeast, which occurs in 37% of OLP cases (Krogh *et al*. 1987). In painful cases, which have not responded to the treatment above, topical corticosteroids, preferably in a paste or an ointment, should be used three times daily for a number of weeks. However, relapses in such cases are very common, and intermittent episodes of treatment may be needed over an extended period.

Pemphigoid

Pemphigoid is a group of disorders in which autoantibodies towards components of the basement membrane result in detachment of the epithelium from the connective tissue. Bullous pemphigoid predominantly affects the skin, but oral mucosal involvement may occur (Brooke 1973; Hodge *et al*. 1981). If only mucous membranes are affected, the term benign mucous membrane pemphigoid (BMMP) is often used. The term cicatricial pemphigoid is also used to describe subepithelial bullous disease limited to the mouth or eyes and infrequently other mucosal areas.

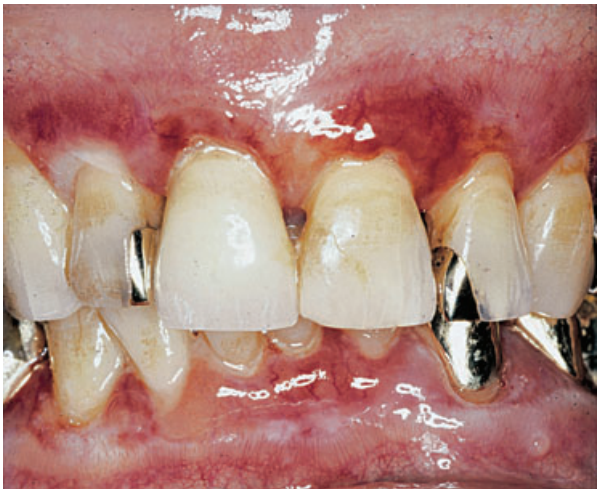

Fig. 16-30 Benign mucous membrane pemphigoid affecting the attached gingiva of both jaws. The lesions are erythematous and resemble atrophic lichen planus lesions. They result in pain associated with oral procedures including eating and oral hygiene.

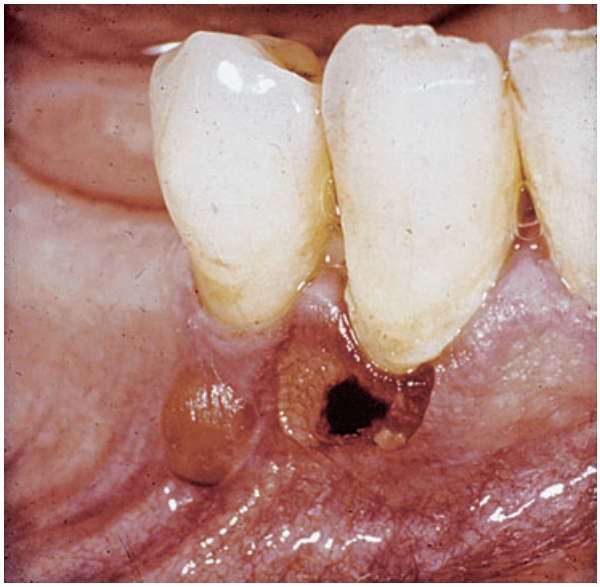

Fig. 16-31 Benign mucous membrane pemphigoid with intact and ruptured gingival bulla.

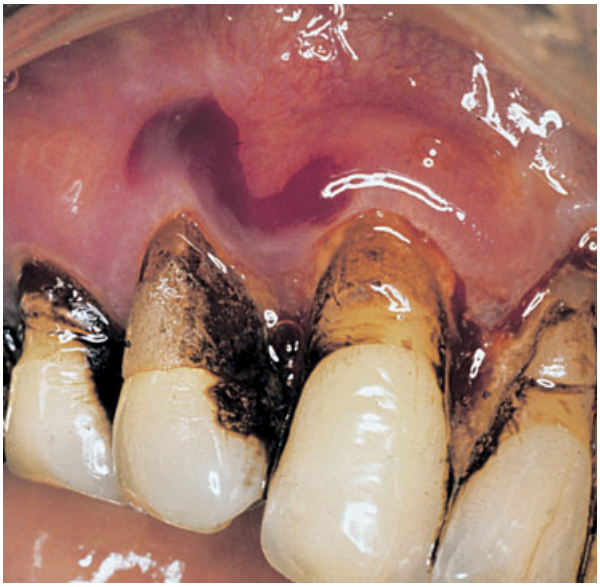

Fig. 16-32 Benign mucous membrane pemphigoid with hemorrhagic gingival bulla. The patient uses chlorhexidine for daily plaque reduction.

This term is problematic at least for the oral lesions, because usually oral lesions do not result in scarring, whereas this is a serious risk in ocular lesions (Scully *et al*. 1998b). It is now evident that BMMP comprises a group of disease entities characterized by an immune reaction involving autoantibodies directed against various basement membrane zone antigens (Scully & Laskaris 1998). These antigens have been identified as hemidesmosome or lamina lucida components (Leonard *et al*. 1982, 1984; Manton & Scully 1988; Domloge-Hultsch *et al*. 1992, 1994), and sera from patients with oral lesions have been shown to recognize the alpha6 integrin subunit (Rashid *et al*. 2006). In addition, complement-mediated cell destructive processes may be involved in the pathogenesis of the disease (Eversole 1994). The trigger mechanisms behind these reactions, however, have not yet been ascertained.

The majority of affected patients are females with a mean age at onset of 50 years or over (Shklar & McCarthy 1971). Oral involvement in BMMP is almost inevitable and usually the oral cavity is the first site of disease activity (Silverman *et al*. 1986; Gallagher & Shklar 1987). Any area of the oral mucosa may be involved in BMMP, but the main manifestation is desquamative lesions of the gingiva presenting intensely erythematous attached gingiva (Laskaris *et al*. 1982; Silverman *et al*. 1986; Gallagher & Shklar 1987) (Fig. 16-30). The inflammatory changes, as always when not caused by plaque, may extend over the entire gingival width and even over the mucogingival junction. Rubbing of the gingiva may precipitate bulla formation (Dahl & Cook 1979). This is denoted a positive Nicholsky sign and is caused by the destroyed adhesion of the epithelium to the connective tissue. The intact bullae are often clear to yellowish or they may be hemorrhagic (Figs. 16-31 and 16-32). This, again, is due to the separation of epithelium from connective tissue at the junction resulting in exposed vessels inside the bullae. Usually, the bullae rupture rapidly leaving fibrin-coated ulcers. Sometimes, tags of loose epithelium can be found due to rupture of bullae. Other mucosal surfaces may be involved in some patients. Ocular lesions are particularly important because scar formation can result in blindness (Williams *et al*. 1984) (Fig. 16-33).

The separation of epithelium from connective tissue at the basement membrane area is the main diagnostic feature of BMMP. A non-specific inflammatory reaction is a secondary histologic finding. In addition, immunohistochemical examination can help distinguish BMMP from other vesiculobullous

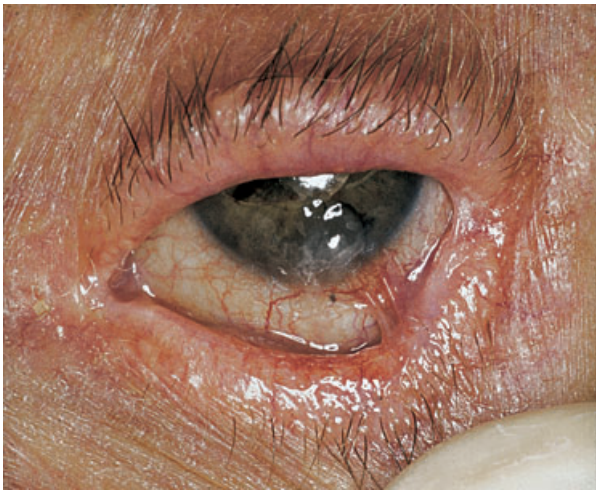

Fig. 16-33 Benign mucous membrane pemphigoid. Eye lesion with scar formation due to coalescence of palpebral and conjunctival mucosa.

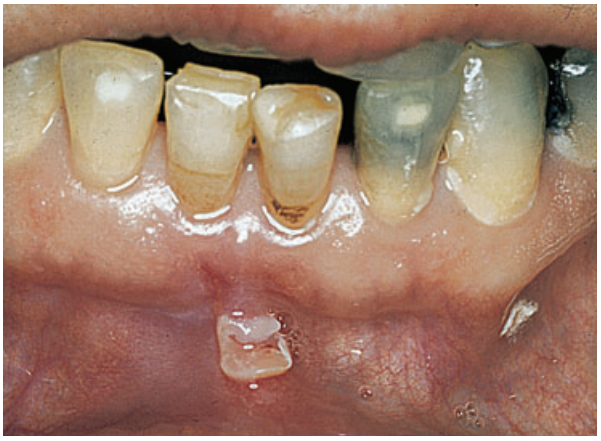

Fig. 16-34 Pemphigus vulgaris. Initial lesion resembling recurrent aphthous stomatitis.

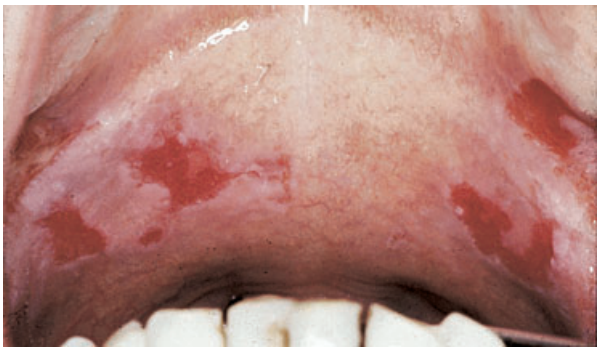

Fig. 16-35 Pemphigus vulgaris. Erosions of soft palatal mucosa. The erosive lesions are due to loss of the superficial part of the epithelium, leaving the connective tissue covered only by the basal cell layers.

diseases, in particular pemphigus, which is life threatening. Deposits of C3, IgG, and sometimes other immunoglobulins as well as fibrin are found at the basement membrane zone in the vast majority of cases (Laskaris & Nicolis 1980; Daniels & Quadra-White 1981; Manton & Scully 1988). It is important to involve peri-lesional tissue in the biopsy because the characteristic features may be lost within lesional tissue (Ullman 1988). Circulating immunoglobulins are found only occasionally in BMMP by indirect immunofluorescence (Laskaris & Angelopoulos 1981).

Therapy consists of professional atraumatic plaque removal and individual instruction in gentle but careful daily plaque control, eventually supplemented with daily use of chlorhexidine and/or topical corticosteroid application if necessary. As for all the chronic inflammatory oral mucosal diseases, oral hygiene procedures are very important and controlling the infection from plaque bacteria may result in considerable reduction of disease activity and symptoms. It is also important to prevent the development of attachment loss due to periodontitis in these patients with difficulties in maintaining oral hygiene (Tricamo *et al*. 2006). However, the disease is chronic in nature and formation of new bullae is inevitable in most patients. Topical corticosteroids, preferably applied as a paste at night, temper the inflammatory reaction.

Pemphigus vulgaris

Pemphigus is a group of autoimmune diseases characterized by formation of intraepithelial bullae in skin and mucous membranes. The group comprises several variants, pemphigus vulgaris (PV) being the most common and most serious form (Barth & Venning 1987).

Individuals of Jewish or Mediterranean background are more often affected by PV than others. This is an indication of a strong genetic background of the disease (Pisanti *et al*. 1974). The disease may occur at any age, but is typically seen in the middle-aged or elderly. It presents with widespread bulla formation often including large areas of skin, and if left untreated the disease is life threatening. Intraoral onset of the disease with bulla formation is very common and lesions of the oral mucosa including the gingiva are frequently seen. Early lesions may resemble aphthous ulcers (Fig. 16-34), but widespread erosions are common at later stages (Fig. 16-35). Gingival involvement may present as painful desquamative lesions or as erosions or ulcerations, which are remains of ruptured bullae (Fig. 16-36). Such lesions may be indistinguishable from BMMP (Zegarelli & Zegarelli 1977; Sciubba 1996). Since the bulla formation is located in the spinous cell layer, the chance of seeing an intact bulla is even more reduced than in BMMP. Involvement of other mucous membranes is common (Laskaris *et al*. 1982). The ulcers heal slowly, usually without scar formation, and the disease runs a chronic course with recurring bulla formation (Zegarelli & Zegarelli 1977).

Diagnosis is based on the characteristic histological feature of PV that is intraepithelial bulla

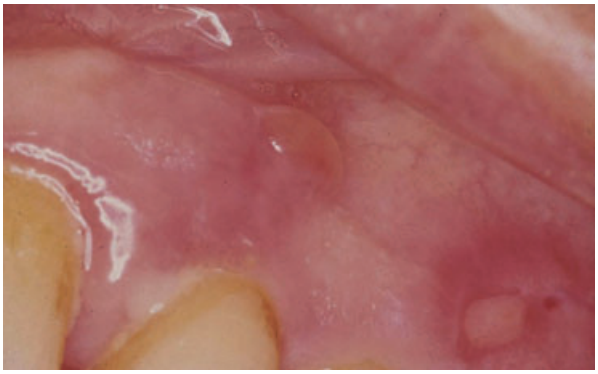

Fig. 16-36 Pemphigus vulgaris. Intact and ruptured gingival bullae.

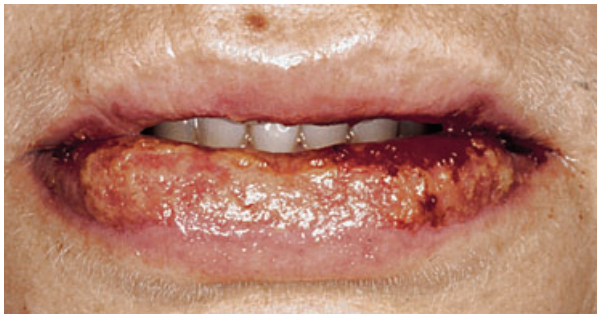

Fig. 16-37 Erythema multiforme with crust formation of the vermilion border of the lower lip.

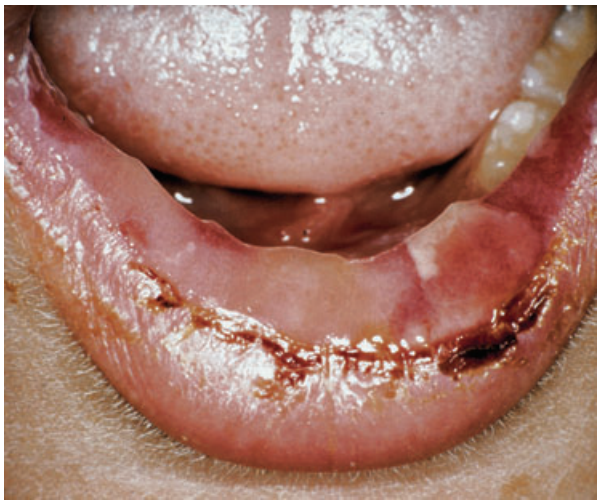

Fig. 16-38 Erythema multiforme with ulceration covered by heavy fibrin exudate.

formation due to destruction of desmosomes resulting in acantholysis. The bullae contain non-adhering free epithelial cells, denoted Tzank cells, which have lost their intercellular bridges (Coscia-Porrazzi *et al*. 1985; Nishikawa *et al*. 1996). Mononuclear cells and neutrophils dominate the associated inflammatory reaction. Immunohistochemistry reveals pericellular epithelial deposits of IgG and C3. Circulating autoantibodies against interepithelial adhesion molecules are detectable in serum samples of most patients, but at the initial stage of intraoral signs antiepithelial antibody may not be elevated (Melbye *et al*. 1987; Manton & Scully 1988; Lamey *et al*. 1992; Lever & Schaumburg-Lever 1997). The background of bulla formation in PV is damage to the intercellular adhesion caused by autoantibodies to cadherin-type epithelial cell adhesion molecules (desmoglein 1 and 3) (Nousari & Anhalt 1995; Nishikawa *et al*. 1996; Lanza *et al*. 2006). The mechanism by which these molecules trigger the formation of autoantibodies has not yet been established.

Immediate referral of patients with PV to a dermatologist or internal medicine specialist is important because when recognized late the disease can be fatal, although systemic corticosteroid therapy can presently solve most cases. Supplementary local treatment consists of gentle plaque control and professional cleaning as mentioned for the chronic inflammatory oral mucosal diseases above. Sometimes, additional topical corticosteroid application is needed to control the intraoral disease.

Erythema multiforme

Erythema multiforme (EM) is a reactive acute, sometimes recurrent, vesiculobullous disease affecting mucous membranes and skin. A general malaise often precedes the lesions. The disease spectrum comprises a self-limiting, mild, exanthematic, cutaneous variant with minimal oral involvement to a progressive, fulminating, severe variant with extensive mucocutaneous epithelial necrosis. The latter form of the disease has been described as Stevens-Johnson syndrome, with widespread mucous membrane lesions, i.e. oral, ocular and genital, in addition to skin lesions (Lozada-Nur *et al*. 1989; Assier *et al*. 1995; Bystryn 1996; Ayangco & Rogers 2003). The multilocular entity has to be differentiated from other disorders such as Reiter and Behçet's syndromes, which also affect the eyes, the oral mucosa, and often the genitalia. The pathogenesis of EM remains unknown, but the disease appears to be a cytotoxic immune reaction towards keratinocytes (Ayangco & Rogers 2003) precipitated by a wide range of factors including herpes simplex virus (Lozada & Silverman 1978; Nesbit & Gobetti 1986; Ruokonen *et al*. 1988; Miura *et al*. 1992; Aurelian *et al*. 1998), *Mycoplasma pneumoniae* (McKellar & Reade 1986; Stutman 1987), and various drugs (Bottiger *et al*. 1975; Gebel & Hornstein 1984; Kauppinen & Stubb 1984).

EM may occur at any age but most frequently affects young individuals. It may or may not involve the oral mucosa, but oral involvement occurs in as many as 25–60% of cases (Huff *et al*. 1983); sometimes it is the only involved site. The characteristic oral lesions comprise swollen lips often with extensive crust formation of the vermilion border (Fig. 16-37). The basic lesions, however, are bullae that rupture and leave extensive ulcers usually covered by heavy yellowish fibrinous exudates sometimes described as pseudomembranes (Figs. 16-38 and 16-39). Such

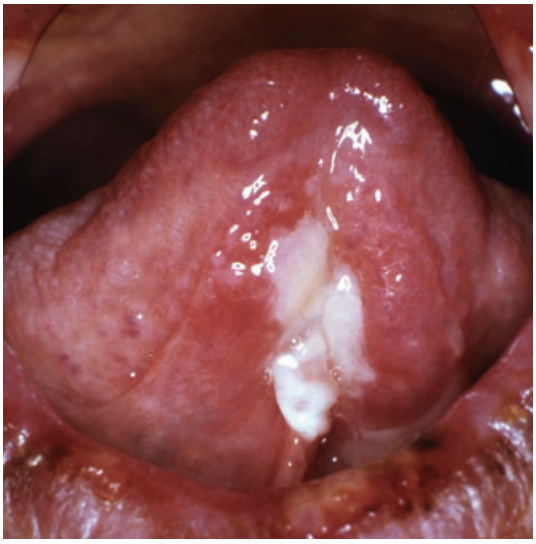

Fig. 16-39 Erythema multiforme. Fibrin-coated ulcerations of ventral surface of tongue and lower lip.

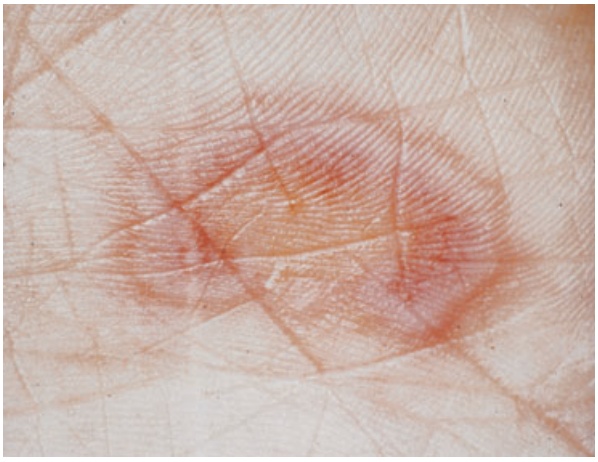

Fig. 16-40 Erythema multiforme. Skin lesion with characteristic iris appearance. Central bulla formation surrounded by a blanched halo within an erythematous zone.

lesions may also involve the buccal mucosa and gingiva (Huff *et al*. 1983; Lozada-Nur *et al*. 1989; Scully *et al*. 1991; Barrett *et al*. 1993). The skin lesions are characteristic due to the iris appearance with a central bulla formation surrounded by a blanched halo within an erythematous zone (Fig. 16-40). Similar intraoral lesions do occur but they are infrequent. The disease is usually self-limiting but recurrences are common. Healing of the lesions may take several weeks (Fabbri & Panconesi 1993).

Histopathology of EM shows intra- or subepithelial separation of epithelium from connective tissue with non-specific inflammation (Reed 1985). Immunohistochemical findings are non-specific and in most instances the diagnosis relies on the clinical findings.

Although periodontal lesions are not the most frequent intraoral manifestation, they can sometimes pose a differential diagnostic problem. The typical crusty ulcerations of the vermilion border and the heavy fibrin exudates covering intraoral lesions are indicative of EM, sometimes therefore denoted erythema multiforme exudativum. The mucosal ulcerations may take weeks to heal and they are painful (Lozada-Nur *et al*. 1989).

As for any intraoral ulcerations, gentle plaque control and professional cleaning are mandatory. The treatment often involves systemic corticosteroids, but topical treatment may be sufficient in cases with minor lesions.

Lupus erythematosus

Lupus erythematosus (LE) is a group of autoimmune connective tissue disorders in which autoantibodies form to various cellular constituents including nucleus, cytoplasmic membrane and others. All parts of the body may be affected, and the disease is much more prevalent among women than among men. The etiology of LE remains unknown, but deposits of antigen–antibody complexes appear to play a role in the tissue damage characteristic of the disease (Schrieber & Maini 1984). LE includes two major traditional forms: discoid LE (DLE) and systemic LE (SLE) which may involve a range of organ systems including kidney, heart, central nervous system, vascular system, and bone marrow. Recently two new forms, acute and subacute cutaneous LE, have been added to the classification, these forms representing different degrees of disease activity and increased risk of development of SLE (Wouters *et al*. 2004). The prevalence of LE has been estimated at 0.05% (Condemi 1987).

DLE is a mild chronic form, which affects skin and mucous membranes, sometimes involving the gingiva as well as other parts of the oral mucosa (Schiødt 1984a,b). The typical lesion presents a central atrophic area with small white dots surrounded by irradiating fine white striae with a periphery of telangiectasia (Fig. 16-41). The lesions can be ulcerated or clinically indistinguishable from leukoplakia or atrophic oral lichen planus (Fig. 16-42) (Schiødt 1984b). Sometimes patients present brownish gingival lesions, which is a side effect of antimalarial drugs prescribed to these patients as part of their treatment (Fig. 16-43). Eight percent of patients with DLE develop SLE, and ulcerations may be a sign of SLE; SLE demonstrates oral lesions in 25–40% of patients (Schiødt 1984a; Pisetsky 1986; Johnsson *et al*. 1988). The characteristic bordeaux-colored "butterfly" skin lesions are photosensitive, scaly, erythematous macules located on the bridge of the nose and the cheeks (Standefer & Mattox 1986). The systemic type, which can still be fatal because of nephrologic and hematologic complications, also has skin lesions on the face but they tend to spread over the entire body.

Diagnosis is based on clinical and histopathologic findings. The epithelial changes, characteristic of oral LE lesions, are hyperkeratosis, keratin plugging and

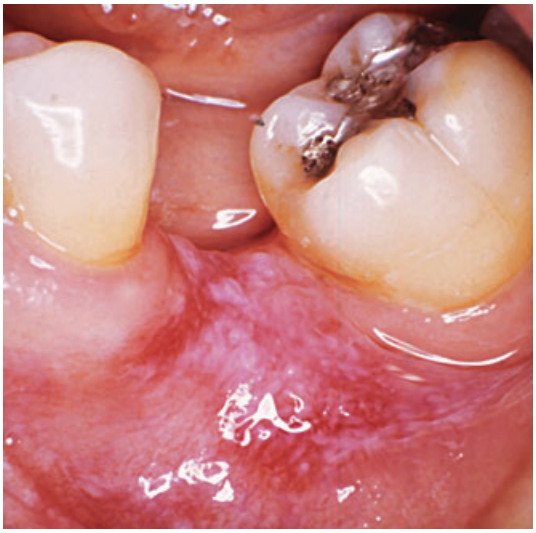

Fig. 16-41 Gingival discoid lupus erythematosus lesion. A central erythematous area with small white dots is surrounded by delicate white striae.

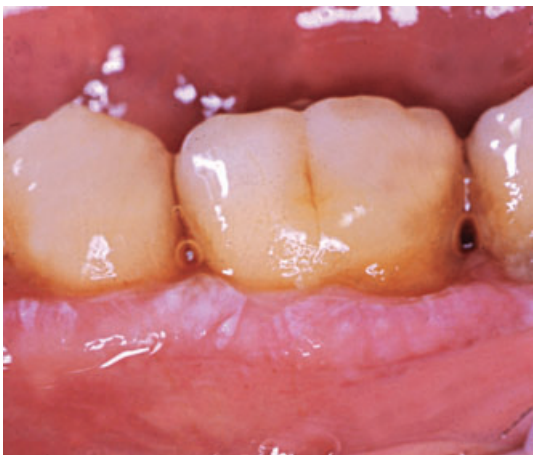

Fig. 16-42 Gingival plaque-type discoid lupus erythematosus lesion resembling frictional keratosis and leukoplakia.

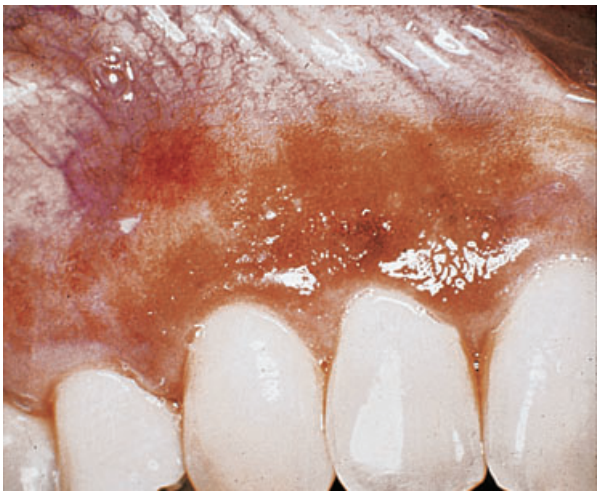

Fig. 16-43 Antimalarial drugs may result in brownish gingival discoloration. This is a patient with discoid lupus erythematosus receiving an antimalarial drug, chloroquine, as part of the treatment regimen.

variation in epithelial thickness, liquefaction degeneration of basal cells, and increased width of the basement membrane. The subepithelial connective tissue harbors inflammation, sometimes resembling OLP but often with a less distinct band-shaped pattern (Schiødt & Pindborg 1984). Immunohistochemical investigation reveals deposits of various immunoglobulins, C3, and fibrin along the basement membrane (Reibel & Schiødt 1986).

Systemic corticosteroid and other anti-inflammatory treatment regimens are required for SLE. Additional topical treatment is sometimes needed for symptomatic intraoral lesions to resolve.

Drug-induced mucocutaneous disorders

A number of drugs cause adverse effects in the oral mucosa. Best known in the periodontal field is gingival hyperplasia related to the intake of phenytoin, cyclosporine, and nifedipine. Because these lesions to some extent are plaque dependent, they are reviewed in Chapter 17. Other types of drugs may give rise to EM as mentioned above.

Several other drugs may be associated with adverse effects that include lesions of the oral mucosa. An example is azathioprine, which is an antimetabolite used for immunosuppression in the treatment of autoimmune and other diseases and to prevent rejection of transplants. Its mode of action is through inhibition of purine base synthesis, resulting in suppression of nucleic acid and protein synthesis, whereby the immune response is inhibited at various stages. Rapidly proliferating tissues such as the bone marrow, the hair follicles, and the gastrointestinal and the oral mucosa may show side effects, e.g. oral ulceration. These ulcerations may include the gingiva. Other examples of drugs frequently resulting in adverse effects in the form of stomatitis are antineoplastic drugs used in cancer chemotherapy. Methotrexate is a cytostatic drug sometimes used in the treatment of leukemia. Epithelial atrophy, superficial sloughing, intense erythema, and ulceration are characteristic findings in the oral mucosa of patients with adverse effects of the chemotherapeutic treatment (Fig. 16-44) (Pindborg 1992). The ulcerative lesions are frequent portals of entry for microorganisms from the mouth, and thereby often sources of serious systemic infection in patients with suppression of the bone marrow and reduced defense systems against infection. Professional plaque removal, mouth rinsing with 0.1% chlorhexidine, and a prophylactic antibiotic regimen are important in such patients (Sonis 1998; Holmstrup & Glick 2002).

Allergic reactions

Allergic manifestations in the oral mucosa are uncommon. Several mechanisms may be involved in allergy, which is an exaggerated immune reaction. Oral mucosal reactions may be type I reactions (immedi-

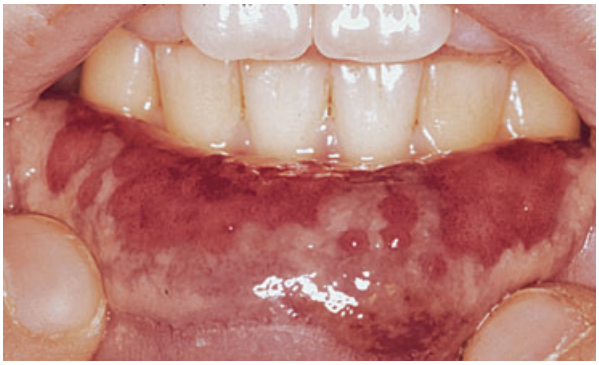

Fig. 16-44 Drug-induced stomatitis sometimes involves the gingiva. This is a mucosal lesion due to azathioprine, which is an antimetabolite used for immunosuppression.

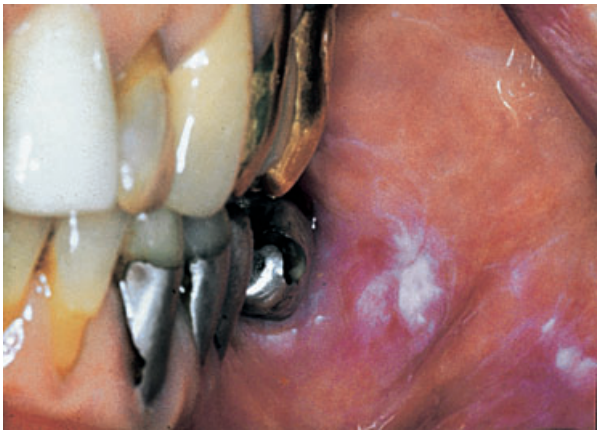

Fig. 16-45 Lichenoid contact lesion of left buccal mucosa due to type IV hypersensitivity to mercury. The lesion is confined to the zone of contact with the amalgam fillings. These lesions usually recover after replacement of the mercury-containing fillings with composites or other materials devoid of allergy-provoking components.

ate type), which is mediated by IgE, or more often they are type IV reactions (delayed type), mediated by T cells. The rare intraoral occurrence may be due to the fact that much higher concentrations of allergen are required for an allergic reaction to occur in the oral mucosa than in skin and other surfaces (Amlot *et al*. 1985; Lüders 1987; Holmstrup 1999). This chapter includes allergies to dental restorative materials, toothpastes, mouthwashes, and food.

Dental restorative materials

The clinical manifestation of type IV allergy (contact allergy) occurs after a period of 12–48 hours following contact with the allergen. The effects on oral mucosa have been denoted contact lesions and prior contact with the allergen resulting in sensitization is prerequisite for these reactions to occur (Holmstrup 1991). Oral mucosal reactions to restorative materials include reactions to mercury, nickel, gold, zinc, chromium, palladium, and acrylics (Ovrutsky & Ulyanow 1976; Zaun 1977; Bergman *et al*. 1980; Council on Dental Materials, Instruments and Equipment Workshop 1984; Fisher 1987). The lesions, which may sometimes affect the gingiva, have clinical similarities with oral lichen planus affections, which is why they are denoted OLL (see earlier in this chapter) or oral leukoplakia (Fig. 16-45). They are reddish or whitish, sometimes ulcerated lesions, but one of the crucial diagnostic observations is that the lesions resolve after removal of the offending material. Additional patch testing to identify the exact allergen gives supplementary information, but for dental amalgam it has been shown that there is no obvious correlation between the result of an epicutaneous patch test and the clinical result after removal of the fillings (Skoglund 1994). A clinical manifestation confined to the area of contact with the offending restorative material and the result after replacing this material indicates the diagnosis (Holmstrup 1999).

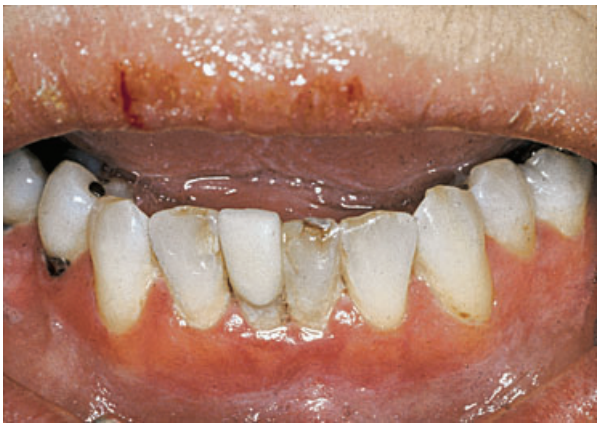

Fig. 16-46 Diffuse gingivitis and cheilitis due to contact allergy to flavor additive in dentifrice.

Reactions to oral hygiene products, chewing gum, and food

Toothpastes, mouthwashes and chewing gum

Contact allergy rarely occurs after the use of toothpastes (Sainio & Kanerva 1995; Skaare *et al*. 1997) and mouthwashes (Sainio & Kanerva 1995). The constituents responsible for the allergic reactions may be flavor additives, for instance carvone and cinnamon (Drake & Maibach 1976) or preservatives (Duffin & Cowan 1985). The flavoring constituents may be used, also, in chewing gum and result in similar forms of gingivostomatitis (Kerr *et al*. 1971). The clinical manifestations of allergy include a diffuse fiery red edematous gingivitis sometimes with ulcerations or whitening (Fig. 16-46). Similar signs may involve the labial, buccal, and tongue mucosa and cheilitis may also be seen. The clinical manifestations, which are characteristic, form the basis of the diagnosis, which may be supported by resolution of the lesions after stopping use of the allergen-containing agent (Holmstrup 1999).

Foods

The gastrointestinal tract is the largest immunologic organ in the body. It is constantly bombarded by a myriad of dietary proteins. Despite the extent of protein exposure, very few patients contract food allergies due to development of oral tolerance to these antigens (Chehade & Mayer 2005). Allergic reactions attributable to food may manifest both as type I and type IV reactions. Type I reaction with severe swelling has been described after intake of food components such as peanuts and pumpkin seed. Birch pollen allergy is associated with some types of oral mucosa allergy, and more than 20% of patients with oral allergy may be hypersensitive to kiwi, peach, apple, chestnut, and salami (Yamamoto *et al*. 1995; Antico 1996; Asero *et al*. 1996; Liccardi *et al*. 1996; Rossi *et al*. 1996; Helbling 1997; Wutrich 1997). Another food allergen resulting in gingivitis or gingivostomatitis is red pepper (Serio *et al*. 1991; Hedin *et al*. 1994). Unless it has been demonstrated that the lesions resolve after removal of the allergen, the diagnosis is difficult to establish.

Other gingival manifestations of systemic conditions

Gastrointestinal diseases

Crohn's disease

Crohn's disease is characterized by chronic granulomatous infiltrates of the wall of the last ileal loops, but any part of the gastrointestinal tract can be affected. The oral cavity is part of the gastrointestinal tract. It is thus not surprising that Crohn's disease can occur from the rectum to the lips.

The number of reports of lesions involving the periodontium is limited (van Steenberghe *et al*. 1976), which is probably related to a tradition by many clinicians of using the term aphthous lesions for any ulcerative disease of the oral mucosa. The oral lesions have striking similarity with those of the intestinal tract as revealed by rectoscopy, i.e. irregular long ulcerations with elevated borders with a cobblestone appearance. Usually, the periodontal lesions appear after the diagnosis has been established on the basis of the intestinal signs, but sometimes the oral lesions are the first findings leading to diagnosis. Characteristic clinical findings are mucosal foldings of the buccal or labial sulcus (Fig. 16-47). Exacerbations of the oral lesions appear in parallel with those of the intestine. An increased risk of periodontal destruction has been reported associated with defective neutrophil function (Lamster *et al*. 1982).

The term orofacial granulomatosis has been used as a collective diagnosis of Crohn's disease, Melkersson-Rosenthal syndrome, and sarcoidosis, because these diseases show the same histopathologic features, i.e. non-caseating, epitheloid cell granulomas in the affected tissue. Rarely, all three diseases

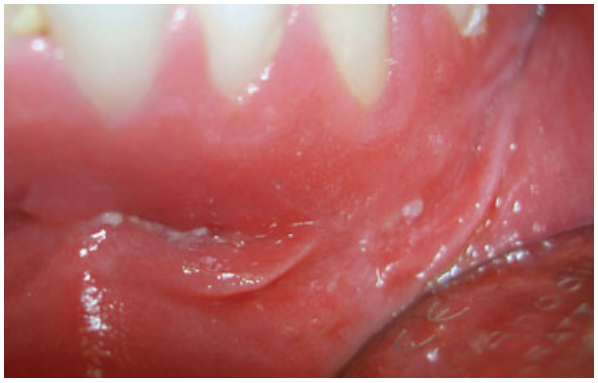

Fig. 16-47 A frequent oral finding in patients with Crohn's disease is mucosal foldings, usually located in the buccal or labial sulcus. Such lesions may be the first clinical finding leading to the diagnosis of the disease. Histopathologic examination of biopsies from these foldings reveal epitheloid cell granulomas. The foldings are characteristic for the other types of orofacial granulomatosis as well.

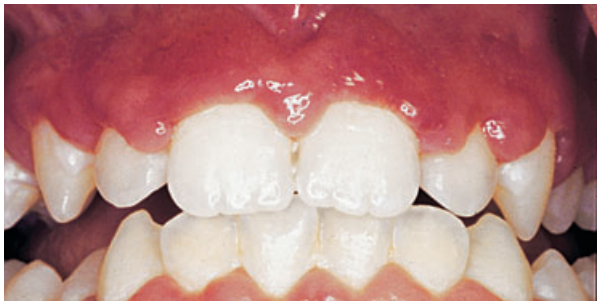

Fig. 16-48 Granulomatous gingival hyperplasia may be due to sarcoidosis, which is one of the orofacial granulomatoses; others are Crohn's disease and Melkersson-Rosenthal syndrome.

may present gingival lesions, characterized by swellings (Pindborg 1992; Mignogna *et al*. 2001); sarcoidosis sometimes causes fiery red granular gingival overgrowth (Fig. 16-48). Among 45 cases of oral sarcoidosis, 13% had gingival lesions (Blinder *et al*. 1997). A recent study of 35 patients with orofacial granulomatosis demonstrated ileal and colonic abnormalities in 54%, and granulomas were revealed in gut biopsies of 64% of the patients. Intestinal abnormality was significantly more likely if the age of onset was less than 30 years (Sanderson *et al*. 2005).

Local treatment consists of intralesional steroid injection (Mignogna *et al*. 2004; El-Hakim & Chauvin 2004) or paste application daily or twice daily during painful exacerbations and meticulous oral hygiene to reduce additional inflammation of the oral cavity. Treatment of any inflammatory condition in the affected oral region, including periodontitis, periapical inflammation, and even mucosal lesions due to hypersensitivity to restorative dental materials, is important for resolution in some cases (Guttman-Yassky *et al*. 2003).

Hematologic disorders

Leukemia

Leukemia is a malignant hematologic disorder with abnormal proliferation and development of leukocytes and their precursors in blood and bone marrow. It can involve any of the subsets of leukocytes, polymorphonuclear leukocytes, lymphocytes or monocytes. Normal hematopoiesis is suppressed and, in most cases of leukemia, the white blood cells appear in the circulating blood in immature forms. The leukemic cell proliferation at the expense of normal hematopoietic cell lines causes bone marrow failure and depressed blood cell count. As a consequence of the inability to produce sufficient functional white blood cells and platelets, death may result from infection or bleeding associated with neutropenia and thrombocytopenia.

The classification of leukemia is based on its course, acute or chronic, and origin of cells involved. The basic forms are: acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myelogenous leukemia (CML). Acute leukemias have an aggressive course resulting in death within 6 months if untreated. They occur rather seldom and patients are usually either under 20 or over 60 years of age. Chronic leukemias, of which the lymphocytic form is the most common, have less pronounced bone marrow failure and a more indolent course usually lasting several years. They occur during adulthood and normally after the age of 40. Whereas the peripheral granulocyte count is markedly elevated in chronic leukemia, it may be elevated, decreased or normal in acute leukemia (McKenna 2000).

Gingival manifestations in leukemia, which include extensive swelling (Fig. 16-49), ulceration (Fig. 16-50), petechiae (Fig. 16-51), and erythema, are much more common in acute than in chronic forms. Sometimes the manifestations lead to the diagnosis of leukemia; 69% of patients with acute leukemia had oral signs of leukemia on examination and 33% of the patients had gingival swelling (Pindborg 1992). In another study gingival swelling was revealed in 21% of AML patients but in no patients with ALL (Meyer *et al*. 2000). In the latter group, on the other hand, 36% showed both gingival erythema and ulcers. In leukemic children, only 10–17% appear to have gingival swelling (Curtis 1971; Michaud *et al*. 1977). The pronounced gingival swelling seen in leukemic patients is mostly due to plaque-induced inflammation, since stringent plaque control appears to resolve the swelling (Barrett 1984); it may also be due to the presence of leukemic infiltrates, although this has been reported to be an uncommon feature of leukemic patients (Barrett 1984). Gingival bleeding, due to secondary thrombocytopenia, is a common sign in leukemic patients. It has been reported as the initial sign in 17.7% of patients with acute leukemias and in 4.4% of patients with chronic forms (Lynch & Ship 1967).

In general, the periodontal treatment of patients with leukemia is important; it aims at reducing plaque as a source of bacteremia and damage to the periodontal tissues both during disease and during periods of chemotherapy. In such periods, potentially pathogenic bacteria occur in plaque simultaneous with granulocytopenia in these patients (Peterson

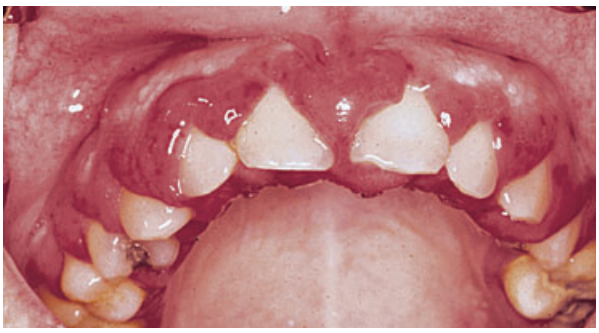

Fig. 16-49 Acute myelogenous leukemia with extensive swelling of the gingiva.

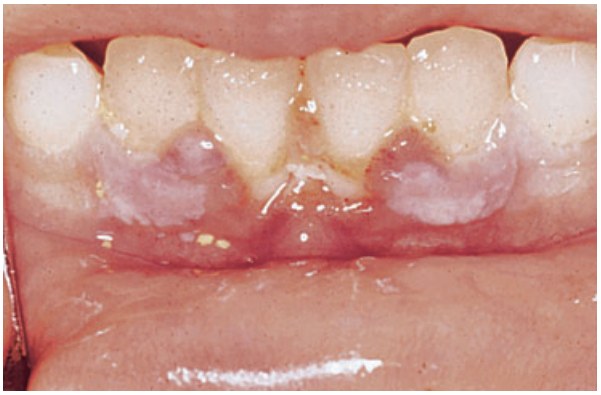

Fig. 16-50 Acute lymphocytic leukemia with gingival ulceration in a child.

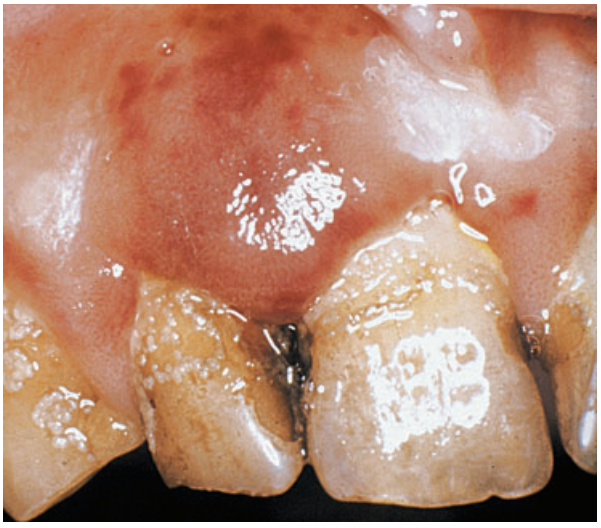

Fig. 16-51 Acute myelogenous leukemia with petechiae and swelling of the gingiva. This patient had several episodes of spontaneous bleeding from the gingiva, which prevented oral hygiene procedures from being undertaken.

et al. 1990). The reduction of periodontal inflammation may also prevent episodes of gingival bleeding. As with many other patients, chemical plaque control in combination with mechanical debridement appears to be most effective and is the preferred method of periodontal therapy in leukemic patients (Holmstrup & Glick 2002). However, the increased tendency to bleeding in many of these patients may necessitate the use of alternative methods to toothbrushing. A study of professional plaque removal preceding mouthrinsing with 0.1% chlorhexidine in patients with AML showed that the additional initial removal of plaque and calculus was more effective in reducing gingival inflammation than mouthrinsing with chlorhexidine alone (Bergman *et al*. 1992). A 1-day antibiotic prophylaxis regimen with a combination of piperacillin and netilmicin was given prior to and after the mechanical debridement. Periodontal treatment always involves a close cooperation with the medical department or specialist responsible for coordination of the patient's treatment.

Traumatic lesions

The background of traumatic lesions of the oral tissues may be self-inflicted, iatrogenic or accidental. Chemical as well as physical and thermal injuries may affect the periodontium (Armitage 1999).

Chemical injury

Surface etching by various chemical products with toxic properties may result in mucosal reactions including reactions of the gingiva. Chlorhexidine-induced mucosal desquamation (Fløtra *et al*. 1971; Almquist & Luthman 1988) (Fig. 16-52), acetylsalicylic acid burn (Najjar 1977), cocaine burn (Dello Russo & Temple 1982), and slough due to dentifrice detergents are examples of such reactions (Muhler 1970). These lesions are reversible and resolve after quitting the toxic influence. Chemical injury to the gingival tissue may be caused by incorrect use of caustics by the dentist. Paraformaldehyde used for pulp mummification may give rise to inflammation and necrosis of the gingival tissue if the cavity sealing is insufficient (Di Felice & Lombardi 1998). Usually, the diagnosis is obvious from the clinical findings and the patient history.

Physical injury

Oral hygiene agents and inexpedient procedures can be injurious to the gingival tissues. If physical trauma is limited, the gingival response is hyperkeratosis, resulting in a white leukoplakia-like, frictional keratosis (Fig. 16-53). In case of more violent trauma the damage varies from superficial gingival laceration to major loss of tissue resulting in gingival recession (Axéll & Koch 1982; Smukler & Landsberg 1984). Abrasiveness of dentifrice, strong brushing force, and horizontal movement of the toothbrush contribute to the gingival injury even in young patients. Characteristic findings in these patients are extremely good oral hygiene, cervical tooth abrasion, and unaffected tops of the interdental papillae at the site of injury (Figs. 16-54 to 16-57). The condition has been termed traumatic ulcerative gingival lesion (Axéll & Koch 1982). Dental flossing may also cause gingival ulceration and inflammation primarily affecting the top of the interdental papillae (Fig. 16-58). The prevalence of such findings is unknown (Gillette & Van House 1980). Diagnosis of physical injuries is based on the clinical findings. An important differential diagnosis is necrotizing gingivitis (Blasberg *et al*. 1981), see Chapter 20. The latter normally reveals itself as a necrotic gingival margin and interdental

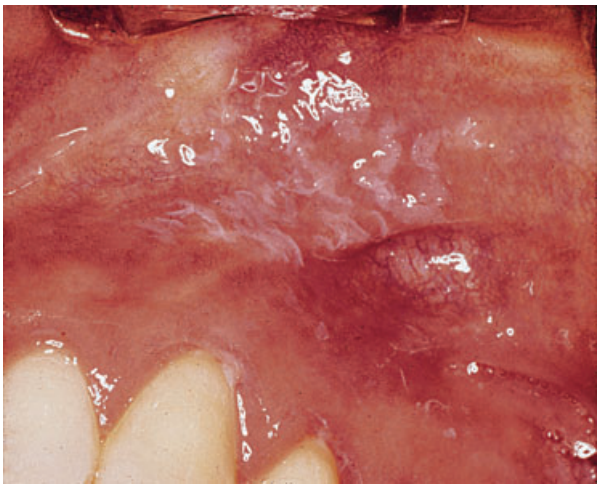

Fig. 16-52 Chlorhexidine-induced mucosal desquamation. This is a reversible type of lesion, which is completely normalized after stopping chlorhexidine use.

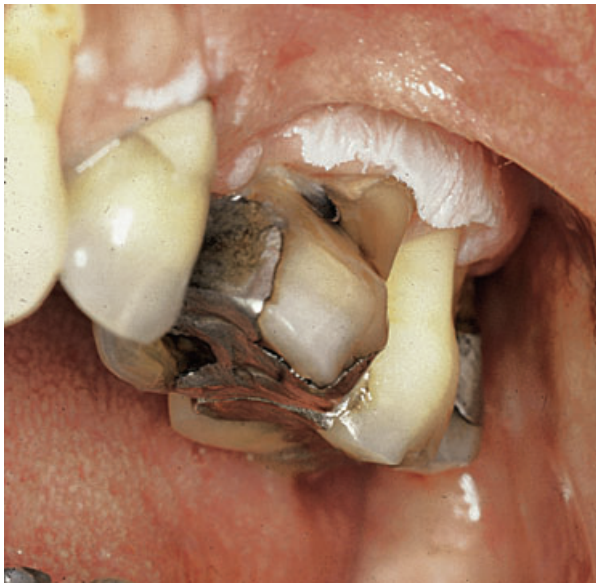

Fig. 16-53 Frictional keratosis due to violent toothbrushing. Note the cervical abrasion of adjacent teeth.

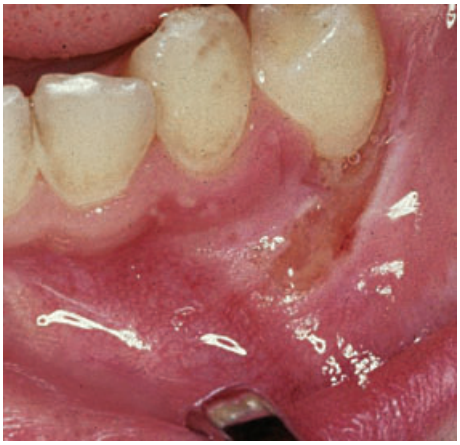

Fig. 16-54 Gingival wounding due to improper toothbrushing. Note the characteristic horizontal extension of the lesion, affecting the most prominent part of the tooth arch.

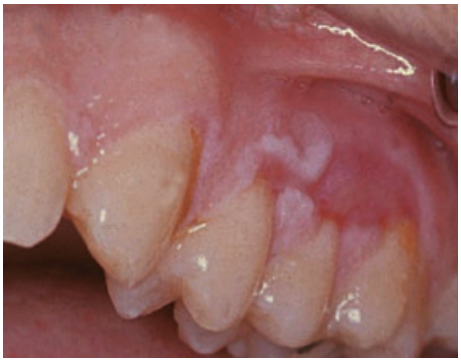

Fig. 16-55 Gingival wounding due to improper toothbrushing. Note the characteristic horizontal extension of the lesion and the uninflamed, unaffected interdental papillae.

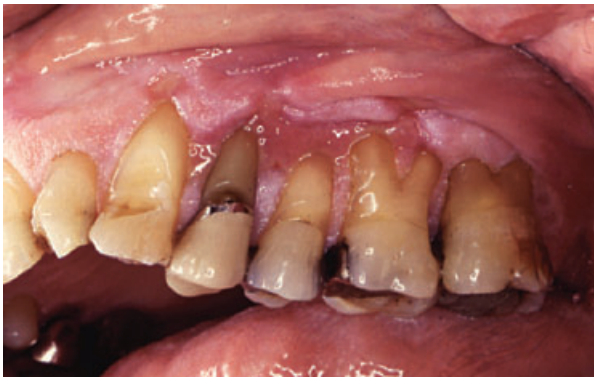

Fig. 16-56 Severe gingival recession and wounding due to improper toothbrushing. Note the unaffected interdental papillae.

papillae, while brushing trauma leads to ulcerations of a few millimeters of the gingival margin.

Self-inflicted physical injury to the gingival tissues can occur; sometimes the lesions are termed gingivitis artefacta. The lesions often show ulceration of the gingival margin often associated with recession (Figs. 16-59 and 16-60). Such lesions are most common in children and young individuals and two thirds appear to involve female patients. The lesions, which may be hemorrhagic, are usually produced by picking at or scratching the gingiva with a finger or a fingernail; sometimes the lesions are made by instruments (Pattison 1983). The correct diagnosis is often difficult to establish based on clinical findings, and identification of the cause may be impossible.

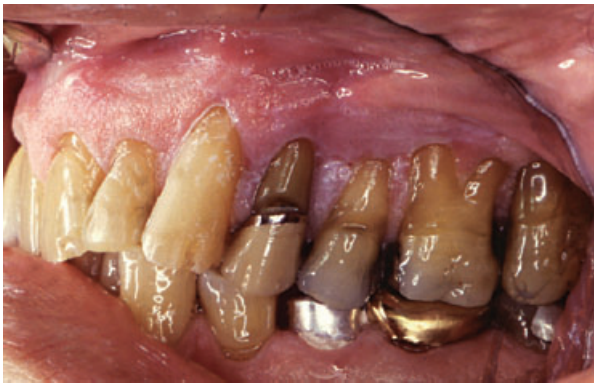

Fig. 16-57 Healing of lesion shown in Fig. 16-56. The damage to the periodontal tissues is severe, leaving extended gingival recession.

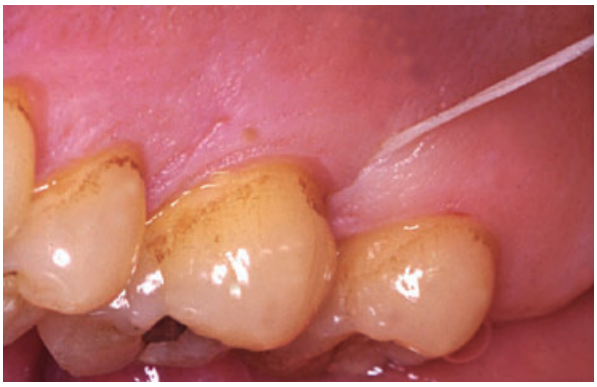

Fig. 16-58 Lesions after dental flossing are common and sometimes result in permanent fissures of the gingival tissue.

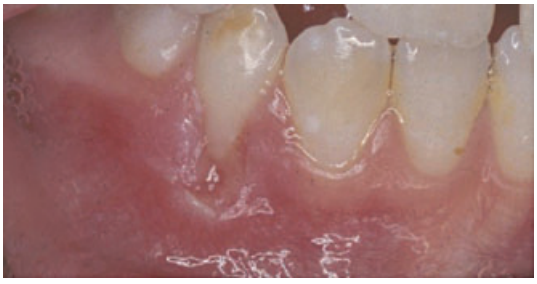

Fig. 16-59 Self-inflicted gingival recession with ulcerated margin due to a 7-year-old boy's scratching with fingernail.

Thermal injury

Extensive thermal burns of the oral mucosa are very rare, but minor burns particularly from hot

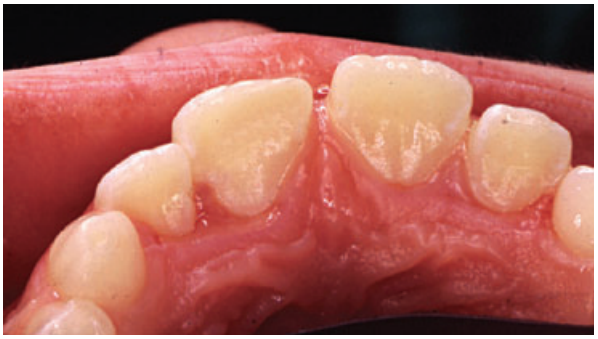

Fig. 16-60 Self-inflicted gingival ulceration of palatal gingiva of the upper right incisor region in the same boy as shown in Fig. 16-59. This lesion was also caused by fingernail scratching.

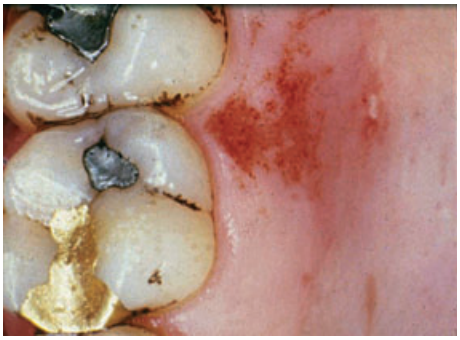

Fig. 16-61 Thermal burn with slight erosion and petechiae of palatal gingiva due to hot coffee intake.

beverages are seen occasionally. Their predilection by site is the palatal and labial mucosa but any part of the oral mucosa can be involved including the gingiva (Colby *et al*. 1961). The area involved is painful and erythematous and may slough a coagulated surface. Vesicles may also occur (Laskaris 1994) and sometimes the lesions present as ulceration, petechia or erosion (Fig. 16-61). Obviously, the history is important for reaching the correct diagnosis. Common causes are hot coffee, pizza, and melted cheese, but dental treatments involving improper handling of hot hydrocolloid impression material, hot wax or cautery instruments are other causes (Colby *et al*. 1961).

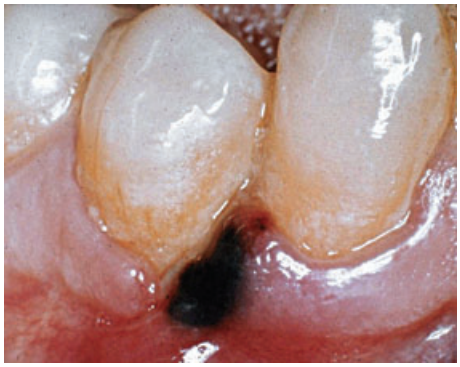

Fig. 16-62 Amalgam tattoo of attached gingiva.

Foreign body reactions

Another type of tissue reaction is established through epithelial ulceration that allows entry of foreign material into gingival connective tissue. This can happen via abrasion or cutting (Gordon & Daley 1997b), a route of tissue injury which is best exemplified by the amalgam tattoo (Buchner & Hansen 1980) (Fig. 16-62). Gingival inflammation associated with foreign bodies has been termed foreign body gingivitis. A clinical study of this condition has shown that it often presents as a red or combined red–white painful chronic lesion frequently misdiagnosed as lichen planus (Gordon & Daley 1997a). An X-ray microanalysis of foreign body gingivitis showed that most of the identified foreign bodies were of dental material origin, usually abrasives (Gordon & Daley 1997b). Another way of introducing foreign substances into the tissues is self-inflicted injury, for instance due to chewing on sticks or self-induced tattooing (Gazi 1986). It is uncertain whether the inflammatory reaction in such cases is due to a toxic or in some instances an allergic reaction.

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Chapter 17

Plaque-Induced Gingival Diseases

Angelo Mariotti

For almost four millennia the clinical manifestations of gingival diseases have been noted by mankind. Throughout the centuries the notion of cause, effect, and management of these diseases was largely dormant, resulting in a dubious realm of remedies that were dominated by superstition, frequently were subjective, often palliative, sometimes painful, and rarely successful. It was not until the last half of the twentieth century that our views about the nature of gingival diseases began to emerge, where pivotal human experiments showed the unmistakable role of dental biofilms in the initiation and progression of gingival inflammation (Löe *et al*. 1965). During the twenty-first century, we are living in a time of radical shifts of culture and science, one in which evidence-based dentistry increasingly plays a pervasive role in our knowledge regarding gingival diseases.

As more clinical evidence becomes available, the scope and nature of various forms of gingivitis become evident. More specifically, there has been growing acceptance that gingivitis does not represent a single disease but rather a spectrum of diseases that are the outcome of a variety of different processes. It is true that inflammation of the gingiva induced by bacteria is the most common form of gingivitis; however, this has created a bias toward naming all manifestations that affect the gingival tissues (e.g. atrophic, desquamative, neoplastic, etc.) as gingivitis. Although inflammation of the gingival tissues can be induced by a variety of methods (e.g. trauma, chemical agents, temperature extremes, ionizing radiation, viruses, fungi, immune defects, etc.), at this time gingival diseases are considered to be disease entities that are initiated by dental plaque and are restricted to gingival tissues. This chapter will focus on the commonly occurring and diverse family of complex and distinct pathological entities found within the gingiva that are initiated by dental plaque and that can be influenced by systemic conditions, endogenous hormones, genetic factors, drugs, and malnutrition.

Classification criteria for gingival diseases

Categorization of diseases affecting the gingiva requires evaluation of patient signs and symptoms, medical and dental histories, a clinical examination that includes the extent, distribution, duration, and physical description of lesions affecting the gingiva, clinical or relative attachment levels, and radiographs. The universal features of gingival diseases include clinical signs of inflammation, signs and symptoms that are confined to the gingiva, reversibility of the diseases by removal of etiology(ies), the presence of bacteria-laden plaque to initiate and/or exacerbate the severity of the lesion, and a possible role as a precursor to attachment loss around teeth (Table 17-1).

Clinical signs of gingival inflammation involve enlarged gingival contours due to edema or fibrosis (Muhlemann & Son 1971; Polson & Goodson 1985), color transition to a red and/or bluish red hue (Muhlemann & Son 1971; Polson & Goodson 1985),

Table 17-1 Universal features of gingival diseases (Mariotti 1999)

Signs and symptoms that are confined to the gingiva
The presence of dental plaque to initiate and/or exacerbate the severity of the lesion
Clinical signs of inflammation (enlarged gingival contours due to edema or fibrosis, color transition to a red and/or bluish red hue, elevated sulcular temperature, bleeding upon stimulation, increased gingival exudate)
Clinical signs and symptoms associated with stable attachment levels on a periodontium with no loss of attachment or on a stable but reduced periodontium (see Fig. 17-1)
Reversibility of the disease by removing the etiology(ies)
Possible role as a precursor to attachment loss around teeth

Table 17-2 Common clinical changes from gingival health to gingivitis

Parameter	Normal gingiva	Gingivitis
Color	Coral pink (correlated to mucocutaneous pigmentation)	Red/bluish red hue
Contour	Scalloped outline that envelops teeth. Papillary gingiva fills interdental space while marginal gingival forms a knife-edged appearance with tooth surface	Edema blunts marginal tissues leading to loss of knife edge adaptation to tooth and produces bulbous papillary tissues resulting in minimization of tissue scalloping
Consistency	Firm and resilient	Tissue is soft and exhibits pitting edema
Bleeding on provocation	Negative	Positive
Gingival exudate	Minimal	Significantly increased
Sulcular temperature	~34°C	Slight increase

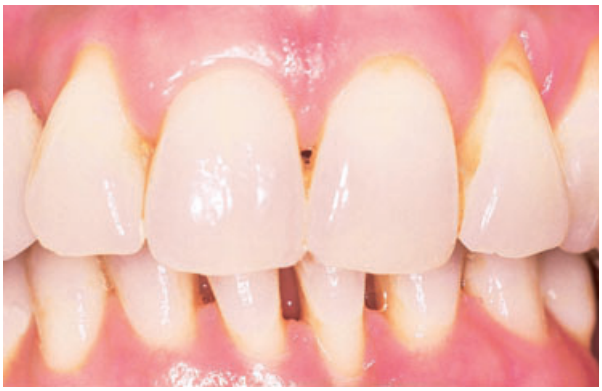

Fig. 17-1 A treated peridontitis case displaying gingival health on a reduced periodontium. If such a case developed inflammation and no further loss of attachment could be demonstrated, the diagnosis of plaque-induced gingivitis would be appropriate.

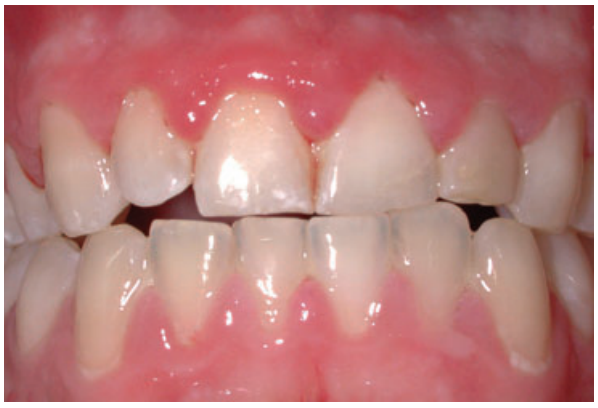

Fig. 17-2 Changes in gingival color and contour associated with plaque-induced gingivitis.

elevated sulcular temperature (Haffajee *et al*. 1992; Wolff *et al*. 1997), bleeding upon probing (Löe *et al*., 1965; Muhlemann & Son, 1971; Greenstein *et al*. 1981; Engelberger *et al*. 1983), and increased gingival exudates (Löe & Holm-Pedersen 1965; Engelberg 1966; Oliver *et al*. 1969; Rudin *et al*. 1970) (see Table 17-2 and Fig. 17-2). Clinical signs of gingival inflammation indicative of a gingival disease must be associated with stable (i.e. unchanging) attachment levels on a periodontium with no loss of attachment or alveolar bone or on a stable but reduced periodontium.

The classification of gingival diseases relies on the presence of dental plaque and factors that modify the inflammatory status of the gingiva. The modification of plaque-induced gingivitis can occur by local or systemic factors. Local factors include tooth anatomic factors (Fig. 17.3), dental restorations (Fig. 17.4) and appliances (Fig. 17.5), root fractures (Fig. 17.6), and cervical root resorption (Fig. 17.7) (Blieden 1999), whereas, systemic factors involve the endocrine system, hematologic diseases, drugs, or malnutrition (Mariotti 1999). Table 17-3 presents a classification of plaque-induced gingival diseases (Mariotti 1999).

Table 17-3 Plaque-induced gingival diseases (modified from Mariotti 1999)

Associated with bacterial plaque only	Associated with a periodontium that exhibits no attachment loss	Plaque-induced gingivitis
	Associated with a stable but reduced periodontium	
Associated with bacterial plaque and modified by systemic factors	Associated with endogenous sex steroid hormones	Puberty-associated gingivitis Menstrual cycle-associated gingivitis Pregnancy-associated gingivitis Pregnancy-associated pyogenic granuloma
	Associated with medications	Drug-influenced gingival enlargements Oral contraceptive-associated gingivitis
	Associated with systemic diseases	Diabetes mellitus-associated gingivitis Leukemia-associated gingivitis
	Associated with malnutrition	Ascorbic acid deficiency gingivitis

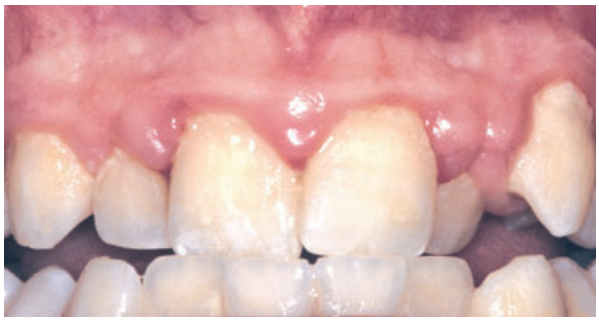

Fig. 17-3 Gingival inflammation as a result of tooth anatomic factors (malocclusion).

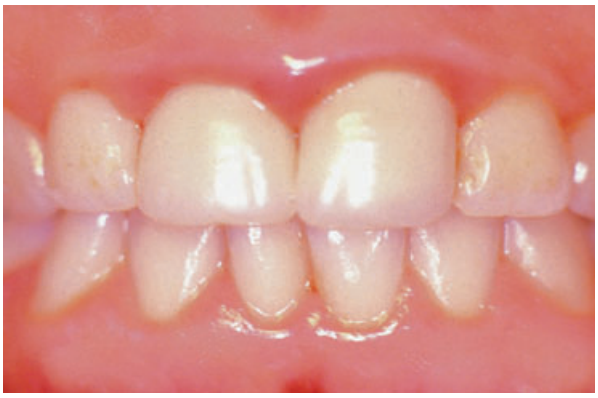

Fig. 17-4 Gingival inflammation associated with violation of the biologic width and overhanging restorations retaining plaque.

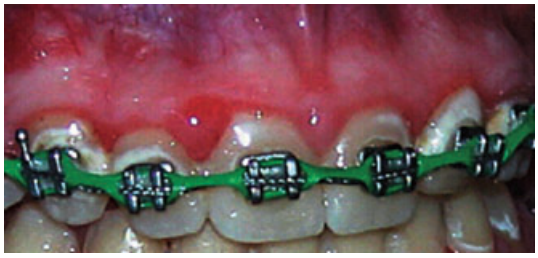

Fig. 17-5 The presence of appliances, such as braces, allows for the accumulation of plaque resulting in gingival inflammation.

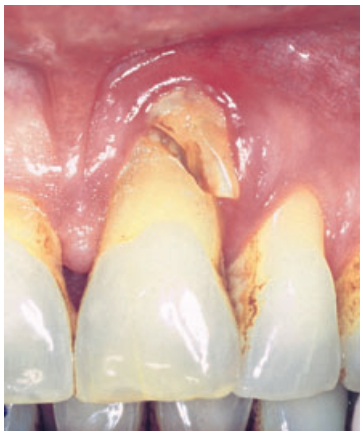

Fig. 17-6 Root fracture with associated periodontal destruction and gingival inflammation.

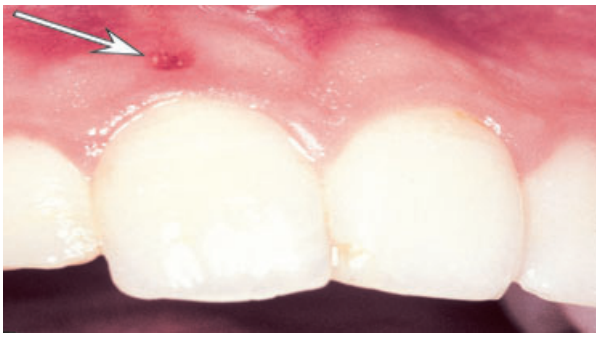

Fig. 17-7 Early cervical resorption and associated inflammation.

Plaque-induced gingivitis

Plaque-induced gingivitis is inflammation of the gingiva resulting from bacteria located at the gingival margin. The relationship of plaque to gingival inflammation has often been postulated as the cause for gingivitis, but it was not until the elegant experimental human gingivitis studies that a plaque bacterial etiology was confirmed (Löe *et al*. 1965). Epidemiological data have shown plaque-induced gingivitis to be prevalent at all ages of dentate

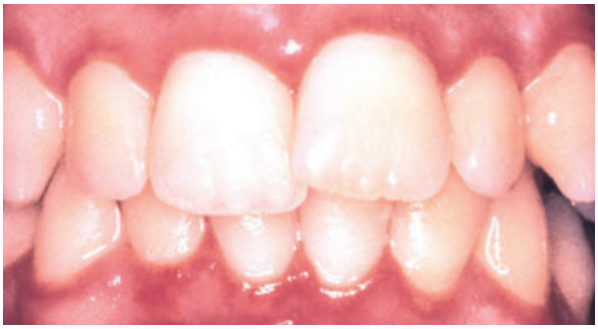

Fig. 17-8 Typical generalized marginal and papillary gingivitis.

populations (US Public Health Service 1965, 1972, 1987; Stamm 1986; Bhat 1991; Albandar 2002; Gjermo *et al*. 2002; Baelum & Schutz 2002; Sheiham & Netuveli 2002; Corbet *et al*. 2002) and this disease has been considered to be the most common form of periodontal disease (Page 1985). In children, the prevalence of plaque-induced gingivitis continues to increase until it reaches a zenith at puberty (Parfitt 1957; Hugoson *et al*. 1981; Stamm 1986). The initial changes from health to plaque-induced gingivitis may not be detectable clinically (Page & Schroeder 1976), but as plaque-induced gingivitis progresses to more advanced forms of this disease, clinical signs and symptoms become more obvious.

Plaque-induced gingivitis begins at the gingival margin and can spread throughout the remaining gingival unit. Clinical signs of gingival inflammation involving changes to gingival contour, color and consistency (Muhlemann & Son 1971; Polson & Goodson 1985), are associated with a stable periodontium which exhibits no loss of periodontal attachment or alveolar bone (Fig. 17-8). In children, gingivitis is not as intense as that found in young adults with similar amounts of dental plaque (Matsson 1978; Matsson & Goldberg 1985). This age-related difference in the development and severity of gingivitis may be associated with the quantity and/or quality of dental plaque, response of the immune system, and/or morphological differences in the periodontium between children and adults (Bimstein & Matsson 1999). More specifically, dental plaque of children usually contains lower concentrations of putative periodontal pathogens and the thicker junctional epithelium is coupled with increased vascularity in the gingival connective tissues and a developing immune system (Bimstein & Matsson 1999). In contrast to children and young adults, gingival inflammation in senior adult populations is more pronounced even when similar amounts of dental plaque are present (Fransson *et al*. 1996). The reason for the difference in senior adults may be the result of age-related differences in cellular inflammatory response to plaque (Fransson *et al*. 1996, 1999).

The intensity of the clinical signs and symptoms of gingivitis will vary between individuals (Tatakis & Trombelli 2004; Trombelli *et al*. 2004) as well as between sites within a dentition. The common clinical findings of plaque-induced gingivitis include erythema, edema, bleeding, sensitivity, tenderness, and enlargement (Löe *et al*. 1965; Suzuki 1988). Radiographic analysis and/or probing attachment levels of individuals with plaque-induced gingivitis will not indicate loss of supporting structures. Histopathologic changes include proliferation of basal junctional epithelium leading to apical and lateral cell migration, vasculitis of blood vessels adjacent to the junctional epithelium, progressive destruction of the collagen fiber network with changes in collagen types, cytopathologic alteration of resident fibroblasts, and a progressive inflammatory/immune cellular infiltrate (Page & Schroeder 1976). Although the composition of bacterial flora associated with plaque-induced gingivitis differs from the flora associated with gingival health, there are no specific bacterial flora that are pathognomonic for plaque-induced gingivitis (Ranney 1993).

Gingival diseases associated with endogenous hormones

Since the nineteenth century, evidence has accumulated to support the concept that tissues of the periodontium are modulated by androgens, estrogens, and progestins. The majority of information concerning sex hormone-induced effects have been gender-specific observations in the gingiva. Much of the evidence that has been documented concerning the effects of sex steroid hormones on the periodontium has come from observing the changes in gingival tissues during distinct endocrinological events (e.g. menstrual cycle, pregnancy, etc.). Although a significant amount of data have shown the gingiva to be a target for sex steroid hormones, the etiology for the changes has not been thoroughly elucidated. The principal explanations for sex steroid hormone-induced changes in the gingiva have pointed to changes of microbiota in dental plaque, immune function, vascular properties, and cellular function in the gingiva (Mariotti 1994, 2005). The actions of sex steroid hormones in the periodontium are multifactorial (Mariotti 1994). Theoretically, sex steroid hormones will affect the host by influencing cellular (i.e. in the blood vessels, epithelium, and connective tissue) and immune function and, together with hormone-selected bacterial populations that occupy the gingival sulcus, induce specific changes in gingival tissues that become clinically observable (Mariotti 1994).

Puberty-associated gingivitis

Puberty is not a single episode but a complex process of endocrinologic events that produce changes in the physical appearance and behavior of adolescents. The incidence and severity of gingivitis in adolescents are influenced by a variety of factors, including

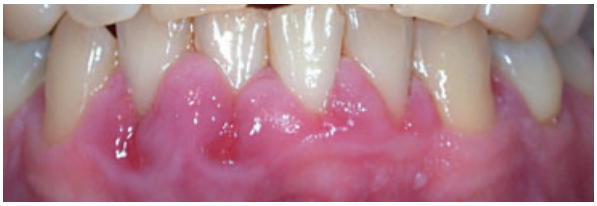

Fig. 17-9 Gingival inflammation can result from an increased secretion of sex steroid hormones during puberty.

plaque levels, dental caries, mouth breathing, crowding of the teeth, and tooth eruption (Stamm 1986); however, the dramatic rise in steroid hormone levels during puberty in both sexes has a transient effect on the inflammatory status of the gingiva (Mariotti 1994). Several studies have demonstrated an increase in gingival inflammation in circumpubertal age individuals of both sexes without a concomitant increase in plaque levels (Parfitt 1957; Sutcliffe 1972; Hefti *et al*. 1981) (Fig. 17-9). Although puberty-associated gingivitis has many of the clinical features of plaque-induced gingivitis, this disease will develop frank signs of gingival inflammation in the presence of relatively small amounts of plaque during the circumpubertal period.

Menstrual cycle-associated gingivitis

Following menarche, there is a periodicity of sex steroid hormone secretion over a 25- to 30-day period: the menstrual cycle. A clinical case report of significant and observable inflammatory changes in the gingiva during the menstrual cycle has been described (Muhlemann 1948); however, women rarely exhibit overt gingival changes that fluctuate in conjunction with the menstrual cycle (Mariotti 1994). The more common gingival inflammatory changes involve less dramatic signs of inflammation in the gingiva during ovulation (Machtei *et al*. 2004). More specifically, gingival exudate increased approximately 20% during ovulation in roughly three quarters of women tested (Hugoson 1971), while observable signs of gingival inflammation have been shown to be clinically insignificant (Machtei *et al*. 2004). Since these changes in crevicular fluid flow and gingival color are not readily observable, most young women with gingival inflammation induced by the menstrual cycle will present with a very mild form of the disease.

Pregnancy-associated gingival diseases

Some of the most remarkable endocrine and oral alterations accompany pregnancy due to the prominent increase in plasma hormone levels over several months. During human gestation, pregnancy-associated gingivitis is characterized by an increase in the prevalence and severity of gingivitis during the second and third trimester of pregnancy (Löe & Silness 1963; Löe 1965; Hugoson 1971; Arafat 1974b) (Fig. 17-10). Both longitudinal and cross-sectional studies have found the prevalence and severity of gingival inflammation significantly higher in the pregnant versus the post-partum subject even though plaque scores remained the same between the two groups (Löe & Silness 1963; Hugoson 1971; Moss *et al*. 2005). In addition, gingival probing depths are deeper (Löe & Silness 1963; Hugoson 1971; Miyazaki *et al*. 1991), bleeding on probing or toothbrushing is increased (Arafat 1974b; Miyazaki *et al*. 1991), and gingival crevicular fluid flow is elevated (Hugoson 1971) in pregnant women. The features of pregnancy-associated gingivitis are similar to plaque-induced gingivitis, except for the propensity to develop frank signs of gingival inflammation in the presence of relatively little plaque during pregnancy.

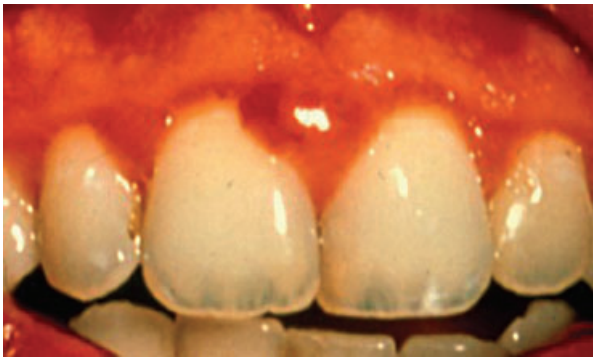

Fig. 17-10 A heightened gingival response to plaque during pregnancy results in pregnancy-associated gingivitis.

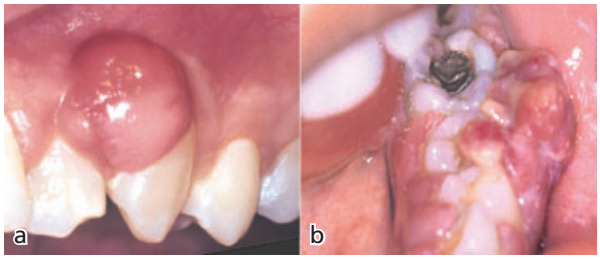

Fig. 17-11 (a) Pyogenic granuloma of pregnancy. (b) Large pyogenic granuloma of pregnancy interfering with occlusal function.

Pregnancy-associated pyogenic granuloma or "pregnancy tumor" was described over a century ago (Coles 1874); this is not a tumor but an exaggerated inflammatory response during pregnancy to an irritation resulting in a solitary polyploid capillary hemangioma which can easily bleed upon mild provocation (Sills *et al*. 1996) (Fig 17-11). Pregnancy-associated pyogenic granuloma presents clinically as a painless protuberant, mushroom-like, exophytic mass that is attached by a sessile or pedunculated base and arises from the gingival margin or more commonly from an interproximal space (Sills *et al*. 1996). Pregnancy-associated pyogenic granuloma has been reported to occur in 0.5–5.0% of pregnant women (Ziskin & Nesse 1946; Maier & Orban 1949;

Arafat 1974a; Kristen 1976). It is more common in the maxilla (Sills *et al*. 1996) and may develop as early as the first trimester (Sills *et al*. 1996), ultimately regressing or completely disappearing following parturition (Ziskin & Nesse 1946).

Gingival diseases associated with medications

In the past century, an astonishing array of medications for the alleviation of human diseases has lead to the creation of new side effects in the oral cavity. Drugs that specifically affect the gingival tissues have principally caused an increase in either inflammation and/or size.

Drug-influenced gingival enlargement

Esthetically disfiguring overgrowth of gingiva is a significant side effect which may be associated with (Hassell & Hefti 1991; Seymour *et al*. 1996; Seymour 2006):

- Anticonvulsant (e.g. phenytoin, sodium valproate, etc.)
- Immunosuppressant (e.g. cyclosporine A) (Fig. 17-12)
- Calcium channel blocking agents (e.g. nifedipine, verapamil, etc.).

The common clinical characteristics of drug-influenced gingival enlargements (Table 17-4) include patient variations in the pattern of enlargement (i.e. genetic predisposition) (Hassell & Hefti 1991; Seymour *et al*. 1996), a tendency to occur more often in anterior gingiva (Hassell & Hefti 1991; Seymour *et al*. 1996), a higher prevalence in younger age groups (Esterberg & White 1945; Rateitschak-Pluss *et al*. 1983; Hefti *et al*. 1994), onset within 3 months of use (Hassell 1981; Hassell & Hefti 1991; Seymour 1991; Seymour & Jacobs 1992) that is usually first observed in the papilla (Hassell & Hefti 1991); although it can be found in a periodontium with or without bone loss, it is not associated with attachment loss or tooth mortality (Hassell & Hefti 1991; Seymour *et al*. 1996). Furthermore, all of these drugs produce clinical lesions and histologic characteristics that are indistinguishable from one another (Hassell & Hefti 1991; Seymour *et al*. 1996).

The influence of plaque on the induction of gingival enlargements by drugs in humans has not been fully elucidated (Hassell & Hefti 1991); however, it does appear that the severity of the lesion is affected by the oral hygiene of the patient (Steinberg & Steinberg 1982; Addy *et al*. 1983; Hassell *et al*. 1984; Tyldesley & Rotter 1984; Daley *et al*. 1986; McGaw *et al*. 1987; Modeer & Dahllof 1987; Yahia *et al*. 1988; Barclay *et al*. 1992).

The first description of a drug causing an enlargement of the gingiva was reported in 1939 and was associated with the use of phenytoin (Kimball 1939). Phenytoin, which is used on a chronic regimen for the control of epileptic seizures, induces gingival enlargements in approximately 50% of patients using this agent (Angelopoulous & Goaz 1972). One prominent theory of the etiology of phenytoin-associated gingival enlargements suggests that the accumulation of genetically distinct populations of gingival fibroblasts results in the accumulation of connective tissues resulting from reduced catabolism of the collagen molecule (Hassell & Hefti 1991).

Calcium channel blockers have also been identified as agents that affect enlargement of the gingiva. Calcium channel blockers are a class of drugs that exert effects principally at voltage-gated Ca^{2+} channels located in the plasma membrane and are commonly prescribed as antihypertensive, anti-arrhythmic and anti-anginal agents. In 1984, calcium channel

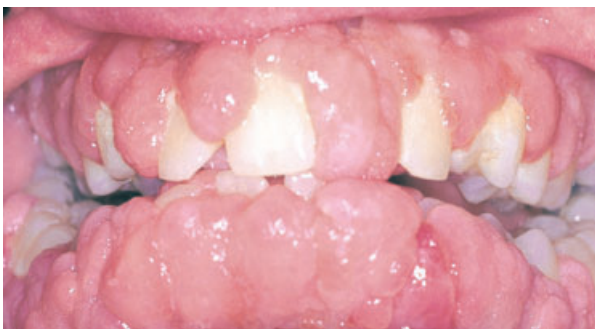

Fig. 17-12 Severe enlargement of the gingiva associated with cyclosporine medication in a kidney transplant patient.

Table 17-4 Characteristics of drug-influenced gingival enlargement (Mariotti 1999)

Variation in interpatient and intrapatient pattern
Predilection for anterior gingiva
Higher prevalence in children
Onset within 3 months
Change in gingival contour leading to modification of gingival size
Enlargement first observed at the interdental papilla
Change in gingival color
Increased gingival exudate
Bleeding upon provocation
Found in gingiva with or without bone loss but is not associated with attachment loss
Pronounced inflammatory response of gingiva in relation to the plaque present
Reductions in dental plaque can limit the severity of lesion
Must be using phenytoin, cyclosporine A or certain calcium channel blockers; the plasma concentrations to induce the lesion have not been clearly defined in humans

blockers were first linked to gingival enlargements (Ramon *et al*. 1984) and the prevalence of gingival lesions associated with these drugs has been estimated to be approximately 20% (Barclay *et al*. 1992), with nifedipine being the primarily calcium channel blocker associated with gingival enlargement (Ellis *et al*. 1999). Presently, the cause(s) of gingival enlargement by calcium channel blockers are still under investigation but these drugs may directly influence gingival connective tissues by stimulating an increase of gingival fibroblasts as well as an increase in the production of the connective tissue matrix (Fu *et al*. 1998).

The final drug class that has been associated with increases in gingival mass is cyclosporine A (CsA), which is a powerful immunoregulating drug used primarily in the prevention of organ transplant rejection (Seymour & Jacobs 1992). The clinical features of cyclosporine-influenced gingival enlargement were first described in 1983 (Rateitschak-Pluss *et al*. 1983) and cyclosporine appears to affect between 25 and 30% of the patients taking this medication (Hassell & Hefti 1991; Seymour *et al*. 1987). Hypotheses explaining why cyclosporine A affects the gingiva are diverse but a leading theory suggests that the principal metabolite of cyclosporine A, hydroxycyclosporine (M-17), in conjunction with the parent compound, stimulates fibroblast proliferation (Mariotti *et al*. 1998). This increase in cell number coupled with a reduction in the breakdown of gingival connective tissues (Hassell & Hefti 1991) has been speculated to be the cause of excessive extracellular matrix accumulation in cyclosporine A associated gingival enlargements.

Oral contraceptive-associated gingivitis

Oral contraceptive agents are one of the most widely utilized classes of drugs in the world. Today, as a result of the early onset of menarche, changing social mores and increased emphasis on family planning, the use of oral contraceptives in adolescents and young adults has increased to reduce unwanted pregnancies. Clinical case reports have described gingival enlargement induced by oral contraceptives in otherwise healthy females with no history of gingival overgrowth (Lynn 1967; Kaufman 1969; Sperber 1969). In all cases, the increased gingival mass was reversed when oral contraceptive use was discontinued or the dosage reduced. Early clinical studies demonstrated that women using hormonal contraceptive drugs had a higher incidence of gingival inflammation in comparison to women who did not use these agents (Lindhe & Bjorn 1967; El-Ashiry *et al*. 1970; Pankhurst *et al*. 1981) and that long-term use of oral contraceptives may affect periodontal attachment levels (Knight & Wade 1974). All studies prior to the 1980s recording changes to gingival tissues by oral contraceptives were completed when contraceptive concentrations were at much higher levels than are currently available today. A recent clinical study evaluating the effects of low-dose oral contraceptives on gingival inflammation in young women found no effect of these hormonal agents on gingival tissues (Preshaw *et al*. 2001). Furthermore, cross-sectional data from NHANES III have failed to show a relationship between low-dose oral contraceptive use and increased levels of gingivitis (Taichman & Eklund 2005). From these data it appears that current low-dose compositions of oral contraceptives are probably not as harmful to the periodontium as the early formulations.

Gingival diseases associated with systemic diseases

Diabetes mellitus-associated gingivitis

Diabetes mellitus (DM) is a chronic systemic disease characterized by disorders in insulin production, metabolism of carbohydrate, fat, and protein, and the structure and function of blood vessels. DM most commonly appears as one of two recognized clinical entities: type 1 DM (insulin-dependent DM or juvenile onset) and type 2 DM (non-insulin-dependent DM or adult onset). DM-associated gingivitis is a consistent feature found in children with poorly controlled type 1 DM (Cianciola *et al*. 1982; Gusberti *et al*. 1983; Ervasti *et al*. 1985). The features of gingivitis associated with DM are similar to plaque-induced gingivitis, except that the level of diabetic control is more of an important aspect than plaque control in the severity of the gingival inflammation (Cianciola *et al*. 1982; Gusberti *et al*. 1983; Ervasti *et al*. 1985). In adults with DM, it is difficult to detect the effects of this endocrine disease on gingival diseases since most studies have evaluated gingival inflammation in association with attachment loss (AAP 1999); however, young adults with type I DM developed an earlier and more pronounced inflammatory response compared to non-diabetic controls in experimental gingivitis studies (Salvi *et al*. 2005). These data suggest that the gingival inflammatory response in adult diabetics is an overt response to the dental biofilm. In addition to the effects of DM on the gingiva, reports in the literature have suggested that reductions in gingival inflammation of diabetic patients will also reduce the amount of insulin needed to control blood glucose levels (Mealey & Oates 2006). This has been a controversial premise given the competing results of numerous studies; however, a meta-analysis of interventional studies suggest that control of gingival inflammation will not substantially affect glycemic control in diabetic patients (Janket *et al*. 2005).

Leukemia-associated gingivitis

Leukemia is a progressive, malignant hematologic disorder characterized by an abnormal proliferation and development of leukocytes and precursors of leukocytes in the blood and bone marrow. Leukemia

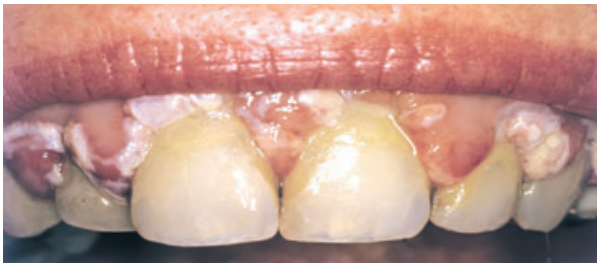

Fig. 17-13 Gingival changes associated with acute monocytic leukemia. Note the acute candidosis superimposed upon the infiltrative gingival changes.

is classified on the duration (acute or chronic) and the type of cell involved (myeloid or lymphoid) and the number of cells in the blood (leukemic or aleukemic). There are noticeable correlations of leukemias with age. For example, acute lymphoblastic leukemia comprise 80% of all childhood leukemias while acute myelogenous leukemia usually affects adults. Oral manifestations have primarily been described in acute leukemias and consist of cervical adenopathy, petechiae, mucosal ulcers, as well as gingival inflammation and enlargement (Fig. 17-13) (Lynch & Ship 1967). Signs of inflammation in the gingiva include swollen, glazed, and spongy tissues which are red to deep purple in appearance (Dreizen *et al*. 1984). Gingival bleeding is a common sign in patients with leukemia and is the initial oral sign and/or symptom in 17.7% and 4.4% of patients with acute and chronic leukemias, respectively (Lynch & Ship 1967). Gingival enlargement has also been reported, initially beginning at the interdental papilla followed by marginal and attached gingiva (Dreizen *et al*. 1984). Although local irritants can predispose and exacerbate the gingival response in leukemia, they are not prerequisites for lesions to form in the oral cavity (Dreizen *et al*. 1984).

Linear gingival erythema

Infection with the human immunodeficiency virus (HIV) produces an irreversible and progressive immunosuppression that renders a person susceptible to a variety of oral diseases. In humans, HIV depletes CD4+ lymphocytes (T helper cells) which leads to the development of a variety of fungal, viral, and bacterial oral infections (Connor & Ho 1992).

Oral manifestations of HIV infection have been used to stage HIV disease (Justice *et al*. 1989; Royce *et al*. 1991; Prevention CDC 1992), identify prophylactic treatment of other serious infections (Force USPHST 1993), and indicate disease prognosis (Dodd *et al*. 1991; Katz *et al*. 1992). In the gingiva, manifestations of HIV infection were formerly known as HIV-associated gingivitis but currently are designated as linear gingival erythema (LGE). LGE is distinguished by a 2–3 mm marginal band of intense erythema in the free gingiva (Winkler *et al*. 1988). This band of gingival erythema may extend into the attached gingiva as a focal or diffuse erythema and/or extend beyond the mucogingival line into the alveolar mucosa (Winkler *et al*. 1988). LGE may be localized to one or two teeth but it is more commonly a generalized gingival condition.

The etiology of this gingival lesion is not well understood; however, research has begun to investigate the relationship of periodontal pathogens and the local host response in regard to how HIV infection affects the gingiva. Although LGE does not respond to conventional scaling, root planing, and plaque control (Winkler & Murray 1987; Grassi *et al*. 1988; Winkler *et al*. 1988, 1989), the anaerobic microflora from subgingival sites of HIV-infected patients with gingivitis seems to be essentially the same as seen in non-infected patients (Moore *et al*. 1993). Despite the similarities in anaerobic microflora between infected and uninfected individuals, organisms not generally associated with gingivitis in HIV-negative patients, such as *Candida* species, have been identified with LGE (Lamster *et al*. 1998). In addition, LGE lesions have been shown to have reduced proportions of T cells and macrophages and an increased number of IgG plasma cells and PMNs (Gomez *et al*. 1995). These host cell responses and unusual microbiota may be responsible for the refractory nature of this lesion to conventional periodontal treatment of gingivitis.

With the advent of antiretroviral therapy for HIV-positive patients, the prevalence of HIV-specific lesions has been dramatically reduced; even so, plaque accumulation with reduced CD4+ counts will still account for a pronounced gingival inflammatory response (Kroidl *et al*. 2005).

Gingival diseases associated with malnutrition

Although some nutritional deficiencies can significantly exacerbate the response of the gingiva to plaque bacteria, the precise role of nutrition in the initiation or progression of periodontal diseases remains to be elucidated. The studies that have attempted to investigate the relationship of nutrition to periodontal disease have examined the periodontal status of individuals in developed and in developing countries and have failed to show a relationship between periodontal disease and nutrition (Russell 1962; Waerhaug 1967; Wertheimer *et al*. 1967). While there is a paucity of information available regarding the effects of a specific, single nutritional deficiency on human periodontal tissues, severe vitamin C deficiency or scurvy has been one of the earliest nutritional deficiencies to be examined in the oral cavity (Lind 1953). Even though scurvy is unusual in areas with an adequate food supply, certain populations on restricted diets (e.g. infants from low socioeconomic families) are at risk of developing this condition (Oeffinger 1993). The classic clinical signs of scurvy describe the gingiva as being bright red,

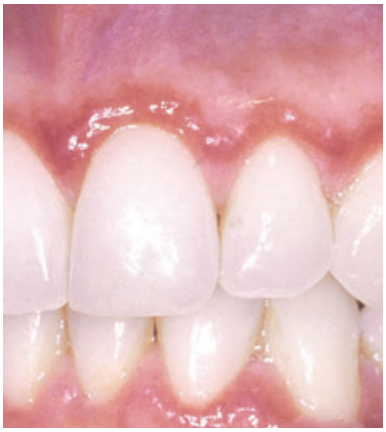

Fig. 17-14 Gingival changes associated with vitamin C deficiency. Note the absence of dental plaque and the distances of the color changes from marginal gingiva.

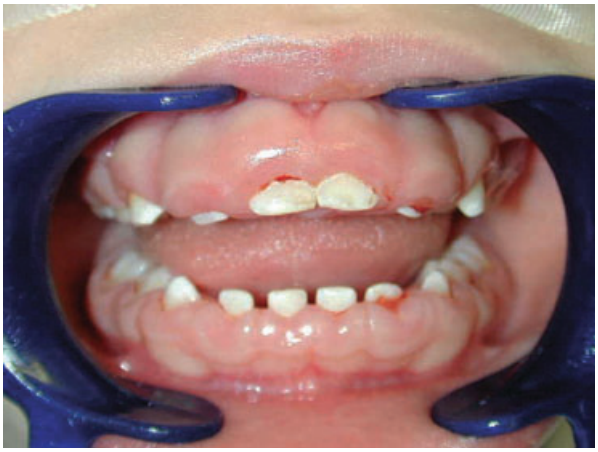

Fig. 17-15 Generalized, benign, non-inflammatory, fibrotic enlargement of gingival tissues.

swollen, ulcerated, and susceptible to hemorrhage (van Steenberghe 1997). Although there is no dispute about the necessity of dietary ascorbic acid for periodontal health, in the absence of frank scurvy the effect of declining ascorbic acid levels on the gingiva can be difficult to detect clinically (Woolfe *et al*. 1980) and when it is detected usually has characteristics that are similar to plaque-induced gingivitis (Fig. 17-14).

Gingival diseases associated with heredity

Benign, non-inflammatory fibrotic enlargement of the maxillary and/or mandibular gingiva associated with a familial aggregation has been designated by such terms as gingivomatosis elephantiasis, familial elephantiasis, juvenile hyaline fibromatosis, congenital familial fibromatosis, idiopathic fibromatosis, idiopathic gingival fibromatosis, hereditary gingival hyperplasia, and hereditary gingival fibromatosis. Although there have been over 100 reports of gingival enlargements associated with heredity in the literature over the past century, our knowledge concerning the natural history of this disease is extremely limited and the etiology of this rare condition has not been determined.

Hereditary gingival fibromatosis appears to be a slowly progressive gingival enlargement that develops upon eruption of the permanent dentition; however, gingival enlargement can also occur in the primary dentition (Emerson 1965; Jorgenson & Cocker 1974; Lai *et al*. 1995; Miyake *et al*. 1995). The disease can be localized or generalized and may ultimately cover the occlusal surfaces of teeth. The enlarged gingiva is non-hemorrhagic and firm but there can be an overlay of gingival inflammation which can augment the enlargement (Fig. 17-15). The histologic features of hereditary gingival fibromatosis include dense fibrotic connective tissue as well as epithelial hyperplasia with elongated and increased rete pegs (Johnson *et al*. 1986; Clark 1987).

Hereditary gingival fibromatosis can be inherited as a simple Mendelian trait in some chromosomal disorders, and as a malformation syndrome (Witkop 1971; Jones *et al*. 1977; Skrinjaric & Bacic 1989; Takagi *et al*. 1991; Goldblatt & Singer 1992; Hallet *et al*. 1995). Currently, a mutation in the *son of sevenless-1* gene has been implicated as a genetic factor responsible for hereditary gingival fibromatosis (Hart *et al*. 2002). Recent research into the cellular responses of this disease suggest an accumulation of specific populations of gingival fibroblasts that result in an abnormal accumulation of connective tissues (Huang *et al*. 1997; Tipton *et al*. 1997; Lee *et al*. 2006).

Gingival diseases associated with ulcerative lesions

Necrotizing ulcerative gingivitis (NUG) has been observed for centuries and has been recognized by numerous names including trench mouth and Vincent's infection. At this time, acute necrotizing ulcerative gingivitis is a term used to describe the clinical onset of the disease and should not be used as a diagnostic classification since some forms of NUG may be recurrent or possibly chronic.

NUG is most often distinguished by a sudden onset. The clinical signs of NUG include intense gingival pain that usually is responsible for the patient seeking professional care, papillary necrosis, that has been described as a "punched out" appearance of the gingival papilla, and gingival bleeding that requires little or no provocation (Fig. 17-16) (Grupe & Wilder 1956; Goldhaber & Giddon 1964; Johnson & Engel 1986). Although these three signs must be present to diagnosis NUG, other signs and symptoms may be present but do not necessarily occur in all individuals with this disease. These signs and symptoms include fever, malaise, lymphadenopathy, metallic taste, and malodor (Schluger 1943; Wilson 1952; Murayama *et al*. 1994). Systemic reactions of acute NUG are usually more severe in children. Significant destruction of the gingival connective tissue is possible with NUG but

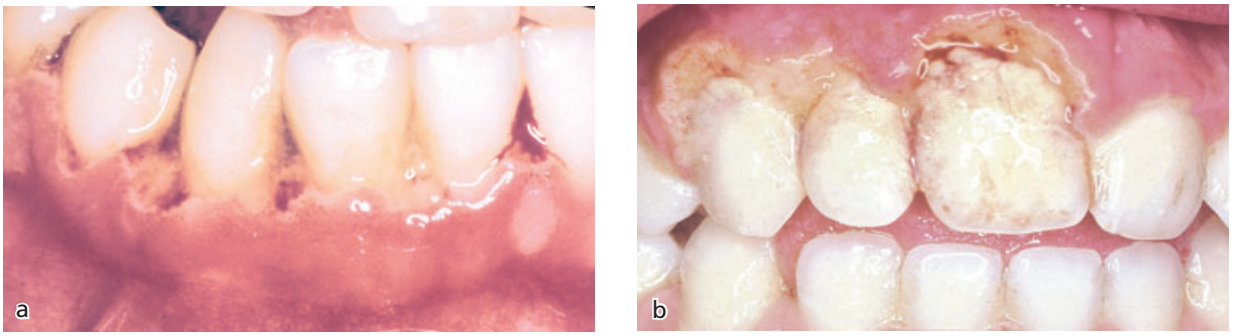

Fig. 17-16 Necrotizing ulcerative gingivitis. (a) Destruction of the interdental papilla, pseudomembrane and spontaneous bleeding. (b) Although usually confined to the papilla, occasionally the marginal tissues are involved.

when attachment loss occurs this condition should be considered as a necrotizing ulcerative periodontitis (NUP).

The etiology of NUG has been associated with a bacterial infection. The four zones of the NUG gingival lesion include the bacterial zone (the superficial area that consists of various bacteria and some spirochetes), neutrophil-rich zone (follows the bacterial zone and contains leukocytes and bacteria including spirochetes), necrotic zone (consists of disintegrated cells and connective tissue elements with many large and intermediate spirochetes) and the spirochetal infiltration zone (the deepest zone that is infiltrated with no other bacteria but intermediate and large spirochetes) (Listgarten 1965). The cultivable flora of NUG that predominates includes *Provetella intermedia* and *Fusobacterium* species while microscopically *Treponema* and *Selenomonas* species are observed (Loesche *et al*. 1982; Rowland *et al*. 1993b). Additional factors such as smoking (AAP 1996), psychological stress (Moulton *et al*. 1952; Cohen-Cole *et al*. 1983), malnutrition (Grupe & Wilder 1956; Goldhaber & Giddon 1964; Johnson & Engel 1986), and immune suppression (Moulton *et al*. 1952; Rowland *et al*. 1993a) can predispose an individual to NUG.

NUG can affect any age group but is considered to be a disease of young adults in industrialized countries (Melnick *et al*. 1988). In developing countries, NUG is a disease found in children from families with a low socioeconomic status (Melnick *et al*. 1988). The onset of NUG in children is associated with inappropriate nutritional intake, especially low protein consumption (Sheiham 1966; Taiwo 1995). In addition, viral infections such as measles can induce NUG in malnourished children (Enwonwu 1972; Osuji 1990). Even though NUG has occurred in epidemic patterns, this disease is not considered communicable (Rosebury 1942).

Treatment of plaque-induced gingival diseases

Personal and professional mechanical oral hygiene measures are critical aspects for the treatment of plaque-induced gingival diseases. Proper oral hygiene reduces the build-up of dental plaque on tooth surfaces and diminishes the incidence of various types of gingival diseases (Garmyn *et al*. 1998). For effective, self-care, mechanical plaque control, the appropriate use of manual (Jepsen 1998) or powered (van der Weijden *et al*. 1998) toothbrushes combined with interdental mechanical cleaning (Kinane 1998) is essential. Dentifrices also have important roles in the reduction of dental plaque. First of all, dentifrices can be used to help in the removal of dental plaque by enhancing the mechanical scrubing and cleaning power of the toothbrush (Mariotti & Burrell 2006). Secondly, since dentifrices are also drug-delivery systems; agents (e.g. tricolsan) present in a toothpaste will provide a pharmacologic advantage by reducing the bacteria found in dental biofilms and/or inflammation in gingival tissues (DeVizio & Davies 2004). Additionally, adjunctive, self-applied, locally delivered, pharmacologic agents (e.g. chlorhexidine) can also be an effective option for individuals with physical or medical limitations that constrain their ability to perform adequate home care.

Professional intervention is required as an adjunct to self-performed hygiene when plaque-retaining factors, such as dental calculus, defective restorations or anatomic factors, prevent an individual from effectively removing dental plaque. In instances where systemic factors modify the gingival response to dental biofilms, a combined treatment plan with the appropriate medical professional can be effective in addressing the root causes of the gingival inflammation.

The significance of gingivitis

The presence of gingival inflammation was at one time considered a normal variant of health but in the mid-twentieth century that concept changed dramatically when it was hypothesized that sites with untreated gingivitis were destined to progress to destructive periodontal disease. Although this concept was supported by some clinical studies showing an association between gingivitis and bone loss (Marshall-Day *et al*. 1955), longitudinal studies examining the natural history of periodontal disease

failed to show complete conversion of chronic gingivitis to periodontitis (Löe *et al*. 1986). Gingival inflammation is probably a necessary precursor for periodontitis (Löe & Morrison 1986; Page & Kornman 1997) but this does not mean that all sites which exhibit gingival inflammation progress to periodontitis (Schätzle *et al*. 2003).

If the majority of the adult population exhibit some form of gingivitis how does one determine which inflamed sites within particular individuals are susceptible to conversion to destructive periodontal disease? There has been an awareness that differences in the inflammatory responsiveness to dental plaque cannot be fully accounted for by the quantity or quality of the plaque (Tatakis & Trombelli 2004). More specifically, there seems to be a differential gingival inflammatory response that is independent of the amount or rate of accumulation of dental plaque (Trombelli *et al*. 2004). Hence, the predilection of inflamed gingival sites to convert to destructive forms of periodontal disease may be dependent on the susceptibility and responsiveness of the individual to gingivitis (van der Velden *et al*. 1985a,b; Abbas *et al*. 1986; Winkel *et al*. 1987; Dietrich *et al*. 2006). In other words, these data suggest that specific types of inflammatory responses in the gingiva are necessary to initiate destruction of connective tissue attachment apical to the cemento-enamel junction. As we learn more about different gingival inflammatory phenotypes our notions about the initiation of periodontal destruction continue to emerge.

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Chapter 18

Chronic Periodontitis

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Chronic periodontitis is considered to start as *plaque-induced gingivitis* (see Chapter 17), a reversible condition that, left untreated, may develop into *chronic periodontitis*. Chronic periodontitis lesions include loss of attachment and bone and are regarded as irreversible. In this chapter, various aspects of chronic periodontitis will be described, including its links to plaque-induced gingivitis.

Clinical features of chronic periodontitis

The clinical features of chronic periodontitis include symptoms such as (1) color, texture and volume alterations of the marginal gingiva, (2) bleeding on probing (BoP) from the gingival pocket area, (3) reduced resistance of the soft marginal tissues to probing (increased pocket depth or periodontal pocketing), (4) loss of probing attachment level, (5) recession of the gingival margin, (6) loss of alveolar bone (even or angular pattern), (7) root furcation exposure, (8) increased tooth mobility, (9) drifting and eventually exfoliation of teeth.

Figure 18-1 illustrates the clinical status of a 30-year-old male with severe chronic periodontitis. The clinical examination revealed that (1) most approximal and lingual/palatal sites exhibited BoP, (2) most teeth showed increased mobility, and (3) gingival recession had occurred at a large number of buccal and interproximal sites. Tooth 16 had erupted beyond the occlusal plane. Teeth 37 and 38 had tilted mesially. The altered position of the molars had evidently compromised the occlusion. Forces elicited during function may have caused the maxillary incisors to tilt in a buccal direction and multiple open spaces, diastemata, had developed in the front tooth segment of the maxilla.

Figure 18-2 presents the radiographic status of the same patient. In the radiographs it can be observed that a large number of teeth have lost substantial amounts of bone support. At teeth 17, 16, 27, 37, 36, and 47 the furcation areas have lost their periodontal tissue support and are open for "through and through" probing.

Overall characteristics of chronic periodontitis

- Chronic periodontitis is prevalent in adults but may occur in children.
- The amount of destruction of the periodontal tissues seen in a given patient is commensurate with oral hygiene and plaque levels, local predisposing factors, smoking, stress, and systemic risk factors.
- The subgingival biofilm harbors a variety of bacterial species; the composition of the biofilm may vary between subjects and sites.
- Subgingival calculus is invariably present at diseased sites.
- Chronic periodontitis is classified as localized when <30% of sites are affected and generalized when this level is exceeded.
- Severity of chronic periodontitis at the site level may be classified based on the degree of probing attachment loss (PAL) as *mild* (PAL = 1–2 mm), *moderate* (PAL = 3–4 mm), and *severe* (PAL ≥ 5 mm).
- Although chronic periodontitis is initiated and sustained by microbial plaque, host factors deter-

Fig. 18-1 A 30-year-old male patient with chronic periodontitis, clinical status prior to treatment.

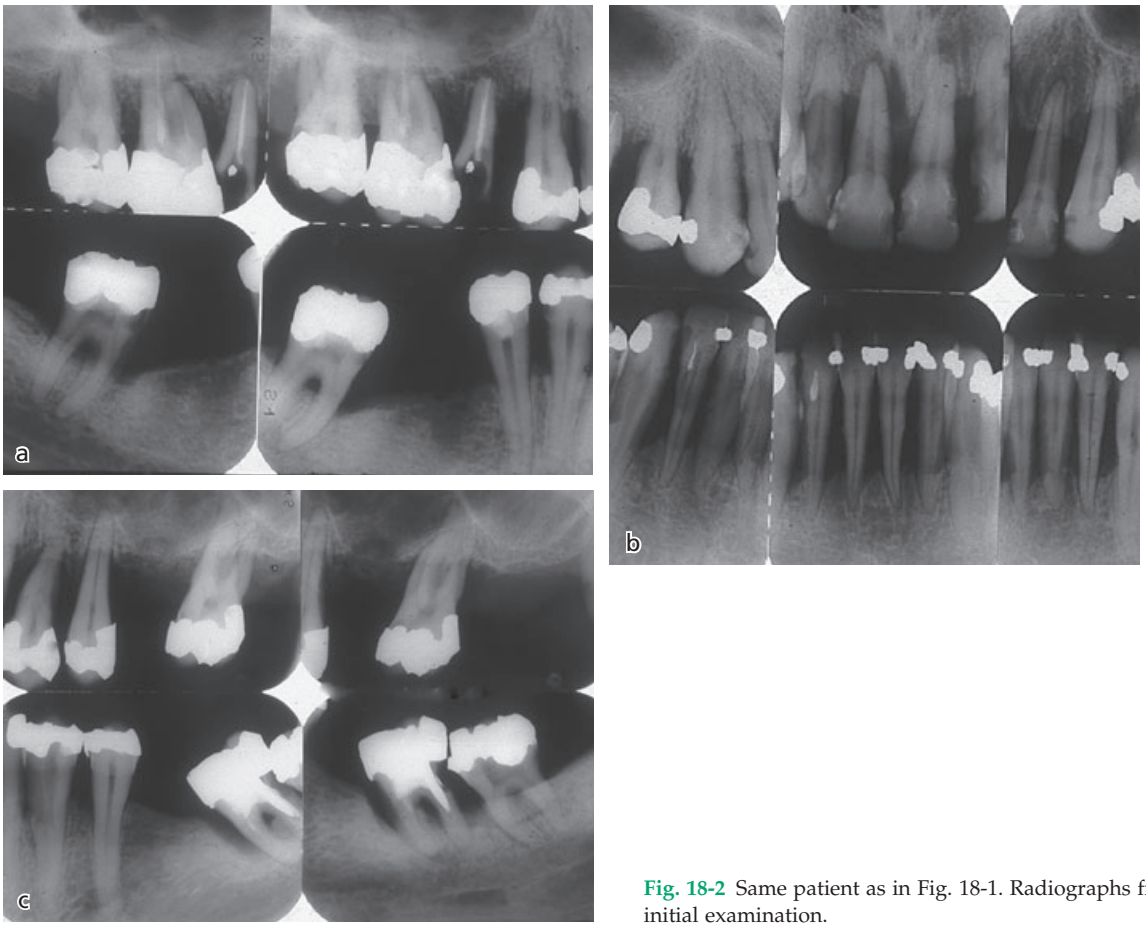

Fig. 18-2 Same patient as in Fig. 18-1. Radiographs from the initial examination.

mine the pathogenesis and (rate of) progression of the disease.
- The rate of progression of chronic periodontitis is in most cases slow to moderate; periods of rapid tissue destruction may, however, occur.
- Additional periodontal tissue breakdown is likely to occur in diseased sites that are left untreated.

Gingivitis as a risk for chronic periodontitis

Findings from epidemiologic studies (cross-sectional as well as longitudinal) indicate that gingival inflammation is invariably a component of chronic periodontitis and that gingivitis precedes the onset of periodontitis (see Chapter 11). The interpretation of data from early cross-sectional studies led to the belief that untreated gingivitis always progressed to chronic periodontitis. More recent studies have demonstrated, however, that this is not the case. Gingivitis lesions may remain stable for many years, and may never progress to become periodontitis lesions that include features such as attachment and bone loss. The two conditions have been considered, therefore, as separate disease entities with the explanation being that the bacterial plaque challenge will induce overt gingivitis but that the degree of response of the host (the susceptibility) will determine whether or not chronic periodontitis will develop. In a review paper, Kinane and Attström (2005) evaluated epidemiologic and experimental data on gingivitis and chronic periodontitis. The independence of these two conditions was called into question. It was proposed that gingivitis and periodontitis most likely represented different aspects of the same disease, namely chronic periodontitis.

Gingivitis becomes manifest after only days or weeks of plaque accumulation (Löe *et al*. 1965) while destructive chronic periodontitis is a condition that in the majority of cases requires far longer periods (years) of plaque and calculus exposure to develop (Lindhe *et al*. 1975; Löe *et al*. 1978). The proportion of untreated gingival lesions in a given subject or in a population that converts to destructive periodontitis lesions is at present unknown. Furthermore, the factors that cause the conversion are not well understood (Schätzle *et al*. 2003).

Findings from epidemiologic studies and prospective clinical trials have indicated that the presence of gingivitis may be regarded as a risk factor for chronic periodontitis. In a 2-year longitudinal study of 15–24-year-old Chinese adolescents from a rural district, it was observed that the percentage of sites that bled on probing at a baseline examination was related to overall attachment loss after 2 years of monitoring (Suda *et al*. 2000). This suggests that gingival inflammation was a risk indicator for additional attachment loss in this cohort. The role of gingivitis in the pathogenesis of chronic periodontitis was further elucidated by Schätzle *et al*. (2004) in longitudinal studies on the initiation and progression of periodontal disease in a Norwegian population. The results demonstrated that gingival sites, which during a 20-year interval never showed signs of inflammation, experienced modest loss of attachment (1.86 mm). For sites which presented with mild inflammation at each examination, the corresponding attachment loss was 2.25 mm, while at sites with severe gingival inflammation, the mean loss of attachment was 3.23 mm. Moreover, while teeth surrounded with healthy gingival tissues were maintained during the study period, teeth with gingivitis lesions were 46 times more likely to be lost.

The above data indicate that gingival inflammation may represent a relevant risk factor not only for destructive chronic periodontitis but also for tooth loss. This conclusion is in agreement with results documenting the absence of gingivitis as a good indicator for long-term maintenance of periodontal health in a subject (Joss *et al*. 1994) as well as at a site (Lang *et al*. 1990) level.

Susceptibility to chronic periodontitis

As stated above plaque-induced gingivitis and chronic periodontitis represent different aspects of the same disease (Kinane & Attström 2005). An important question is whether both gingivitis and chronic periodontitis are affected by the same subject response (the host response) to plaque. If this is the case, the corollary is that susceptibility to gingivitis will reflect susceptibility to chronic periodontitis and may have prognostic utility.

Even in the very first reports from studies called "Experimental gingivitis in man" (Löe *et al*. 1965; Theilade *et al*. 1966) (see Chapters 11 and 17), evidence was presented that suggested that the onset and severity of the inflammatory response of the gingiva to plaque accumulation differed markedly among participants. The differences were, however, at that time attributed to differences in plaque accumulation rates (quantitative plaque differences) and/or differences in bacterial species present in plaque (qualitative plaque differences). More recent studies utilizing the "Experimental gingivitis" model have documented that significant differences in the inflammatory response occurred in different subjects although their plaque accumulation was quantitatively and/or qualitatively similar (Trombelli *et al*. 2004, 2005). It was suggested that the intensity of the inflammatory response to the plaque challenge may represent an individual trait (Tatakis & Trombelli 2004). Thus, an individual's susceptibility to gingivitis may be dependent on host-related factors, possibly of genetic origin (Shapira *et al*. 2005; Scapoli *et al*. 2005).

With the use of the "Experimental gingivitis" model it was also demonstrated that the susceptibility to gingivitis differed between two groups of patients consistent with different susceptibilities to

periodontitis (Abbas *et al*. 1986; Winkel *et al*. 1987). Thus, the group with greater periodontitis susceptibility had also a greater susceptibility to gingivitis. Furthermore, in more recent studies it was documented that subjects with a history of aggressive periodontitis presented significantly more gingivitis in response to *de novo* plaque accumulation when compared to periodontally healthy subjects matched for extent and rate of supragingival plaque accumulation (Trombelli *et al*. 2006).

Prevalence of chronic periodontitis

From epidemiologic studies (see Chapter 7) it was concluded that chronic periodontitis is the most commonly occurring form of periodontal disease. While most subjects over 50 years of age have suffered moderate amounts of periodontal tissue destruction, advanced forms of chronic periodontitis are seen in only a small (<10%) subset of the population. Both age of onset of chronic periodontitis and subsequent rate of progression of the disease vary between individuals and are probably influenced by genetics (see Chapter 13) and environmental risk factors (see Chapters 7 and 12). Findings from examination of dizygotic and monozygotic twins (Michalowicz *et al*. 1991, 2000) indicated that (1) between 38% (regarding probing attachment loss) and 82% (regarding gingivitis) of the population variance could be attributed to genetic factors (Michalowicz *et al*. 1991), and (2) chronic periodontitis has about 50% heritability (Michalowicz *et al*. 2000).

On a population basis chronic periodontitis is often classified according to number (prevalence) of diseased sites (extent) and severity of tissue breakdown (probing attachment loss) at such sites. For the extent of chronic periodontitis, the low category would involve one to ten diseased (probing attachment loss) sites, the medium category would involve 11–20 sites, while the high category would involve more than 20 diseased sites. The amount of PAL at a given site may be used to describe the severity of chronic periodontitis. The severity may be considered as mild (PAL = 1–2 mm), moderate (PAL= 3–4 mm) or severe (PAL ≥ 5 mm). It has been documented that the extent and severity of chronic periodontitis are useful predictors of future disease progression.

Clinical (probing) attachment loss of 1–2 mm at one or several sites can be found in nearly all members of an adult population. The prevalence of subjects with one or more sites with PAL ≥ 3 mm increases with age. Furthermore the number of diseased sites in any one individual increases with age, as does the population prevalence (extent and severity) of chronic periodontitis with age.

Progression of chronic periodontitis

Chronic periodontitis is generally a slowly progressing form of periodontal disease that at any stage may undergo exacerbation resulting in additional loss of attachment and bone.

Tissue destruction in chronic periodontitis does not affect all teeth evenly, but has site predilection. In other words, in the same dentition some teeth may be severely affected with periodontal tissue destruction while other teeth are almost free of signs of attachment and bone loss. Figure 18-3 illustrates the clinical condition of a subject with chronic periodontitis. Clinically (Fig. 18-3a) it can be observed that most teeth exhibit advanced recession of the soft tissue margin. In the corresponding radiographs (Fig. 18-3b) it is noted that the mesial surface of tooth 16 has a normal periodontal tissue support, while the neighboring tooth, i.e. the first premolar (tooth 14), has lost several millimeters of bone support on the distal aspect. The mesial surface of tooth 14, on the

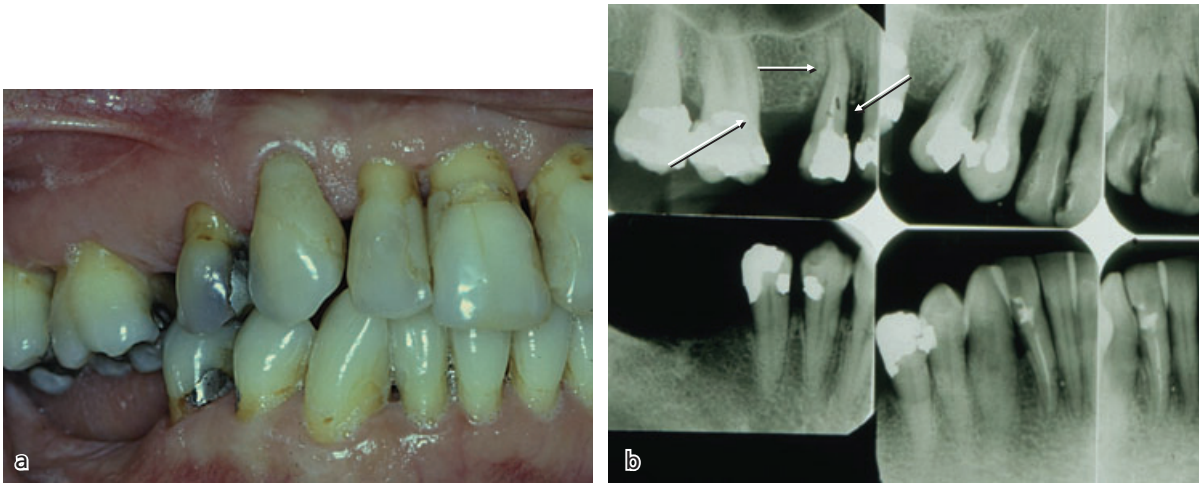

Fig. 18-3 (a) The clinical condition in quadrants 1 and 3 of a subject with chronic periodontitis. Most teeth in both quadrants exhibit advanced recession of the soft tissue margin. (b) Corresponding radiographs: the mesial surface of tooth 16 (arrow) has a normal periodontal tissue support, while the neighboring tooth, tooth 14, has lost several millimeters of bone support on the distal aspect (arrow). The mesial surface of tooth 14 has a comparatively normal tissue support (arrow).

other hand, has a comparatively normal tissue support.

When considering changes in attachment level over time, it is also peculiar that only relatively few sites in a subject with chronic periodontitis undergo marked, additional tissue destruction during any given observation period. Based on data from a series of longitudinal studies, Socransky *et al*. (1984) proposed that chronic periodontitis progressed in episodes of exacerbation and remission. They termed this the "burst hypothesis" of disease progression. Findings from other similar studies, however, indicated that the progression of chronic periodontitis may be a continuous, slowly destructive process rather than exhibiting a "burst" pattern. The current consensus is that the progression of chronic periodontitis in most subjects and at most sites is a continuous process but that periods of exacerbation occasionally may occur. Clinically, the progressive nature of the disease can only be confirmed by repeated examinations over time but it is a safe assumption that untreated lesions of chronic periodontitis will progress and cause additional attachment and bone loss. Flemmig (1999) reported a mean additional PAL of ≥3 mm in up to 27% of subjects in untreated populations during a 1-year period. When progression was studied on a site basis, the overall annualized incidence ranged from 0.3–4.2% (Flemmig 1999). This indicates that the number of sites that actually exhibited progression within a given time varied considerably between subjects.

It is important to realize that factors associated with the initiation of chronic periodontitis may also influence disease progression. Furthermore, the extent and severity of disease within an individual, i.e. number of sites with attachment loss, bone loss, and/or deep pockets, are good predictors of future disease occurrence. In fact the best predictor of disease progression is previous disease experience.

Risk factors for chronic periodontitis

The term "risk factor" means an aspect of lifestyle, an environmental exposure, or an inborn or inherited characteristic, which on the basis of epidemiologic evidence is known to be associated with a given disease. Risk factors may be part of the causal chain of a disease and/or may predispose the host to develop a disease. An individual presenting with one or more risk factors has an increased probability of contracting the disease or of the disease being made worse.

Bacterial plaque

Bacterial aspects of periodontal disease are dealt with in Chapters 8 and 9. From the data presented it is obvious that a cumulative risk for a given microbiota can be estimated. It is not clear, however, if the specific microbiota is the principal disease-causing factor or whether it reflects the disease process. Specific microorganisms have been considered as potential periodontal pathogens but it is clear that, although pathogens are necessary, their mere presence may not be enough for the progressive disease to occur. Microbial plaque (biofilm) is a crucial factor in inflammation of the periodontal tissues, but the progression of gingivitis to periodontitis is largely governed by host-based risk factors (Michalowicz 1994; Shapira *et al*. 2005). Microbial biofilms of particular compositions will initiate chronic periodontitis (Marsh 2005) in certain individuals whose host response and cumulative risk factors predispose them to periodontal tissue destruction and attachment loss.

Age

Although the prevalence of periodontal disease increases with age it is unlikely that becoming older in itself greatly increases susceptibility to periodontal disease. It is more likely that the cumulative effects of disease over a lifetime, i.e. deposits of plaque and calculus, and the increased number of sites capable of harboring such deposits, as well as attachment and bone loss experience, explain the increased prevalence of disease in older people.

Smoking

The association between periodontal disease and smoking is dealt with in detail in Chapter 12. Only a brief discussion of smoking as a risk factor for chronic periodontitis is thus given here. The literature consistently indicates a positive association between smoking and chronic periodontitis across the many cross-sectional and longitudinal studies performed over the years (Kinane & Chestnutt 2000) and the risk attributable to tobacco for chronic periodontitis is between 2.5 and 7.0. It is not only the risk of developing the disease that is enhanced by smoking, but also the response to periodontal therapy is impaired in smokers. A further feature in smokers is that their signs and symptoms of both gingivitis and chronic periodontitis, mainly gingival redness and bleeding on probing (BOP), are masked by the dampening of inflammation seen for smokers as compared to non-smokers.

Systemic disease

It is difficult to determine the precise role any systemic disease may play in the pathogenesis of chronic periodontitis. There are several reasons for this. Firstly, in epidemiologic studies attempting to evaluate the effect of systemic disease, control groups should be carefully matched in respect of age, sex, oral hygiene, and socioeconomic status. Many studies, particularly before the etiologic importance of dental plaque was recognized, failed to include such controls. Secondly, because of the chronic nature of periodontal disease, longitudinal studies spanning several years are preferable in individuals both with

and without systemic disease. Unfortunately, most of the available data are derived from cross-sectional studies (Kinane 1999).

A reduction in number or function of polymorphonuclear leukocytes (PMNs) generally results in increased rate and severity of periodontal tissue destruction (Wilton *et al*. 1988). Many drugs, such as phenytoin, nifedipine, and cyclosporine, predispose to gingival overgrowth in response to plaque and thus may modify pre-existing chronic periodontitis (Ellis *et al*. 1999). Changes in circulating hormone levels may increase severity of plaque-induced gingival inflammation but typically do not result in any increased susceptibility to periodontitis. Hormonal changes following menopause have been associated with osteoporosis but studies are lacking to link this disease or an estrogen deficient state to a higher susceptibility to periodontal disease. Immunosuppressive drug therapy and any disease resulting in suppression of inflammatory and immune processes (such as HIV infection) may predispose the individual to exaggerated periodontal tissue destruction (Barr *et al*. 1992).

Nutritional deficiencies in animals have been shown to affect the periodontal tissues. Epidemiologic data do not support the suggestion that such deficiencies play an important role in chronic periodontal disease although nutritional influences on inflammation are now accepted and are now actively being researched (Ritchie & Kinane 2005). Gingival bleeding is the most consistent oral feature of vitamin C deficiency or scurvy but there is also some evidence to suggest that avitaminosis-C may aggravate established chronic periodontitis.

The periodontal features of *histiocytosis X* and other conditions in the rare histiocytoses disease group may present as necrotizing ulcerative periodontitis (Kinane 1999). Diabetes appears to be one of the most fascinating systemic diseases that interacts with periodontitis. On the one hand periodontitis severity and prevalence are increased in subjects with long-duration diabetes and more so in poorly controlled diabetics, than non-diabetics. On the other hand, periodontitis may also exacerbate diabetes as it may decrease glycemic control (Thorstenson 1995).

Despite the paucity of high quality data on individuals both with and without systemic disease the following general conclusions can be drawn (Kinane 1999):

- The *blood cells* have a vital role in supplying oxygen, hemostasis and protection to the tissues of the periodontium. Systemic hematological disorders can thus have profound effects on the periodontium by denying any of these functions necessary for the integrity of the periodontium.
- The *polymorphonuclear leukocyte* (PMN cell) is undoubtedly crucial to the defense of the periodontium. To exert this protective function several activities of PMNs must be integrated, namely chemotaxis, phagocytosis, and killing or neutralization of the ingested organism or substance. Individuals with either quantitative (neutropenia) or qualitative (chemotactic or phagocytic) PMN deficiencies, exhibit severe destruction of the periodontal tissues, which is strong evidence that PMNs are an important component of the host's protective response to the subgingival biofilm. Quantitative deficiencies are generally accompanied by destruction of the periodontium of all teeth, whereas qualitative defects are often associated with localized destruction affecting only the periodontium of certain teeth (i.e. chronic periodontitis may be modified).
- *Leukemias* which give excessive numbers of leukocytes in the blood and tissues also cause a greatly depleted bone marrow function with concomitant anemia, thrombocytopenia, neutropenia, and reduced range of specific immune cells which give some characteristic periodontal features: anemic gingival pallor; gingival bleeding; gingival ulceration. Leukemic features are further complicated by the potential for the proliferating leukocytes to infiltrate the gingiva and result in gingival enlargement. In broad terms leukemias result in gingival pathologies, whereas periodontal bone loss is the consequence of neutrophil functional defects or deficient numbers and other severe functional defects such as deficiency of leukocyte adhesion receptors.
- *Diabetes mellitus:* there are numerous confounding variables which must be considered in determining the true relationship between periodontitis and diabetes. The current consensus is that diabetics are at increased risk of periodontal disease, and whilst periodontitis can be successfully treated, both disease susceptibility and the outcome of therapy are influenced by poor metabolic control. Thus, it may be of benefit to the dentist to have knowledge of the control status of diabetes in an individual patient, as in the longer term metabolic control could indicate the probable outcome of periodontal therapy. In addition, it is now accepted that periodontal therapy can improve metabolic control in diabetics, meaning that the relationship is two-way and periodontal therapy is beneficial to the control of both diseases.
- *Medications* such as phenytoin, cyclosporine, and nifedipine may predispose to gingival overgrowth in patients with gingivitis.
- *Genetic traits*, which result in diseases that modify the periodontal structures or change the immune or inflammatory responses, can result in gross periodontal destruction in the affected individual; although the destruction seen may imitate periodontitis, this is not etiopathologically chronic periodontitis.

Stress

Stressful life events and negative emotions have been shown to modulate several physiologic systems,

including the endocrine and the immune system, leading to health changes (Kiecolt-Glaser *et al*. 2002; LeResche & Dworkin 2002). The association between stress and disease is particularly strong for infectious diseases, inflammatory conditions, and impaired wound healing (Kiecolt-Glaser *et al*. 2002; LeResche & Dworkin 2002; Broadbent *et al*. 2003). Specific periodontal conditions have been associated with psychosocial variables, including chronic periodontitis (Green *et al*. 1986; Linden *et al*. 1996; Genco *et al*. 1999; Wimmer *et al*. 2002; Pistorius *et al*. 2002), necrotizing ulcerative gingivitis (Shields 1977; Cohen-Cole *et al*. 1983; Horning & Cohen 1995), chronic and experimental gingivitis (Minneman *et al*. 1995; Deinzer *et al*. 1998; Waschul *et al*. 2003). In adults, the reported contribution of psychosocial factors to enhanced gingivitis expression (Deinzer *et al*. 1998) may relate to the stress-associated increase in plaque accumulation (Deinzer *et al*. 2001). However, the possible association of other psychosocial variables, such as personality traits and coping behavior, which are associated with either susceptibility or resistance to stress, with changes in the inflammatory response of the gingiva to *de novo* plaque accumulation, remains uncertain (Trombelli *et al*. 2005).

Most of the literature on stress and periodontal conditions is quite old, and reports of acute necrotizing ulcerative gingivitis (or trench mouth) were made on stressed soldiers on the front line during World War I. It is understood that stress may be immunosuppressive and that acute necrotizing ulcerative gingivitis may occur in the immunosuppressed (also in HIV patients), but there is insufficient data as yet to substantiate the assumption that psychosocial factors are indeed of etiologic importance in chronic periodontitis.

Genetics

There is convincing evidence from twin studies for a genetic predisposition to the periodontal diseases. The twin studies have indicated that risk of chronic periodontitis has a high inherited component. A great deal of research is underway attempting to identify the genes and polymorphisms associated with all forms of periodontitis. It is likely that chronic periodontitis involves many genes, the composition of which may vary across individuals and races. Much attention has focused on polymorphisms associated with the genes involved in cytokine production (Shapira *et al*. 2005). Such polymorphisms have been linked to an increased risk for chronic periodontitis but these findings have yet to be corroborated (Kinane & Hart 2003; Kinane *et al*. 2005).

Scientific basis for treatment of chronic periodontitis

Chronic periodontitis is initiated and sustained by microorganisms living in biofilm communities which are present in supra- and subgingival plaque in the form of uncalcified and calcified biofilms. Prevention of initiation or primary prevention of periodontitis is clearly related to preventing formation and/or eradication of the microbial biofilm and it follows that prevention of gingivitis is a primary preventive measure for chronic periodontitis. Initial periodontal therapy or basic treatment of periodontitis involves the removal of both sub- and supragingival plaque. The clinical outcome is largely dependent on the skill of the operator in removing subgingival plaque and the skill and motivation of the patient in practicing adequate home care. A further variable is the innate susceptibility of the patient which is related to the way in which their innate, inflammatory, and immune systems operate in response to the microbial challenge. In addition, local and systemic risk factors can influence the quantity and quality of both the microbial challenge and the host response to these pathogens. The relative contribution of these risk factors has yet to be fully determined but their influence would be limited if the periodontium were kept free of microbial plaque. Thus, sub- and supragingival debridement and the quality of the patient's home care are of vital importance in preventing inflammation that manifests as both gingivitis and periodontitis.

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Chapter 19

Aggressive Periodontitis

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Periodontitis is an infection that can have many different clinical presentations. This has led to the recognition of different clinical syndromes. Until recently, the question of whether or not these dissimilar clinical presentations represented different forms of disease has been open to discussion. Today several lines of evidence support the existence of truly different forms of periodontitis. These include:

1. The growing clinical consensus of differential prognosis and need for specific treatment approaches for the various syndromes
2. Heterogeneity in etiology with possible therapeutic implications
3. Heterogeneity in genetic and environmental susceptibility.

At the 1999 international classification workshop, the different forms of periodontitis were reclassified into three major forms (chronic, aggressive, and necrotizing forms of periodontitis) and into periodontal manifestations of systemic diseases. This chapter deals with aggressive, type 1, periodontitis. Until recently, this group of diseases was defined primarily based on the age of onset/diagnosis and was thus named early onset periodontitis (EOP). Features of this form of disease, however, can present themselves at any age and this form of periodontitis is not necessarily confined to individuals under the arbitrarily chosen age of 35.

Aggressive periodontitis (AgP) comprises a group of rare, often severe, rapidly progressive forms of periodontitis often characterized by an early age of clinical manifestation and a distinctive tendency for cases to aggregate in families. At the above mentioned classification workshop, AgP was characterized by the following major common features (Lang *et al*. 1999):

- Non-contributory medical history
- Rapid attachment loss and bone destruction
- Familial aggregation of cases.

Frequently AgP presents early in the life of the individual; this implies that etiologic agents have been able to cause clinically detectable levels of disease over a relatively short time. This fact is central to the current understanding of these diseases, since it implies infection with a highly virulent microflora and/or a high level of subject susceptibility to periodontal disease. AgP, however, can occur at any age. Diagnosis of AgP requires exclusion of the presence of systemic diseases that may severely impair host defenses and lead to premature tooth loss (periodontal manifestations of systemic diseases).

The existence of specific forms of AgP has also been recognized based on specific clinical and laboratory features: localized aggressive periodontitis (LAP, formerly known as localized juvenile periodontitis or LJP) and generalized aggressive periodontitis (GAP, formerly termed generalized juvenile periodontitis (GJP) or generalized early onset periodontitis, G-EOP) (Tonetti & Mombelli 1999).

In spite of its rare occurrence AgP has been the focus of many investigations aimed at understanding its etiology and pathogenesis. Difficulties in gathering sufficiently large populations, however, have resulted in few clinical studies addressing both diagnostic and therapeutic procedures for these subjects. Utilization of both clinical and advanced diagnostic

procedures as well as a variety of treatment approaches remains largely anecdotal and based on the specific experience of individual clinicians rather than on well documented scientific evidence.

Classification and clinical syndromes

In the absence of an etiologic classification, aggressive forms of periodontal disease have been defined based on the following primary features (Lang *et al*. 1999):

- Non-contributory medical history
- Rapid attachment loss and bone destruction
- Familial aggregation of cases.

Secondary features that are considered to be generally but not universally present are:

- Amounts of microbial deposits inconsistent with the severity of periodontal tissue destruction
- Elevated proportions of *Actinobacillus actinomycetemcomitans* (recently renamed *Aggregatibacter actinomycetemcomitans*) and, in some Far East populations, *Porphyromonas gingivalis*
- Phagocyte abnormalities
- Hyper-responsive macrophage phenotype, including elevated production of prostaglandin E_2 (PGE_2) and interleukin-1β (IL-1β) in response to bacterial endotoxins
- Progression of attachment loss and bone loss may be self-arresting.

The international classification workshop identified clinical and laboratory features deemed specific enough to allow subclassification of AgP into localized and generalized forms (Lang *et al*. 1999; Tonetti & Mombelli 1999). The following features were identified:

- *Localized aggressive periodontitis* (LAP) (Fig. 19-1):
  - Circumpubertal onset
  - Localized first molar/incisor presentation with interproximal attachment loss on at least two permanent teeth, one of which is a first molar, and involving no more than two teeth other than first molars and incisors
  - Robust serum antibody response to infecting agents
- *Generalized aggressive periodontitis* (GAP) (Fig. 19-2):
  - Usually affecting persons under 30 years of age, but patients may be older
  - Generalized interproximal attachment loss affecting at least three permanent teeth other than first molars and incisors
  - Pronounced episodic nature of the destruction of attachment and alveolar bone
  - Poor serum antibody response to infecting agents.

Diagnosis of one of these AgP forms requires the absence of systemic diseases that may severely impair host defenses and lead to premature exfoliation of teeth. In such instances the appropriate clinical diagnosis will be periodontal manifestation of systemic disease.

GAP represents the most heterogeneous group and includes the most severe forms of periodontitis. They comprise forms originally described as generalized juvenile periodontitis (emphasis on a possible relationship with LAP), severe periodontitis (emphasis on the advanced destruction in comparison with patient age), or rapidly progressing periodontitis (emphasis on the fast rate of progression of lesions in these forms). Each of these GAP forms, however, remains highly heterogeneous in terms of clinical presentation and response to therapy. The European Workshop on Periodontology has therefore suggested that, while a better etiologic classification remains unavailable, these forms should be considered as a group to be further defined by the use of various clinical descriptors of the disease based on clinical, microbiologic, and immunologic parameters (Attström & Van der Velden 1993). Further rationale for an imprecise classification of these GAP forms comes from the fact that, given the severity of the disease and the heterogeneity of clinical presentation, each of these rare cases deserves individual consideration.

Subjects often present with attachment loss that does not fit the specific diagnostic criteria established for AgP or chronic periodontitis; this occurrence has been termed *incidental attachment loss*. It includes: recession associated with trauma or tooth position; attachment loss associated with impacted third molars; attachment loss associated with removal of impacted third molars, etc. It may include initial clinical presentations of periodontitis. Patients with this clinical diagnosis should be considered as a high-risk group for AgP or chronic periodontitis.

Besides clinical presentation, a variety of radiographic, microbiologic, and immunologic parameters are currently being used, along with the assessment of environmental exposures such as cigarette smoking, to further describe the AgP affecting the individual subject. These descriptors are important in treatment selection and to establish long-term prognosis. They will be further discussed in the section on diagnosis later in this chapter.

It is also important to underline that, in the present state of uncertainty regarding both the causative agents and the genetic and environmental susceptibility to AgP, it is possible that, in spite of the lines of evidence presented above, LAP and GAP may simply represent phenotypic variations of a single disease entity. Conversely, it is possible that different AgP forms may manifest themselves with a common clinical presentation. This aspect is of great diagnostic and therapeutic importance.

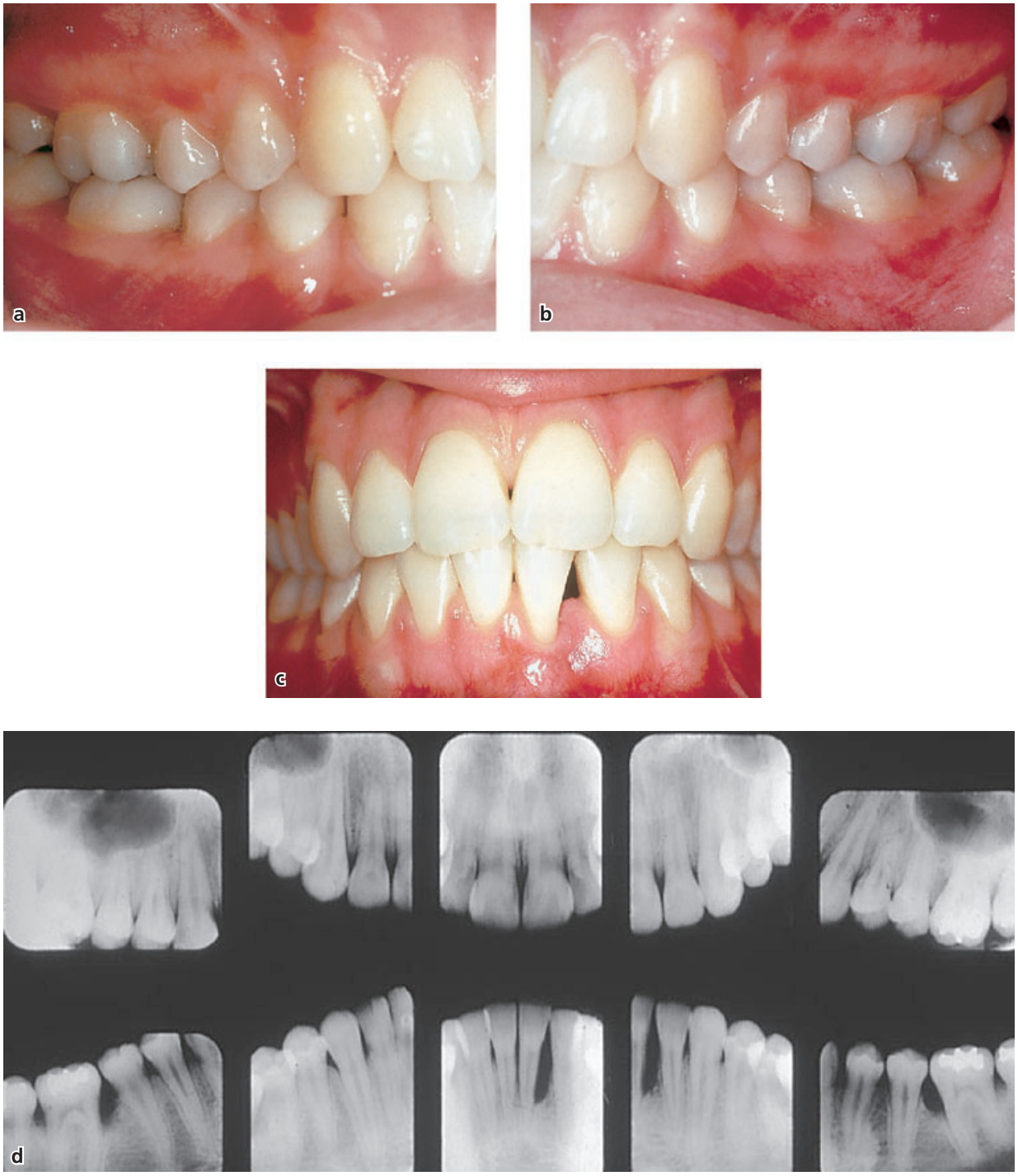


Fig. 19-1 (a–c) Clinical appearance of the periodontal tissues of a 15-year-old girl suffering from localized aggressive periodontitis. Note the proper oral hygiene conditions and the scalloped outline of the gingival margin. In the lower anterior region, the interdental papilla between teeth 31 and 32 has been lost. (d) Intraoral radiographs show the presence of localized angular bony defects, associated with clinical attachment level loss, at the mesial aspect of tooth 46, 36 and at the distal aspect of tooth 31. No significant bone loss and/or attachment loss was detectable in other areas of the dentition. Diagnosis: localized aggressive periodontitis (LAP). (e–g) Clinical appearance of the 14-year-old sister of the proband depicted in (a–d). Note that in spite of the excellent oral hygiene status, bleeding on probing was provoked in the mesial of the molars, where deep pockets were present. (h) Angular bone loss is evident on the mesial of 16, 26 and 46.

Some case reports have indicated that some subjects may experience periodontitis affecting the primary dentition, followed by LAP and later by GAP (Shapira *et al*. 1994). One investigation indicated that the primary dentition of LAP patients presented bone loss at primary molars in 20–52% of cases, suggesting that at least some LAP cases may initially affect the primary dentition (Sjodin *et al*. 1989, 1993). Furthermore, in LAP subjects an association between the number of lesions and the age of the subject has

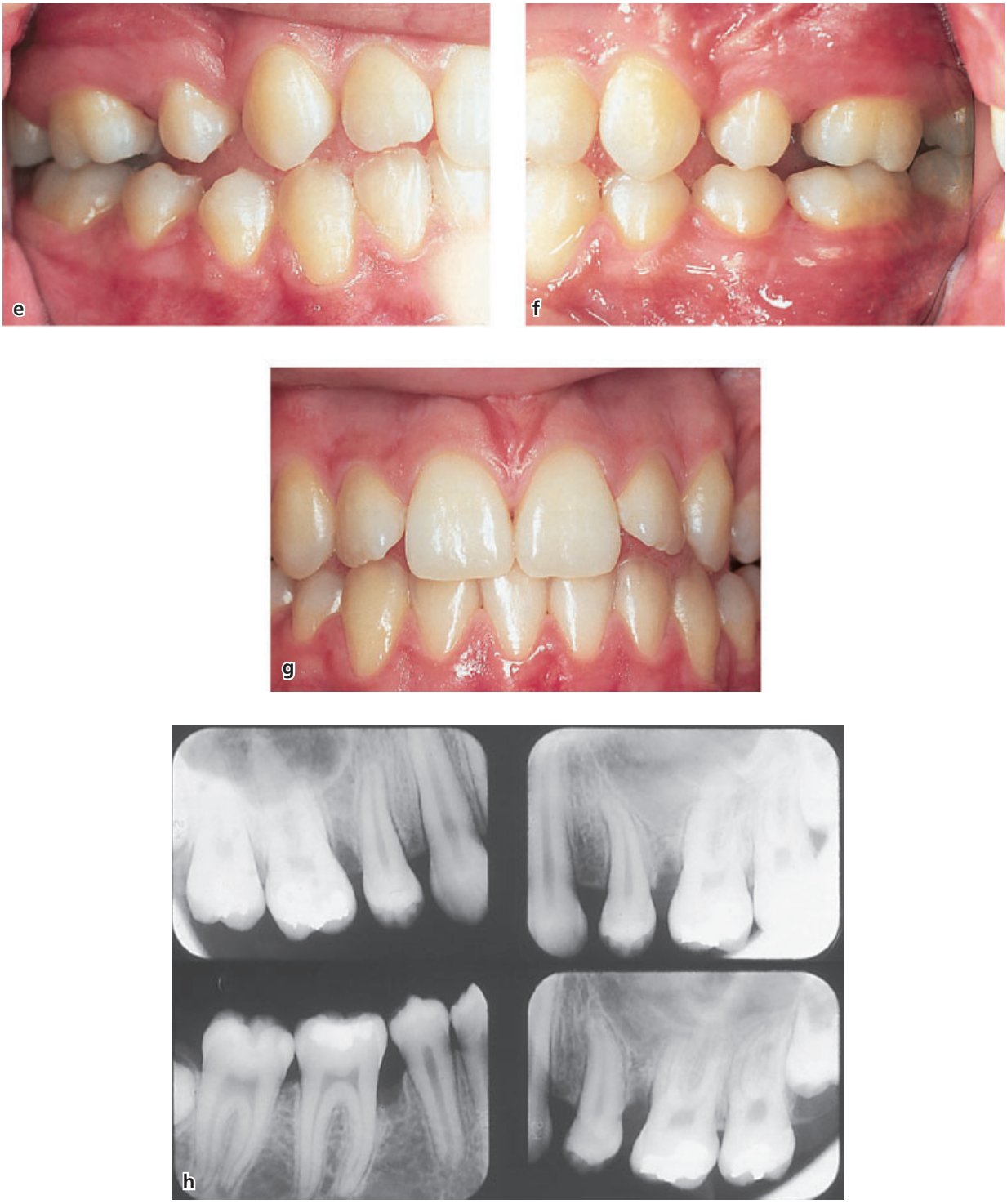


Fig. 19-1 *Continued*

been described, suggesting an age-dependent shift from localized to generalized forms of AgP (Hormand & Frandsen 1979; Burmeister *et al*. 1984).

Epidemiology

Given the recent definition of AgP and the fact that it does not represent just a new term for the previously defined EOP, epidemiologic studies available relate primarily to EOP. Relatively few investigations employing different epidemiologic techniques have estimated the prevalence and the progression of EOP in the primary and permanent dentition(s) of children and young adults. All available investigations, however, indicate that early onset (aggressive) forms of periodontal diseases are detectable in all age and ethnic groups (Papapanou 1996). Wide variation in prevalence, however, has been reported, with some

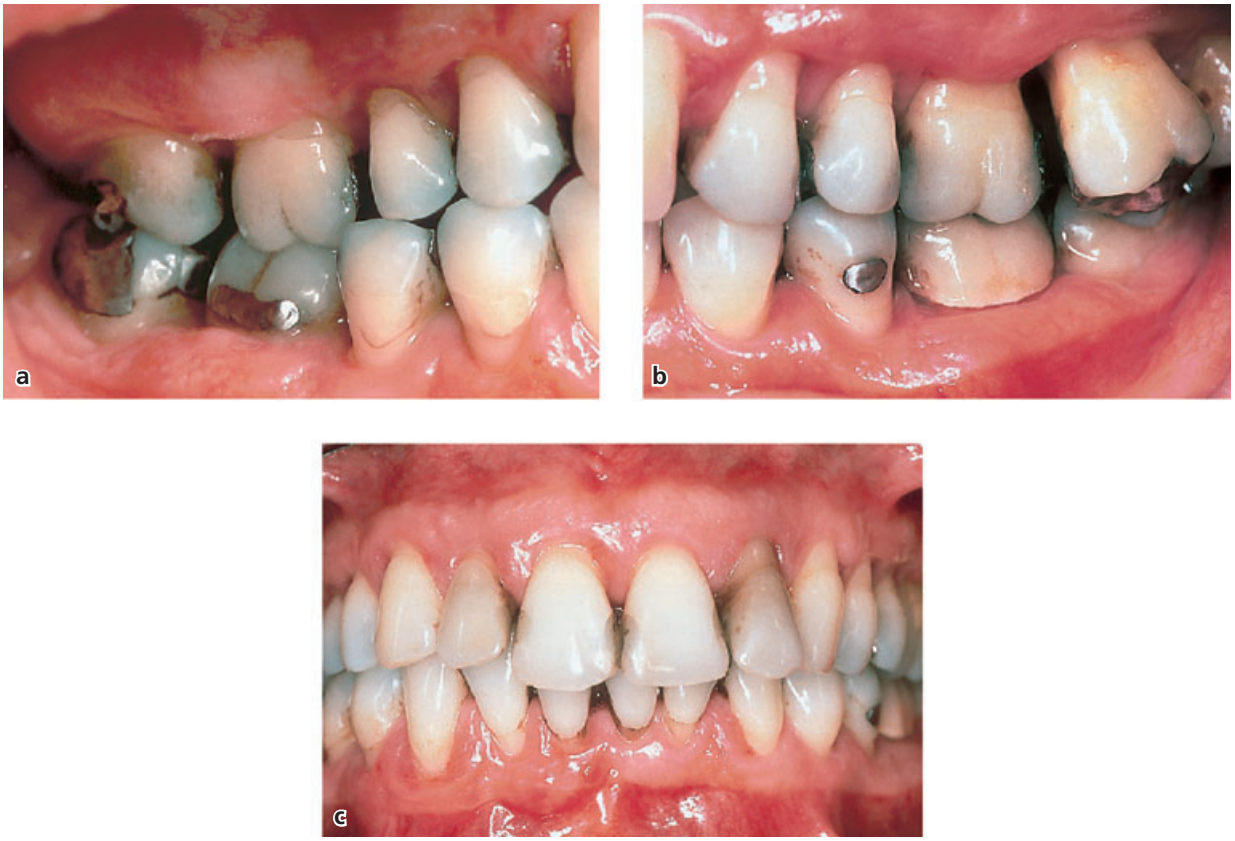


Fig. 19-2 (a–c) Clinical presentation in 1990 of a 32-year-old female with generalized severe bone loss and clinical attachment loss, recession of the gingival margin and presence of deep periodontal pockets. Presence of local factors, and intense inflammation and edema of the gingival margin are evident. (d–f). Previous radiographic examinations were available from 1984 and 1987. Comparison of the radiographs obtained over the 6-year period from 1984 to 1990 indicates that most of the periodontal destruction occurred during the last 3 years. The patient had been smoking 20 cigarettes/day for more than 10 years. Diagnosis: generalized aggressive periodontitis (GAP) in a cigarette smoker.

studies showing up to 51.5% affected individuals. These differences are probably due to differences in the employed epidemiologic methodologies and definition of EOP.

Primary dentition

Little evidence is available concerning the prevalence of AgP affecting the primary dentition. In the few studies from industrialized countries, marginal alveolar bone loss has been found to affect the primary dentition of 5–11-year-olds with frequencies ranging from 0.9–4.5% of subjects (Sweeney *et al*. 1987; Bimstein *et al*. 1994; Sjodin & Mattson 1994). In this respect, it should be emphasized that periodontitis affecting the primary dentition does not necessarily mean presence of an aggressive form of periodontitis, but may indicate a chronic form of disease with relative abundance of local factors (plaque and calculus). A clinical case of localized periodontitis affecting the primary dentition is illustrated in Fig. 19-3. More severe cases affecting the primary dentition and leading to tooth exfoliation early in life are usually interpreted as periodontal manifestations of systemic (hematologic) diseases, such as leukocyte adhesion deficiency (see Chapter 7 and Fig. 19-4).

Permanent dentition

In the permanent dentition of 13–20-year-old individuals, the majority of studies have reported a prevalence of periodontitis of less than 1% (usually 0.1–0.2% in Caucasian populations). The risk of developing periodontitis at such an early age, however, does not seem to be shared equally in the population: among US schoolchildren 5–17 years of age, the prevalence of periodontitis has been estimated to range from about 0.2% for white subjects to about 2.6% for black subjects (Löe & Brown 1991). Furthermore, in these young age groups higher prevalence of periodontitis has been reported in studies from some developing countries (see Chapter 7).

Longitudinal studies of disease progression in adolescents indicate that subjects with signs of destructive periodontitis at a young age are prone to further deterioration. Such deterioration appears to be more pronounced at initially affected sites, and in patients diagnosed with LAP and from low socioeconomic groups. Deterioration of the periodontal status involves both an increase in extent (number of lesions within the dentition) and in severity of lesions (further alveolar bone loss at initially diseased sites) (Fig. 19-5)

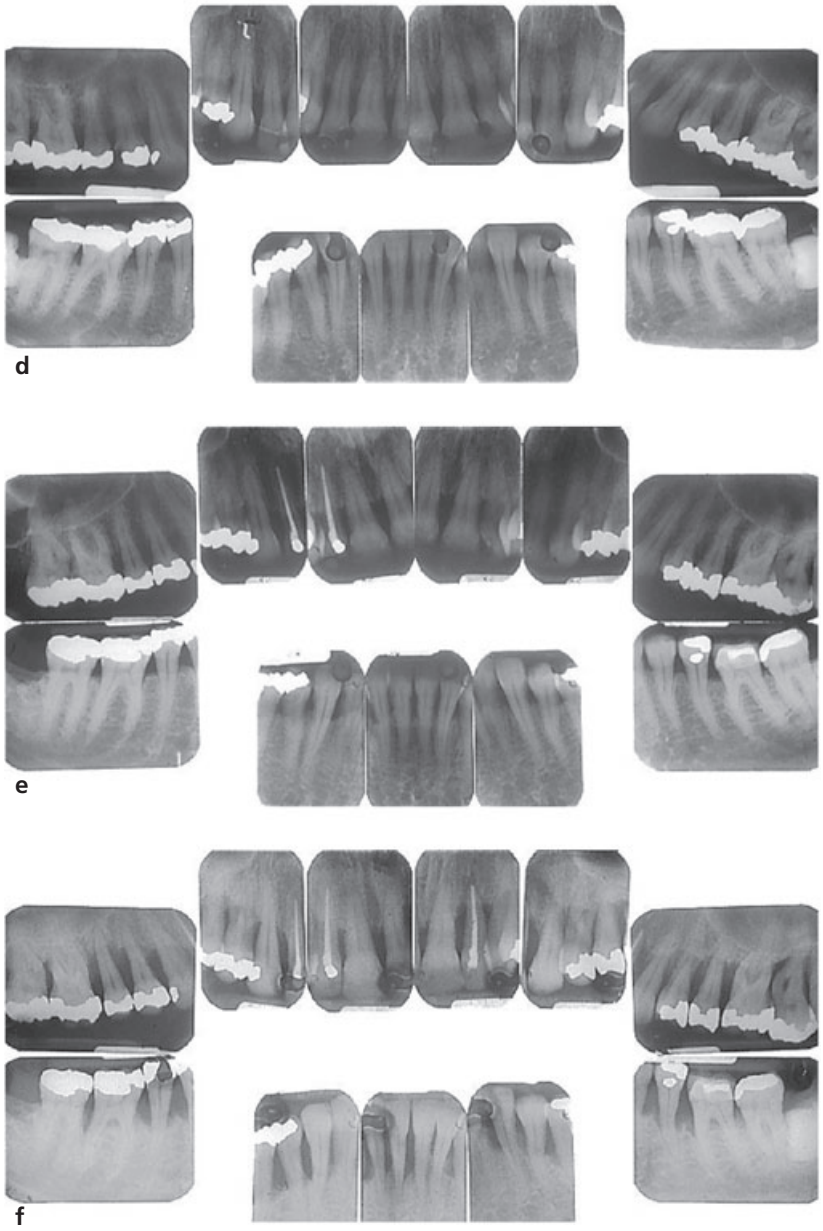


Fig. 19-2 *Continued*

(Clerehugh *et al*. 1990; Lissau *et al*. 1990; Albandar *et al*. 1991a,b; Albandar 1993; Aass *et al*. 1994).

Some epidemiologic investigations have reported high prevalence of attachment loss in adolescents and young adults that did not fit the characteristics of recognized periodontitis clinical syndromes. Such occurrences have been termed *incidental attachment loss*, and have been reported in 1.6–26% of the subjects. This group is thought to comprise both initial forms of periodontitis (including AgP) and a variety of defects, such as recession due to traumatic toothbrushing, attachment loss associated with removal of impacted third molars, etc.

Conclusion

A small but significant proportion of children and young adults is affected by some form of periodontitis. A substantial proportion of these subjects is thought to be affected by AgP. Given the severity of these forms of periodontal disease and their tendency to progress, early detection of periodontitis, and AgP in particular, should be a primary concern of both practitioners and public health officers. The whole population, including children and young adults, should receive a periodontal screening as part of their routine dental examination.

Screening

Given the low prevalence of AgP patients within the population, cost-effective detection of cases requires utilization of a sensitive screening approach, i.e. the application of a diagnostic approach able to correctly identify most of the cases with disease. The objective of screening is the detection in a population of

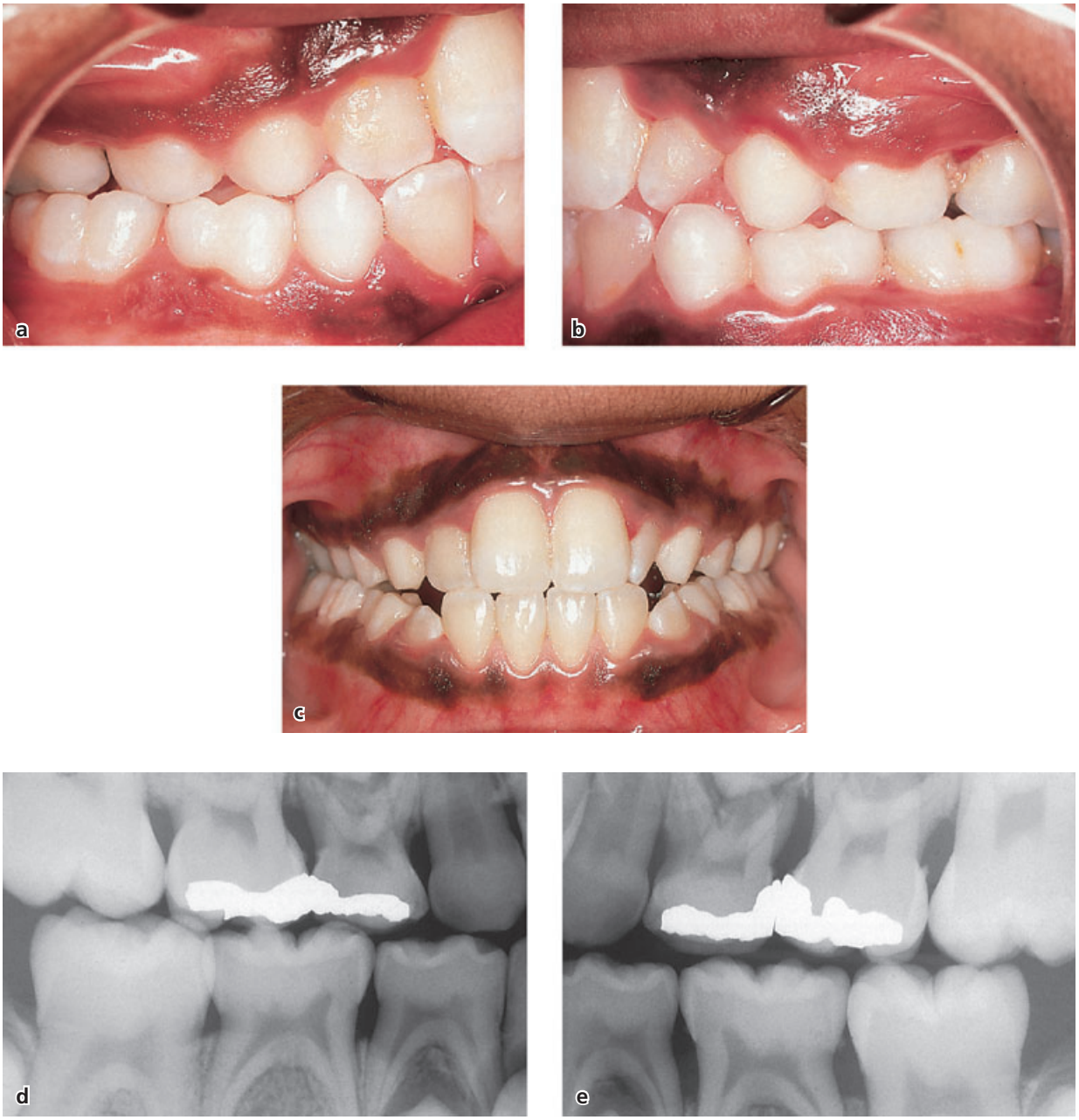


Fig. 19-3 Seven-year-old African American female presenting with radiographic alveolar bone loss and probing attachment loss at the primary molars and permanent first molars and incisors. (a–c) Clinical photographs, buccal view. (d–e) Bite-wing radiographs. Clinical presentation shows moderate plaque accumulation, localized gingival inflammation, with ulceration of the gingival margin and loss of the interdental papilla mesial of #65. In the primary molar regions there were 4–6 mm pockets with bleeding on probing. Bone loss and attachment loss were limited to the molar region. The mesial aspects of the first permanent molars are also initially involved. Radiographic subgingival calculus is evident. Note that the upper left posterior sextant seems to be more severely affected than the other posterior segments. Diagnosis: localized aggressive (type 1) periodontitis.

possibly diseased subjects that would require a more comprehensive examination. In periodontology, the most sensitive diagnostic test for the detection of periodontitis is the measurement of attachment loss by probing. Application of this diagnostic procedure in the mixed dentition and in teeth that are not fully erupted, however, may be difficult.

In younger subjects, therefore, a currently utilized screening approach is the measurement of the distance between the alveolar crest and the cemento-enamel junction on bite-wing radiographs. An advantage of this approach relates to the fact that in most industrialized countries bite-wing radiographs of children and young adolescents in mixed dentition are routinely taken for caries prevention programs; these radiographs should therefore be screened not only for carious lesions but also for the presence of marginal alveolar bone loss.

Recent investigations have attempted to determine the "normal" distance between the cemento-enamel junction and the alveolar crest of primary and permanent molars in 7–9-year-old children (Sjodin &

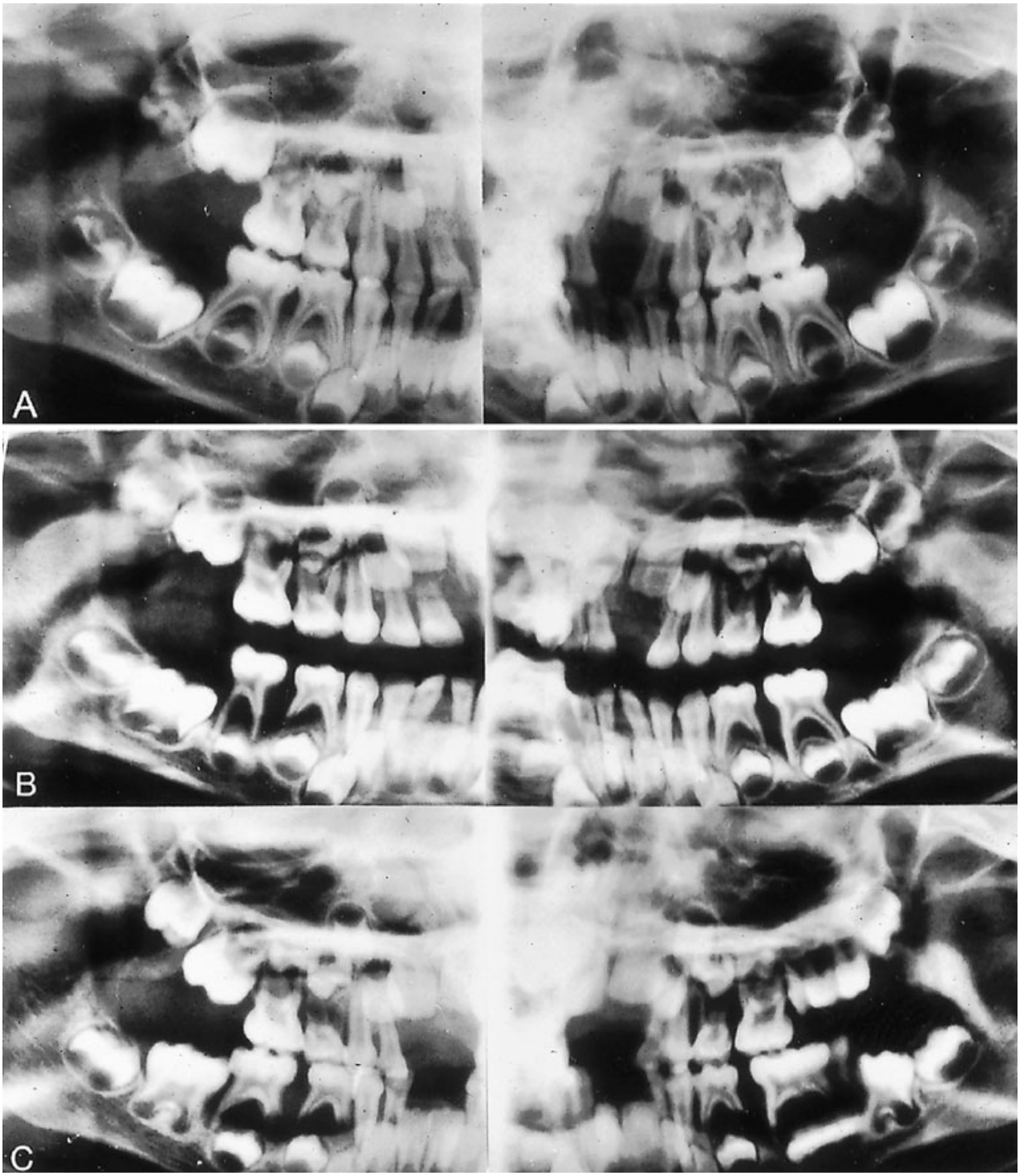


Fig. 19-4 Radiographs obtained from a Caucasian female with generalized pre-pubertal periodontitis. Radiographic situation in (A) April 1978 when she was 4–5 years old, (B) December 1978, and (C) August 1979. The radiographs illustrate the extent of alveolar bone loss that occurred over the 15-month period. Note the widespread bone loss. During infancy, this patient had severe, recurrent skin and ear infections sustained by *Staphylococcus aureus* and *Pseudomonas aeruginosa*, respectively. Delayed healing was also observed following minor injuries. White cell counts revealed a persistent leukocytosis, with absolute neutrophil counts always above 8000/mm^3. Gingival biopsy indicated that the inflammatory infiltrate consisted almost completely of plasma cells and lymphocytes. No neutrophils were present, in spite of the abundance of these cells in the circulation. This history and clinical manifestation appears to be consistent with the diagnosis of periodontal manifestations of systemic disease in a subject with leukocyte adhesion deficiency (LAD). From Page *et al*. (1983b) with permission from the American Academy of Periodontology.

Mattson 1992; Needleman *et al*. 1997). Median distances at primary molars were 0.8–1.4 mm. These values were in agreement with those previously reported for primary molars of 3–11-year-old children (Bimstein & Soskolne 1988). The cemento-enamel junction of permanent molars was 0–0.5 mm apical to the alveolar crest in 7–9-year-olds. These values were age-dependent, and related to the state of eruption of the tooth. In general, however, it should be noted that the majority of children present with

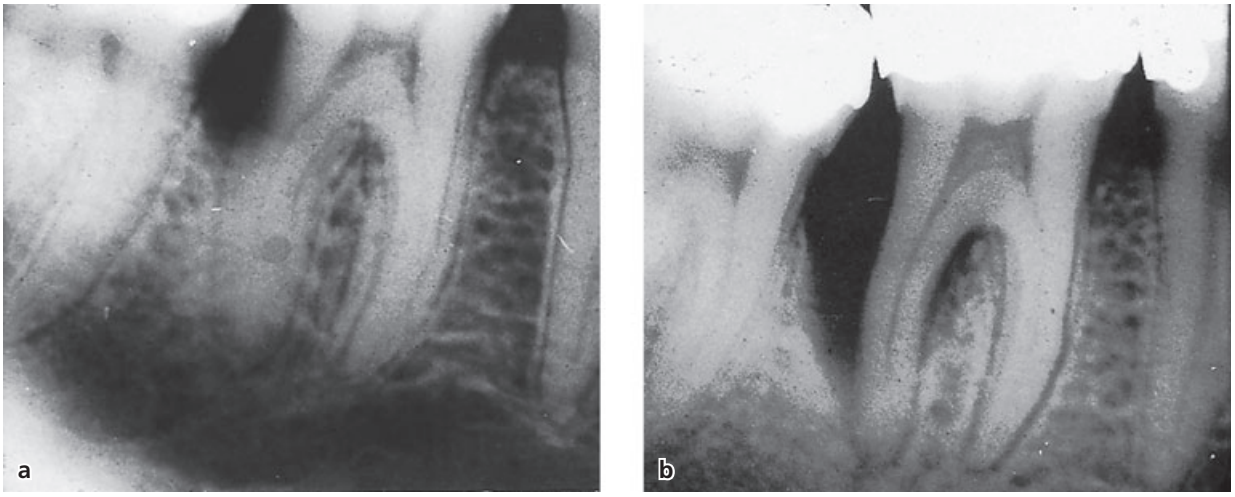


Fig. 19-5 Radiographs illustrating bone loss at the distal aspect of the mandibular first molar in a 15-year-old girl (a) and progression of disease 1 year later (b).

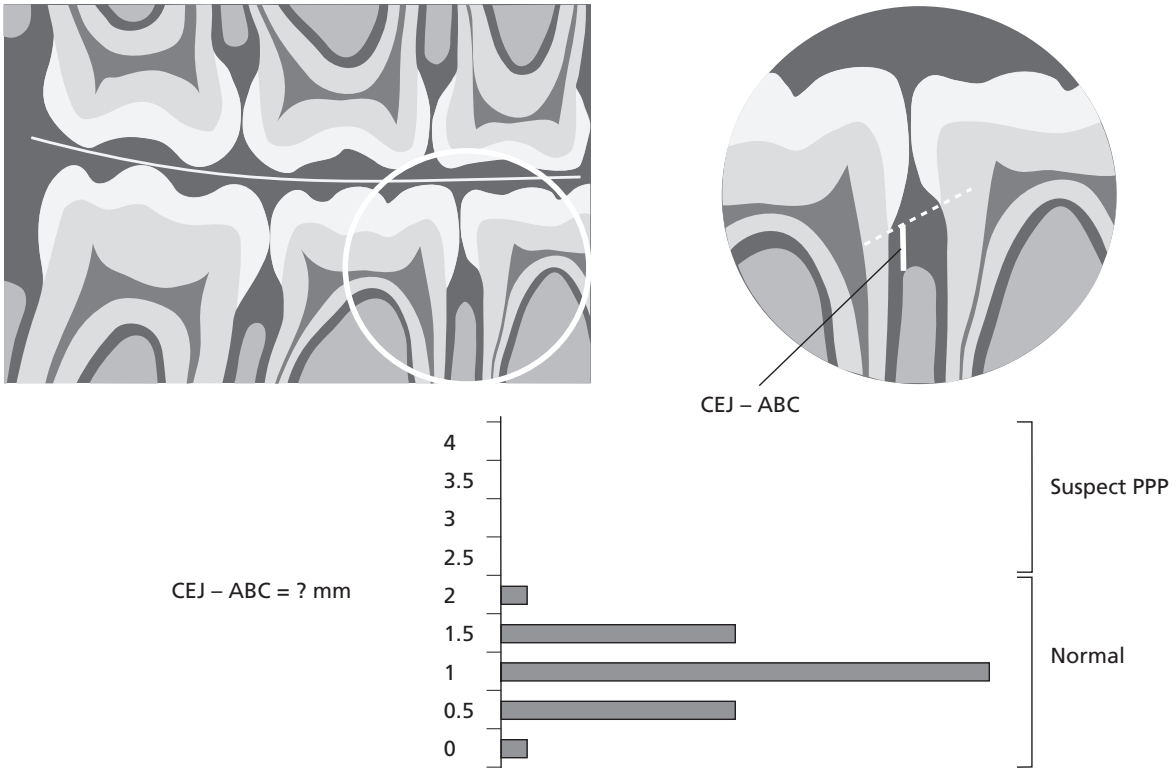


Fig. 19-6 Diagrammatic representation of the use of bite-wing radiographs to screen for prepubertal periodontitis in mixed dentition. The distance from the cemento-enamel junction (CEJ) and the alveolar bone crest (ABC) is measured from a line connecting the CEJ of the two adjacent teeth. Measurements are taken for each mesial and distal surface. Normal CEJ-ABC distances for 7–9 year olds are less than 2.0 mm. If the measurement exceeds this value, prepubertal periodontitis should be suspected, and a comprehensive periodontal examination should be performed.

distances significantly smaller than the 2–3 mm considered normal for the completely erupted dentitions of adults. In children, significantly greater distances have been detected at sites with caries, fillings or open contacts, indicating that these factors may contribute to bone loss in similar ways to those in adult patients. Furthermore, presence of one of these local factors may suggest a local cause of bone loss, other than periodontitis. A distance of 2 mm between the cemento-enamel junction and the alveolar crest, in the absence of the above-mentioned local factors, argues therefore for a suspected diagnosis of periodontitis (Figs. 19-6 and 19-7) (Sjodin & Mattson 1992). This tentative diagnosis will have to be confirmed by a complete periodontal examination. In utilizing bite-wing radiographs for the screening of

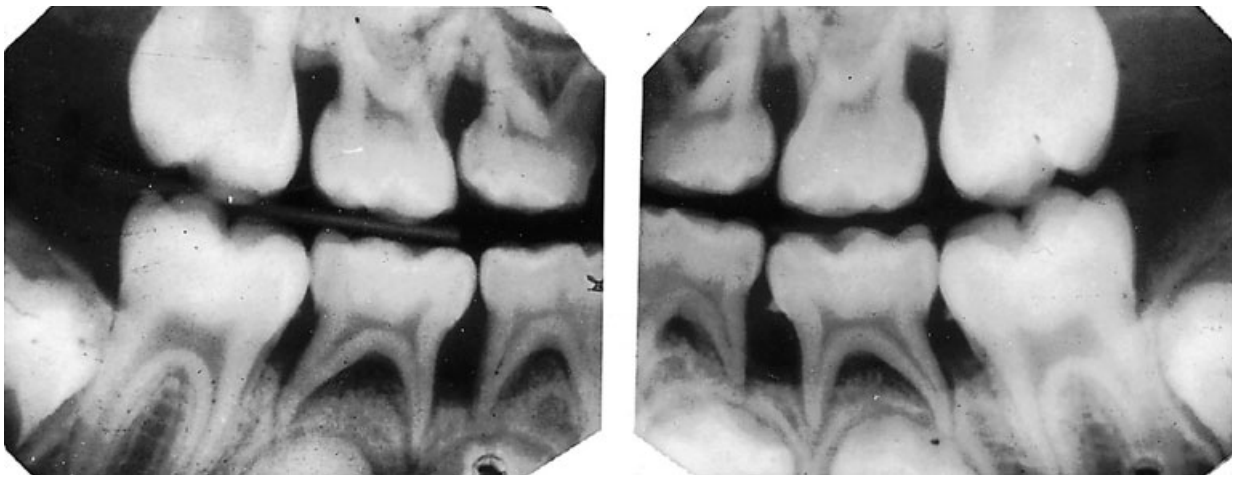


Fig. 19-7 Bite-wing radiographs illustrating advanced bone loss at primary molars, and initial involvement of the mesial aspect of the first molar in a child with early onset periodontitis. Note the marginal pattern of bone loss, which is significantly different from the pattern expected in association with the normal exfoliation of deciduous teeth. Subgingival calculus can also be observed.

patients, clinicians should be aware that radiographic marginal bone loss (in the presence of probing attachment loss) is a highly specific diagnostic sign of periodontitis. Its sensitivity, however, is lower than that of periodontal probing because initial intrabony lesions may not appear on radiographs as a result of the masking effects of intact cortical plates (Suomi *et al*. 1968; Lang & Hill 1977). Some initial cases of periodontitis may therefore remain undetected.

In older adolescents and adults, periodontal probing is a more appropriate screening examination than the use of radiographs. It is important to differentiate between clinical use of periodontal probing to perform a complete periodontal examination, and its use as a screening tool. Using probing to detect attachment loss during a screening examination requires circumferential probing to evaluate all sites around the tooth. In a screening examination, however, attachment loss values for all sites are usually not recorded. Furthermore, the screening examination can be stopped once evidence of attachment loss has been detected, and therefore the need for a comprehensive examination has been established. The American Academy of Periodontology has recently endorsed a simplified screening examination for this purpose. This examination is based on a modification of the Community Periodontal Index of Treatment Needs (CPITN) (Ainamo *et al*. 1982; American Academy of Periodontology & American Dental Association 1992).

Once a case has been detected by a screening examination, a comprehensive periodontal examination will be necessary to establish a proper diagnosis. At this stage, once a case of periodontitis has been confirmed, a differential diagnosis between aggressive (type 1) periodontitis and chronic (type 2) periodontitis needs to be made in accordance with the criteria mentioned above and keeping in mind that cases which do not fit the AgP criteria should be diagnosed as chronic periodontitis.

Conclusion

Screening periodontal examinations should be performed as part of every dental visit. Marginal bone loss assessed on bite-wing radiographs, though less sensitive than periodontal probing, may be used as a screening tool in subjects with primary and mixed dentitions. Attachment loss evaluated by periodontal probing is the most sensitive screening approach currently available; it should be used in older adolescents and adults. Differential diagnosis between AgP and chronic periodontitis is made based on exclusion of AgP.

Etiology and pathogenesis

As a group, aggressive forms of periodontitis are characterized by severe destruction of the periodontal attachment apparatus at an early age. This early manifestation of clinically detectable lesions is generally interpreted as being the expression of highly virulent causative agents or high levels of susceptibility of the individual patient, or a combination of the two.

Bacterial etiology

The evidence implicating bacteria in the etiology of periodontitis has been described in Chapter 9. The most abundant evidence regarding a bacterial etiology of AgP comes from studies of LAP. Evidence relating to other forms of AgP (GAP) will be discussed only when specifically different from LAP.

Acceptance of bacterial etiology of aggressive forms of periodontitis has been particularly difficult

since clinical presentation of cases frequently shows little visible plaque accumulation, and proximal caries, another dental disease of bacterial origin affecting younger individuals, seems much less prevalent in LAP patients than in age-, gender-, and race-matched controls (Fine *et al*. 1984; Sioson *et al*. 2000). Of great importance, in this respect, were microscopic studies demonstrating the presence of a layer of bacterial deposits on the root surface of advanced AgP lesions (Listgarten 1976; Westergaard *et al*. 1978). Early studies attempting the identification of the involved bacteria using culture techniques were performed by Newman *et al*. and by Slots (Newman *et al*. 1976; Slots 1976; Newman & Socransky 1977). In these studies, Gram-negative organisms comprised approximately two thirds of the isolates from deep periodontal pockets. In contrast, these organisms averaged only about one third of the isolates in control sites with normal gingiva. A substantial part of the isolates was not identifiable at that time due to methodological limitations and ambiguous classification schemes. Dominant microorganisms in LAP included *Actinobacillus actinomycetemcomitans* (*A.a.*, now termed *Aggregatibacter actinomycetemcomitans)*, *Capnocytophaga* sp., *Eikenella corrodens*, saccharolytic Bacteroides-like organisms now classified as *Prevotella* sp., and motile anaerobic rods today labeled *Campylobacter rectus*. Gram-positive isolates were mostly streptococci, actinomycetes, and peptostreptococci. *A.a.*, *Capnocytophaga* sp., and *Prevotella* sp. were also shown to be the most prominent members of the subgingival microbiota of periodontitis lesions in the primary dentition. The microbial patterns observed in periodontal lesions of the primary dentition seemed, however, to be more complex than the ones found in LAP patients.

One of these organisms, *A. actinomycetemcomitans*, a short, facultatively anaerobic, non-motile, Gram-negative rod, received particular attention and was increasingly viewed as a key microorganism in LAP. This view was principally based on four lines of evidence (Socransky & Haffajee 1992):

1. Association studies, linking the organism to the disease: *A.a.* was isolated in periodontal lesions from more than 90% of LAP patients and was much less frequent in periodontally healthy individuals (Table 19-1) (for more recent investigations, see also Ashley *et al*. 1988; Van der Velden *et al*. 1989; Albandar *et al*. 1990; Gunsolley *et al*. 1990; Slots *et al*. 1990; Asikainen *et al*. 1991; Aass *et al*. 1992; Ebersole *et al*. 1994; Listgarten *et al*. 1995). In some studies it was possible to demonstrate elevated levels of *A.a.* in sites showing evidence of recent or ongoing periodontal tissue destruction (Haffajee *et al*. 1984; Mandell 1984; Mandell *et al*. 1987).
2. Demonstration of virulence factors: *A.a.* was shown to produce several potentially pathogenic substances, including a leukotoxin, was capable of translocating across epithelial membranes, and could induce disease in experimental animals and non-oral sites (for review see Zambon *et al*. 1988; Slots & Schonfeld 1991).
3. Findings of immune responses towards this bacterium: investigators repeatedly reported significantly elevated levels of serum antibodies to *A.a.* in LAP patients (Listgarten *et al*. 1981; Tsai *et al*. 1981; Altman *et al*. 1982; Ebersole *et al*. 1982, 1983; Genco *et al*. 1985; Vincent *et al*. 1985; Mandell *et al*. 1987; Sandholm *et al*. 1987). Such patients were furthermore shown to produce antibodies locally against this organism at diseased sites (Schonfeld

Table 19-1 Classical studies on the distribution of *A.a.* in LAP, gingivitis, adult periodontitis, and in normal non-diseased subjects

Study	Diagnosis	No. of subjects (sites)	% *A.a.*-positive subjects	% *A.a.*-positive sites
Slots *et al*. 1980	LAP	10 (34)	90	79
	Adult periodontitis	12 (49)	50	35
	Normal juveniles	10 (60)	20	3
	Normal adults	11 (66)	36	17
Mandell & Socransky 1981	LAP	6 (18)	100	79
	Adult periodontitis	25 (50)	0	–
	Gingivitis	23 (46)	0	–
Zambon *et al*. 1983	LAP	29	97	–
	Adult periodontitis	134	21	–
	Normal juveniles/adults	142	17	–
Eisenmann *et al*. 1983	LAP	12 (12)	100	100
	Normal juveniles	10 (10)	60	60
Moore *et al*. 1985	LAP	14 (31)	36	5
Asikainen *et al*. 1986	LAP	19 (38)	89	68

See text for a selection of more recent investigations.

& Kagan 1982; Ebersole *et al*. 1985b; Tew *et al*. 1985).

4. Clinical studies showing a correlation between treatment outcomes and levels of *A.a.* after therapy: unsuccessful treatment outcomes were linked to a failure in reducing the subgingival load of *A.a.* (Slots & Rosling 1983; Haffajee *et al*. 1984; Christersson *et al*. 1985; Kornman & Robertson 1985; Mandell *et al*. 1986, 1987; Preus 1988).

In consideration of these findings, *A.a.* was one of the few oral microorganisms recognized by many to be a true infectious agent, and LAP as an infection essentially caused by *A.a.* Accepting such a concept has far-reaching consequences with regards to strategies for prevention and therapy. For example, if *A.a.* is a real exogenous pathogen for LAP, or AgP in general, avoidance of exposure to the organism becomes a relevant issue in prevention (the mere presence of *A.a.* would be an indication for intervention), and the elimination of *A.a.* may be a valid treatment goal. Consequently, highly sensitive tests to detect the bacterium would be useful diagnostic tools. Several studies have, in fact, provided evidence for transmission of *A.a.* between humans, e.g. from parent to child or between spouses (DiRienzo *et al*. 1990, 1994b; Preus *et al*. 1992; Petit *et al*. 1993a,b; Poulsen *et al*. 1994; Von Troil-Lindén *et al*. 1995). Other studies have indicated that *A.a.* can be eliminated with appropriate mechanical treatment and adjunctive antibiotic therapy (Rams *et al*. 1992; Pavicic *et al*. 1994).

However, the view of LAP as an *A.a.* infection did not remain undisputed. It was contested by citing cross-sectional studies showing a high general *A.a.* prevalence in certain populations, particularly from developing countries (Eisenmann *et al*. 1983; Dahlén *et al*. 1989; McNabb *et al*. 1992; Al-Yahfoufi *et al*. 1994; Gmür & Guggenheim 1994). It was also argued that *A.a.* could be detected in subgingival plaque samples from sites with and without disease, and that there were patients with LAP who apparently neither showed presence of *A.a.* in the oral flora nor had elevated antibody titers to the organism (Loesche *et al*. 1985; Moore 1987). A systematic review with the purpose of determining to what extent adjunctive microbiological testing could distinguish between chronic and aggressive periodontitis concluded that the presence or absence of *A.a.* (as well as of four other suspected periodontal pathogens) could not discriminate between subjects with aggressive periodontitis from those with chronic periodontitis (Mombelli *et al*. 2002). Although a diagnosis of AgP was more likely in a subject positive for *A.a.* than in an individual negative for this organism, any *A.a.*-positive individual with periodontitis was three times more likely to be suffering from chronic than from aggressive periodontitis.

If a putative pathogen can be detected frequently in subjects without a given clinical diagnosis, this suggests that not all humans are equally susceptible and/or that there is variation in virulence and pathogenic potential. Strong evidence has been produced in recent years demonstrating that the virulence of *A.a.* is in fact variable, and proving the existence of at least one particularly virulent subpopulation of *A.a.*

Using monoclonal antibody technology, five serotypes (a, b, c, d, e) of *A.a.* can be distinguished. Each of these serotypes represents a separate evolutionary lineage. A serotype-dependent pattern of association with LAP was found in the United States, where serotype b strains were more often isolated from patients with localized juvenile periodontitis than from other subjects (Zambon *et al*. 1983b, 1996). A higher frequency of serotype b strains was also reported from Finnish subjects with periodontitis (Asikainen *et al*. 1991, 1995). Differing results were, however, reported from other parts of the world, suggesting that there may be specific distribution patterns in ethnically distinct populations (Chung *et al*. 1989; Gmür & Baehni 1997; Hölttä *et al*. 1994). Using restriction fragment length polymorphism (RFLP) analysis, DiRienzo *et al*. (1994a,b) could discriminate twelve genotypes of *A.a.* One of them (RFLP type II) was uniquely associated with periodontal disease. Others, however, were linked to healthy periodontal conditions.

Several properties of *A.a.* are regarded as important determinants of virulence and pathogenic potential (Table 19-2). All Gram-negative bacteria are enveloped by two membranes, of which the outer is rich in endotoxin. This identifying feature of Gram-negative bacteria consists of a lipid and a polysaccharide part and is therefore frequently termed lipopolysaccharide (LPS). LPS is set free when bacterial cells die or multiply. *A.a.* can also secrete membrane vesicles that can serve as transport vehicles to spread endotoxin as well as other pathogenic substances produced by the bacterium. The LPS of *A.a.* can activate host cells, and macrophages in

Table 19-2 Determinants of virulence and pathogenic potential of *A. actinomycetemcomitans*

Factor	Significance
Leukotoxin	Destroys human polymorphonuclear leukocytes and macrophages
Endotoxin	Activates host cells to secrete inflammatory mediators (prostaglandins, interleukin-1β, tumor necrosis factor-α)
Bacteriocin	May inhibit growth of beneficial species
Immunosuppressive factors	May inhibit IgG and IgM production
Collagenases	Cause degradation of collagen
Chemotactic inhibition factors	May inhibit neutrophil chemotaxis

particular, to secrete inflammatory mediators such as prostaglandins, interleukin-1β and tumor necrosis factor-α. It is also highly immunogenic, since high titers of antibodies against its antigenic determinant are frequently detected in infected individuals. Additional virulence factors interfering with fibroblast proliferation have been identified for certain strains of *A.a.* Immunosuppressive properties of *A.a.*, as well as collagenolytic activity and inhibition of neutrophil chemotaxis, have been demonstrated (for review see Fives-Taylor *et al*. 1996). The key element of virulence and pathogenicity of *A.a.*, however, is considered to be the production of a leukotoxin, playing an important role in the evasion of local host defenses. The leukotoxin produced by *A.a.* exhibits cytotoxic specificity and destroys human polymorphonuclear leukocytes and macrophages, but neither epithelial and endothelial cells nor fibroblasts. It belongs to the family of the RTX (Repeats in ToXin) toxins, which are pore-forming lytic toxins (for details see Lally *et al*. 1996).

Leukotoxin production varies significantly among strains of *A.a.* (Brogan *et al*. 1994; Kolodrubetz *et al*. 1989; Spitznagel *et al*. 1991; Zambon *et al*. 1983a). The strain-specific difference in leukotoxin production seems to be regulated at the level of transcription (Spitznagel *et al*. 1991). Brogan *et al*. (1994) detected a 530 bp deletion in the promoter region of the leukotoxin operon and found that strains with this feature produced 10–20 times more leukotoxin. Subsequent analysis showed that the occurrence of such highly toxigenic strains coincided with the high frequency of serotype b in patients with localized juvenile periodontitis, and that these strains actually constituted a specific clone of serotype b, now referred to as the JP2 clone (the initial isolate of this clone is strain JP2, from an African American child with prepubertal periodontitis) (Tsai *et al*. 1984). Extensive further research (Poulsen *et al*. 1994; Haubek *et al*. 1995, 1996, 1997, 2001; Tinoco *et al*. 1997; Bueno *et al*. 1998; He *et al*. 1999; Macheleidt *et al*. 1999; Mombelli *et al*. 1999; Contreras *et al*. 2000; Haraszthy *et al*. 2000; Tan *et al*. 2001; Cortelli *et al*. 2005) has clearly identified the JP2 clone as a common isolate in patients of North and West African descent suffering from aggressive periodontitis, even if they lived in another geographical region (e.g. North and South America or Europe). The disease association of RFLP type II reflects the fact that the JP2 clone represents a subpopulation of strains showing the RFLP type II pattern.

Our current knowledge with regards to the genetic and phenotypic diversity of *A.a.*, and its distribution in various populations and cohorts, with or without a clinical diagnosis of LAP, suggests that *A.a.* may be considered an opportunistic pathogen, or even a commensal bacterial species as a whole. However, at least one distinct subpopulation, the JP2 clone, displays the properties of a true pathogen in at least one group of humans of North and West African descent (Kilian *et al*. 2006). Prevention of vertical transmission of such virulent clones may a be feasible measure to prevent AgP (Van Winkelhoff & Boutaga 2005).

Generalized aggressive periodontitis (GAP), formerly named generalized early onset periodontitis (G-EOP) and rapidly progressive periodontitis (RPP), has been frequently associated with the detection of *Porphyromonas gingivalis*, *Bacteroides forsythus* and *A.a.* In contrast to *A.a.*, which is facultatively anaerobic, *P. gingivalis* and *B. forsythus* are fastidious strict anaerobes. *P. gingivalis* produces several potent enzymes, in particular collagenases and proteases, endotoxin, fatty acids, and other possibly toxic agents (Shah 1993). A relationship between the clinical outcome of therapy and bacterial counts has also been documented for *P. gingivalis*, and non-responding lesions often contain this organism in elevated proportions. High local and systemic immune responses against this bacterium have been demonstrated in patients with GAP (Tolo & Schenck 1985; Vincent *et al*. 1985; Ebersole *et al*. 1986; Murray *et al*. 1989).

Bacterial damage to the periodontium

Disease-associated bacteria are thought to cause destruction of the marginal periodontium via two related mechanisms: (1) the direct action of the microorganisms or their products on the host tissues, and/or (2) as a result of their eliciting tissue-damaging inflammatory responses (see Chapter 11) (Tonetti 1993). The relative importance of these two mechanisms in AgP remains speculative. Human investigations have indicated that *Aggregatibacter actinomycetemcomitans* is able to translocate across the junctional epithelium and invade the underlying connective tissue (Saglie *et al*. 1988). These data support the hypothesis that direct bacterial invasion may be responsible for some of the observed tissue breakdown. Data from chronic periodontitis, however, seem to indicate that two thirds of attachment loss and alveolar bone resorption is preventable through the action of non-steroidal anti-inflammatory drugs, and therefore tissue destruction seems to be driven by the inflammatory process (Williams *et al*. 1985, 1989). Apical spread of bacteria loosely adhering to the hard, non-shedding surface of the tooth is thought to be controlled through a first line of defense consisting of mechanisms such as the high turnover of junctional epithelium keratinocytes, the outward flow of crevicular fluid, and the directed migration of polymorphonuclear leukocytes through the junctional epithelium; the efficiency of these innate immune mechanisms is highly enhanced by the presence of specific antibodies and complement fragments in the gingival crevicular fluid (Page 1990) (Table 19-3) (see Chapter 11).

Host response to bacterial pathogens

Both local and systemic host responses to AgP-associated microflora have been described. Local

Table 19-3 Host defense mechanisms in the gingival sulcus (modified from Page 1990)

Intact epithelial barrier and epithelial attachment
Salivary flushing action, agglutinins, antibodies
Sulcular fluid flushing action, opsonins, antibodies, complement and other plasma components
Local antibody production
High levels of tissue turnover
Presence of normal flora or beneficial species
Emigrating PMNs and other leukocytes

inflammatory responses have been characterized by an intense recruitment of polymorphonuclear leukocytes (PMNs) both within the tissues and into the periodontal pocket. Such a preponderance of PMNs underlines the importance of these cells in the local defense against bacterial aggression and their potential role in host-mediated tissue destruction. B cells and antibody-producing plasma cells represent a significant component of the mononuclear cell-dominated connective tissue lesion (Liljenberg & Lindhe 1980). Plasma cells have been shown to be predominantly IgG-producing cells, with a lower proportion of IgA-producing cells (Mackler *et al*. 1977, 1978; Waldrop *et al*. 1981; Ogawa *et al*. 1989). Local IgG_4-producing cells, in particular, seem to be elevated. Another important component of the local inflammatory infiltrate are T cells. Subset analysis of local T cells has indicated a depressed T-helper to T-suppressor ratio as compared to both healthy gingiva and peripheral blood. These findings have been interpreted to suggest the possibility of altered local immune regulation (Taubman *et al*. 1988, 1991). Peripheral blood mononuclear cells from AgP patients have been reported to exhibit a reduced autologous mixed lymphocyte reaction, as well as a higher than normal response to B cell mitogens (for review see Engel 1996). Local inflammatory responses are characterized by high levels of PGE_2, IL-1α and IL-1β in both crevicular fluid and tissue (Masada *et al*. 1990; Offenbacher *et al*. 1993). PGE_2 production, in particular, has been shown to be highly elevated in AgP subjects when compared to periodontally healthy individuals and chronic periodontitis patients.

Specific antibodies against AgP-associated microorganisms (Lally *et al*. 1980; Steubing *et al*. 1982; Ebersole *et al*. 1984, 1985a,b) and cleaved complement fragments (Schenkein & Genco 1977; Patters *et al*. 1989) have also been detected in crevicular fluid from AgP lesions. Of interest is the evidence indicating that crevicular fluid titers of antibodies against AgP-associated microorganisms are frequently higher than in the serum of the same patient (Ebersole *et al*. 1984, 1985a,b). This observation, together with substantial *in vitro* and *ex vivo* data, strongly suggests that substantial fractions of these antibodies are locally produced in the inflammatory infiltrate (Steubing *et al*. 1982; Hall *et al*. 1990, 1991, 1994). Substantial titers of antibodies against *A.a.* and *P. gingivalis* have also been detected in the serum of AgP patients. Furthermore, in some patients, titers of antibodies reactive with *A.a.* have been shown to be as high as the ones against *Treponema pallidum* present in tertiary syphilis (0.1–1 g/ml); this clearly indicates the extent of host response that can be mounted against these periodontal pathogens (for a review see Ebersole 1990, 1996).

Recent investigations have identified the immunodominant *A. actinomycetemcomitans* antigen to be the serotype-specific carbohydrate; furthermore, it has been shown that the vast majority of antibodies reactive with this carbohydrate in AgP patients consist of IgG_2 (Califano *et al*. 1992). High titers and high avidity of *A.a.*-specific IgG_2 have been demonstrated in LAP patients, where high antibody titers are thought to be associated with the host's ability to localize attachment loss to few teeth; conversely, GAP patients are frequently seronegative for *A.a.* or display low titers and avidity. Anti-*A.a.* serotype polysaccharide IgG_2, therefore, are considered to be protective against widespread AgP (Tew *et al*. 1996).

Of importance are findings reporting antibody response to *P. gingivalis* in GAP forms. Patients suffering from these forms of disease frequently show both low levels of serum antibodies against *P. gingivalis* and low levels of antibody avidity, indicating a specific inability of some GAP patients to cope effectively with these bacteria. Importantly, however, both titers and avidity of antibodies reacting with *P. gingivalis* can be improved as a result of therapy.

Another important aspect of host response towards AgP microorganisms has been the recognition that PMNs of some LAP and GAP patients present decreased migration and antibacterial functions (Genco *et al*. 1980, 1986; Van Dyke *et al*. 1982, 1986, 1988). These abnormalities are frequently minor in the sense that they are usually not associated with infections other than periodontitis. A key report has indicated that PMN abnormalities in LAP patients seem to cluster in families much in the same way as AgP does (Fig. 19-8) (Van Dyke *et al*. 1985). This evidence has been interpreted as a suggestion that the LAP-associated PMN defect may be inherited. Other recent reports have indicated that PMN abnormalities in LAP patients may be, at least in part, the result of a hyper-inflammatory state resulting in the presence of pro-inflammatory cytokines in the serum of some AgP patients (Shapira *et al*. 1994; Agarwal *et al*. 1996).

Genetic aspects of host susceptibility

Several family studies have indicated that the prevalence of AgP is disproportionately high among certain

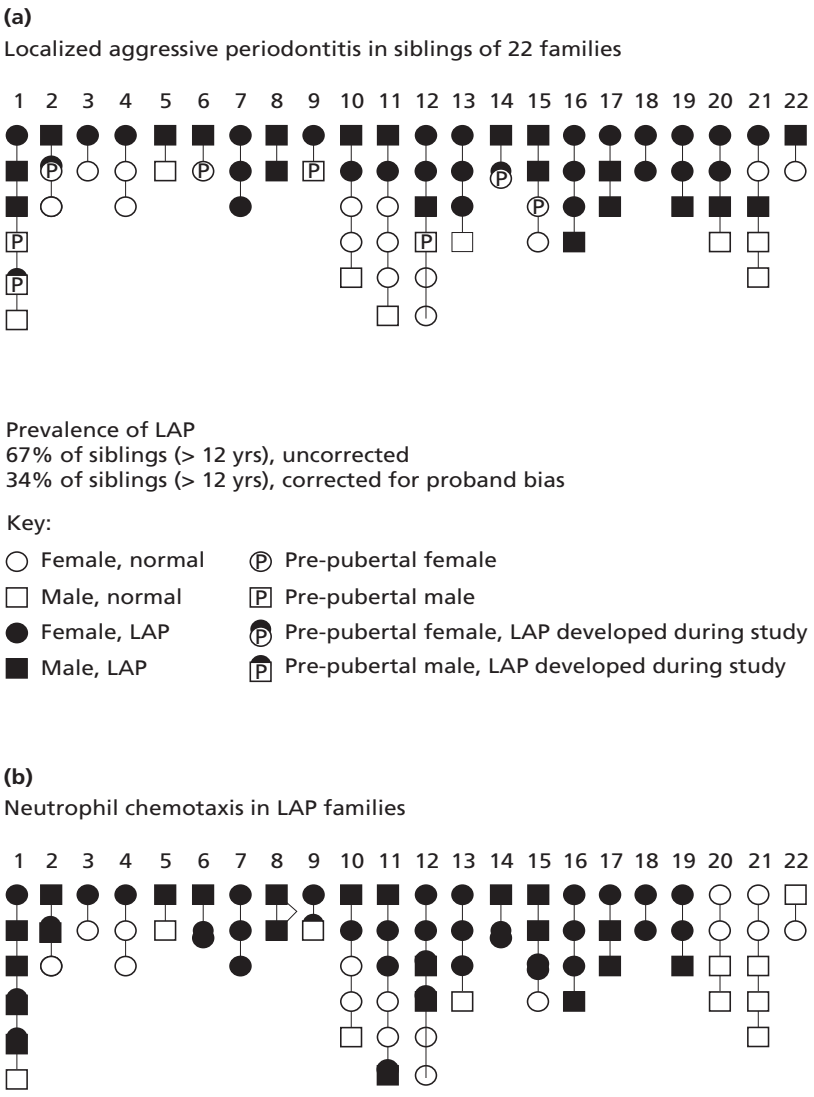


Fig. 19-8 (a) Patients suffering from LAP in 22 families are represented by solid black figures. In each family the proband is on the left. (b) Diagrammatic representation of sibships involved in study group. Numbers are the same as in (a). Solid black figures represent patients exhibiting depressed neutrophil chemotaxis. In this group, after correcting for sampling bias, 40% of subjects present with abnormal chemotaxis. Subjects in sibship 8 are identical twins. From Van Dyke *et al.* (1985).

families, where the percentage of affected siblings may reach 40–50% (Saxen & Nevanlinna 1984; Beaty *et al*. 1987; Long *et al*. 1987; Boughman *et al*. 1992; Marazita *et al*. 1994; Llorente & Griffiths 2006). Such a dramatic familial aggregation of cases indicates that genetic factors may be important in susceptibility to AgP. Genetic studies in these families suggest that the pattern of disease transmission is consistent with mendelian inheritance of a gene of major effect (Saxen & Nevanlinna 1984; Beaty *et al*. 1987; Boughman *et al*. 1992; Hart *et al*. 1992; Marazita *et al*. 1994). This means that the observed familial pattern can be partly accounted for by one or more genes that could predispose individuals to develop AgP.

Segregation analyses have indicated that the likely mode of inheritance is autosomal dominant (Fig. 19-9a) (Saxen & Nevanlinna 1984; Beaty *et al*. 1987; Hart *et al*. 1992; Marazita *et al*. 1994). Most of these investigations, however, were carried out in African-American populations; it is therefore possible that other modes of inheritance may exist in different populations. Segregation analysis can provide information about the mode of inheritance of a genetic trait but does not provide information about the specific gene(s) involved. The chromosomal location of a gene of major effect for a trait such as AgP susceptibility can be determined by linkage analysis. An investigation utilizing this methodology reported linkage of LAP to the vitamin D binding locus on region q of chromosome 4 in a large family of the Brandywine population (Boughman *et al*. 1986). These results, however, were not confirmed in a subsequent study utilizing a different population (Hart *et al*. 1993). A recent study has linked localized AgP with the q25 region of chromosome 1 in an area close to the cyclo-oxygenase 2 (COX-2) gene (Li *et al*. 2004). Another has established evidence of linkage with the q13–14 region of chromosome 2 that contains the IL-1 gene complex (Scapoli *et al*. 2005). Such data are currently considered to support the existence of genetic heterogeneity in LAP forms, and of distinct forms of AgP. Therefore, it is currently maintained that although formal genetic studies of AgP support the existence of a gene of major effect, it is unlikely that all forms of AgP are due to the same genetic variant (Hart 1996; Loos *et al*. 2005). This notion is consistent

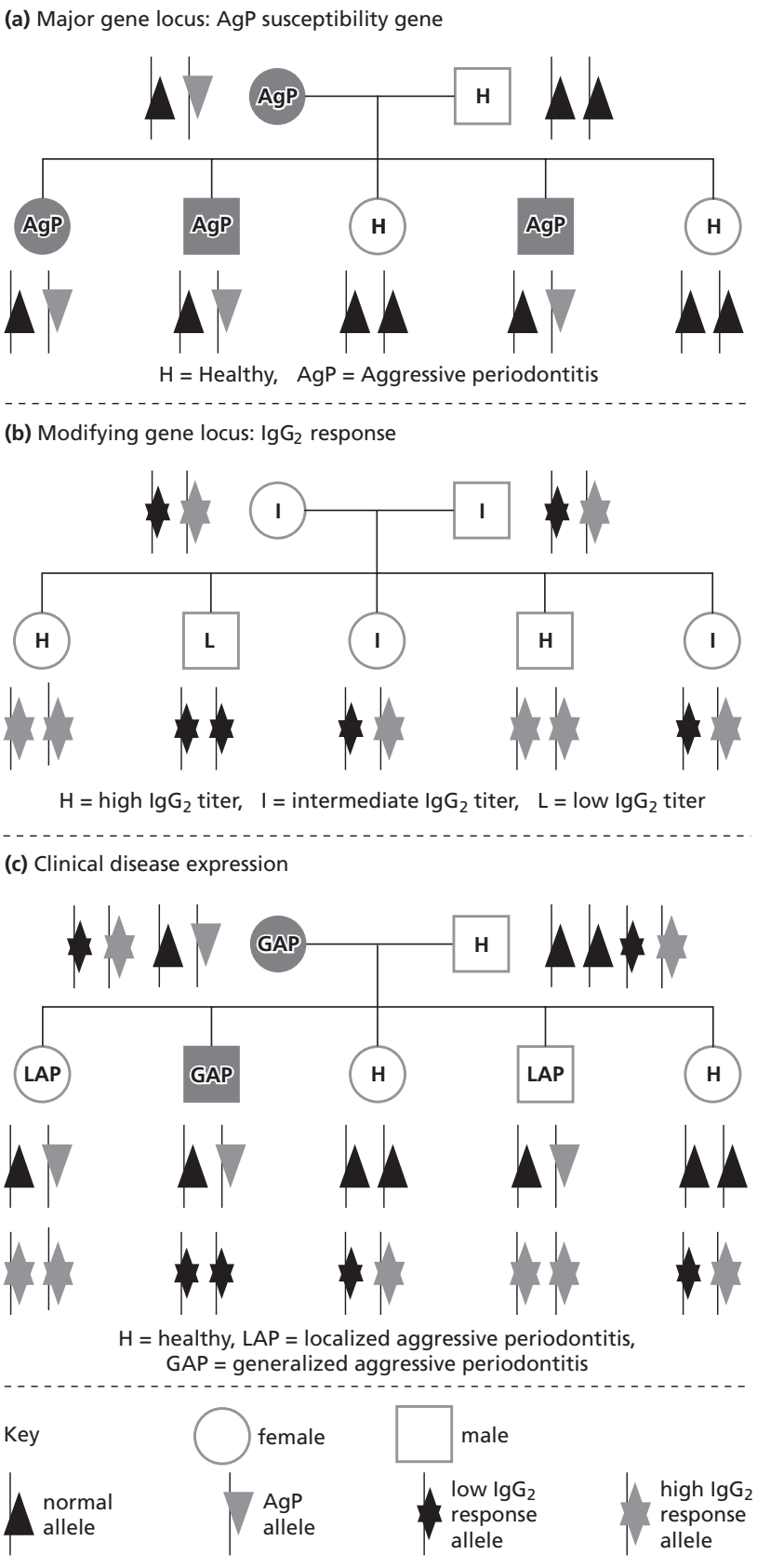


Fig. 19-9 (a) Genetic predisposition to AgP is determined by a single gene of major effect, inherited as an autosomal dominant trait. (b) Modifying genes may control immune responses that determine the clinical extent and severity of periodontal destruction in AgP. Here an allele controlling IgG_2 levels is inherited as a codominant trait. (c) Independent inheritance of major locus and modifying locus illustrating how LAP and GAP may segregate within the same family. The propensity to develop AgP is dependent upon inheritance of a major susceptibility gene. The clinical phenotype is dependent upon host ability to produce IgG_2 in response to periodontopathic bacteria. High IgG_2 titers limit disease extension. Intermediate and low IgG_2 titers are less effective in limiting intermediate disease progression. From Schenkein (1994), as modified by Hart (1996), with permission from the American Academy of Periodontology.

with the fact that numerous diseases and syndromes with similar clinical appearance are known to result from different genetic polymorphisms.

A recent study providing an additional line of evidence for a genetic component to aggressive periodontitis has shown that quantitative measures of periodontal parameters show substantial levels of hereditability in AgP patients (Diehl *et al*. 2005).

Based on current knowledge that AgP subjects present high prevalence of PMN function defects,

Table 19-4 Genes known to affect human PMN function or host response to LPS load and/or thought to be among the candidate genes of major effect in EOP susceptibility

Condition	OMIM*	Transmission	Chromosome location	Comments
Bactericidal permeability increasing protein (BPIP)	109195	AD	20q11–12	BPIP is associated with PMN granules and is bactericidal to Gram organisms. It binds to LPS with high affinity. BPIP is 45% homologous to LPS binding protein
Lipopolysaccharide binding protein (LBP)	151990	AD	20q11–12	Produced during acute phase of infection: binds to LPS and functions as a carrier for LPS; functions in monocyte response
Monocyte differentiation antigen (CD14)	158126	AD	5q31	Receptor for LBP-LPS complex
Prostaglandin synthase 2 (PTGS2)	600262	AR	1q25.2–3	Major role in regulation of prostaglandin synthesis. Dramatic induction of PTGS2 mRNA occurs in normal peripheral blood leukocytes in response to LPS
PMN actin dysfunction (NAD)	257150	AR	?	Carriers (heterozygotes) have a 50% decrease in actin filament assembly; affected individuals (homozygotes) have recurrent bacterial infections. PMN severely defective in migration and particle ingestion; basic defect due to failure of PMN actin polymerization
Myeloperoxidase deficiency (MPO)	254600	AR	17q12–21	Absence of MPO. MPO is a dimeric protein that catalyzes the production of oxidating agents with microbicidal activity against a wide range of microbes. Several variants have been described
IgE elevation with PMN chemotaxis defect	147060	AD	?	Impaired lymphocyte response to *Candida* antigen; recurrent bacterial infections
Fc receptor gamma IIA polymorphism (FCGR2A)	146790	AD	1q21-q23	Allelic variants of the Fc-gamma receptor 2A confer distinct phagocytic capacities providing a possible mechanism for hereditary susceptibility to infection. The H131 allele is the only FGR2A that recognizes IgG_2 efficiently, and optimal IgG_2 handling occurs only in the homozygous state for H131. The allelic variant R131 has low binding of IgG_2
Immunoglobulin G_2m allotypes	N/A	?	N/A	Specific allotypes associated with IgG_2 response to specific bacterial antigens. Subjects lacking specific allotypes may be selectively unable to mount efficient antibody response against specific antigens

* Online Mendelian Inheritance in Man (OMIM). Modified from Hart (1996).

that they have been shown to produce high levels of inflammatory mediators in response to LPS stimulation, and of the relevance of connective tissue homeostasis in periodontitis, several loci have been proposed as genes conferring increased susceptibility to AgP. Hart (1996) compiled a list of candidate genes (Table 19-4) associated with increased susceptibility to AgP.

A series of studies has been performed to assess whether or not specific polymorphisms in these candidate genes were associated with AgP (for a recent review see Shapira *et al*. 2005 and Loos *et al*. 2005). Significant associations have been observed for genes encoding for proteins that are associated with neutrophil function (Fu *et al*. 2002; Loos *et al*. 2003; Kaneko *et al*. 2004; Jordan *et al*. 2005; Nibali *et al*. 2006; de Souza & Colombo 2006), with inflammation and with the host ability to effectively deal with exposure to bacterial components such as endotoxin (Suzuki *et al*. 2004; Scapoli *et al*. 2005; Brett *et al*. 2005; Noack *et al*. 2006), and with connective tissue homeostasis (Suzuki *et al*. 2004; Park *et al*. 2006; Soedarsono *et al*. 2006). It should be emphasized, however, that the validity of the conclusions of the majority of these studies suffers

from small sample sizes, study of a single or few specific polymorphisms in the gene, as well as failure to account for ethnic variations and correction for environmental factors (e.g. cigarette smoking) (Tonetti & Claffey 2005). These three factors may be responsible for false-positive associations and bigger studies need to be performed to establish consistent associations.

Besides genes of major effect that may determine susceptibility to AgP, other genes may act as modifying genes and influence clinical expression of the disease. In this respect, particular interest has been focused on the impact of genetic control on antibody responses against specific AgP-associated bacteria and against *A.a.* in particular. These studies have indicated that the ability to mount high titers of specific antibodies is race-dependent and probably protective (Gunsolley *et al*. 1987, 1988). This has been shown to be under genetic control as a co-dominant trait, independent of the risk for AgP. In individuals susceptible to AgP, therefore, the ability to mount high titers of antibodies (IgG_2 in particular) may be protective and prevent extension of disease to a generalized form (Schenkein 1994; Diehl *et al.* 2003) (Fig. 19-9b,c). Allelic variations in the Fc receptor for IgG_2 immunoglobulins have also been suggested to play a role in suboptimal handling of *A.a*. infections. PMN expressing the R131 allotype of FcγRIIa (i.e. an Fc receptor containing an arginine instead of a histidine at amino acid 131) show decreased phagocytosis of *A.a*. (Wilson & Kalmar 1996).

Environmental aspects of host susceptibility

Recent evidence has indicated that, besides genetic influences, environmental factors may affect the clinical expression of AgP. In a large study, cigarette smoking was shown to be a risk factor for patients with generalized forms of AgP (Schenkein *et al*. 1995). Smokers with GAP had more affected teeth and greater mean levels of attachment loss than patients with GAP who did not smoke (Table 19-5). Environmental exposure to cigarette smoking, therefore, seems to add significant risk of more severe and prevalent disease to this group of already highly susceptible subjects. The mechanism(s) for this observation are not completely understood, but findings from the same group indicate that IgG_2 serum levels as well as antibody levels against *A.a.* are significantly depressed in subjects with GAP who smoke. Since these antibodies are considered to represent a protective response against *A.a.*, it is possible that depression of IgG_2 in smokers may be associated with the observed increase in disease extent and severity in these subjects.

Table 19-5 Effect of smoking on extent and severity of GAP

Smoking status	Mean percentage of sites with PAL ≥5 mm*	Mean PAL (mm)*
Smokers	49.0 ± 3.9	2.78 ± 0.2
Non-smokers	36.8 ± 3.8	2.14 ± 0.2

* Values adjusted for age and mean plaque index, subject as unit of analysis. Smokers showed significantly greater extent and severity of periodontal disease than non-smokers after correcting for age and oral hygiene level.
Modified from Schenkein *et al.* (1995).

Current concepts

Aggressive forms of periodontitis are currently considered to be multifactorial diseases developing as a result of complex interactions between specific host genes and the environment. Inheritance of AgP susceptibility is probably insufficient for the development of disease: environmental exposure to potential pathogens endowed with specific virulence factors is also a necessary step. Host inability to effectively deal with the bacterial aggression and to avoid inflammatory tissue damage results in the initiation of the disease process. Interactions between the disease process and environmental (e.g. cigarette smoking) and genetically controlled (e.g. IgG_2 response to *A.a.*) modifying factors are thought to contribute to determining the specific clinical manifestation of disease (Figs. 19–9a-c and 19-10).

Diagnosis

Clinical diagnosis

Clinical diagnosis is based on information derived from a specific medical and dental history and from the clinical examination of the periodontium. Limitations that will be discussed in this section, however, frequently require supplementation of clinical and anamnestic parameters with other, more advanced aids to properly diagnose, plan treatment for and monitor these diseases. The purpose of clinical diagnosis is the identification of patients suffering from AgP and of factors that have an impact on how the case should be treated and monitored.

In the diagnosis of AgP the initial question that the clinician should ask is:

- Is there periodontitis?

This may sound like a trivial question, but in fact many cases of AgP are currently not identified because of a failure to detect signs of periodontitis. Conversely, some clinicians attribute to periodontitis pathological changes associated with other unrelated and sometimes self-limiting processes. Correctly answering this question requires systematic collection of clinical information regarding the following items:

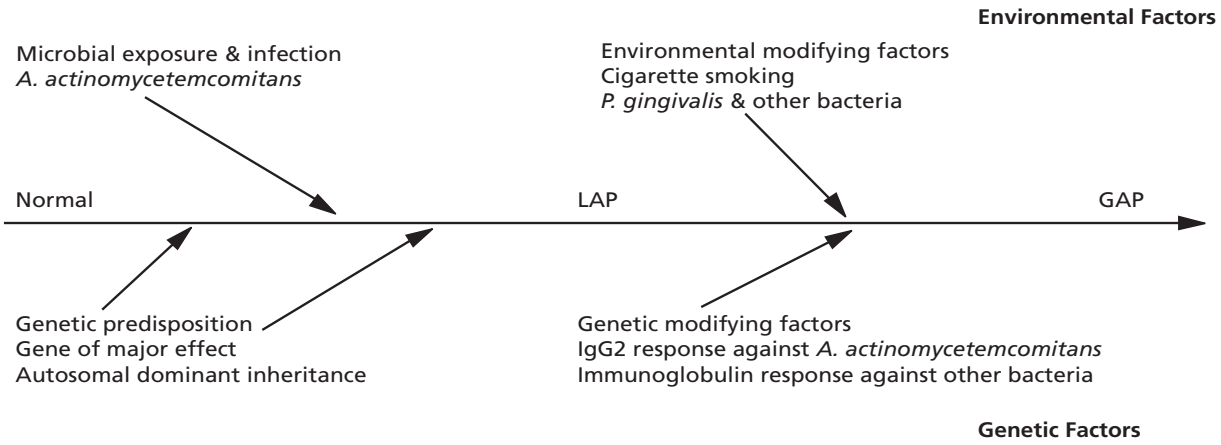


Fig. 19-10 Diagrammatic representation of the current understanding of the eco-genetic interactions leading to development of LAP and GAP in African-American populations. (See text for explanation.)

- Is there loss of periodontal support (loss of clinical attachment and marginal resorption of alveolar bone)?
- Is the loss of attachment accompanied by pocket formation or mostly the result of recession?
- Is there a plausible cause for attachment loss other than periodontitis?
- Is there another process imitating periodontal disease by pseudopocket formation?

From a clinical standpoint, it is important to realize that clinically detectable loss of attachment may occur as a result of pathological events other than periodontitis. Examples are traumatic injuries, removal or presence of impacted teeth (Kugelberg 1992), tooth position, orthodontic tooth movement, advanced decay, subgingival margins of restorations, etc. This means that the clinician must recognize different causes for attachment loss and must rule out other causes of attachment loss by a combination of careful clinical examination and assessment of the dental history. Orthodontic considerations are necessary to evaluate attachment loss without pocket formation (recession). In such instances the appropriate clinical diagnosis may be *incidental attachment loss*.

After establishing the presence of periodontitis, the clinician should determine which clinical diagnosis best describes the disease in the individual patient: chronic, aggressive or necrotizing periodontitis. Since the current classification is based on the combination of clinical presentation, rate of disease progression, and pattern of familial aggregation of cases in the absence of a systemic cause for the clinical observations, the next questions should address these parameters:

- Does the patient have a systemic condition that would in itself explain the presence of periodontitis?

As indicated, the diagnosis of chronic, aggressive or necrotizing periodontitis implies presence of periodontal destruction in the absence of systemic diseases that may severely impair host defense. A well constructed and well taken medical history is fundamental for identifying the presence of systemic involvements accompanied with periodontitis (see Chapter 7). Careful questioning regarding recurrent infections, their familiarity, presence of severe diseases or their symptoms and signs should be part of the evaluation of all periodontal patients. Consultation with the attending physician and evaluation of laboratory parameters are frequently necessary. Understanding of the medical condition that may be associated with periodontitis is fundamental. Some conditions are relatively frequent disorders such as poorly controlled diabetes mellitus; others are rare inherited disorders such as the palmo-plantar keratosis (Papillon-Lefèvre and Heim-Munk syndromes) or hypophosphatasia. Some are inborn defects such as the leukocyte adhesion deficiencies (LAD); others are acquired following exposure to pharmacological agents such as drug-induced granulocytopenia. Positive confirmed history of a significant systemic condition results in the diagnosis of *periodontal manifestation of systemic disease*.

In such instances, the periodontitis is likely to represent an oral manifestation of the systemic disease. Examples of significant conditions are AIDS, leukemia, neutropenia, diabetes or rare genetic diseases such as histiocytosis X, Papillon-Lefèvre syndrome or Chediak-Steinbrinck-Higashi syndrome (see Chapter 11 and Fig. 19-4).

In the absence of significant systemic components, the next questions relate to the exclusion of the rare but clearly identified necrotizing/ulcerative forms. The question will then be:

- Does the patient have signs or symptoms of necrotizing periodontitis?

If the answer to both of the previous questions is negative, differential diagnosis between chronic or aggressive periodontitis will be required. In this

respect it is important to observe that chronic periodontitis has been defined as the common form of periodontitis whose diagnosis is done by excluding the presence of aggressive periodontitis (Armitage 1999). Diagnosis of AgP is made by verification of the satisfaction by the individual cases of the primary and secondary features described in the international classification workshop (see discussion above).

In this respect it must be recognized that the features include both clinical and laboratory aspects. In the diagnosis of a case, clinical and history parameters are initially utilized to suspect the presence of AgP, while laboratory tests are frequently utilized to confirm the diagnosis. In this respect, it is important to realize that periodontal diagnosis based only on periodontal probing and dental radiography does not classify causes; rather, it describes destruction patterns.

A tentative clinical diagnosis of AgP is made based on the following criteria:

- Absence of significant systemic conditions
- Rapid attachment loss and bone destruction
- Familial aggregation of cases
- Lack of consistency between clinically visible bacterial deposits and severity of periodontal breakdown.

A rapid rate of destruction of the periodontium is a major criterion for the diagnosis of AgP. It is aimed at identifying subjects characterized by high virulence of the microflora and/or high levels of susceptibility. Although correct application of this criterion requires availability of clinical or radiographic data from more than one time point, presence of severe destruction in relation to the age of the subject is frequently considered to be sufficient information to infer rapid progression.

Establishing the presence of familial aggregation of cases is based on a combination of history and clinical examination of family members of the affected individual. At this stage there is inadequate evidence to establish the best approach to obtain a significant estimation of familial aggregation. A recent study, in particular, questioned the reliability of family history as a way to establish familial aggregation (Llorente & Griffiths 2006).

It is maintained that in the majority of AgP cases the amount of periodontal destruction seems to be higher than that expected from the mere accumulation of local factors. This observation, however, may not be true for all cases. In general, a discrepancy between local factors and the amount of periodontal tissue breakdown is considered to be an indication for either infection with particularly virulent microorganisms, or presence of a highly susceptible host. This information may be consequential in determining surgical goals of therapy, the impact of antibiotics, and the possible impact of sub-optimal hygiene as a risk factor for disease recurrence.

The international classification workshop consensus indicated that not all listed primary and secondary features need to be present in order to assign an AgP diagnosis and that the diagnosis may be based on clinical, radiographic, and historical data alone. It also indicated that laboratory testing, although helpful, might not be essential in making an AgP diagnosis.

Once an AgP diagnosis has been made based on the criteria above, differential diagnosis between LAP and GAP needs to be made. In this respect specific clinical features have been suggested. A diagnosis of LAP is made based on evidence of circumpubertal onset and localized first molar/incisor presentation with interproximal attachment loss on at least two permanent teeth, one of which is a first molar, and involving no more than two teeth other than first molars and incisors. A diagnosis of GAP takes into account the fact that this form of disease usually affects persons under 30 years of age (but patients may be older) and that it presents with generalized interproximal attachment loss affecting at least three permanent teeth other than first molars and incisors. Furthermore this pathology is characterized by a pronounced episodic nature of the destruction of attachment and alveolar bone. The differential diagnosis may benefit from additional laboratory investigations of the individual host response to the infecting organisms.

In order to properly describe the specific AgP case, modifying factors should also be explored by addressing the question of the presence of modifying or contributory factors such as smoking or drug abuse. Such additional information is relevant since these factors may explain a specific presentation of disease in terms of its extent and severity. Furthermore, these factors, unlike genetic factors, are amenable to modification through appropriate intervention. Therapy should therefore include an approach aimed at controling the impact of these factors.

Even though differential diagnosis between AgP and chronic periodontitis and differentiation between LAP and GAP is mostly based on history and clinical presentation, it must be emphasized that clinical parameters alone cannot further discriminate between forms of disease with similar clinical appearance. Inferences regarding a specific etiology are speculative under such circumstances and require further laboratory testing for confirmation.

In the previous classification system, age at onset or age at diagnosis was considered helpful to further characterize specific clinical syndromes. LAP, in particular, is thought to occur in adolescents, 13–14 years old to 25 years, while GAP is generally found in adolescents or young adults of less than 30–35 years. It should be realized, however, that (1) some cases may present initial LAP at an earlier age, (2) LAP may start before puberty and affect the primary dentition, (3) patterns of periodontal destruction compatible with LAP may be initially detected at an age

older than 25, and (4) there may be a tendency toward spreading from a localized to a generalized pattern of AgP in older subjects of these groups.

Another difficulty is related to the fact that periodontal destruction is often diagnosed when the attachment loss is already fairly advanced. In general, distinct alterations in the morphology of the periodontium and substantial tissue damage are necessary for establishing a clear diagnosis. Milder or initial stages of disease or sites at risk for future periodontal breakdown cannot be detected based on clinical parameters. This makes it difficult to intercept and treat initial forms of AgP. Furthermore, such difficulty makes it extremely important to examine the other members of the family of the proband as well: siblings may present with clinically undetectable disease in spite of the presence of the putative pathogens. A common strategy employed to overcome the insufficient ability of clinical parameters to detect early disease is to closely monitor high-risk patients such as the siblings of the probands. It is in this respect important to underline that "incidental attachment loss" may, in some cases, represent an initial manifestation of AgP. In such a case an isolated periodontal lesion characterized by attachment loss with pocketing may represent the only clinically evident AgP lesion. Such subjects should, therefore, be considered at high risk for the development of AgP and require close monitoring and possibly further microbiologic diagnosis.

Microbiologic diagnosis

The presence of specific microorganisms is considered as one of the secondary features of AgP. A systematic review has, however, clearly indicated that the presence or absence of suspected periodontal pathogens such as *A.a.* on the species level cannot fully discriminate subjects with AgP from subjects with chronic periodontitis. Although it is more than ten times more likely that *A.a.*-negative patients suffer from chronic than from aggressive periodontitis, any *A.a.*-positive individual with periodontitis is three times more likely to be suffering from chronic than from aggressive periodontitis (Mombelli *et al*. 2002). The noted limitations in discriminating power to distinguish AgP from ChP should not be interpreted to mean that a test aiming at the detection of target microorganisms is completely useless in any clinical situation. Treatment studies suggest that *A.a.* is particularly difficult to suppress with conventional mechanical therapy (Mombelli *et al*. 1994a, 2000), longitudinal and retrospective studies have indicated an increased risk for periodontal breakdown in positive sites (Fine 1984; Slots *et al*. 1986; Bragd *et al*. 1987; Slots & Listgarten 1988; Rams *et al*. 1996), and results of treatment seemed to be better if *A.a.* could not be detected any more at follow up (Bragd *et al*. 1987; Carlos *et al*. 1988; Haffajee *et al*. 1991; Grossi *et al*. 1994; Haffajee & Socransky 1994). Therefore, even if microbiologic testing alone cannot distinguish between chronic and aggressive periodontitis, access to microbiologic data may improve the outcome of periodontal therapy. This should be taken into account particularly with regards to the highly leukotoxic variant of *A.a.*, which shows a stronger association with AgP than *A.a.* as a whole. In discussing the diagnostic potential of a test, one should also consider that the main difference between clinical groups may not be the prevalence but rather the amount of putative pathogens found in positive samples (Gunsolley *et al*. 1990).

Microbiologic data may be useful to establish a differential diagnosis in patients clinically diagnosed with AgP. Knowledge of whether a clinical condition is associated with *A.a.*, and/or with other periodontal pathogens, such as *P. gingivalis*, has an impact on the need to supplement conventional therapy with antibiotics and on the choice of the antimicrobial drug (see Chapter 42). Microbiologic information can be useful at different stages of the treatment plan, i.e. as a part of the initial diagnosis, at re-evaluation or during the recall phase. The need for microbiologic information before therapy depends on the general strategy for treatment. Many clinicians prefer to remove bacterial deposits mechanically in a first treatment phase without the adjunctive use of systemic antibiotics. As microbiologic findings have no influence on the way this initial treatment is performed, microbiologic testing may be postponed until the first phase is completed. One should keep in mind, however, that the reduction in bacterial load might increase the possibility of false-negative results when an insensitive microbiologic test is used. If the specific clinical diagnosis is LAP, then the clinician can assume even without a microbiologic test that the treatment should be directed towards a maximal suppression of *A.a.* This is due to the fact that the great majority of LAP patients are infected with this organism. This is different for all other forms of AgP, where such a close association of one microbial species with the disease cannot be assumed, and therefore microbial testing should be performed.

Since *A.a.* and *P. gingivalis* can be transmitted from periodontal patients to family members, microbial testing of spouses, children or siblings of AgP patients may be indicated to intercept early disease in susceptible individuals.

Evaluation of host defenses

Several forms of AgP have been associated with impairment of host defenses. Classic studies have indicated that in some populations both LAP and GAP forms are associated with high incidence of phagocyte functional disturbances, such as depressed neutrophil chemotaxis and other phagocyte antibacterial dysfunctions. In many of these patients, AgP was the only infection that was associated with the reduced phagocyte function(s); this observation

is important in two respects. First, AgP-associated phagocyte defects are frequently insignificant in terms of increasing susceptibility to infections other than periodontitis. Furthermore, it is likely that such "mild" leukocyte defects may go unnoticed until laboratory testing is performed in conjunction with periodontal diagnosis. Reports of such phagocyte defects relate mostly to AgP subjects from African American groups; systematic evaluations of PMN and monocyte functions associated with clinical diagnosis of AgP in European Caucasians failed to confirm a high prevalence of abnormalities (Kinane *et al*. 1989a,b). Testing for these host defense parameters, therefore, may be more restricted to specific populations. Another important aspect is that, so far, no specific study has attempted to associate treatment response or incidence of recurrent disease with the presence of the above-mentioned abnormalities.

More recent investigations have indicated that specific patterns of host response to bacterial pathogens are associated with different forms of AgP; this early evidence may be extremely helpful for the development of clinically useful tests to estimate the risk of developing AgP. In this respect two findings deserve to be mentioned:

1. AgP patients present significantly higher levels of crevicular fluid PGE_2 than chronic periodontitis patients or healthy subjects. This finding may indicate that monocytes from these patients respond to bacterial and inflammatory stimuli with very high levels of local release of inflammatory mediators. These may induce an exuberant inflammatory reaction associated with high levels of activation of tissue-degrading matrix-metalloproteinases.
2. GAP patients have a decreased ability to mount high titers of specific IgG_2 antibodies to *A.a.* These subjects exhibit a tendency towards progressive periodontal destruction leading to tooth loss over a relatively short period of time. LAP patients, on the other hand, seem to have better prognosis and do not express this trait. Since there are indications that at least some LAP cases may progress into generalized forms, early detection of patients infected with *A.a.* but producing low levels of specific antibodies may allow early identification of a high-risk group for development of GAP. Serum antibody titers (IgG_2 in particular) and/or avidity to *A.a.* may be particularly useful in the differential diagnosis of GAP and LAP syndromes and in the early detection of the LAP cases with high risk for progression into the more widespread forms of disease.

Genetic diagnosis

Given the disproportionately high incidence of AgP in the families of affected individuals, evaluation of siblings of the proband and other family members is a requirement. Clinical determination of different disease forms in the family should be followed by construction of a pedigree of the AgP trait. Such diagnosis may bring considerable information regarding the level of risk eventually shared within the family. Furthermore, it helps to establish the need for monitoring clinically unaffected individuals.

All the evidence gathered during the diagnostic process should contribute to the definition of a specific diagnosis. An example of such diagnosis is illustrated in Fig. 19-11: LAP in a 22-year-old systemically healthy African American female patient, associated with *A.a.* infection without detectable levels of *P. gingivalis*, inconsistency between local factors and amount of clinically detectable breakdown, absence of demonstrable leukocyte defects, no known contributory factors, and no siblings displaying clinically detectable periodontitis.

Principles of therapeutic intervention

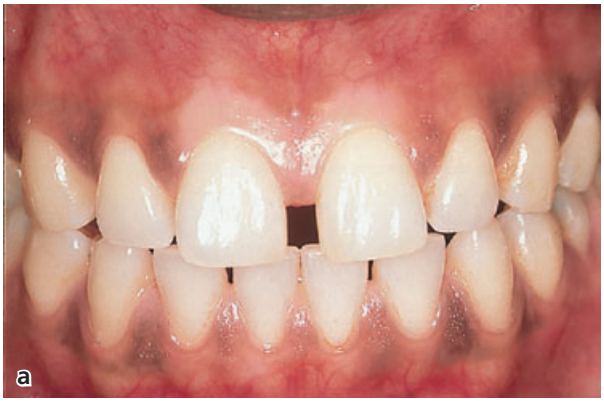
Treatment of AgP should only be initiated after completion of a careful diagnosis by a specifically trained periodontist. The severity of some of the AgP forms suggests that specialists, possibly working in association with highly specialized centers, could best perform both diagnosis and treatment of these rare forms of periodontitis. The roles of the general practitioner, the pedodontist or the orthodontist, however, are fundamental in the detection of possible cases to be referred for further evaluation and therapy.

Successful treatment of AgP is considered to be dependent on early diagnosis, directing therapy towards elimination or suppression of the infecting microorganisms and providing an environment conducive to long-term maintenance. The differential element of treatment of AgP, however, relates to specific efforts to affect the composition and not only the quantity of the subgingival microbiota.

Elimination or suppression of the pathogenic flora

A.a. elimination has been associated with successful therapy; conversely, recurrent lesions have been shown to still harbor this organism. Several investigators have reported that scaling and root planing of juvenile periodontitis lesions could not predictably suppress *A.a.* below detection levels (Slots & Rosling 1983; Christersson *et al*. 1985; Kornman & Robertson 1985). Soft tissue curettage and access flap therapy also had limited success in eliminating *A.a.* (Christersson *et al*. 1985).

A.a. is also difficult to eliminate by conventional mechanical therapy in adult periodontitis patients, and it is therefore not surprising to observe the presence of this microorganism in the subgingival microflora of many non-responding periodontitis patients (Bragd *et al*. 1985; van Winkelhoff *et al*. 1989; Renvert



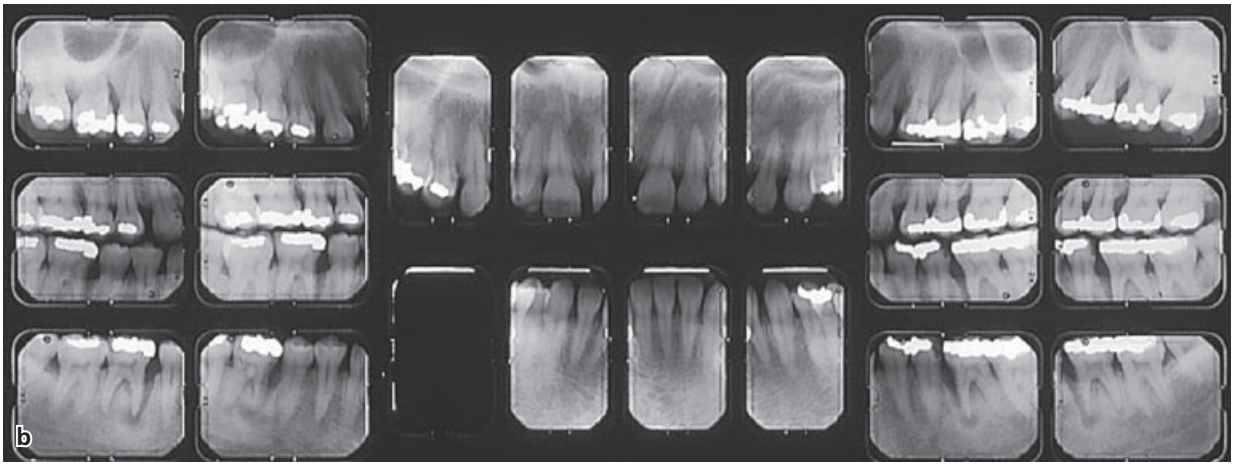


Fig. 19-11 (a,b) Clinical and radiographic presentation of a 22-year-old African-American female. Clinical attachment loss and alveolar bone loss are localized on the mesial aspect of the first molars, where deep, vertical defects are apparent. (c–e) Detailed views of the defect on the mesial aspect of 26. No other tooth appears to be affected. Microbiology (DNA probe analysis of *A. actinomycetemcomitans*, *P. gingivalis* and *P. intermedia*) confirmed the presence of high levels (>104 bacteria/sample) of *A. actinomycetemcomitans* in all four deep lesions. *Pr. intermedia* was also detectable in three of four sites, while *P. gingivalis* was undetectable. The patient did not display abnormal leukocyte functions; furthermore, she had a non-contributory medical history, and did not smoke. She had a younger brother (15 years old) and an older sister (27 years old); on clinical examination, the periodontium of both of them appeared to be within normal limits. The following diagnosis was made: "LAP in a 22-year-old systemically healthy African-American female; associated with *A. actinomycetemcomitans* infection without clinically detectable levels of *P. gingivalis*; absence of demonstrable leukocyte defects; no known contributory factors; no cigarette smoking; no siblings displaying clinically detectable AgP".

et al. 1990a,b; Rodenburg *et al*. 1990; Mombelli *et al*. 1994a). Similar, but less systematic observations have also been reported for the ability to suppress the microflora associated with some GAP forms, where high subgingival loads of *P. gingivalis*, *B. forsythus*, *A.a.*, and other highly virulent bacteria are frequently detected.

Use of antibiotics has been suggested as a rational complement to mechanical debridement in these cases. Regimens, including the adjunctive administration of tetracyclines or metronidazole, have been tested for the treatment of LAP and other forms of AgP (see Chapter 42).

The choice of antibiotic can either be empiric (based on published information on the efficacy of the regimen in similar populations) or guided by information about the nature of the involved pathogenic microorganism(s) and/or their antibiotic susceptibility profile. Both approaches have been suggested but currently there is no direct evidence that microbiologic diagnosis and targeted selection of the antibiotic regimen provides an additional benefit compared to empiric use.

With regards to empiric use, effectiveness is based on outcomes of a series of trials that have specifically assessed the clinical outcomes following administration of a specific antibiotic regimen or placebo in combination with mechanical instrumentation of the root surface and oral hygiene instructions. The approach is supported by a meta-analysis (Haffajee *et al.* 2003) indicating significantly greater clinical improvements following systemic antibiotic administration upon completion of subgingival instrumentation. Metronidazole in combination with amoxicillin may suppress *A.a.* more effectively than single antibiotic regimes and has thus become increasingly popular. Substantial evidence indicates that subgingival *A.a.* can be eliminated or suppressed for a

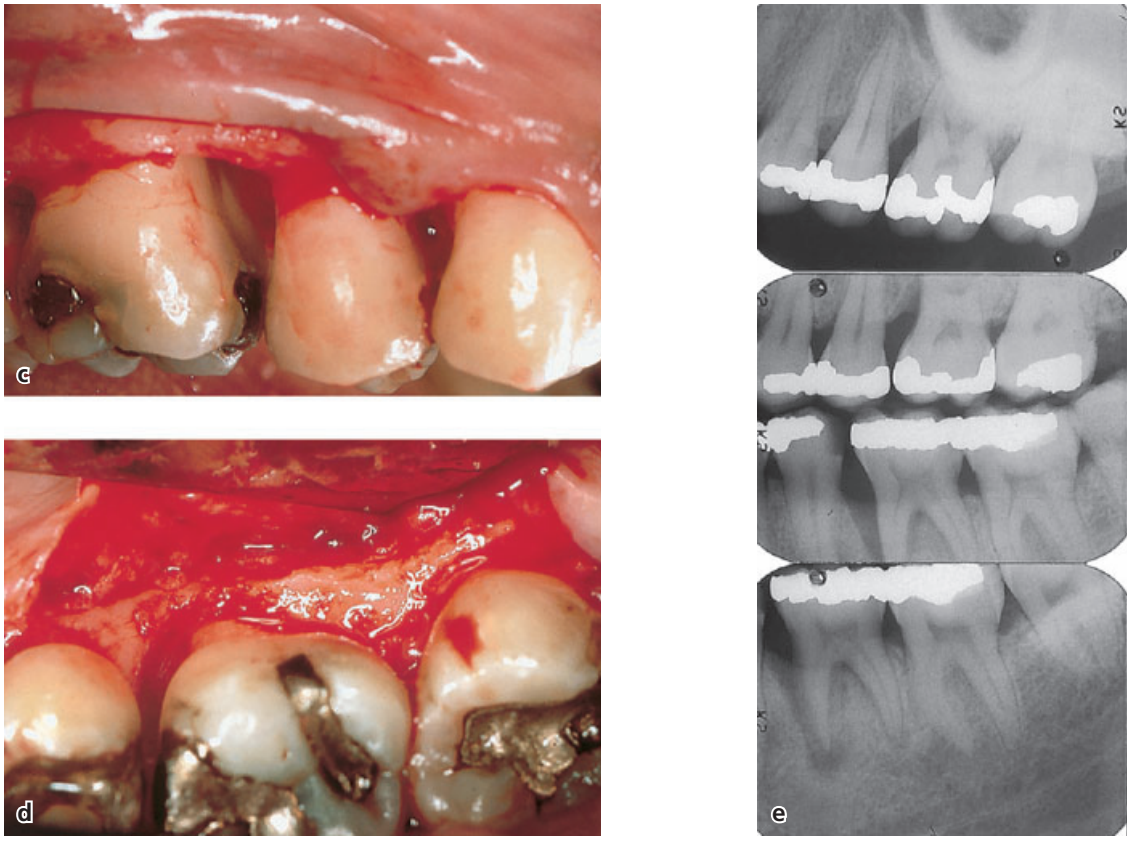


Fig. 19-11 *Continued*

prolonged period by mechanical debridement supplemented with systemic metronidazole plus amoxicillin.

Systemic antibiotics should only be administered as an adjunct to mechanical debridement because in undisturbed subgingival plaque the target organisms are effectively protected from the antibiotic agent due to the biofilm effect (see Chapter 42).

Antibiotics have been used in essentially two ways for the treatment of AgP: (1) in combination with intensive instrumentation over a short period of time after achievement of adequate plaque control in a pretreatment motivation period; or (2) as a staged approach after completion of the initial therapy.

A recent randomized controlled clinical trial (Guerrero *et al.* 2005) has provided evidence of a significant benefit arising from a treatment approach consisting of: (1) achievement of adequate supragingival plaque control (less than 25% of tooth sites with detectable plaque); (2) subgingival instrumentation with a combination of hand and mechanical instruments delivered intensively over a 2-day period; (3) an adjunctive systemic antibiotic regimen consisting of metronidazole (500 mg, tid for 7 days) combined with amoxicillin (500 mg, tid for 7 days). The results of the placebo arm showed highly significant improvements in clinical parameters including reductions of probing depth and improvement of clinical attachment levels throughout the dentition. The adjunctive antibiotic provided additional benefits in the deeper pockets in terms of all parameters.

As part of the second option, treatment is started with an initial phase of mechanical therapy, including systematic scaling and planing of all accessible root surfaces and the introduction of meticulous oral hygiene. After a period of 4–6 weeks, the case is reassessed clinically. Based on persistence of periodontal lesions, a second phase of therapy is planned. Decisions are made as to how to gain access to deep lesions with appropriate surgical procedures and concerning the administration of antimicrobial agents. Microbial samples from the deepest pocket in each quadrant may provide additional information about the presence and relative importance of putative pathogens. Systemic antimicrobial therapy with the appropriate agent is usually initiated immediately upon completion of the surgical interventions or immediatedly after another round of mechanical instrumentation to ensure that subgingival plaque deposits have been reduced as much as possible and to disrupt the subgingival biofilm.

Microbiologic testing, if performed, may be repeated at 1–3 months after completion of therapy to verify the elimination or marked suppression of the putative pathogen(s). After resolution of the periodontal infection, the patient should be placed on an individually tailored maintenance care program, including continuous evaluation of the occurrence

and of the risk of disease progression. Optimal plaque control by the patient is of paramount importance for a favorable clinical and microbiologic response to therapy. Recurrence of disease is an indication for a repetition of microbiologic tests, for re-evaluation of the host immune response, and re-assessment of the local and systemic modifying factors. Further therapy should be targeted against putative periodontal pathogens and should take into account the systemic immune responses of the subject.

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Chapter 20

Necrotizing Periodontal Disease

Palle Holmstrup and Jytte Westergaard

Nomenclature

Necrotizing gingivitis (NG), necrotizing periodontitis (NP), and necrotizing stomatitis (NS) are the most severe inflammatory periodontal disorders caused by plaque bacteria. The necrotizing diseases usually run an acute course and therefore the term acute is often included in the diagnoses. They are rapidly destructive and debilitating, and they appear to represent various stages of the same disease process (Horning & Cohen 1995). A distinction between NG and NP has not always been made in the literature, but parallel to the use of the term gingivitis, NG should be limited to lesions only involving gingival tissue with no loss of periodontal attachment (Riley *et al*. 1992). Most often, however, the disease results in loss of attachment (MacCarthy & Claffey 1991), and a more correct term in cases with loss of attachment is NP, provided the lesions are confined to the periodontal tissues including gingiva, periodontal ligament, and alveolar bone. Further progression to include tissue beyond the mucogingival junction is characteristic of necrotizing stomatitis and distinguishes this disease from NP (Williams *et al*. 1990).

The necrotizing periodontal diseases have had several names, including ulceromembranous gingivitis, acute necrotizing ulcerative gingivitis (ANUG), Vincent's gingivitis or Vincent's gingivostomatitis, necrotizing gingivostomatitis, and trench mouth (Pickard 1973; Johnson & Engel 1986; Horning & Cohen 1995). Vincent first described the mixed fusospirochetal microbiota of the so-called "Vincent's angina", characterized by necrotic areas in the tonsils (Vincent 1898). A similar mixed microbiota has been isolated from NG lesions, but Vincent's angina and NG usually occur independently of each other, and should be regarded as separate disease entities.

NS has features in common with the far more serious *cancrum oris*, also denoted noma. This is a destructive and necrotizing, frequently fatal, stomatitis in which the same mixed fusospirochetal flora dominates. It occurs almost exclusively in certain developing countries, mostly in children suffering from systemic diseases including malnutrition (Enwonwu 1972, 1985). It has been suggested that cancrum oris always develops from pre-existing NG (Emslie 1963) but this connection has not been confirmed (Pindborg *et al*. 1966, 1967; Sheiham 1966).

In the literature, a distinction between NG, NP, and NS is seldom made. However, the reader should be aware of this uncertainty and the consequences of the lack of distinction between the three diagnoses in reports. The uncertainty is reflected in the present chapter by the use of the term necrotizing periodontal disease (NPD) as a common denominator for necrotizing gingivitis, necrotizing periodontitis, and necrotizing stomatitis.

Prevalence

During World War II, up to 14% of Danish military personnel encountered NPD (Pindborg 1951a). Large numbers of civilians also suffered from the disease (King 1943; Stammers 1944). After World War II, the prevalence of NPD declined substantially and it is now rare in industrialized countries. It occurs particularly among young adults. In the 1960s NPD was found in 2.5% of 326 US students during their first college year, but over the next year more students became affected, with a total of 6.7% demonstrating the disease during their first two college years (Giddon *et al*. 1964). Among 9203 students in Chile, 6.7% showed at least one necrotic ulcerated lesion on the papillae (Lopez *et al*. 2002), and the presence of necrotizing lesions was associated with the occurrence of clinical attachment loss (Lopez & Bælum 2004). Other studies in industrialized countries have reported prevalence of 0.5% or less (Barnes *et al*. 1973; Horning *et al*. 1990). In Scandinavia, the disease is now very rare among otherwise healthy individuals, with a prevalence of 0.001% among young Danish military trainees (personal communication, F. Prætorius). NPD can be observed in all age groups but there are geographic differences in the age distribution.

The disease seems to occur slightly more often among HIV-infected individuals. Studies among groups of HIV-infected individuals have revealed prevalences of NPD between 0% and 27.7% (Reichart *et al*. 2003; Holmstrup & Westergaard 1994). However, most studies have included cohorts of individuals connected with hospitals or dental clinics. Studies conducted outside these environments have shown relatively low prevalence figures. NP was found in 1% of 200 HIV-seropositive individuals in Washington, DC (Riley *et al*. 1992), and the prevalence may not, in fact, differ so much from that of the general population (Drinkard *et al*. 1991; Friedman *et al*. 1991; Barr *et al*. 1992); this is particularly true after introduction of antiretroviral therapy (Tappuni & Flemming 2001).

In developing countries, the prevalence of NPD is higher than in the industrialized countries, and the disease frequently occurs in children. This is practically never seen in western countries. In Nigerian villages, between 1.7% and 26.9% of 2–6-year-old children were found with NPD (Sheiham 1966). In India, 54–68% of NPD cases occurred in children below 10 years of age (Migliani & Sharma 1965; Pindborg *et al*. 1966).

Clinical characteristics

Development of lesions

NG is an inflammatory destructive gingival condition, characterized by ulcerated and necrotic papillae and gingival margins resulting in a characteristic punched-out appearance. The ulcers are covered by a yellowish white or grayish slough, which has been termed "pseudomembrane". However, the sloughed material has no coherence, and bears little resemblance to a membrane. It consists primarily of fibrin and necrotic tissue with leukocytes, erythrocytes, and masses of bacteria. Consequently, the term is misleading and should not be used. Removal of the sloughed material results in bleeding and ulcerated underlying tissue becomes exposed.

The necrotizing lesions develop rapidly and are painful, but in the initial stages, when the necrotic areas are relatively few and small, pain is usually moderate. Severe pain is often the chief reason for patients to seek treatment. Bleeding is readily provoked. This is due to the acute inflammation and necrosis with exposure of the underlying connective tissue. Bleeding may start spontaneously as well as in response to even gentle touch. In early phases of the disease lesions are typically confined to the top of a few interdental papillae (Fig. 20-1). The first lesions are often seen interproximally in the mandibular anterior region, but they may occur in any interproximal space. In regions where lesions first appear, there are usually also signs of pre-existing chronic gingivitis, but the papillae are not always edematous at this stage and gingival stippling may be maintained. Usually, however, the papillae swell rapidly and develop a rounded contour; this is particularly evident in the facial aspect. The zone between the marginal necrosis and the relatively unaffected gingiva usually exhibits a well demarcated narrow erythematous zone, sometimes referred to as the linear erythema. This is an expression of hyperemia due to dilation of the vessels in the gingi-

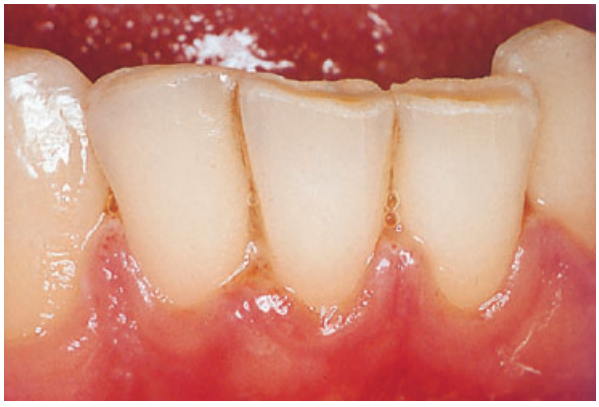

Fig. 20-1 Necrotizing gingivitis with initial punched out defects at the top of the interdental papillae of the mandibular incisor region. Courtesy of Dr. Finn Prætorius.

val connective tissue in the periphery of the necrotic lesions (see Fig. 20-17a).

A characteristic and pronounced *foetor ex ore* is often associated with NPD, but can vary in intensity and in some cases is not very noticeable. Strong *foetor ex ore* is not pathognomonic of NPD as it can also be found in other pathologic conditions of the oral cavity such as chronic destructive periodontal disease.

Interproximal craters

The lesions are seldom associated with deep pocket formation, because extensive gingival necrosis often coincides with loss of crestal alveolar bone. The gingival necrosis develops rapidly and within a few days the involved papillae are often separated into one facial and one lingual portion with an interposed necrotic depression, a negative papilla, between them. The central necrosis produces considerable tissue destruction and a regular crater is formed. At this stage of the disease, the disease process usually involves the periodontal ligament and the alveolar bone, and loss of attachment is now established. The diagnosis of the disease process is consequently NP.

Along with the papilla destruction, the necrosis usually extends laterally along the gingival margin at the oral and/or facial surfaces of the teeth. Necrotic areas originating from neighboring interproximal spaces frequently merge to form a continuous necrotic area (Figs. 20-2 and 20-3). Superficial necrotic lesions only rarely cover a substantial part of the attached gingiva, which becomes reduced in width as the result of disease progression. The palatal and lingual marginal gingiva is less frequently involved than the corresponding facial area. Frequently, gingiva of semi-impacted teeth and in the posterior maxillary region are affected (Figs. 20-4 and 20-5). Progression of the interproximal process often results in destruction of most interdental alveolar bone (Fig. 20-6). In more advanced cases, pain is often considerable and may be associated with a markedly increased salivary flow. As a result of pain it is often difficult for

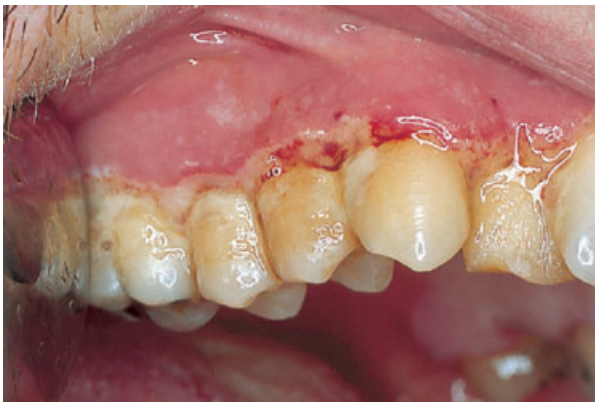

Fig. 20-2 Necrotizing gingivitis progressing along the gingival margin of the right maxilla. The interproximal necrotizing processes have merged.

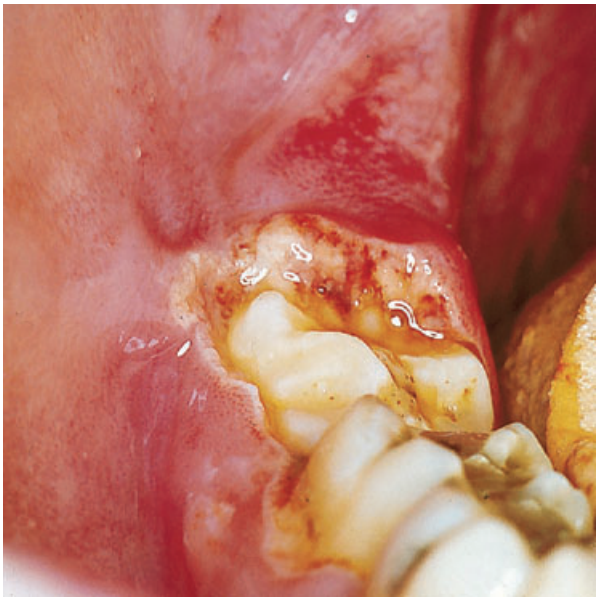

Fig. 20-4 Necrotizing gingivitis affecting gingiva of semi-impacted right mandibular third molar. Courtesy of Dr. Finn Prætorius.

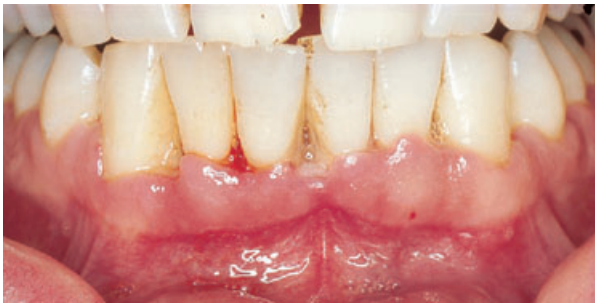

Fig. 20-3 Necrotizing periodontitis with more advanced lesions of interdental papillae and gingival margin. Note the irregular morphology of the gingival margin as determined by the progressive loss of the interdental papillae.

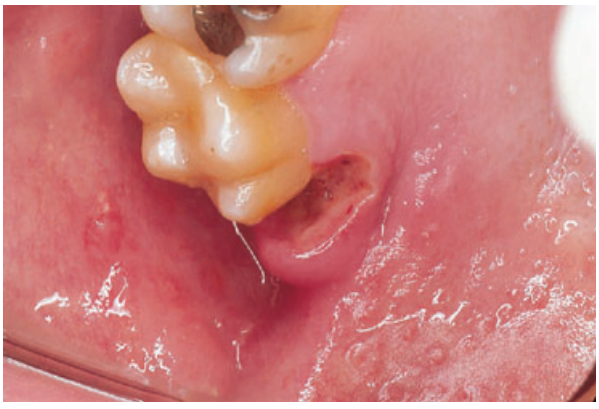

Fig. 20-5 Necrotizing periodontitis affecting right maxillary second molar periodontium. Note the extensive punched out lesion.

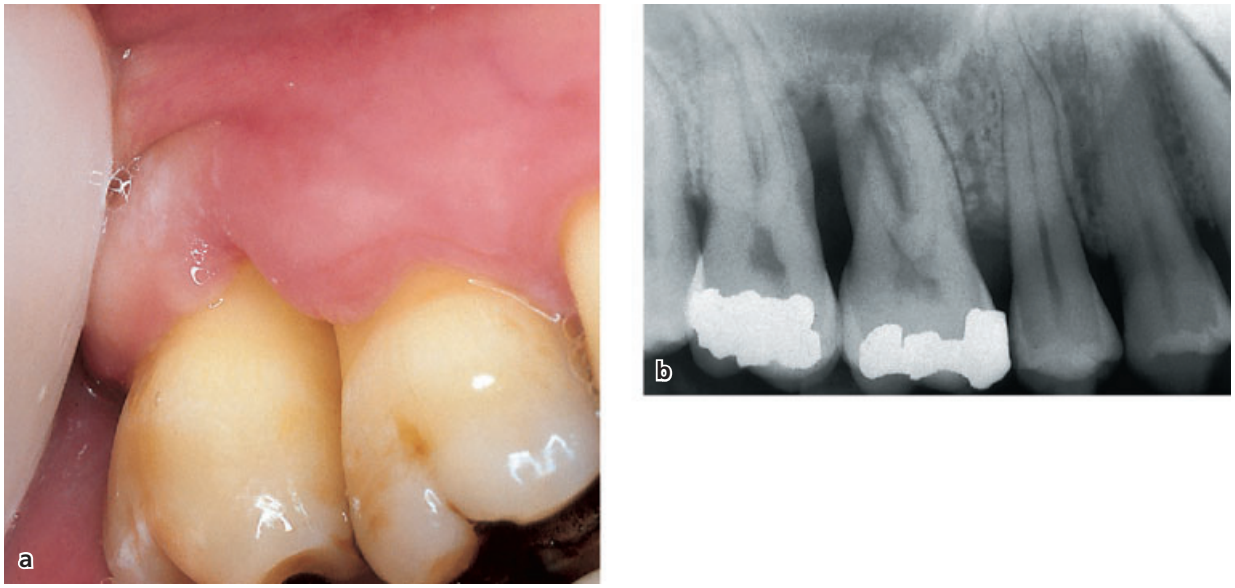

Fig. 20-6 (a) Necrotizing periodontitis often results in major loss of interdental tissue including alveolar bone of the molar regions as demonstrated in the radiograph (b).

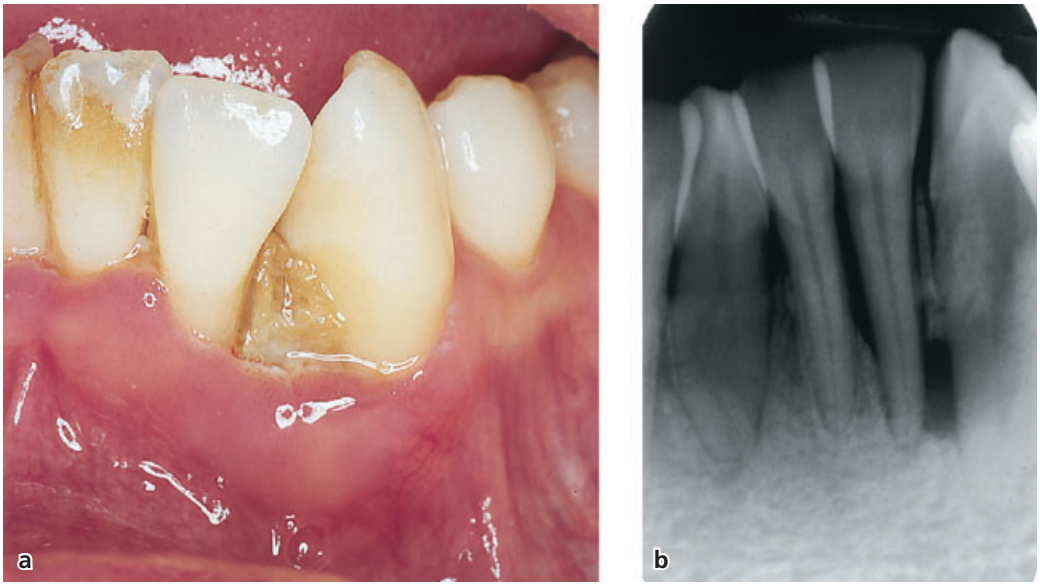

Fig. 20-7 (a) Necrotizing periodontitis with sequestration of alveolar bone between left mandibular lateral incisor and canine. (b) The extension of the sequestrum as seen in the radiograph covers the interdental septum almost to the apices of the roots.

the patients to eat, and a reduced food intake may be critical to HIV-infected patients because they may already lose weight in association with their HIV infection.

Sequestrum formation

The disease progression may be rapid and result in necrosis of small or large parts of the alveolar bone. Such a development is particularly evident in severely immunocompromised patients including HIV-seropositive individuals. The necrotic bone, denoted a sequestrum, is initially irremovable but after some time becomes loosened, whereafter it may be removed with forceps. Analgesia may not be required. A sequestrum may not only involve interproximal bone but also include adjacent facial and oral cortical bone (Fig. 20-7).

Involvement of alveolar mucosa

When the necrotic process progresses beyond the mucogingival junction, the condition is denoted NS (Figs. 20-8 and 20-9) (Williams *et al*. 1990). The severe tissue destruction characteristic of this disease is related to seriously compromised immune functions typically associated with HIV infection and malnutrition (Fig. 20-10). Importantly, it may be life-threatening. NS may result in extensive denudation of bone, resulting in major sequestration with the development of oro-antral fistula and osteitis (SanGiacomo *et al*. 1990; Felix *et al*. 1991).

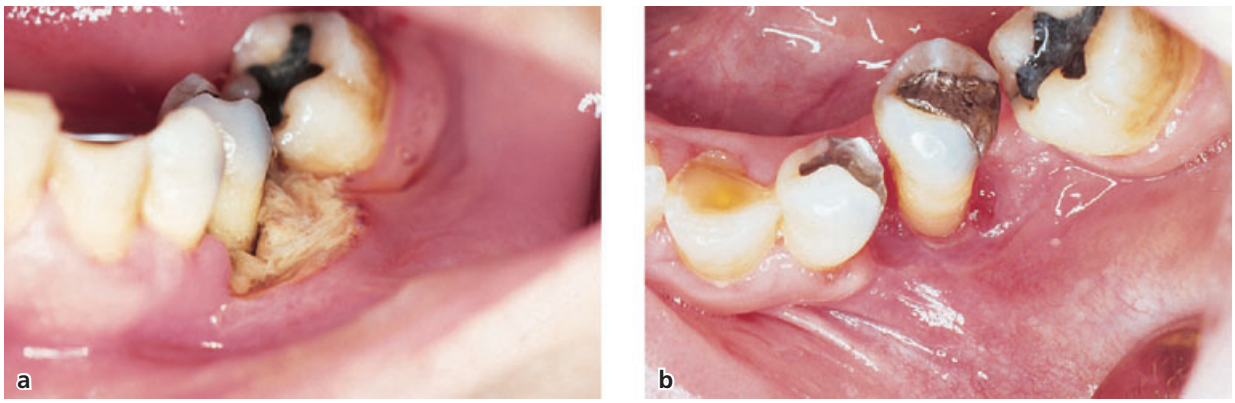

Fig. 20-8 (a) Necrotizing stomatitis affecting periodontium of left mandibular premolar region and adjacent alveolar mucosa. (b) After treatment and healing, no attached gingiva remains.

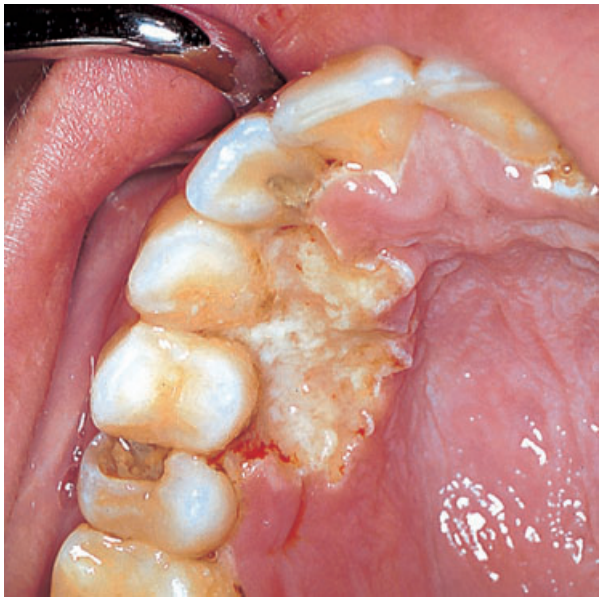

Fig. 20-9 Necrotizing stomatitis of right maxilla with extensive necrotic ulcer of palatal mucosa.

Swelling of lymph nodes

Swelling of the regional lymph nodes may occur in NPD but is particularly evident in advanced cases. Such symptoms are usually confined to the submandibular lymph nodes, but the cervical lymph nodes may also be involved. In children with NPD, swelling of lymph nodes and increased bleeding tendency are often the most pronounced clinical findings (Jiménez & Baer 1975).

Fever and malaise

Fever and malaise is not a consistent characteristic of NPD. Some investigations indicate that elevated body temperature is not common in NG and that, when present, the elevation of body temperature is usually moderate (Grupe & Wilder 1956; Goldhaber & Giddon 1964; Shields 1977; Stevens *et al*. 1984). A small decrease in body temperature in NG has even been described. The disagreement on this point may, in fact, be due to misdiagnosis of primary herpetic gingivostomatitis as NG (see below).

Oral hygiene

The oral hygiene in patients with NPD is usually poor. Moreover, brushing of teeth and contact with the acutely inflamed gingiva is painful. Therefore, large amounts of plaque on the teeth are common, especially along the gingival margin. A thin, whitish film sometimes covers parts of the attached gingiva (Fig. 20-11). This film is a characteristic finding in patients who have neither eaten nor performed oral hygiene for days. It is composed of desquamated epithelial cells and bacteria in a meshwork of salivary proteins. The film is easily removed.

In general, the clinical characteristics of NPD in HIV-seropositive patients do not essentially differ from those in HIV-seronegative patients. However, the lesions in HIV-seropositive patients may not be associated with large amounts of plaque and calculus. Thus, the disease activity in these patients sometimes shows limited correlation with etiologic factors as determined by the amount of bacterial plaque (Holmstrup & Westergaard 1994). Further, lesions of NPD in HIV-seropositive patients have sometimes been revealed in gingival tissue affected by Kaposi's sarcoma (Fig. 20-12).

Acute and recurrent/chronic forms of necrotizing gingivitis and periodontitis

In most instances the course of the diseases is acute, characterized by the rapid destruction of the periodontal tissue. However, if inadequately treated or left untreated, the acute phase may gradually subside. The symptoms then become less unpleasant to the patient, but the destruction of the periodontal tissues continues, although at a slower rate, and the necrotic tissues do not heal completely. Such a condition has been termed chronic necrotizing gingivitis, or periodontitis in the case of attachment loss (Fig. 20-13).

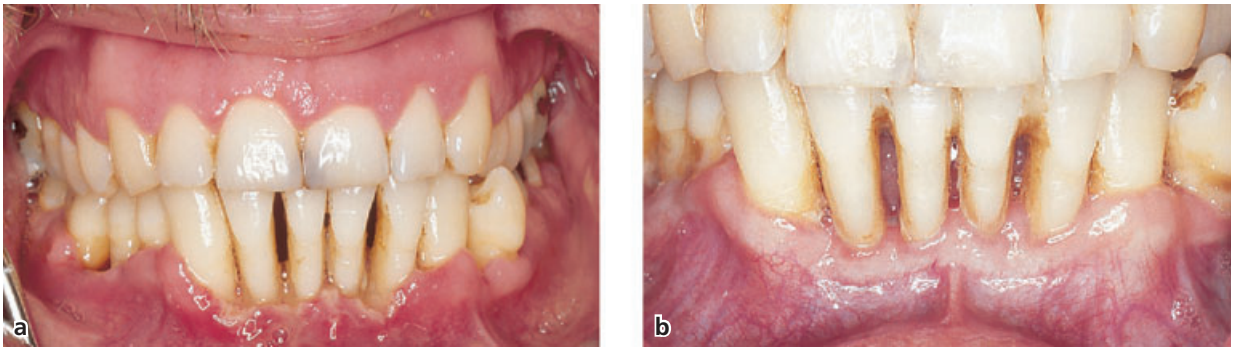

Fig. 20-10 (a) Necrotizing stomatitis affecting the mandible of an HIV-seropositive patient. (b) Two years after treatment the result of treatment is satisfactory, and there has been no recurrence.

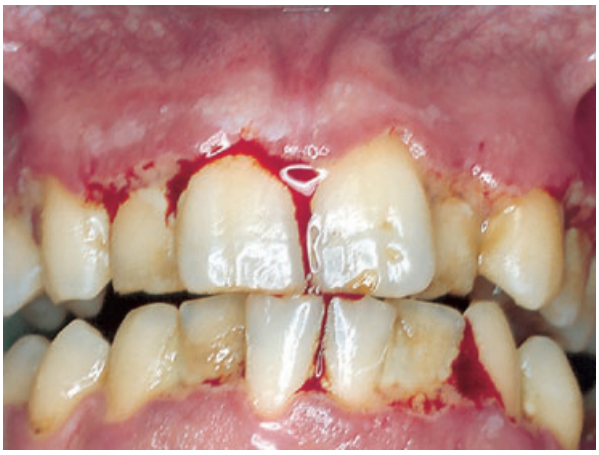

Fig. 20-11 A whitish film sometimes covers parts of the attached gingiva in patients with NPD as demonstrated in the maxillary gingiva. The film is composed of desquamated epithelial cells which have accumulated because the patient has not eaten or performed oral hygiene for days.

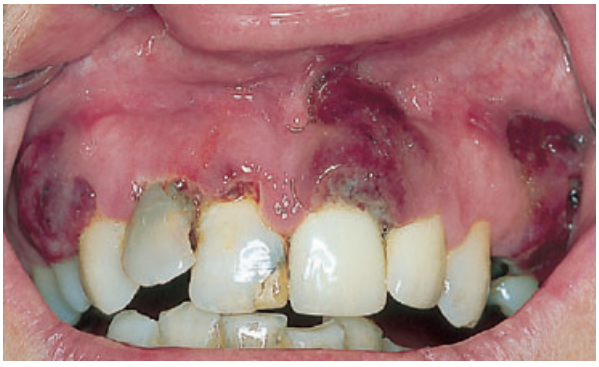

Fig. 20-12 Necrotizing periodontitis affecting Kaposi's sarcoma of left maxillary central incisor gingiva in an HIV-infected patient. The sarcoma affected almost the entire maxillary gingiva after 9 months.

The necrotizing lesions persist as open craters, frequently with a content of subgingival calculus and bacterial plaque. Although the characteristic ulcerative, necrotic areas of the acute phase usually disappear, acute exacerbations with intervening periods of quiescence may also occur. In recurrent acute phases, subjective symptoms again become more prominent

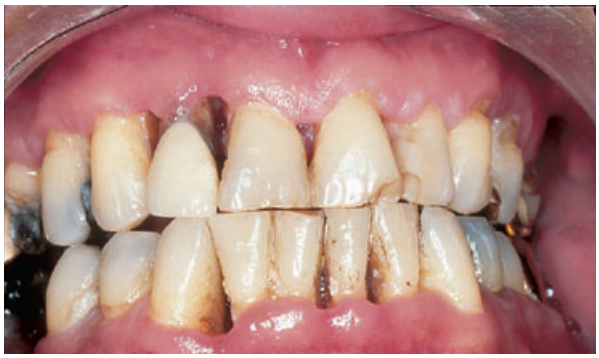

Fig. 20-13 Chronic necrotizing periodontitis with edematous gingiva particularly of mandible. The slightly active necrotizing processes at the bottom of the negative papillae are not visible.

and necrotic ulcers reappear. Some authors prefer the term recurrent rather than chronic to describe this category of necrotizing disease (Johnson & Engel 1986). Plaque and necrotic debris are often less conspicuous in these phases than in the acute forms, because they are located in pre-existing interdental craters. Several adjoining interdental craters may fuse, resulting in total separation of facial and oral gingivae, which form two distinct flaps. Recurrent forms of NG and NP may produce considerable destruction of supporting tissues. The most pronounced tissue loss usually occurs in relation to the interproximal craters.

Diagnosis

The diagnosis of NG, NP, and NS is based on clinical findings as described above. The patient has usually noticed pain and bleeding from the gingiva, particularly upon touch. The histopathology of the necrotizing diseases is not pathognomonic for NG, and biopsy is certainly not indicated in the heavily infected area.

Differential diagnosis

NPD may be confused with other diseases of the oral mucosa. Primary herpetic gingivostomatitis (PHG) is

Table 20-1 Important characteristics for differential diagnosis between NPD and PHG

	NPD	PHG
Etiology	Bacteria	Herpes simplex virus
Age	15–30 years	Frequently children
Site	Interdental papillae. Rarely outside the gingiva	Gingiva and the entire oral mucosa
Symptoms	Ulcerations and necrotic tissue and a yellowish white plaque	Multiple vesicles which disrupt, leaving small round fibrin-covered ulcerations
	Foetor ex ore	*Foetor ex ore*
	Moderate fever may occur	Fever
Duration	1–2 days if treated	1–2 weeks
Contagious	–	+
Immunity	–	Partial
Healing	Destruction of periodontal tissue remains	No permanent destruction

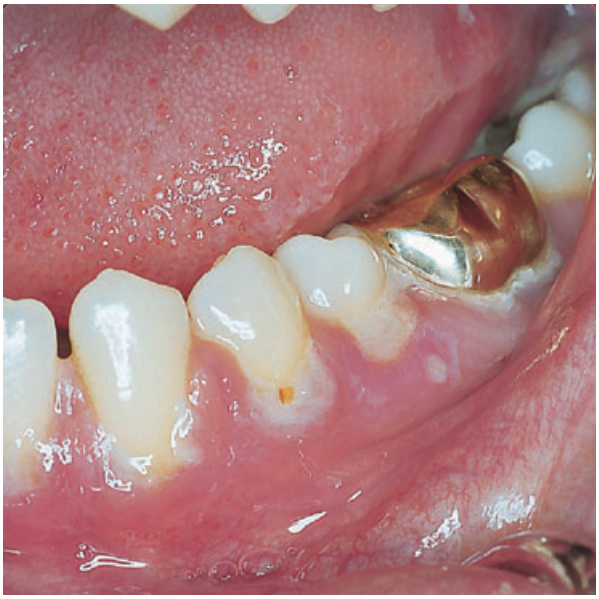

Fig. 20-14 Primary herpetic gingivostomatitis. Note that the ulcers affect the gingival margin but not primarily interdental papillae. A circular ulcer of the second premolar gingiva is highly suggestive of the diagnosis.

not infrequently mistaken for NPD (Klotz 1973). The important differential diagnostic criteria for the two diseases are listed in Table 20-1. It should be noted that in the USA and in northern Europe, NPD occurs very rarely in children, whereas PHG is most commonly found in children. If the body temperature is markedly raised, to 38°C or more, PHG should be suspected. NG and NP has a marked predilection for the interdental papillae, while PHG shows no such limitation and may occur anywhere on the free or the attached gingiva, or in the alveolar mucosa (Fig. 20-14). In PHG erythema is of a more diffuse character and may cover the entire gingiva and parts of the alveolar mucosa. The vesicular lesions in PHG, which disrupt and produce small ulcers surrounded by diffuse erythema, occur both on the lips and tongue as well as on the buccal mucosa. PHG and NPD may occur simultaneously in the same patient, and in such cases there may be mucosal lesions outside the gingiva, and fever and general malaise tend to occur more frequently than with NPD alone.

Oral mucosal diseases that have been confused with NPD include desquamative gingivitis, benign mucous membrane pemphigoid, erythema multiforme exudativum, streptococcal gingivitis, gonococcal gingivitis, and others. All of these are clinically quite distinct from NPD.

In some forms of leukemia, especially acute leukemia, necrotizing ulcers may occur in the oral mucosa and are not infrequently seen in association with the gingival margin, apparently as an exacerbation of an existing chronic inflammatory condition. The clinical appearance can resemble NPD lesions, and the symptoms they produce may be the ones that first make the patient seek professional consultation. In acute leukemia the gingiva often appears bluish red and edematous with varying degrees of ulceration and necrosis. Generally, the patient has more marked systemic symptoms than with ordinary NPD, but can feel relatively healthy for a while. The dentist should be aware of the possibility that leukemias present such oral manifestations, which require medical examination of the patient, whereas biopsy is usually not indicated.

Histopathology

Histopathologically, NG lesions are characterized by ulceration with necrosis of epithelium and superficial layers of the connective tissue and an acute, nonspecific inflammatory reaction (Fig. 20-15). An important aspect is the role of the microorganisms in the lesions, because they have been demonstrated not only in the necrotic tissue components but also in vital epithelium and connective tissue.

Sometimes the histologic findings demonstrate the formation of regular layers with certain characteristics (Listgarten 1965) but there may be variations in regularity. The surface cover of yellowish white or grayish slough can be observed clinically; under the light microscope it appears to be a meshwork of fibrin with degenerated epithelial cells, leukocytes and erythrocytes, bacteria, and cellular debris. At the ultrastructural level, bacteria of varying sizes and forms including small, medium-sized, and large spirochetes have been revealed between the inflammatory cells, the majority of which are neutrophilic granulocytes. Moreover, in presumably vital parts of the surface epithelium, compact masses of spirochetes and short, fusiform rods have been found intercellularly.

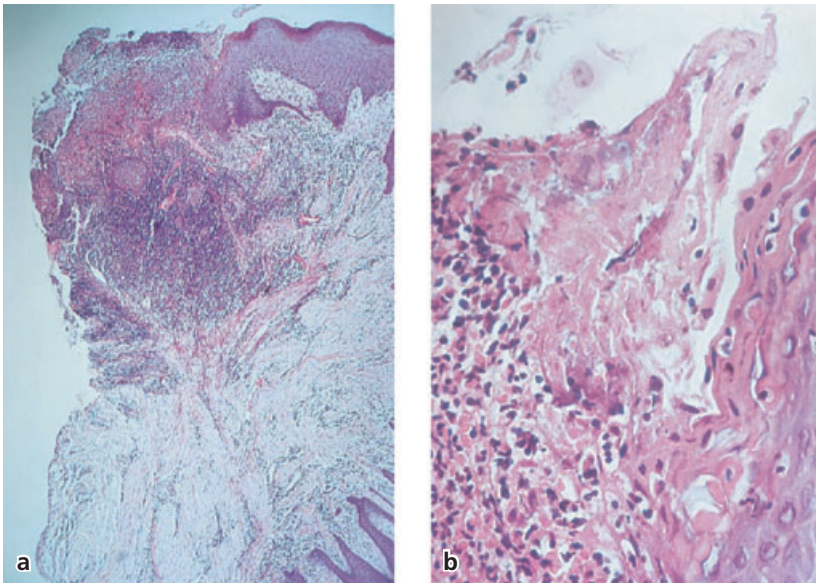

Fig. 20-15 Photomicrograph of gingival tissue affected by necrotizing gingivitis. (a) Upper right part of gingival biopsy shows gingival oral epithelium whereas upper left is ulcerated surface. Underneath the ulcer the connective tissue is heavily infiltrated by inflammatory cells. (b) Higher magnification of margin of ulcer shows necrotic tissue infiltrated with neutrophils. Right border is covered by epithelium. Courtesy of Dr. Finn Prætorius.

The vital connective tissue in the bottom of the lesion is covered by necrotic tissue, characterized by disintegrated cells, many large and medium-sized spirochetes, and other bacteria which, judging from their size and shape, may be fusobacteria. In the superior part of the vital connective tissue, characterized by intact tissue components, the tissue is infiltrated by large and medium-sized spirochetes, but no other microorganisms have been seen. In the vital connective tissue the vessels are dilated. They also proliferate to form granulation tissue, and the tissue is heavily infiltrated by leukocytes. As always in acute processes the inflammatory infiltrate is dominated by neutrophils (Figs. 20-15b and 20-16). In the deeper tissue, the inflammatory process also comprises large numbers of monocytes and plasma cells (Listgarten 1965; Heylings 1967).

Microbiology

Microorganisms isolated from necrotizing lesions

Microbial samples from NPD lesions have demonstrated a constant and a variable part of the flora. The "constant flora" primarily contained *Treponema* sp., *Selenomonas* sp., *Fusobacterium* sp., and *B. melaninogenicus* ss *intermedius* (*Prevotella intermedia*), and the "variable flora" consisted of a heterogeneous array of bacterial types (Loesche *et al*. 1982). Although the characteristic bacterial flora of spirochetes and fusobacteria has been isolated in large numbers from the necrotic lesions in several studies, their presence is not evidence of a primary etiologic importance. Their presence could equally well result from secondary overgrowth. Moreover, the microorganisms associated with NG are also harbored by healthy mouths and mouths with gingivitis or periodontitis (Johnson & Engel 1986). An important role for *Treponema* sp. and *B. intermedius* (*P. intermedia*) has been suggested by studies of antibodies in NPD patients to such bacteria, compared to levels in age- and sex-matched controls with healthy gingiva or simple gingivitis (Chung *et al*. 1983).

There is little available information about the microbiology of HIV-associated NPD. *Borrelia*, Gram-positive cocci, β-hemolytic streptococci and *Candida albicans* have been isolated from the lesions (Reichart & Schiødt 1989). It has also been proposed that human cytomegalovirus (HCMV) may play a role in the pathogenesis of NPD (Sabiston 1986). This virus has been found in the digestive tract of HIV-patients (Kanas *et al*. 1987; Langford *et al*. 1990), and a case of oral HCMV infection with similarities to necrotizing periodontitis has been reported (Dodd *et al*. 1993). An increased frequency of HCMV and other herpes viruses found in necrotizing lesions among Nigerian children supports a contributory role of the viruses (Contreras *et al*. 1997), although it remains to be demonstrated in future studies whether cytomegalovirus does play a causal role.

Pathogenic potential of microorganisms

Our knowledge of the pathogenic mechanisms by which the bacterial flora produces the tissue changes characteristic of NPD is limited. One reason is that it has been difficult to establish an acceptable animal experimental model. However, several of the pathogenic mechanisms which have been associated with chronic gingivitis and periodontitis may also be of etiologic importance in the necrotizing forms of the diseases.

An important aspect in the pathogenesis of periodontitis is the capacity of the microorganisms to invade the host tissues. Among the bacteria isolated from necrotizing lesions, spirochetes and fusiform bacteria can, in fact, invade the epithelium (Heylings 1967). The spirochetes can also invade the vital

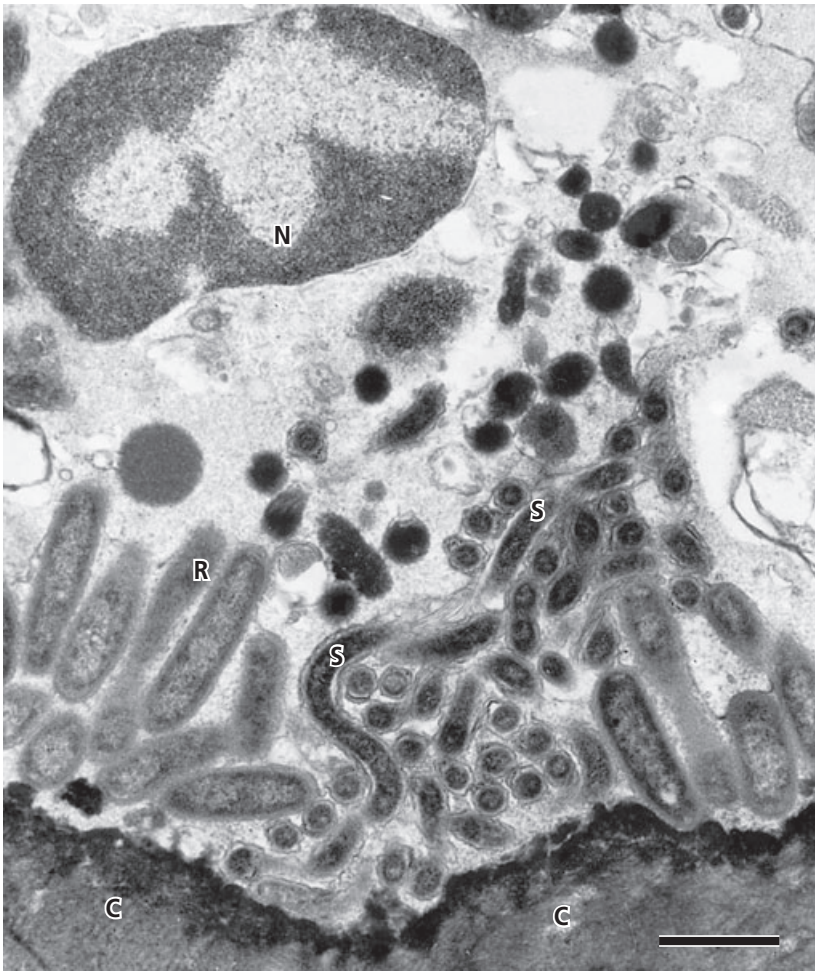

Fig. 20-16 Electronmicrograph demonstrating phagocytosing neutrophil (N) close to the surface of a sequestrum (C), covered by numerous microorganisms including spirochetes (S) and rods (R). Bar = 1 µm.

connective tissue (Listgarten 1965). The pathogenic potential is further substantiated by the fact that both fusobacteria and spirochetes can liberate endotoxins (Mergenhagen *et al*. 1961; Kristoffersen & Hofstad 1970).

A number of observations indicate that the effects of endotoxins are more prominent in NPD than in chronic gingivitis and periodontitis. The large masses of Gram-negative bacteria liberate endotoxins in close contact with connective tissue. Endotoxins may produce tissue destruction both by direct toxic effects and indirectly, by activating and modifying tissue responses of the host (Wilton & Lehner 1980). Through a direct toxic effect, endotoxins may lead to damage of cells and vessels. Necrosis is a prominent feature in the so-called "Shwartzman reaction", which is caused by endotoxins. Indirectly, endotoxins can contribute to tissue damage in several ways: they can function as antigens and elicit immune reactions; they can activate complement directly through the alternative pathway and thereby liberate chemotoxins; but they can also activate macrophages, B and T lymphocytes, and influence the host's immune reactions by interfering with cytokines produced by these cells. Studies have shown that endotoxins can stimulate catabolic processes with degradation of both connective tissue and bone induced by the released cytokines. The extent to which such reactions contribute to host defense or to tissue damage is not yet known.

An aspect which has been of major concern, especially in wartime, is the communicability of the disease. Several reports have considered this aspect but it has been concluded that the necrotizing diseases are not transmissible by ordinary means of contact (Johnson & Engel 1986). Attempts to transmit the disease from one animal to another, or to produce necrotic lesions in experimental animals, have failed to yield conclusive results (MacDonald *et al*. 1963). Several suspect microorganisms and several combinations of microorganisms can produce similar lesions in experimental animals. A combination of four different bacteria, none of them fusobacteria or spirochetes, has been found to possess such properties and there are indications that among the four bacterial species, *Bacteroides melaninogenicus* was the true pathogen (MacDonald *et al*. 1956, 1963). *B. melaninogenicus* may, under certain conditions, produce an enzyme which degrades native collagen (Gibbons & MacDonald 1961). It is still not clear, however, whether this microorganism is of particular importance in the pathogenesis of NPD. NG lesions have

also been induced in dogs pretreated with steroids and inoculated with a fusiform–spirochete culture from dogs which had gingival lesions similar to the NG lesions seen in humans (Mikx & van Campen 1982). The lesions produced in experimental animals may not be identical to those which occur in humans. It is also important to note that even if necrotic lesions can be transmitted by transmission of infectious material or bacterial cultures, this does not necessarily mean that the disease is truly contagious.

It is obvious from the above observations and assumptions that a fundamental question remains to be answered, and at this point it may be stated that the necrotizing periodontal diseases belong to those diseases to which Pasteur referred when he said: "there are some bacteria that cause a disease, but there are some diseases that bring about a condition that is ideal for the growth of some bacteria" (Wilson 1952). If the microorganisms mentioned above play a role in the etiology of the disease, then, presumably, the disease is an opportunistic infection. Consequently, the pathogenic characteristics of the microorganisms are normally overcome by the host defenses, and disease occurs when the host defenses are impaired. The isolated microorganisms do possess biologic activities which may contribute to the pathogenesis, but the exact role of the various microorganisms has not yet been clarified (Johnson & Engel 1986).

Host response and predisposing factors

It is particularly evident for HIV-infected patients that the disease is associated with diminished host resistance; among other predisposing factors, the basic mechanism may include altered host immunity. Changes in leukocyte function and the immune system have been observed in some studies, although the biologic reason for, and significance of, these findings are unclear (Johnson & Engel 1986).

Significantly increased IgG and IgM antibody titers to intermediate-sized spirochetes and higher IgG titers to *B. melaninogenicus* ssp *intermedius* have been found in NG patients as compared to age- and sex-matched healthy and gingivitis control groups (Chung *et al*. 1983). These results, however, are in disagreement with other data showing no differences in serum antibody levels to bacterial antigens (Wilton *et al*. 1971).

Total leukocyte counts have been found to be similar for patients and controls. NG patients, however, displayed marked depression in polymorphonuclear leukocyte chemotaxis and phagocytosis as compared with control individuals. Reduced mitogen-induced proliferation of peripheral blood lymphocytes has also been found in NG patients. It was suggested that elevated blood steroids may account for the reduced chemotactic and phagocytic responses (Cogen *et al*. 1983).

For many years it has been known that a number of predisposing factors may interact with the host defense systems and render the patient susceptible to NPD. Usually, a single one of these factors is not sufficient to establish disease. The various factors, which have been focused upon, comprise systemic diseases, including HIV infection and malnutrition, poor oral hygiene, pre-existing gingivitis and history of previous NPD, psychologic stress and inadequate sleep, smoking and alcohol use, Caucasian background, and young age.

A recent analysis of suspected predisposing factors among American patients with NPD has shown that HIV seropositivity overwhelmed all other factors in importance when present (Horning & Cohen 1995). Among the HIV-seronegative patients the ranked importance of the predisposing factors was: history of previous NPD; poor oral hygiene; inadequate sleep; unusual psychologic stress; poor diet; recent illness; social or greater alcohol use; smoking; Caucasian background; and age under 21 years. The various predisposing factors mentioned below are obviously not equally important in industrialized and developing countries, but many of these factors are known to relate to impaired immunity.

Systemic diseases

Systemic diseases which impair immunity predispose to NPD. This is why NPD occurs more frequently in HIV-infected individuals and in patients with other leukocyte diseases including leukemia (Melnick *et al*. 1988). Examples of other diseases predisposing to NPD are measles, chicken pox, tuberculosis, herpetic gingivostomatitis, and malaria, but malnutrition is also important. Whereas these examples of predisposing factors are rare in western patients, they are evident in developing countries, where they often predispose to NPD and noma in children (Emslie 1963; Pindborg *et al*. 1966, 1967; Sheiham 1966; Enwonwu 1972, 1985). It is important to note that NPD is sometimes an early signal of impending serious illness (Enwonwu 1972).

HIV infection

In Africa, the general population shows a high HIV-seropositive prevalence rate, ranging up to 33% in some populations. In Europe, prevalence figures have been established for areas in the UK, where the prevalence figures were 0.1–0.2% (Nicoll *et al*. 2000). In South Africa NPD in otherwise systemically healthy individuals was correlated with HIV infection, with a predictive value of 69.6% (Shangase *et al*. 2004). In industrialized countries, a significant portion of patients with NPD are HIV-infected patients, and no characteristics have been revealed that distinguish NPD in HIV-seropositive from that in HIV-seronegative patients. A history of frequent relapses and poor response to traditional or drug therapy may

be suggestive (Greenspan *et al*. 1986; Horning & Cohen 1995). Suspicion of HIV infection is also supported by the simultaneous presence of oral candidosis, "hairy leukoplakia", or Kaposi's tumor, but these lesions are far from always present in HIV-infected patients.

HIV infection attacks the T-helper cells of the body, causing a drastic change in the T-helper(CD4+)/T-suppressor(CD8+) ratio with severe impairment of the host's resistance to infection. Depleted peripheral T-helper lymphocyte counts correlate closely with the occurrence of NG as demonstrated in a study of 390 US HIV-seropositive soldiers (Thompson *et al*. 1992). Furthermore, a complete absence of T cells in gingival tissue of HIV-infected patients with periodontitis has been reported (Steidley *et al*. 1992). The lack of local immune effector and regulatory cells in HIV-seropositive patients could in fact explain the characteristic and rapidly progressive nature of periodontitis in these patients. Moreover, a protective effect has been encountered with antiviral treatment of the HIV infection against NPD (Tappuni & Fleming 2001) as well as against HIV-associated gingivitis and periodontitis (Masouredis *et al*. 1992). NP has been revealed as a marker for immune deterioration, with a 95% predictive value that CD4+ cell counts were below 200 cells/mm^3, and, if untreated, a cumulative probability of death within 24 months (Glick *et al*. 1994). As a consequence of this finding, if possible all NPD patients should be recommended to have a test for HIV infection.

Malnutrition

In developing countries malnutrition has often been mentioned as a predisposing factor to NPD (Enwonwu 1972; Osuji 1990). Malnutrition results in lowered resistance to infection and protein malnutrition has been emphasized as the most common public health problem affecting underprivileged Nigerian children who are most often affected by NPD (Enwonwu 1985, 1994). In response to periodontal pathogens, phagocytes elaborate destructive oxidants, proteinases, and other factors. Periodontal damage may occur as the result of the balance between these factors, the antioxidants and host-derived antiproteinases. Malnutrition is characterized by marked tissue depletion of the key antioxidant nutrients, and impaired acute-phase protein response to infections. This is due to impairment in the production and cellular action of the cytokines. Other features of malnutrition include inverted helper/suppressor T lymphocyte ratio, histaminemia, hormonal imbalance with increased blood and saliva levels of free cortisol, and defective mucosal integrity. Malnutrition usually involves concomitant deficiencies of several essential macro- and micronutrients, and therefore has the potential to adversely influence the prognosis of periodontal infections (Enwonwu 1994).

Poor oral hygiene, pre-existing gingivitis, and history of previous NPD

Many of the early studies of NPD showed that a low standard of oral hygiene contributed to the establishment of the disease (Johnson & Engel 1986). This has been supported by recent studies in the USA and Nigeria (Taiwo 1993; Horning & Cohen 1995). Consequently, NPD is usually established on the basis of preexisting chronic gingivitis (Pindborg 1951b). It should be emphasized, however, that plaque accumulation as seen in NPD patients may also be enhanced by the discomfort experienced with oral hygiene practices due to the disease. Based on questionnaires and personal interviews, 28% of NPD patients have been found with a history of previous painful gingival infection and 21% had gingival scars suggestive of previous NPD (Horning & Cohen 1995).

Psychologic stress and inadequate sleep

Just as other ulcerative gastrointestinal conditions have been shown to have psychogenic origins, psychologic stress has often and for many years been mentioned as a predisposing factor (Johnson & Engel 1986). Epidemiologic investigations seem to indicate a more frequent occurrence of necrotizing diseases in periods when the individuals are exposed to psychologic stress (Pindborg 1951a,b; Giddon *et al*. 1963; Goldhaber & Giddon 1964). New recruits and deploying military personnel, college students during examination periods, patients with depression or other emotional disorders, and patients feeling inadequate at handling life situations are more susceptible to NPD (Pindborg 1951a,b; Moulton *et al*. 1952; Giddon *et al*. 1963; Cohen-Cole *et al*. 1983). Urine levels of corticosteroids have been used as a physiologic measure of stress, and increased free cortisol levels have been encountered in the urine of NPD patients as compared with controls. The NPD patients showed significantly higher levels of trait anxiety, depression, and emotional disturbance than did control individuals (Cohen-Cole *et al*. 1983). The role of anxiety and psychologic stress in the pathogenesis of NG has been borne out by both psychiatric and biochemical investigations (Moulton *et al*. 1952; Shannon *et al*. 1969; Maupin & Bell 1975). There are several ways by which psychologic stress factors may interfere with host susceptibility. Host tissue resistance may be changed by mechanisms acting through the autonomic nervous system and endocrine glands resulting in elevation of corticosteroid and catecholamine levels. This may reduce gingival microcirculation and salivary flow and enhance nutrition of *Prevotella intermedia*, but also depress neutrophil and lymphocyte functions which facilitate bacterial invasion and damage (Johnson & Engel 1986; Horning & Cohen 1995).

Inadequate sleep, often as the result of lifestyle choices or job requirements, has been mentioned

by many patients with NPD (Horning & Cohen 1995).

Smoking and alcohol use

Smoking has been listed as a predisposing factor to NPD for many years and presumably predisposes to other types of periodontitis as well (The American Academy of Periodontology 1996). Two studies from the 1950s found that 98% of the patients were smokers (Pindborg 1951a; Goldhaber 1957). More recent data have confirmed this by finding only 6% non-smokers among NPD patients in contrast to 63% in a matched control group (Stevens *et al*. 1984). The amount smoked also appears important since 41% of subjects with NG smoked more than 20 cigarettes daily whereas only 5% of controls smoked that much (Goldhaber & Giddon 1964).

The relationship between tobacco usage and NPD appears to be complex. It has often been stated that smokers in general have poorer oral hygiene than non-smokers but studies have shown that there is little difference in the level of plaque accumulation in smokers versus non-smokers. Also, there have been no conclusive studies to show that smoking adversely affects periodontal tissues by altering the microbial composition of plaque (The American Academy of Periodontology 1996). Smoking could lead to increased disease activity by influencing host response and tissue reactions. As examples, smokers have depressed numbers of T-helper lymphocytes, and tobacco smoke can also impair chemotaxis and phagocytosis of oral and peripheral phagocytes (Eichel & Shahrik 1969; Kenney *et al*. 1977; Ginns *et al*. 1982; Costabel *et al*. 1986; Lannan *et al*. 1992; Selby *et al*. 1992). Nicotine-induced secretion of epinephrine resulting in gingival vasoconstriction has been proposed as one possible mechanism by which smoking may influence tissue susceptibility (Schwartz & Baumhammers 1972; Kardachi & Clarke 1974; Bergström & Preber 1986). The exact mechanism of tobacco smoking predisposing to NPD, however, remains to be determined.

Social or heavy drinking has been admitted by NPD patients and its role as a predisposing factor has been accounted for by its numerous physiologic effects which add to other factors as general sources of debilitation (Horning & Cohen 1995).

Caucasian background

A number of American studies have demonstrated a 95% preponderance of Caucasian patients with NPD including a study in which the referring population was 41% African American (Barnes *et al*. 1973; Stevens *et al*. 1984; Horning & Cohen 1995), but a proportion of 49% of African Americans in another study casts doubt on race as a predisposing factor alone, and the mechanism for this factor is unknown.

Young age

In industrialized countries, young adults appear to be the most predisposed to NPD. The disease can occur at any age, the reported mean age for NPD being between 22 and 24 years. This may reflect a number of factors such as military population age, wartime stress, and probably is related to the involvement of other factors such as smoking (Horning & Cohen 1995).

Treatment

The treatment of the necrotizing periodontal diseases is divided into two phases: acute and maintenance phase treatment.

Acute phase treatment

The aim of the acute phase treatment is to eliminate disease activity as manifest by ongoing tissue necrosis developing laterally and apically. A further aim is to avoid pain and general discomfort which may severely compromise food intake. Among patients suffering from systemic diseases resulting in loss of weight, further weight loss due to reduced food intake should be avoided by rapid therapeutic intervention.

At the first consultation scaling should be attempted, as thoroughly as the condition allows. Ultrasonic scaling may be preferable to the use of hand instruments. With minimal pressure against the soft tissues, ultrasonic cleaning may accomplish the removal of soft and mineralized deposits. The continuous water spray combined with adequate suction usually allows good visibility. How far it is possible to proceed with debridement at the first visit usually depends on the patient's tolerance of pain during instrumentation. Obviously toothbrushing in areas with open wounds does not promote wound healing. Therefore, patients should be instructed in substituting toothbrushing with chemical plaque control in such areas until healing is accomplished.

Hydrogen peroxide and other oxygen-releasing agents also have a long-standing tradition in the initial treatment of NPD. Hydrogen peroxide (3%) is still used for debridement in necrotic areas and as a mouth rinse (equal portions 3% H_2O_2 and warm water). It has been thought that the apparently favorable effects of hydrogen peroxide may be due to mechanical cleaning, and the influence on anaerobic bacterial flora of the liberated oxygen (Wennström & Lindhe 1979; MacPhee & Cowley 1981). Further adjunctive local oxygen therapy of NDP showed a more rapid clinical restitution with less periodontal destruction than in a group without oxygen therapy (Gaggl *et al*. 2006).

Twice daily rinsing with a 0.2% chlorhexidine solution is a very effective adjunct to reduce plaque formation, particularly when toothbrushing is not

performed. It also assists self-performed oral hygiene during the first weeks of treatment. Its effect is discussed elsewhere in this book. For an optimal effect of this medicament, it should be used only in conjunction with and in addition to systematic scaling and root planing. The chlorhexidine solution does not penetrate subgingivally and the preparation is readily inactivated by exudates, necrotic tissues, and masses of bacteria (Gjermo 1974). The effectiveness of chlorhexidine mouth rinses is therefore dependent upon a simultaneous, thorough mechanical, debridement.

In some cases of NPD the patient's response to debridement is minimal or the general health is affected to such an extent that the supplementary use of systemic antibiotics or chemotherapeutics is indicated. This also applies to patients with malaise, fever, and lassitude. The choice of drug aims at a direct action on bacteria which are the cause of the inflammatory process in NPD. Supplementary treatment with metronidazole 250 mg three times daily has been found effective against spirochetes and appears to be the first choice in the treatment of NPD (Proctor & Baker 1971; Shinn 1976; Loesche *et al*. 1982). The adjunctive use of metronidazole in HIV-associated NPD is reported to be extremely effective in reducing acute pain and promoting rapid healing (Scully *et al*. 1991). Acute pain usually disappears after a few hours (Fig. 20-17).

Antibiotics such as penicillins and tetracyclines are also effective. Penicillin (1 million i.u. three times daily) should be used as an adjunct to scaling as for metronidazole until the ulcers are healed. Topical application of antibiotics is not indicated in the treatment of NPD, because intralesional bacteria are frequent, and topical application does not result in sufficient intralesional concentration of antibiotics.

It is important to emphasize that many HIV-seropositive patients with NPD at their initial visit are not aware of their serostatus. If HIV infection is a suspected predisposing factor, the patient can be referred to her or his physician for further examination. Some patients may prefer referral to a hospital department. Information on HIV-serostatus is frequently not available at initiation of therapy, but the lack of information has no serious implications for the choice of treatment or for the handling of the patient. As a consequence of a lack of information on HIV-serostatus of patients seeking dental treatment in general, all procedures in the dental office must always include precautions to protect against transmission of the virus to the dentist, to the dental auxiliaries, and to other patients.

If the dentist asks the patient about his or her possible chance of having contracted HIV infection this should be done with great care, because HIV infection has serious implications for the patient. Consequently, a successful outcome depends on a

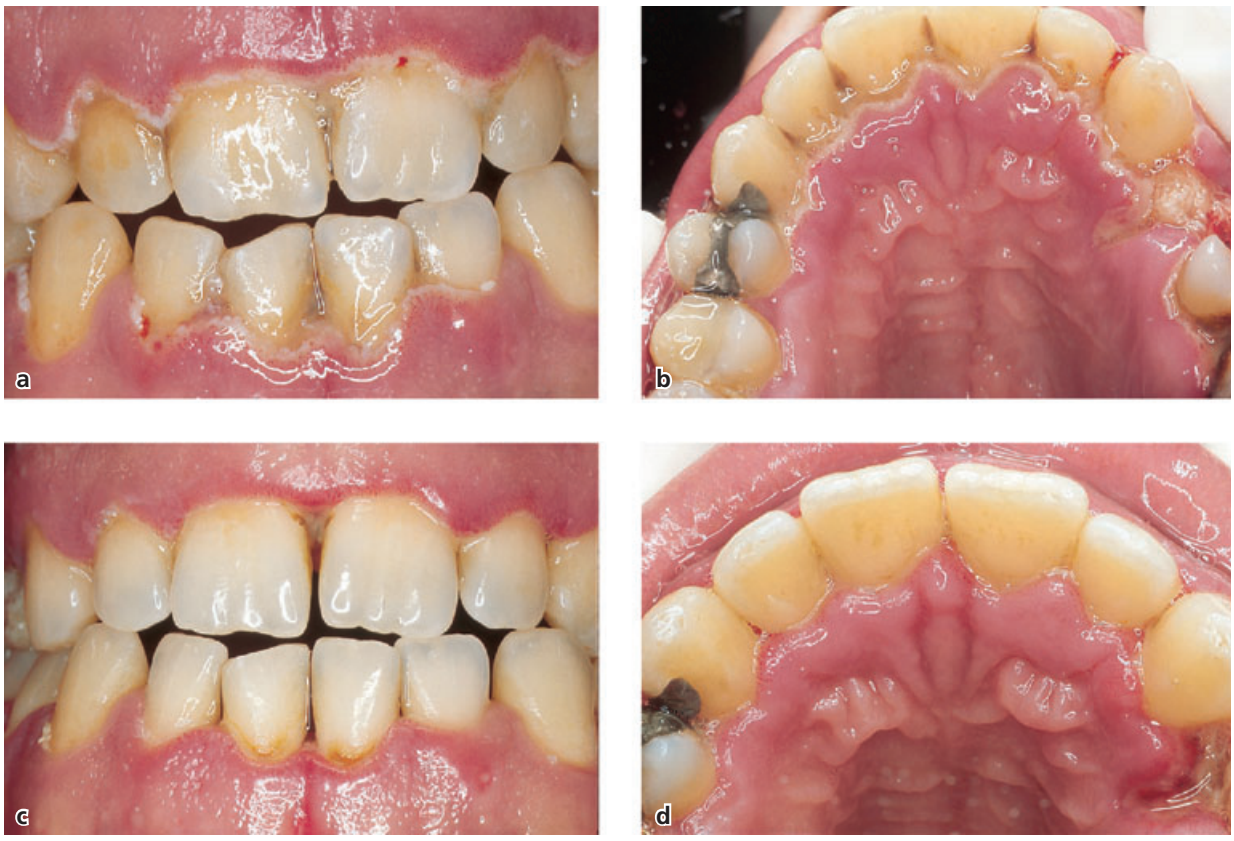

Fig. 20-17 Necrotizing periodontitis with severe pain. The entire gingival margin is the seat of a necrotic ulcer. (a) Facial aspect. (b) Palatal aspect. (c,d) The patient was treated with scaling supplemented with metronidazole and the next day the patient was free of symptoms and the clinical features were significantly improved.

confidential relationship between patient and dentist. In the case of a new patient, such a relationship is first established after at least a couple of appointments in the clinic.

In HIV-infected patients antibiotic prophylaxis in relation to scaling does not usually appear to be necessary. Bacteria recovered from venipuncture 15 minutes after scaling were not detectable in samples obtained at 30 minutes (Lucartoto *et al*. 1992). Neither does removal of sequestra always appear to require antibiotic cover (Robinson 1991). HIV-infected patients are susceptible to candidal infections (Holmstrup & Samaranayake 1990) and if oral candidosis is present or occurs throughout the period of antibiotic treatment, treatment with appropriate antimycotic drugs such as miconazole may be necessary.

Patients with NPD should be seen almost daily as long as the acute symptoms persist. Appropriate treatment alleviates symptoms within a few days. Thereafter the patient should return in approximately 5 days. Systematic subgingival scaling should be continued with increasing intensity as the symptoms subside. Correction of restoration margins and polishing of restorations and root surfaces should be completed after healing of ulcers. When the ulcerated areas are healed, local treatment is supplemented with oral hygiene instruction and patient motivation. Instruction in gentle but effective toothbrushing and approximal cleaning is mandatory. In many cases the extensive tissue destruction results in residual soft tissue defects that are difficult for the patient to keep clean. Oral hygiene in these areas often requires the use of interproximal devices and soft, smaller brushes. Sometimes healing is delayed in HIV-infected patients and intensive professional control may be necessary for prolonged periods of time.

Patients with NPD are not always easily motivated to carry out a proper program of oral hygiene. They frequently have poor oral hygiene habits and possibly a negative attitude to dental treatment in general. As a result, some patients discontinue treatment as soon as pain and other acute symptoms are alleviated. Motivation and instruction should be planned to prevent this happening, and should be reinforced during later visits. Patients with severely impaired immune function, for instance due to HIV infection, may suffer from other infections or diseases during the period of treatment. This may complicate the treatment, because patients may be hospitalized.

Maintenance phase treatment

When the acute phase treatment has been completed, necrosis and acute symptoms in NPD have disappeared. The formerly necrotic areas are healed and the gingival craters are reduced in size, although some defects usually persist. Bacterial plaque readily accumulates in such areas, and the craters, therefore, predispose to recurrence of NPD or to further destruction because of a persisting chronic inflammatory process, or both. These sites, therefore, may require surgical correction. Shallow craters can be removed by simple gingivectomy, while the elimination of deep defects may require flap surgery. Treatment of necrotizing gingivitis has not been completed until all gingival defects have been eliminated and optimal conditions for future plaque control have been established. If possible, elimination of predisposing factors is also very important to prevent recurrence. Due to delayed healing in HIV-infected patients, periodontal surgery is not recommended in these patients. Instead, intensive approximal cleaning is necessary to prevent recurrence of disease.

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Chapter 21

Periodontal Disease as a Risk for Systemic Disease

Ray C. Williams and David W. Paquette

Throughout the history of mankind, there has been the belief that diseases which affect the mouth, such as periodontal disease, can have an effect on the rest of the body. Over the centuries, writings from the ancient Egyptians, Hebrews, Assyrians, Greeks, and Romans, to name a few, have all noted the importance of the mouth in overall health and wellbeing. Thus, one could say that the concept linking systemic disease and periodontitis can be traced back to the beginning of recorded history and medicine (O'Reilly & Claffey 2000).

This chapter examines the evidence which has emerged since the early 1990s implicating periodontal disease as a risk factor for several systemic conditions such as cardiovascular disease, adverse pregnancy outcomes, diabetes, and pulmonary disease. But first, it is helpful for the student of dentistry to understand the historical perspective under which this relationship emerged. The concept of "focal infection" which emerged around 1900 has resurfaced and has stimulated much new interest and research into the role of periodontitis as a risk for systemic disease.

Early twentieth century concepts

At the beginning of the twentieth century, medicine and dentistry were searching for reasons to explain why people became afflicted with a wide range of systemic diseases. Medicine at that time had very little insight into what caused diseases such as arthritis, pneumonia, and pancreatitis. Through the writings and lectures of principally two individuals, Willoughby D. Miller, a microbiologist in Philadelphia, and William Hunter, a London physician, the concept that oral bacteria and infection were likely causes of most systemic illnesses suddenly became very popular (O'Reilly & Claffey 2000). For the next 40 years, physicians and dentists would embrace the idea that infections, especially those originating in the mouth, caused most human suffering and illness. This era, which came to be known as the "era of focal infection", can be attributed primarily to Willoughby D. Miller and William Hunter (O'Reilly & Claffey 2000).

Willoughby Miller was an instructor at the University of Pennsylvania School of Dental Medicine around the turn of the twentieth century. Miller had earlier trained in microbiology in Berlin in Robert Koch's institute. Koch was a pioneer in microbiology and the father of the modern "germ theory" of disease. While under the influence of Robert Koch, Miller too became intensely interested in the role of "germs" or bacteria in causing diseases. Miller returned to the US following his training, convinced that the bacteria residing in the mouth could cause or be attributed to most systemic diseases in patients. In a paper published in 1891, entitled "The human mouth as a focus of infection", Miller argued that the oral flora caused ostitis, osteomyelitis, septicemia, pyemia, disturbances of the alimentary tract, noma, dyptheria, tuberculosis, syphilis, and thrush (Miller 1891). Clearly from this one publication, one can appreciate just how extensively the mouth and oral infection were blamed for causing systemic disease (O'Reilly & Claffey 2000).

While attending one of Miller's lectures at the International Congress of Hygiene in London, William Hunter, a physician from the London Fever Hospital, noted that he and Miller were in strong agreement about the systemic impact of oral infections or oral sepsis. Shortly after, Hunter was invited to speak at the opening of the Strathcona Medical Building at McGill University in Montreal in 1910. In

his address to the audience, he blamed poor dentistry and the resulting oral sepsis for causing most of mankind's systemic disease. Hunter remarked that the crowns, bridges and partial dentures he saw in his patients in London were built on teeth surrounded by a "mass of sepsis". Indeed, this oral sepsis could explain why most individuals developed chronic diseases (Hunter 1900; O'Reilly & Claffey 2000). It is likely that Hunter was referring to the untreated periodontal diseases, caries, and defective restorations he was noting in his adult patients at the London Fever Hospital. But whatever Hunter thought he observed in the mouths of his sick patients, his speech at McGill University and his subsequent publication on the role of sepsis and antisepsis in medicine (Hunter 1910) ushered in an era of belief that periodontitis, caries, and poor oral hygiene were the primary cause of systemic illness. The term "oral sepsis" used by Hunter was replaced with the term "focal infection" in 1911 (Billings 1912). Focal infection implied that there was a nidus of infection somewhere in the body, such as periodontitis, which could affect distant sites and organs via the bloodstream. Throughout the 1920s and 1930s, dentists and physicians believed that the bacteria on the teeth and the resultant infectious diseases, such as caries, gingivitis, and periodontitis, were a focus of infection that led to a wide variety of systemic problems. It became popular during this period to extract teeth as a means of ridding the body of oral bacteria and preventing and/or treating diseases affecting the joints, as well as diseases of the heart, liver, kidneys, and pancreas (Cecil & Angevine 1938; O'Reilly & Claffey 2000).

However, by 1940, medicine and dentistry were realizing that there was much more to explain a patient's general systemic condition than bacteria in the mouth. Dentists and physicians realized that (1) extracting a person's teeth did not necessarily make the person better or make their disease go away, (2) people with very healthy mouths and no obvious oral infection developed systemic disease, and (3) people who had no teeth and thus no apparent oral infection still developed systemic diseases (Galloway 1931; Cecil & Angevine 1938).

By 1950, it was apparent to medicine and dentistry that oral infections, such as dental caries, gingivitis, and periodontitis, could not explain why individuals developed a wide range of systemic diseases. By this time medicine was making strides in discovering the true etiologies of many diseases, and dentistry was making great strides in the prevention as well as the treatment of caries and periodontal disease. Thus, the era of focal infection as a primary cause of systemic diseases came to an end (O'Reilly & Claffey 2000).

Throughout the second half of the twentieth century, several researchers and clinicians continued to question whether oral infection (and inflammation) might in some way contribute to a person's overall health, but the reasons given were mostly speculative. Clinicians continued to propose that bacteria and bacterial products within the periodontal pocket, and which could enter the bloodstream from the mouth, could surely in some way be harmful to the body as a whole (Thoden van Velzen *et al*. 1984). However, it was not until the last decade of the twentieth century that dentistry and medicine again began to examine the relationship of periodontitis as a risk for systemic disease. The student of dentistry thus needs to appreciate the intense focus on oral infection as a "likely" cause of many systemic diseases from 1900–1950, then the era of retreat from the focal infection theories of disease causation from 1950 to around 1989, and now the new look at emerging science that suggests periodontitis as a possible risk factor for several systemic diseases, including cardiovascular disease, adverse pregnancy outcomes, diabetes mellitus, and bacterial pneumonia.

Periodontitis as a risk for cardiovascular disease

In 1989 Kimmo Mattila and co-workers in Finland conducted a case–control study on patients who had experienced an acute myocardial infarction and compared these patients to control subjects selected from the community. A dental examination was performed on all of the subjects studied and a dental index computed. The dental index used by Mattila was the sum of scores from the number of carious lesions, missing teeth and periapical lesions, and probing depth measures to indicate periodontitis and the presence or absence of pericoronitis. Mattila and his group reported a highly significant association between poor dental health, as measured by the dental index, and acute myocardial infarction. The association was independent of other risk factors for heart attack such as age, total cholesterol, high density lipoprotein (HDL) triglycerides, C peptide, hypertension, diabetes, and smoking (Mattila *et al*. 1989).

Mattila's findings initiated a great deal of interest in the scientific community. Might it be possible that there was a significant association between periodontitis and cardiovascular disease? Physicians and dentists noted the following commonalities. Patients with periodontal disease share many of the same risk factors as patients with cardiovascular disease, including age, gender (predominantly male), lower socioeconomic status, stress, and smoking (Beck *et al*. 1998). Additionally, a large proportion of patients with periodontal disease also exhibit cardiovascular disease (Umino & Nagao 1993). These observations suggest that periodontal disease and atherosclerosis share similar or common etiologic pathways. Scannapieco and colleagues (2003a) conducted a systematic review of the evidence supporting or refuting any relationship. In response to the focused questions, "Does periodontal disease influence the initiation/progression of atherosclerosis and therefore cardiovascular disease, stroke and peripheral vascular disease?" the investigators identified 31 human

Table 21-1 Summary of select case–control and cohort observational studies supporting an association between periodontal disease and cardiovascular disease

Reference	Study design	Population	Periodontal outcome or exposure	Cardiovascular outcome	Findings and conclusions
Matilla *et al*. 1989	Case–control	Finland; 100 cases and 102 controls	Dental Severity Index (sum of scores for caries, periodontal disease, periapical pathosis and pericoronitis)	Evidence of myocardial infarction (MI) from EKG and elevated enzyme levels (creatinine phosphokinase isoenzyme MB)	Dental health significantly worse in patients with MI versus controls after adjusting for smoking, social class, smoking, serum lipids, and diabetes
Beck *et al*. 2001	Cohort	United States; 6017 subjects (ARIC Study)	Severe periodontitis defined as clinical attachment loss ≥3 mm at ≥30% of sites	Carotid artery intima media wall thickness (IMT) ≥1 mm	Periodontitis may influence atheroma formation (OR = 1.3)
Beck *et al*. 2005	Cohort	United States; 15 792 subjects (ARIC Study)	Serum antibodies to periodontal pathogens	Carotid artery IMT ≥1 mm	Presence of antibody to *C. rectus* was associated with carotid atherosclerosis (OR = 2.3)
Hung *et al*. 2004	Cohort	United States; 41 407 males from the HPFS and 58 974 females from the NHS	Self-reported tooth loss at baseline	Incident fatal and non-fatal MI or stroke	For males with tooth loss, the relative risk for coronary heart disease was 1.36. For females with tooth loss, the relative risk was 1.6
Engebretson *et al*. 2005	Cohort	United States; 203 subjects from INVEST	Radiographic alveolar bone loss	Carotid plaque thickness via ultrasonography	Severe periodontal bone loss was independently associated with carotid atherosclerosis (OR = 3.64)
Desvarieux *et al*. 2005	Cohort	United States; 1056 subjects from INVEST	Subgingival bacterial burden	Carotid artery IMT ≥1 mm	Severe periodontal bone loss was independently associated with carotid atherosclerosis (OR = 3.64)
Pussinen *et al*. 2004	Cohort	Finland; 6950 subjects in the Mobile Clinic Health Survey	Serum antibodies to *P. gingivalis* or *A. actinomycetemcomitans*	Incident fatal or non-fatal stroke	Seropositive subjects had an OR of 2.6 for stroke
Abnet *et al*. 2005	Cohort	China; 29 584 rural subjects	Tooth loss	Incidence of fatal MI or stroke	Tooth loss was associated with an increased odds for death from MI (RR = 1.29) and stroke (RR = 1.1)

studies. Table 21-1 lists selected influential studies identified in the review plus additional recent observational studies discussed below. Although the authors did not perform a meta-analysis due to differences in reported outcomes, the authors noted relative (not absolute) consistency and concluded, "Periodontal disease may be modestly associated with atherosclerosis, myocardial infarction and cardiovascular events." An accompanying consensus report approved by the American Academy of Periodontology recommends, "Patients and health care providers should be informed that periodontal intervention may prevent the onset or progression of atherosclerosis-induced diseases."

Since Scannapieco's review and consensus report, other meta-analyses on the cardiovascular–periodontal disease association have been conducted and published. Meurman and co-workers (2004) reported a 20% increase in the risk for cardiovascular disease among patients with periodontal disease (95% CI

1.08–1.32), and an even higher risk ratio for stroke varying from 2.85 (95% CI 1.78–4.56) to 1.74 (CI 1.08–2.81). Similarly, Vettore and co-workers reported relative risk estimates of 1.19 (95% CI 1.08–1.32) and 1.15 (95% CI 1.06–1.25) respectively (Khader *et al*. 2004; Vettore 2004). These meta-analyses of the available observational human data suggest a modest but statistically significant increase in the risk for cardiovascular disease with periodontal disease.

Recent findings from several worldwide population studies also should be noted. These studies include the Atherosclerosis Risk in Communities Study (ARIC), the Health Professional Follow-up Study (HPFS), the Nurses Health Study (NHS), and the Oral Infections and Vascular Disease Epidemiology Study (INVEST) conducted in the United States. Other studies have involved populations from Sweden, Finland, and China.

Periodontal probing data were collected on 6017 persons, 52–75 years of age, participating in the ARIC study (Beck *et al*. 2001, 2005; Elter *et al*. 2004). The investigators assessed both the presence of clinical cardiovascular disease (MI or revascularization procedure) and subclinical atherosclerosis (carotid artery intima media wall thickness (IMT) using B-mode ultrasound) as dependent variables in the population. Individuals with both high attachment loss (≥10% of sites with attachment loss >3 mm) and high tooth loss exhibited elevated odds of prevalent cardiovascular disease as compared to individuals with low attachment loss and low tooth loss (OR = 1.5, 95% CI 1.1–2.0 and OR = 1.8, CI 1.4–2.4 respectively) (Elter *et al*. 2004). A second logistic regression analysis indicated a significant association between severe periodontitis and thickened carotid arteries after adjusting for covariates like age, gender, diabetes, lipids, hypertension, and smoking (Beck *et al*. 2001). Accordingly, the odds ratio for severe periodontitis (i.e. 30% or more of sites with ≥3 mm clinical attachment loss) and subclinical carotid atherosclerosis was 1.31 (95% CI 1.03–1.66). In a third report, these investigators quantified serum IgG antibody levels specific for 17 periodontal organisms using a whole bacterial checkerboard immunoblotting technique (Beck *et al*. 2005). Analyzing mean carotid IMT (≥1 mm) as the outcome and serum antibody levels specific as exposures for this same population, the investigators noted the presence of antibody to *Campylobacter rectus* increased the risk for subclinical atherosclerosis two-fold (OR = 2.3, 95% CI 1.83–2.84). In particular, individuals with both high *C. rectus* and *Peptostreptococcus micros* antibody titers had almost twice the prevalence of carotid atherosclerosis as compared to those with only a high *C. rectus* antibody (8.3% versus 16.3%). Stratification by smoking indicated that all microbial models significant for smokers were also significant for never smokers except for *Porphyromonas gingivalis*. Thus, clinical signs of periodontitis are associated with cardiovascular disease and subclinical atherosclerosis in the ARIC population, and exposures to specific periodontal pathogens significantly increase the risk for atherosclerosis in smoking and non-smoking subjects.

Self-reported periodontal disease outcomes and incident cardiovascular disease were assessed in two extant databases, HPFS (n = 41 407 males followed for 12 years) and NHS (n = 58 974 females followed for 6 years) (Hung *et al*. 2004). After controlling for important cardiovascular risk factors, males with a low number of teeth (≤10 at baseline) had a significantly higher risk of cardiovascular disease (RR = 1.36; 95% CI 1.11–1.67) as compared to males with a higher number of teeth (25 or more). For females with the same reported extent of tooth loss, the relative risk for cardiovascular disease was 1.64 (95% CI 1.31–2.05) as compared to women with at least 25 teeth. The relative risks for fatal cardiovascular disease events increased to 1.79 (95% CI 1.34–2.40) for males and 1.65 (95% CI 1.11–2.46) for females with tooth loss respectively. In a second report, the investigators evaluated the association between self-reported periodontal disease and serum elevations in cardiovascular disease biomarkers cross-sectionally in a subset of HPFS participants (n = 468 males) (Joshipura *et al*. 2004). Serum biomarkers included C-reactive protein (CRP), fibrinogen, factor VII, tissue plasminogen activator (t-PA), LDL cholesterol, von Willebrand factor, and soluble TNF receptors 1 and 2. In multi-variate regression models controlling for age, cigarette smoking, alcohol intake, physical activity, and aspirin intake, self-reported periodontal disease was associated with significantly higher levels of CRP (30% higher among periodontal cases compared with non-cases), t-PA (11% higher), and LDL cholesterol (11% higher). These analyses reveal significant associations between self-reported number of teeth at baseline and risk of cardiovascular disease and between self-reported periodontal disease and serum biomarkers of endothelial dysfunction and dyslipidemia.

One population study called INVEST has been planned *a priori* and conducted exclusively to evaluate the association between cardiovascular disease and periodontal outcomes in a cohort population. It was reported that for a group of 203 stroke-free subjects (ages 54–94) at baseline, mean carotid plaque thickness (measured with B-mode ultrasound) was significantly greater among dentate subjects with severe periodontal bone loss (≥50% measured radiographically) as compared to those with less bone loss (<50%) (Engebretson *et al*. 2005). These investigators noted a clear dose–response relationship when they graphed subject tertiles of periodontal bone loss versus carotid plaque thickness. The investigators next collected subgingival plaque from 1056 subjects and tested for the presence of 11 known periodontal bacteria using DNA techniques (Desvarieux *et al*. 2005). The investigators found that cumulative periodontal bacterial burden was significantly related to carotid IMT after adjusting for cardiovascular disease risk factors. Whereas mean IMT values were similar

across burden tertiles for putative (orange complex) and health-associated bacteria, IMT values rose with each tertile of etiologic bacterial burden (*Actinobacillus acinomycetemcomitans* (recently renamed *Aggregatibacter acinomycetemcomitans*), *P. gingivalis, Treponema denticola* and *Tannerella forsythia*). Similarly, white blood cell values (but not serum CRP) increased across these burden tertiles. These data from INVEST provide evidence of a direct relationship between periodontal microbiology and subclinical atherosclerosis independent of CRP.

Consistent associations between periodontal outcomes and atherosclerosis have been recently demonstrated among populations in Europe and Asia. For 131 adult Swedes, mean carotid IMT values were significantly higher in subjects with clinical and/or radiographic evidence of periodontal disease compared to periodontally healthy controls (Soder *et al*. 2005). Multiple logistic regression analysis identified periodontal disease as a principal independent predictor of carotid atherosclerosis with an odds ratio of 4.64 (95% CI 1.64–13.10). Pussinen *et al*. (2004) monitored antibody responses for *A. actinomycetemcomitans* and *P. gingivalis* among 6950 Finnish subjects for whom cardiovascular disease outcomes over 13 years were available (Mobile Clinic Health Survey). Compared with the subjects who were seronegative for these pathogens, seropositive subjects had an odds ratio of 2.6 (95% CI 1.0–7.0) for a secondary stroke. In a second report on 1023 males (Kuopio Ischemic Heart Disease Study), Pussinen and co-workers (2005) observed that cases with myocardial infarction or cardiovascular disease death were more often seropositive for *A. actinomycetemcomitans* than those controls who remained healthy (15.5% versus 10.2%). In the highest tertile of *A. actinomycetemcomitans* antibodies, the relative risk for MI or coronary heart disease death was 2.0 (95% CI 1.2–3.3) compared with the lowest tertile. For *P. gingivalis* antibody responses, the relative risk was of 2.1 (95% CI 1.3–3.4). Abnet and co-workers (2005) recently published findings from a cohort study of 29 584 healthy, rural Chinese adults monitored for up to 15 years. Tooth loss was evaluated as an exposure outcome for periodontal disease, and mortality from heart disease or stroke were modeled as dependent variables. Individuals with greater than the age-specific median number of teeth lost exhibited a significantly increased risk of death from MI (RR = 1.28, 95% CI 1.17–1.40) and stroke (RR = 1.2, 95% CI 1.02–1.23). These elevated risks were present in male and females irrespective of smoking status. Collectively, these findings indicate consistent associations for periodontal disease and pathogenic exposures with cardiovascular disease for European and Asian populations.

Biologic rationale

Many investigators have asked the question: what is the biologic rationale to explain how periodontitis may be related to cardiovascular disease? Scientists have noted that a patient who has, for example, 28 teeth with pocket depths of 6–7 mm and bone loss, has a large overall surface area of infection and inflammation (Waite & Bradley 1965). In patients with moderate periodontitis, the surface area could be the size of the palm of the hand or larger. In addition, the subgingival bacteria in periodontal pockets exists in a highly organized biofilm. Since periodontal infections result in low-grade bacteremias and endotoxemias in affected patients (Sconyers *et al*. 1973; Silver *et al*. 1980), systemic effects on vascular physiology via these exposures appear biologically plausible. Four specific pathways have been proposed to explain the plausibility of a link between cardiovascular disease and periodontitis (Fig. 21-1). These pathways (acting independently or collectively) include: (1) direct bacterial effects on platelets, (2) autoimmune responses, (3) invasion and/or uptake of bacteria in endothelial cells and macrophages, and (4) endocrine-like effects of pro-inflammatory mediators. In support of the first pathway, two oral bacteria, *P. gingivalis* and *Streptococcus sanguis* express virulence factors called "collagen-like platelet aggregation associated proteins" (PAAP) that induce platelet aggregation *in vitro* and *in vivo* (Hertzberg & Meyer 1996, 1998). Secondly, autoimmune mechanisms may play a role since antibodies that cross react with periodontal bacteria and human heat shock proteins have been identified (Hinode *et al*. 1998; Sims *et al*. 2002). Deshpande *et al*. (1998) have thirdly demonstrated that *P. gingivalis* can invade aortic and heart endothelial cells via fimbriae. Several investigative groups have independently identified specific oral pathogens in atheromatous tissues (Chui 1999; Haraszthy *et al*. 2000). In addition, macrophages incubated *in vitro* with *P. gingivalis* and LDL uptake the bacteria intracellularly and transform into foam cells (Giacona *et al*. 2004). In the last potential pathway, systemic pro-inflammatory mediators are up-regulated for endocrine-like effects in vascular tissues, and studies consistently demonstrate elevations in CRP and fibrinogen among periodontally diseased subjects (Slade *et al*. 2000; Wu *et al*. 2000a,b).

Experiments with animal models demonstrate that specific infections with periodontal pathogens accelerate atherogenesis. For example, inbred heterozygous and homozygous apoE-deficient mice exhibit increased aortic atherosclerosis when challenged orally or intravenously with invasive strains of *P. gingivalis* (Li *et al*. 2002; Lalla *et al*. 2003; Chi *et al*. 2004; Gibson *et al*. 2004). While *P. gingivalis* challenges increased aortic atherosclerosis in apoE-deficient mice in a hypercholesterolemic background only, normocholesterolemic pigs were recently shown to develop both coronary and aortic lesions with *P. gingivalis* challenges (Brodala *et al*. 2005). This finding suggests that *P. gingivalis* bacteremia may exert an atherogenic stimulus independent of high cholesterol

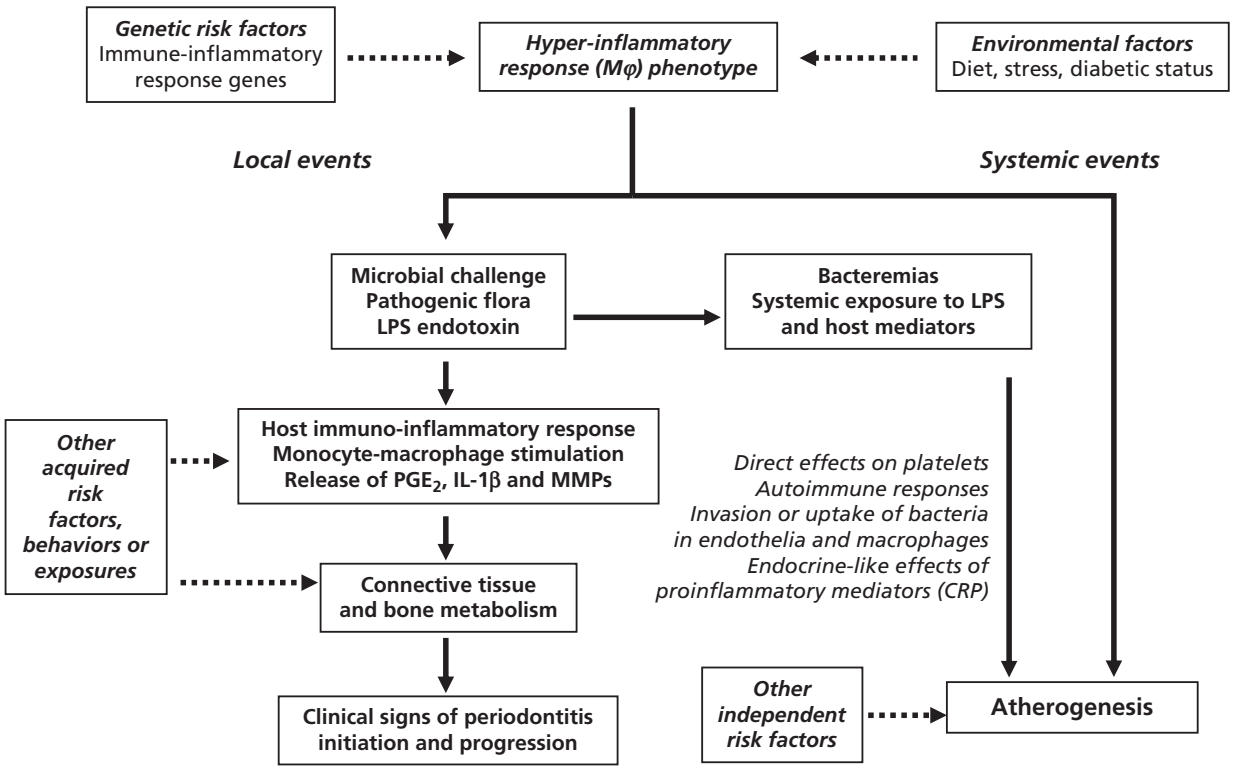

Fig. 21-1 Proposed model and mechanisms linking periodontal disease and cardiovascular disease.

levels in pigs. It is worth noting that a wide range of *P. gingivalis* doses was used in these animal studies. While the clinically relevant dose for human subjects is unknown at present, it probably varies greatly (Daly *et al*. 2001; Haynes & Stanford 2003; Ide *et al*. 2004). Importantly, *P. gingivalis* challenges enhance atherosclerosis despite these different routes of administration and dosing regimens in both species. *P. gingivalis* 16 ribosomal DNA was detected by polymerase chain reaction (PCR) in atheromas from some but not all of these mutant mice and the pigs. These experiments suggest that both the host response and the virulence of the specific *P. gingivalis* strains appear to be important variables in these infection–atherogenesis models. Collectively, when one looks at the body of evidence gathered so far since 1989, there appears to be a compelling association between periodontitis and coronary heart disease.

Periodontitis as a risk for adverse pregnancy outcomes

In 1996, following a landmark report by Offenbacher and colleagues (1996), there has been much interest and research into whether periodontitis may be a possible risk factor for adverse pregnancy outcomes. Adverse pregnancy outcomes that have been linked to periodontal disease include preterm birth, low birthweight, miscarriage or early pregnancy loss, and pre-eclampsia. Pre-eclampsia and preterm births are major causes of maternal and prenatal morbidity and mortality.

Preterm infants who are born with low birthweights represent a major social and economic public health problem, even in industrialized nations. Although there has been an overall decline in infant mortality in the US over the past 40 years, preterm low birthweight remains a significant cause of perinatal mortality and morbidity. A 47% decrease in the infant mortality rate to a level of 13.1 per 1000 live births occurred between 1965 and 1980. But from 1980 to 2000, the percentage of low birthweight infants increased by 11.8% and that of very low birthweight infants increased by 24.3% in the US; among survivors, low birthweight is a major contributor to long-term disability.

Preterm low birthweight deliveries represent approximately 10% of annual births in industrialized nations and account for two-thirds of overall infant mortality. Approximately one-third of these births are elective while two-thirds are spontaneous preterm births. About a half of the spontaneous preterm births are due to premature rupture of membranes and the other half are due to preterm labor. For the spontaneous preterm births, 10–15% occur before 32 weeks gestation, result in very low birthweight (<1500 g) and often cause long-term disability, such as chronic respiratory diseases and cerebral palsy (Offenbacher *et al*. 1996, 1998; Champagne *et al*. 2000; Scannapieco *et al*. 2003c; Xiong *et al*. 2006).

Among the known risk factors for preterm low birthweight deliveries are young maternal age (<18 years), drug, alcohol and tobacco use, maternal stress, genetic background, and genitourinary tract infec-

tions. Although 25–50% of preterm low birthweight deliveries occur without any known etiology, there is increasing evidence that infection may play a significant role in preterm delivery (Hill 1998; Goldenberg *et al*. 2000; Sobel 2000; Williams *et al*. 2000; Scannapieco *et al*. 2003c; Xiong *et al*. 2006).

One of the more important acute exposures that has been implicated in preterm birth is an acute maternal genitourinary tract infection at some point during the pregnancy. Bacterial vaginosis (BV) is a Gram-negative, predominantly anaerobic infection of the vagina, usually diagnosed from clinical signs and symptoms. It is associated with a decrease in the normal lactobacillus-dominated flora and an increase in anaerobes and facultative species including *Gardenerella vaginalis*, *Mobiluncus curtsii*, *Prevotella bivia*, and *Bacteroides ureolyticus.* Bacterial vaginosis is a relatively common condition that occurs in about 10% of all pregnancies. It may ascend from the vagina to the cervix and even result in inflammation of the maternal fetal membranes (chorioamnionitis). Extending beyond the membranes, the organisms may appear in the amniotic fluid compartment that is shared with the fetal lungs and/or involve placental tissues and result in exposure to the fetus via the bloodstream. Despite the observed epidemiologic linkage of bacterial vaginosis with preterm birth, the results from randomized clinical trials to determine the effects of treating bacterial vaginosis with systemic antibiotics on incident preterm birth are equivocal (Goldenberg *et al*. 2000). Still, there are compelling data linking maternal infection and the subsequent inflammation to preterm birth. It appears that inflammation of the uterus and membranes represents a common effector mechanism that results in preterm birth, and, thus, either clinical infection or subclinical infection is a likely stimulus for increased inflammation.

In the early 1990s, it was hypothesized that oral infections, such as periodontitis, could represent a significant source of both infection and inflammation during pregnancy. It was noted that periodontal disease is a Gram-negative anaerobic infection with the potential to cause Gram-negative bacteremias in persons with periodontal disease. It was hypothesized that periodontal infections, which serve as reservoirs for Gram-negative anaerobic organisms, lipopolysaccharide (LPS, endotoxin), and inflammatory mediators including prostaglandin E_2 (PGE_2) and tumor necrosis factor-α (TNF-α), may be a potential threat to the fetal–placental unit (Fig. 21-2) (Collins *et al*. 1994a,b).

As a first step in testing this hypothesis, Greg Collins in Offenbacher's laboratory conducted a series of experiments in the pregnant hamster animal model. It had been noted earlier by Lanning *et al*. (1983) that pregnant hamsters challenged with *Escherichia coli* LPS had malformation of fetuses, spontaneous abortions, and low fetal weight. The work by Lanning and co-workers clearly demonstrated that

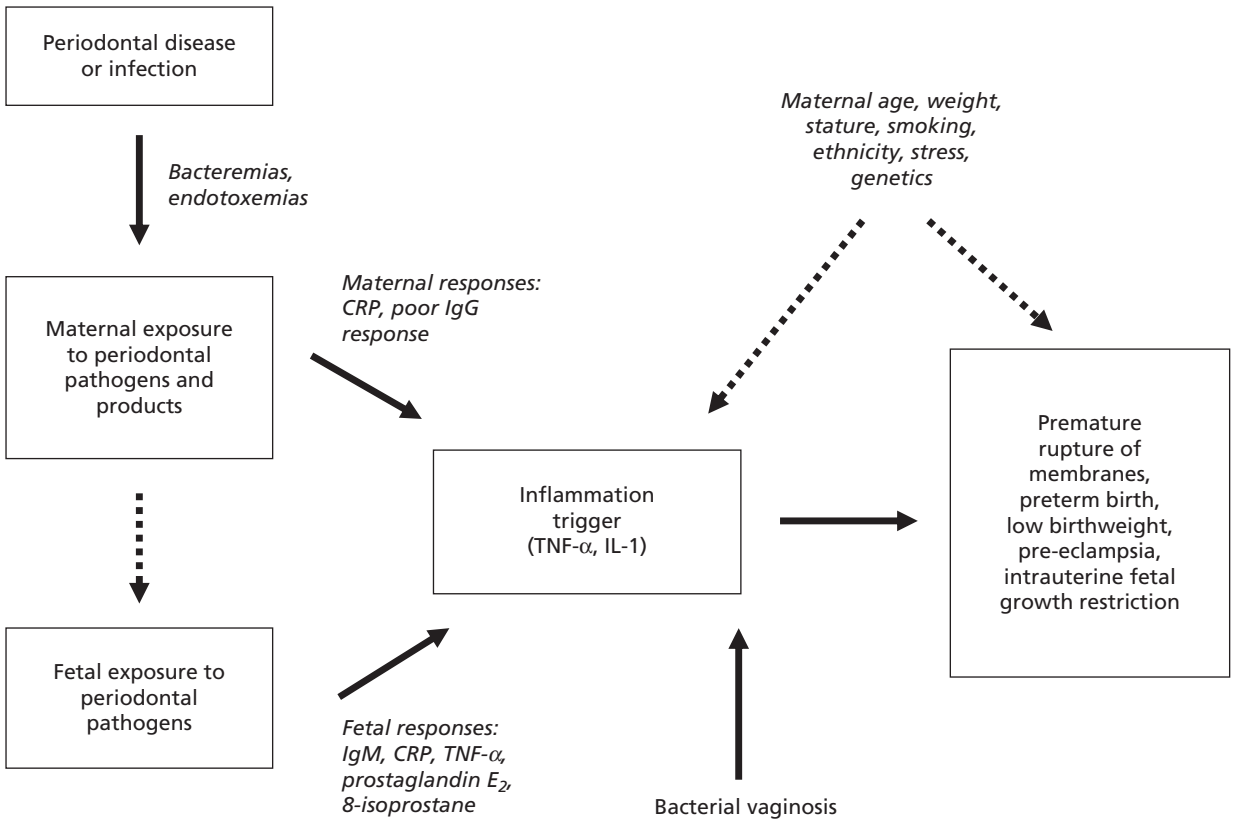

Fig. 21-2 Proposed model for relationship between periodontal disease and adverse pregnancy outcomes.

infections in pregnant animals could elicit many pregnancy complications including spontaneous abortion, preterm labor, low birthweight, fetal growth restriction, and skeletal abnormalities. It was not clear, however, if these findings from *E. coli* would be similar if endotoxin from oral anaerobes was studied. First of all, LPS from Gram-negative enteric organisms differs in structure and biological activity from oral LPS. Thus, Collins needed to demonstrate that LPS from oral organisms had similar effects on fetal outcomes when administered to pregnant animals. Secondly, the oral cavity represents a distant site of infection. Although pneumonia has been a recognized example of a distant site of infection triggering maternal obstetric complications, it was important to demonstrate that distant, non-disseminating infections with oral pathogens could elicit pregnancy complications in animal models. Thirdly, oral infections are chronic in nature. Increased obstetric risk is generally associated with acute infections that occur during pregnancy. Thus, in concept, maternal adaptation to a chronic infectious challenge was assumed to afford protection to the fetus, even during acute flare-ups that may occur during pregnancy.

Collins' landmark hamster studies (Collins *et al*. 1994a,b) demonstrated that chronic exposure to oral pathogens like *P. gingivalis* in a chamber model (Genco & Arko 1994) does not in fact afford protection, but actually enhances the fetal–placental toxicity of exposure during pregnancy. Thus during pregnancy the mother does not become "tolerant" of infectious challenge from oral organisms. Collins and Offenbacher also wanted to demonstrate that the low-grade infections with low numbers of oral pathogens were not of sufficient magnitude to induce maternal malaise or fever. They noted however a measurable local increase of PGE_2 and TNF-α in chamber fluid with *P. gingivalis* as well as a 15–18% decrease in fetal weight. Further, the magnitude of the PGE_2 and TNF-α response was inversely related to the weight of the fetuses, mimicking the intra-amniotic changes seen in humans with preterm low birthweight. LPS dosing experiments demonstrated that higher levels of LPS could induce fever and weight loss in pregnant animals and resulted in more severe pregnancy outcomes including spontaneous abortions and malformations. These more noteworthy outcomes were not seen in the low-challenge oral infection models, but rather resulted in a consistent decrease in fetal weight. Previous sensitization or exposures to these pathogens prior to pregnancy enhanced the severity of the fetal growth restriction when a secondary exposure occurred during pregnancy.

Collins and colleagues (1994b) next studied infection and pregnancy in the hamster by experimentally inducing periodontal disease in the animal model. Four groups of animals were fed either control chow or plaque-promoting chow for an 8-week period to induce experimental periodontitis prior to mating. Two additional groups of animals (i.e. one control chow and one plaque-promoting chow) received exogenous *P. gingivalis* via oral gavage. Animals fed the plaque-promoting diet beginning 8 weeks prior to mating developed periodontitis. These animals also had litters with a mean fetal weight of 1.25 ± 0.07 g that was 81% of the weight of the control groups. Animals receiving both plaque-promoting diet and *P. gingivalis* gavage also had significantly smaller fetuses. The mean fetal weight for this group was 1.20 ± 0.19 g which represented a significant 22.5% reduction in fetal weight compared to controls. Exogenous *P. gingivalis* challenge by gastric gavage did not appear to promote either more severe periodontal disease or more severe fetal growth restriction. This experiment indicated that experimentally induced periodontitis in the hamster could also alter fetal weight in the hamster.

More recently this group has focused on a possible role for *Campylobacter rectus* in contributing to adverse pregnancy outcomes (Madianos *et al*. 2001). In recent animal studies utilizing the BALB/C mouse model, Yeo *et al*. (2005) have reported that maternal *Campylobacter rectus* infection mediates fetal growth restriction in pregnant mice. More recently, Bobetsis and colleagues (Offenbacher *et al*. 2005) found that maternal *C. rectus* infection induced placental inflammation and decidual hyperplasia as well as a concomitant increase in fetal brain IFN-γ. Maternal infection with *C. rectus* increased mouse pup mortality and also affected the hippocampal region of the neonatal brain, suggesting that maternal infection with *C. rectus* may also affect perinatal neurological growth and development (Offenbacher *et al*., 2005).

In what is now viewed as a landmark human study, Offenbacher and colleagues (1996) conducted a case–control study on 124 pregnant or postpartum women (Table 21-2). Preterm low birthweight cases were defined as a mother whose infant had a birthweight of less than 2500 g and also had one or more of the following: gestational age <37 weeks, preterm labor or preterm premature rupture of membranes. Controls were all mothers whose infant had a normal birthweight. Assessments included a broad range of known obstetric risk factors such as tobacco usage, drug use, and alcohol consumption, level of prenatal care, parity, genitourinary tract infections, and weight gain during pregnancy. Each subject received a full-mouth periodontal examination to determine clinical attachment levels. Mothers of preterm low birthweight (PLBW) cases and first birth PLBW cases had significantly more advanced periodontal disease as measured with attachment loss than the respective mothers of normal birthweight controls. Multi-variate logistic regression models, controlling for other known risk factors and co-variates, demonstrated that periodontitis was a statistically significant risk factor for preterm low birthweight, with adjusted odds ratios of 7.9 and 7.5 for all PLBW cases and primiparous PLBW cases respectively. This research

Table 21-2 Summary of case–control observational studies on periodontal disease and adverse pregnancy outcomes

Reference	Population	Periodontal outcome or exposure	Adverse pregnancy outcome	Findings and conclusions
Offenbacher *et al*. 1996	United States; 93 cases and 31 controls	≥60% of sites with clinical attachment levels ≥3 mm	Birthweight <2500 g, gestational age <37 weeks, preterm labor and/or premature rupture of membranes	Significant association between periodontal disease and preterm low birthweight (LBW) (OR = 7.5)
Davenport *et al*. 2002	United Kingdom; 236 cases and 507 controls	Mean pocket depth (mm)	Preterm delivery <37 weeks and birthweight <2499 g	No association detected for periodontal disease and preterm LBW (OR = 0.83)
Goepfert *et al*. 2004	United States; 59 cases and 44 controls	Clinical attachment levels ≥5 mm	Spontaneous preterm birth <32 weeks	Significantly higher risk for preterm birth for mothers with periodontal disease (OR = 3.4)
Radnai *et al*. 2004	Hungary; 41 cases and 44 controls	One or more sites with probing depth ≥4 mm and bleeding on probing ≥50%	Premature labor, spontaneous rupture of membranes and/or the birthweight of the newborn ≤2499 g	Significant association between periodontal disease and preterm LBW (OR = 5.4)
Jarjoura *et al*. 2005	United States; 83 cases and 120 controls	Five or more sites with clinical attachment levels ≥3 mm	Preterm delivery <37 weeks	Significant association between periodontal disease and preterm delivery (OR = 2.75, 95% CI 1.01–7.54)
Moliterno *et al*. 2005	Brazil; 76 cases and 75 controls	Four or more sites with pocket depth >4 mm and clinical attachment levels ≥3 mm	Preterm delivery <37 weeks and birthweight <2500 g	Significantly higher risk for preterm LBW for mothers with periodontal disease (OR = 3.48)
Buduneli *et al*. 2005	Turkey; 53 cases and 128 controls	Mean pocket depth (mm)	Preterm delivery <37 weeks or birthweight <2500 g	No statistically significant differences between the cases and controls with regard clinical periodontal parameters
Moore *et al*. 2005	United Kingdom; 61 cases and 93 controls	Number of sites with pocket depth ≥5 mm	Preterm delivery <37 weeks	No association between periodontal disease and preterm birth
Bosnjak *et al*. 2006	Croatia; 17 cases and 64 controls	>60% of sites with clinical attachment levels ≥4 mm	Spontaneous preterm birth <37 weeks	Significant association between periodontal disease and preterm birth (OR = 8.13)
Skuldbol *et al*. 2006	Denmark; 21 cases and 33 controls	Pocket depth ≥4 mm and bleeding on probing	Preterm delivery <35 weeks	No difference in mean periodontal parameters between the two groups; no association between periodontal disease and preterm birth
Radnai *et al*. 2006	Hungary; 77 cases and 84 controls	One or more sites with probing depth ≥4 mm and bleeding on probing ≥50%	Preterm delivery <37 weeks and birthweight <2500 g	Significant association between periodontal disease and preterm LBW (OR = 3.32)
Contreras *et al*. 2006	Colombia; 130 cases and 243 controls	Pocket depth and clinical attachment loss ≥4 mm and bleeding on probing	Pre-eclampsia: blood pressure ≥140/90 mmHg and ≥2+ proteinuria	Significant association for periodontal disease and pre-eclampsia (OR = 3.0)

was the first to demonstrate an association between periodontal infection and adverse pregnancy outcomes in humans (Offenbacher *et al*. 1996).

Offenbacher and co-workers proceeded to conduct a prospective cohort study, entitled Oral Conditions and Pregnancy (OCAP), which was designed to determine whether maternal periodontal disease was predictive of preterm (<37 weeks) or very preterm (<32 weeks) birth. One thousand and twenty pregnant women were periodontally examined antepartum (<26 weeks gestation) and postpartum. Again, logistic regression models were developed using maternal exposure to either periodontal disease at enrollment or disease progression during pregnancy (clinical attachment loss ≥2 mm at one or more sites) as independent variables and adjusting for known risk factors (e.g. previous preterm delivery, race, smoking, social domain variables, and other infections). Overall, the incidence of preterm was 11.2% among periodontally healthy women, compared with 28.6% in women with moderate–severe periodontal disease (adjusted risk ratio or RR = 1.6, 95% CI 1.1–2.3). Antepartum moderate–severe periodontal disease was associated with an increased incidence of spontaneous preterm births (15.2% versus 24.9%, adjusted RR = 2.0, 95% CI 1.2–3.2). Similarly, the unadjusted rate of very preterm delivery was 6.4% among women with periodontal disease progression, significantly higher than the 1.8% rate among women without disease progression (adjusted RR = 2.4, 95% CI 1.1–5.2). This second study by the Offenbacher group implicated maternal periodontal disease exposure and progression as independent risk factors for PTB outcomes (Offenbacher *et al*. 2001, 2006; Lieff *et al*. 2004).

A subsequent analysis of OCAP data further indicates that maternal periodontal disease is associated with small-for-gestational-age births (Boggess *et al*. 2006). Defining "small-for-gestational-age" as birthweight less than the tenth percentile for gestational age, Boggess *et al*. (2006) reported that its prevalence was significantly higher among women with moderate or severe periodontal disease, compared with those with health or mild disease (13.8% versus 3.2%). Indeed, mothers with moderate or advanced periodontal disease were 2.3 times (RR, 95% CI 1.1–4.7) more likely to have small-for-gestational-age infants as compared to mothers with periodontal health even after adjusting for age, smoking, drugs, marital/insurance status, and pre-eclampsia (i.e. pregnancy-related hypertension with proteinuria or edema).

Jeffcoat and co-workers (2001a,b) also found a positive association between maternal periodontal disease and preterm birth in a comparable US cohort study involving 1313 pregnant subjects. Complete periodontal, medical, and behavioral assessments were made between 21 and 24 weeks gestation for each subject. Gestational ages of the infants were determined following delivery, and logistic regression modeling was performed to assess any relationship between periodontal disease and preterm birth while making adjustments for other known risk factors. Notably, subjects with severe or generalized periodontal disease had an adjusted OR of 4.45 (95% CI 2.16–9.18) for preterm delivery (<37 weeks) as compared with periodontally healthy subjects. The adjusted OR increased with advancing prematurity to 5.28 (95% CI 2.05–13.60) before 35 weeks gestational age and to 7.07 (95% CI 1.70–27.4) before 32 weeks gestational age. Hence, mothers with severe periodontal disease were four to seven times more likely to deliver a preterm infant relative to mothers with periodontal health.

Two other observational studies involving US populations report a consistent association for maternal periodontal disease and preterm low birthweight. One case–control study, involved 59 women with early spontaneous preterm births (<32 weeks of gestation), 36 women with early indicated preterm births (<32 weeks of gestation), and 44 controls with uncomplicated births at term (≥37 weeks) (Goepfert *et al*. 2004). Severe periodontal disease (clinical attachment loss ≥5 mm) was more common in the spontaneous preterm birth group (49%) as compared to the indicated preterm and term control groups (25% and 30% respectively). The odds for severe periodontal disease and spontaneous preterm birth were 3.4 (95% CI 1.5–7.7). For the second observational study involving 83 preterm cases (<37 weeks gestation) and 120 term delivery controls, preterm birth was associated with severe periodontitis, i.e. five or more sites with clinical attachment loss ≥3 mm, adjusted OR = 2.75, (95% CI 1.1–7.54) (Jarjoura *et al*. 2005).

This relationship has been explored in other cross-sectional and cohort populations around the globe (Tables 21-2 and 21-3). Bosnjak *et al*. (2006) reported an adjusted OR of 8.13 (95% CI 2.73–45.9) for maternal periodontal disease and preterm birth for a Croatian population (17 preterm cases and 64 controls). Similarly, a Finnish study (Oittinen *et al*. 2005) involving 130 consecutively enrolled pregnant mothers found that those with periodontal disease were 5.5 times (95% CI 1.4–21.2) more likely to have preterm deliveries or adverse pregnancy outcomes. Two case–control studies involving Hungarian subjects found positive associations between maternal early localized periodontitis (more than one site with probing depth ≥4 mm and bleeding on probing ≥50%) and preterm low birth weight (OR = 5.4, 95% CI 1.7–17.3; OR = 3.32, 95% CI 1.64–6.69) (Radnai *et al*. 2004, 2006). Another observational study with 96 Spanish pregnant women found a higher severity of periodontal disease (percentage of sites with probing depths ≥4 mm) among those having low birthweight infants relative to those with normal weight infants (Moreu *et al*. 2005). Moliterno and co-workers (2005) measured periodontal disease and birth outcomes for 150 Brazilian mothers and reported a significant association between periodontitis and low birthweight with an OR of 3.48 (95% CI 1.17–10.36). Chilean

Table 21-3 Summary of cohort observational studies on periodontal disease and adverse pregnancy outcomes

Reference	Population	Periodontal outcome or exposure	Adverse pregnancy outcome	Findings and conclusions
Offenbacher *et al*. 2001, 2006; Lieff *et al*. 2004	United States; 1020 subjects	Moderate–severe disease: four or more sites with pocket depths ≥5 mm and clinical attachment levels ≥2 mm; progressive disease: one or more sites with clinical attachment loss ≥2 mm	Preterm delivery <37 weeks; very preterm <32 weeks	Moderate–severe periodontal disease (RR = 1.6) and progressive disease (RR = 2.4) are significant risk factors for preterm delivery
Jeffcoat *et al*. 2001	United States; 1313 subjects	Severe or generalized disease: ≥90 sites with clinical attachment levels ≥3 mm	Preterm delivery <37 weeks	Severe or generalized periodontal disease is associated with preterm delivery (OR = 4.5)
Lopez *et al*. 2002b	Chile; 639 subjects	Four or more teeth showing one or more sites with pocket depth ≥4 mm and with clinical attachment level ≥3 mm	Preterm delivery <37 weeks and birthweight <2500 g	Significant association between periodontal disease and preterm LBW (RR = 3.5)
Boggess *et al*. 2003	United States; 763 subjects	Severe disease: ≥15 sites with pocket depths ≥4 mm; progressive disease: four or more sites with increases in pocket depth ≥2 mm and resulting in pockets ≥4 mm in depth	Pre-eclampsia: blood pressure >140/90 mm Hg and ≥1+ proteinuria	Significantly higher risk for pre-eclampsia among women with severe (OR = 2.4) or progressive (OR = 2.1) periodontal disease
Holbrook *et al*. 2004	Iceland; 96 subjects	Pocket depth ≥4 mm	Preterm delivery <37 weeks or birthweight <2500 g	No association between periodontal disease and preterm LBW
Moore *et al*. 2004	United Kingdom; 3738 subjects	Percentage of sites with pocket depth >4 or 5 mm	Preterm delivery <37 weeks or birthweight <2500 g	No association between periodontal disease case definitions and preterm delivery or LBW
Moreu *et al*. 2005	Spain; 96 subjects	Percentage sites with pocket depths ≥3 mm	Preterm delivery <37 weeks and birthweight <2500 g	Higher severity of periodontal disease among those having LBW infants
Rajapakse *et al*. 2005	Sri Lanka; 227 subjects	Pocket depth, bleeding and plaque scores > median value in the total cohort	Preterm delivery < 37 weeks and birthweight <2500 g	No association between periodontal disease and preterm delivery (OR = 2.3)
Boggess *et al*. 2006	United States; 1017 subjects	Moderate–severe disease: ≥15 sites with pocket depths ≥4 mm	Small-for-gestational-age births: birthweight <10% for gestational age	Association between periodontal disease and small-for-gestational-age births (RR = 2.3)
Meurman *et al*. 2006	Finland; 207 subjects	Community Periodontal Index for Treatment Needs	Preterm delivery <37 weeks, birthweight <2500 g, caesarean section, gestational diabetes or hypertension, pre-eclampsia or infant Apgar score <7	No association between poor periodontal health and pregnancy or delivery complications

mothers with periodontal disease appear to be 3.5 times (RR, 95% CI 1.5–7.9) more likely to have a preterm low birthweight infant versus mothers with periodontal health (Lopez *et al*. 2002a).

A smaller number of observational studies involving populations in Europe and Asia have failed to detect any significant association between maternal periodontal disease and adverse pregnancy outcomes (Davenport *et al*. 2002; Holbrook *et al*. 2004; Buduneli *et al*. 2005; Moore *et al*. 2005; Rajapakse *et al*. 2005; Skuldbol *et al*. 2006; Meurman *et al*. 2006). One prospective study finding no association was conducted at Guy's and St. Thomas' Hospital Trust in London and involved a large cohort of 3738 pregnant subjects (Moore *et al*. 2004). Regression analysis indicated no significant relationships between the severity of periodontal disease (periodontal pocketing or clinical attachment loss) and either preterm birth or low birthweight. The investigators did note a correlation between poorer periodontal health and mothers who experienced a late miscarriage. A subsequent analysis on non-smokers within this same population confirmed no associations between poor periodontal health and either preterm birth or low birthweight (Farrell *et al*. 2006). Again, non-smoking mothers who experienced late miscarriages exhibited a higher mean probing depth as compared with the subjects with term births. This same group of investigators performed genetic testing (restriction fragment length polymerase techniques) on a sub-cohort of 48 preterm cases and 82 control subjects (Moore *et al*. 2004). There were no significant associations reported for the tested cytokine polymorphisms (interleukin-1β+3953 and TNF-α-308 allelic variants), prematurity, and the severity of periodontal disease. In addition, the combination of genotype and periodontal disease did not increase the risk of preterm delivery in this subcohort. These studies reporting no association are a small proportion of the total available evidence collected to date and suggest that differences in the susceptibility to periodontal disease-associated prematurity may occur in certain global populations.

Association of periodontal disease and pre-eclampsia

Pre-eclampsia is a common hypertensive disorder of pregnancy that independently contributes to maternal and infant morbidity and mortality. Accordingly, atherosclerotic-like changes in placental tissues involving oxidative and inflammatory events are thought to initiate the development of pre-eclampsia (Ramos *et al*. 1995). Boggess and co-workers (2003) hypothesized that maternal exposure to periodontal disease or infection may be associated with the development of pre-eclampsia. Using data collected as part of the OCAP study, the investigators conducted logistic regression analyses on outcomes collected from 763 women who were enrolled at less than 26 weeks gestation and who delivered live infants. Pre-eclampsia (defined here as blood pressure >140/90 mmHg on two separate occasions, and ≥1+ proteinuria on catheterized urine specimen) affected 5.1% of subjects. The adjusted OR for severe periodontal disease at delivery (≥15 sites with pocket depths ≥4 mm in depth) and pre-eclampsia was 2.4 (95% CI 1.1–5.3). For women exhibiting periodontal disease progression during pregnancy (four or more sites with increases in pocket depth ≥2 mm and resulting in pockets ≥4 mm in depth) the adjusted OR was 2.1 (95% CI 1.0–4.4). After adjusting for other risk factors, such as maternal age, race, smoking, gestational age at delivery, and insurance status, the results from this cohort study indicate that severe and progressive maternal periodontal disease during pregnancy is associated with an increased risk for pre-eclampsia.

This same hypothesis was tested in a case–control study conducted in Colombia and including 130 pre-eclamptic (blood pressure ≥149/90 mmHg and ≥2+ proteinuria) and 243 non-pre-eclamptic women recruited between 26 and 36 weeks of pregnancy (Contreras *et al*. 2006). In addition to sociodemographic data, obstetric risk factors, and clinical periodontal outcomes, Contreras and co-workers examined the maternal subgingival microbial flora with sampling and anaerobic culture techniques. Sixty-four percent of pre-eclamptic women had chronic periodontitis (pocket depth and clinical attachment loss ≥4 mm and bleeding on probing) (OR = 3.0, 95% CI 1.91–4.87) versus 37% of controls. Notably, a higher proportion of pre-eclamptic women were infected subgingivally with periodontal pathogens including *P. gingivalis* (OR = 1.77, 95% CI 1.12–2–8), *T. forsythia* (OR = 1.8, 95% CI 1.06–3.00), and *Eikenella corrodens* (OR = 1.8, 95% CI 1.14–2.84). This case–control report demonstrates a consistent relationship between exposure to periodontal disease or subgingival pathogens and pre-eclampsia in pregnant women.

Xiong and co-workers (2006) have recently reviewed all of the existing evidence to date that examines the influence of periodontitis on adverse pregnancy outcomes. Twenty-two studies (13 case–control and 9 cohort) focused on preterm low birthweight, low birthweight, preterm birth, birthweight by gestational age, miscarriage or pregnancy loss, and pre-eclampsia. Fifteen studies suggested an association between periodontal disease and increased risk of adverse pregnancy outcome (odds ratio ranging from 1.10 to 20.0) while seven found no evidence of an association (odds ratio ranging from 0.78 to 2.54). This report concludes that more methodologically vigorous studies are needed and those studies are currently being conducted.

Periodontitis as a risk for diabetic complications

Similar to cardiovascular disease, diabetes mellitus is a common, multifactorial disease process involving

genetic, environmental, and behavioral risk factors. Affecting up to 5% of the general population and over 124 million persons worldwide (King *et al*. 1998), this chronic condition is marked by defects in glucose metabolism that produce hyperglycemia in patients. Diabetes mellitus is broadly classified under two major types (American Diabetes Association Expert Committee on the Diagnosis and Classification of Diabetes Mellitus 1997). In patients with type I diabetes, (formerly called insulin-dependent diabetes mellitus), the defect occurs at the level of the pancreatic beta cells that are destroyed. Consequently type 1 diabetics produce insufficient levels of the hormone insulin for homeostasis. In contrast, patients with type 2 diabetes (formerly called non-insulin-dependent diabetes mellitus), exhibit the defect at the level of the insulin molecule or receptor. Cells in type 2 diabetics cannot respond or are resistant to insulin stimulation.

Diabetes mellitus is usually diagnosed via laboratory fasting blood glucose levels that are greater than 7 mmol/L (126 mg/dL). Additionally, casual or non-fasting blood glucose values are elevated above 11.1 mmol/L (200 mg/dL). Thirdly, diabetic patients exhibit abnormal glucose tolerance tests (i.e. blood glucose levels greater than 8.3 mmol/L (150 mg/dL) at 2 hours following a 100 g glucose load). Elevated glycated hemoglobin levels (HbA1 and HbA1c) comprise a fourth laboratory parameter and one that provides a 30–90-day record of the patient's glycemic status. Classic signs and symptoms of diabetes include polyuria, polydipsia, polyphagia, pruritis, weakness, and fatigue. End-stage diabetes mellitus is characterized by problems with several organ systems including micro- and macrovascular disease (atherosclerosis), retinopathy, nephropathy, neuropathy, and periodontal disease.

Although environmental exposures, viral infection, autoimmunity, and insulin resistance are currently considered to play principal roles in the etiology of diabetes mellitus (Yoon 1990; Atkinson & Maclaren 1990), pathogenesis of the disease and end-organ damage relies heavily on the formation and accumulation of advanced glycation end-products (AGEs) (Brownlee 1994). Accordingly, the chronic hyperglycemia in diabetes results in the non-enzymatic and irreversible glycation of body proteins. These AGEs, in turn, bind to specific receptors for advanced glycation end-products (RAGEs) on monocytes, macrophages, and endothelial cells, and alter intracellular signaling (transduction) pathways (Esposito *et al*. 1992; Kirstein *et al*. 1992). With AGE–RAGE binding, monocytes and macrophages are stimulated to proliferate, up-regulate pro-inflammatory cytokines, and produce oxygen free radicals (Vlassara *et al*. 1988; Yan *et al*. 1994; Yui *et al*. 1994). While oxygen free radicals directly damage host tissues, pro-inflammatory cytokines like IL-1, IL-6 and TNF-α exacerbate this damage via a cascade of catabolic events and the recruitment of other immune cells (T and B lymphocytes). Patients with diabetes exhibit elevated levels of AGEs in tissues including those of the periodontium (Brownlee 1994; Schmidt *et al*. 1996). Diabetics also present with elevated serum and gingival crevicular fluid levels of pro-inflammatory cytokines (Nishimura *et al*. 1998; Salvi *et al*. 1998). Furthermore, monocytes isolated from diabetics and stimulated with LPS secrete higher concentrations of pro-inflammatory cytokines and prostaglandins (Salvi *et al*. 1998). Chronic hyperglycemia, the accumulation of AGEs and the hyper-inflammatory response may promote vascular injury and altered wound healing via increased collagen cross-linking and friability, thickening of basement membranes, and altered tissue turnover rates (Weringer & Arquilla 1981; Lien *et al*. 1984; Salmela *et al*. 1989; Cagliero *et al*. 1991). Lastly, diabetic patients exhibit impairments in neutrophil chemotaxis, adherence, and phagocytosis (Bagdade *et al*. 1978; Manouchehr-Pour *et al*. 1981; Kjersem *et al*. 1988), and thus are at high risk for infections like periodontitis.

Numerous epidemiologic surveys demonstrate an increased prevalence of periodontitis among patients with uncontrolled or poorly controlled diabetes mellitus. For example, Cianciola *et al*. (1982) reported that 13.6% and 39% of type 1 diabetics, 13–18 and 19–32 years of age respectively, had periodontal disease. In contrast, none of the non-diabetic sibling controls and 2.5% of the non-diabetic, unrelated controls exhibited clinical evidence of periodontitis. In a classic study, Thorstensson and Hugoson (1993) examined the severity of periodontitis in patients with diabetes mellitus and compared severity of periodontitis with the duration a patient had been diagnosed with diabetes. In looking at three age cohorts, 40–49 years, 50–59 years, and 60–69 years, the 40–49 years age group diabetics had more periodontal pockets ≥6 mm and more extensive alveolar bone loss than non-diabetics. In this same age group, there were also more subjects with severe periodontal disease experience among the diabetics than among the non-diabetics. In noting that the younger age diabetics had more periodontitis than the older age diabetics, these authors reported that early onset of diabetes is a much greater risk factor for periodontal bone loss than mere disease duration.

Safkan-Seppala and Ainamo (1992) conducted a cross-sectional study of 71 type 1 diabetics diagnosed with the condition for an average of 16.5 years. Diabetics identified with poor glycemic control demonstrated significantly more clinical attachment loss and radiographic alveolar bone resorption as compared to well controlled diabetics with the same level of plaque control. Two longitudinal cohort studies monitoring type 1 diabetics for 5 and 2 years respectively documented significantly more periodontitis progression among diabetics overall and among those whose diabetes was poorly controlled (Seppala *et al*. 1993; Firatli 1997).

Investigators from the State University of New York at Buffalo have published a number of papers documenting the periodontal status of Pima Indians,

a population with a high prevalence of type 2 diabetes mellitus. Shlossman *et al*. (1990) first documented the periodontal status of 3219 subjects from this unique population. Diagnosing type 2 diabetes with glucose tolerance tests, the investigators found a higher prevalence of clinical and radiographic periodontitis for diabetics versus non-diabetics independent of age. This investigative group next focused on a cross-sectional analysis of 1342 dental subjects (Emrich *et al*. 1991). A logistic regression analysis indicated that type 2 diabetics were 2.8 times more likely to exhibit clinical attachment loss and 3.4 times more likely to exhibit radiographic alveolar bone loss indicative of periodontitis relative to non-diabetic controls. In a larger study of 2273 Pima subjects, 60% of type 2 diabetics were affected with periodontitis versus 36% of non-diabetic controls (Nelson *et al*. 1990). When a cohort of 701 subjects with little or no evidence of periodontitis at baseline were followed for approximately 3 years, diabetics were 2.6 times more likely to present with incident alveolar bone resorption as compared to non-diabetics. Taylor *et al*. (1998a,b) similarly reported higher odds ratios of 4.2 and 11.4 for the risk of progressive periodontitis among diabetic Pima Indians in general and poorly controlled diabetics (i.e. with glycated hemoglobin levels >9%) respectively.

The studies cited above review the evidence that diabetes is a modifier or risk factor for periodontitis. Of tremendous importance also are the data that have emerged indicating that the presence of periodontitis or periodontal inflammation can increase the risk for diabetic complications, principally poor glycemic control. Taylor *et al*. (1996) tested this hypothesis using longitudinal data on 88 Pima subjects. Severe periodontitis at baseline as defined clinically or radiographically was significantly associated with the risk of worsening glycemic control (glycated hemoglobin >9%) by six-fold over a 2-year period. Other significant co-variates in the regression modeling included subject age, smoking, and baseline severity and duration of type 2 diabetes. Collin and co-workers (1998) studied older adults in Finland and found that people with advanced periodontitis were more likely to have higher HbAlc levels than those who had no or moderate periodontitis at follow-up.

With the emerging evidence reviewed earlier in this chapter that periodontal disease is a significant risk factor for cardiovascular disease, Saremi *et al*. (2005) conducted a longitudinal trial to examine the effect of periodontal disease on overall mortality and cardiovascular disease-related mortality in 600 subjects with type 2 diabetes. In subjects with severe periodontitis, the death rate from ischemic heart disease was 2.3 times as high as the rate in subjects with no or mild periodontitis after accounting for other known risk factors. The death rate from diabetic nephropathy was 8.5 times higher in those with severe periodontitis. When deaths from renal and cardiac causes were analyzed together, the mortality rate from cardiorenal disease was 3.5 times higher in patients with severe periodontitis. These findings further suggest that periodontal disease is a risk for cardiovascular and renal mortality in people with diabetes (Janket *et al*. 2003; Scanniapieco *et al*. 2003a; Mealey & Rose 2005; Saremi *et al*. 2005; Mealey & Oates 2006).

Periodontitis as a risk for respiratory infections

There is emerging evidence that in certain at risk populations, periodontitis and poor oral health may be associated with several respiratory conditions. Respiratory diseases contribute considerably to morbidity and mortality in human populations. Lower respiratory infections were ranked as the third most common cause of death worldwide in 1990, and chronic obstructive pulmonary disease (COPD) was ranked sixth (Scannapieco 1999; Scannapieco *et al*. 2003).

Bacterial pneumonia is either community-acquired or hospital-acquired (nosocomial). Community-acquired pneumonia is usually caused by bacteria that reside on the oropharyngeal mucosa, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Hospital-acquired pneumonia is often caused by bacteria within the hospital or health care environment, such as Gram-negative bacilli, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* (Scannapieco 1999; Mealey & Klokkvold 2006). As many as 250 000 to 300 000 hospital-acquired respiratory infections occur in the US each year with an estimated mortality rate of about 30%. Pneumonia also contributes to a significant number of other deaths by acting as a complicating or secondary factor with other diseases or conditions.

COPD is another common severe respiratory disease characterized by chronic obstruction to airflow with excess production of sputum resulting from chronic bronchitis and/or emphysema. Chronic bronchitis is the result of irritation to the bronchial airway causing an expansion of the propagation of mucus-secreting cells within the airway epithelium. These cells secrete excessive tracheobronchial mucus sufficient to cause cough with expectoration for at least 3 months of the year over 2 consecutive years. Emphysema is the distention of the air spaces distal to the terminal bronchiole with destruction of the alveolar septa (Scannapieco 1999).

Beginning in 1992 with a report by Scannapieco's group at SUNY-Buffalo (Scannapieco *et al*. 1992), several investigators have hypothesized that oral and/or periodontal infection may increase the risk for bacterial pneumonia or COPD. It seems plausible from all the evidence reviewed in this chapter that the oral cavity may have a critical role in respiratory infections. For example, oral bacteria from the periodontal pocket can be aspirated into the lung to cause

aspiration pneumonia. The teeth may also serve as a reservoir for respiratory pathogen colonization and subsequent nosocomial pneumonia. Typical respiratory pathogens have been shown to colonize the dental plaque of hospitalized intensive care and nursing home patients. Once established in the mouth, these pathogens may be aspirated into the lung to cause infection. Also, periodontal disease-associated enzymes in saliva may modify mucosal surfaces to promote adhesion and colonization by respiratory pathogens, which are then aspirated into the lungs. These same enzymes may also destroy salivary pellicles on pathogenic bacteria to hinder their clearance from the mucosal surface. Lastly, cytokines originating from periodontal tissues may alter respiratory epithelium to promote infection by respiratory pathogens (Scannapieco 1999).

Data from a longitudinal study of more than 1100 men revealed that alveolar bone loss was associated with the risk of COPD. Over a 25-year period, 23% of subjects were diagnosed with COPD. Subjects who had more severe bone loss at the baseline dental examination had a significantly increased risk of subsequently developing COPD compared with subjects with less bone loss (Hayes *et al*. 1998). Scannapieco and co-workers (1998) found that individuals with poor oral hygiene were at increased risk for chronic respiratory diseases such as bronchitis and emphysema. Scannapieco and Ho (2001) reported that patients with a history of COPD had significantly more periodontal attachment loss (1.48 ± 1.35 mm) than subjects without COPD (1.17 ± 1.09 mm). However, two recent systematic reviews of all of the current evidence indicate that at present there is not sufficient evidence to say that there is an association between periodontal disease and COPD (Scannapieco *et al*. 2003; Azarpazhooh & Leake 2006). There is emerging evidence for an association between hospital-acquired (nosocomial) bacterial pneumonia and periodontal disease. It is thought that potential respiratory pathogens, usually from the gastrointestinal tract, can colonize the oral cavity, where they are subsequently aspirated, leading to pneumonia (Mealey & Klokkevold 2006).

Effects of treatment of periodontitis on systemic diseases

This chapter has examined the evidence, gathered by many investigators since the early 1990s, which suggests that periodontitis may be a risk for certain systemic conditions such as cardiovascular disease, adverse pregnancy outcomes, diabetes mellitus, and pulmonary disease. Collectively, the findings gathered from investigators world-wide are very compelling. It would certainly appear that periodontal disease is strongly associated with systemic conditions.

Students of dentistry will next ask, "If you treat periodontitis, do you prevent the onset or reduce the severity of these systemic complications?" It is clear that dentistry must now focus on intervention studies to determine whether treating periodontitis will have a beneficial effect on systemic diseases. This is not an easy task and some studies will take considerable time before we know the answer. However, there are initial data which examine intervention and the impact of periodontal treatment on several systemic conditions and the results are promising.

Regarding cardiovascular disease, evidence in human subjects demonstrating the beneficial effects of periodontal therapy on cardiovascular disease outcomes is limited and indirect at present. D'Aiuto and co-workers (2004) demonstrated that periodontitis patients treated with scaling and root planing exhibited significant serum reductions in the cardiovascular disease biomarker, CRP, and IL-6. In particular, patients who clinically responded to periodontal therapy in terms of pocket depth reductions were four times more likely to exhibit serum decreases in CRP relative to patients with a poor clinical periodontal response. Elter and colleagues (2006) also reported decreases in these serum biomarkers plus improved endothelial functions (i.e. flow-mediated dilation of the brachial artery) for 22 periodontitis patients treated with "complete mouth disinfection" (i.e. scaling and root planing, periodontal flap surgery, and extraction of hopeless teeth within a 2-week interval). Similarly, Seinost and co-workers (2005) tested endothelial function in 30 patients with severe periodontitis versus 31 periodontally healthy control subjects. Prior to interventions, flow-mediated dilation was significantly lower in patients with periodontitis than in control subjects. Periodontitis patients with favorable clinical responses to non-surgical periodontal therapy (i.e. scaling and root planing, topical and peroral antimicrobials plus mechanical retreatment) exhibited concomitant improvements in flow-mediated dilatation of the brachial artery and serum CRP concentrations. While the effects of periodontal therapy on cardiovascular disease events in patients have yet to be determined, the available pilot data suggest that periodontal therapies can improve surrogate cardiovascular disease outcomes like serum biomarkers and endothelial dysfunction.

In considering adverse pregnancy outcomes, four published intervention studies provide early evidence that preventive and treatment interventions aimed at reducing maternal periodontal infection and inflammation may reduce the likelihood of preterm low birthweight infants, while one study did not find an effect. Mitchell-Lewis and co-workers (2000) conducted a non-randomized pilot trial involving 164 US inner-city minority pregnant women. One group received full mouth debridement (scaling with hand and/or ultrasonic instruments) plus tooth polishing and oral hygiene instructions. The second group received no periodontal intervention. No differences in clinical periodontal status were observed

between preterm low birthweight cases and women with normal birth outcomes, but preterm low birthweight mothers had significantly higher levels of subgingival pathogens like *T. forsythia* and *C. rectus.* Strikingly, while 18.9% of women receiving no periodontal intervention delivered preterm low birthweight infants, only 13.5% of the treated women had preterm low birthweight infants.

A second pilot trial conducted in the US involved 366 women with periodontitis recruited between 21 and 25 weeks gestation (Jeffcoat *et al*. 2003). Subjects were stratified for risk factors (previous spontaneous PTB at <35 weeks, body mass index <19.8 or bacterial vaginosis as assessed by Gram stain) and randomized to one of three treatment groups as follows: (1) dental prophylaxis plus placebo capsule; (2) scaling and root planing plus placebo capsule; or (3) scaling and root planing plus metronidazole capsule (250 mg tid for 1 week). An additional group of 723 pregnant women meeting the same criteria for periodontitis but receiving no intervention served as the negative control. Women treated with scaling and root planing plus placebo capsules exhibited the lowest incidence rate for PTB <35 weeks (0.8%). Those treated with dental prophylaxis plus placebo capsules or scaling and root planing plus metronidazole capsules exhibited intermediate incidence rates for preterm deliveries (4.9% and 3.3% respectively). In contrast, the rate of PTB for the untreated reference group was 6.3%. This trial supported the hypothesis that mechanical periodontal therapy alone may reduce PTB in pregnant women with periodontitis.

Lopez and co-workers (2002a, 2005) have reported results from two intervention studies conducted in Chile demonstrating consistent, significant, and beneficial effects of mechanical periodontal therapy on preterm low birthweight outcomes. In the first trial, the investigators enrolled 351 pregnant women with clinical evidence of periodontitis (four or more teeth with one or more site exhibiting pocket depth ≥4 mm and clinical attachment loss ≥3 mm) and randomized them to immediate mechanical periodontal therapy (scaling and root planing) versus delayed (postpartum) treatment. The total incidence of PLBW in this cohort of periodontitis subjects was 6.26%. For women treated for periodontal disease, the incidence of PLBW was only 1.84%, while the incidence was 10.11% in untreated women. When a multivariate logistic regression analysis was performed controlling for other risk factors, delayed periodontal disease treatment was the strongest factor related to PLBW with an OR of 4.70 (95% CI 1.29–17.13). In the second trial, 870 pregnant women with gingivitis (≥25% of sites bleeding on probing but no clinical attachment loss ≥2 mm) were randomly assigned to immediate versus postpartum periodontal treatment (supra- and subgingival scaling, tooth polishing, and daily rinsing with 0.12% chlorhexidine gluconate). Those receiving immediate periodontal treatment also received maintenance therapy plus oral hygiene instructions every 2–3 weeks until delivery. Accordingly, the incidence of preterm low birthweight in the immediate treatment group was 2.14% versus 6.71% for the control group (OR = 3.26, 95% CI 1.56–6.83). After adjusting for other known risk factors, women with gingivitis receiving delayed intervention were almost three times more likely to deliver preterm as compared to women who received periodontal treatment (OR = 2.76, 95% CI 1.29–5.88). One trial did not find an effect of scaling and root planing on adverse pregnancy outcomes (Michalowicz *et al*. 2006). Overall, these clinical trials suggest that mechanical intervention in pregnant mothers with gingivitis or periodontitis can reduce the incidence of preterm low birthweight.

Clinicians and investigators working with patients who have diabetes mellitus have studied whether periodontal treatment can improve glycemic control. Several investigators have sought to answer this question using periodontal mechanical treatment as the intervention (Seppala & Ainamo 1994; Aldridge *et al*. 1995; Smith *et al*. 1996; Christgau *et al*. 1998; Stewart *et al*. 2001). Some of these studies have failed to detect an improvement in glycated hemoglobin level with scaling and root planing alone, while others have shown an improvement.

Kiran and co-workers conducted a study of patients with well controlled type 2 diabetes who had gingivitis or mild periodontitis. Prophylaxis and scaling and root planing, without systemic antibiotic therapy, was examined for the effect on periodontal disease and glycemic control. Control diabetic subjects with periodontal disease received no treatment. The treated subjects had a 50% reduction in the prevalence of gingival bleeding 3 months after treatment. In addition these subjects had a significant improvement in glycemic control, with a reduction in the mean HbAlc value of 0.8%. The control subjects who were not treated had no change in periodontal status or glycemic control (Kiran *et al*. 2005).

Grossi *et al*. (1997) reported positive findings from an intervention trial featuring 113 Pima Indians with type 2 diabetes and periodontitis who received both mechanical and antimicrobial treatment. At baseline, participants were treated with scaling and root planing plus one of five antimicrobial regimens: (1) water (placebo) rinse and peroral doxycycline (100 mg qid for 2 weeks), (2) 0.12% chlorhexidine rinse and peroral doxycycline, (3) povidone–iodine rinse and peroral doxycycline, (4) 0.12% chlorhexidine rinse and peroral placebo, or (5) povidone–iodine rinse and peroral placebo. Subjects were evaluated using clinical, microbiologic, and laboratory parameters prior to therapy and at 3 and 6 months. All treatment groups on average demonstrated clinical and microbiological improvements; however, those groups treated with adjunctive peroral tetracycline exhibited significant and greater reductions in pocket depth and subgingival detection rates for *P. gingivalis* as compared to the groups receiving peroral placebo.

Most strikingly, diabetic subjects receiving mechanical therapy plus peroral tetracycline demonstrated significant, 10% reductions in their glycated hemoglobin levels. Two small, uncontrolled cohort studies with type 1 diabetic–periodontitis patients each similarly reported improvements in glycemic control with combination mechanical–antimicrobial therapy (Williams & Mahan 1960; Miller *et al*. 1992).

At present it is still not clear what can be expected from treating or reducing periodontal disease in diabetic subjects on glycemic control. There are enough available data to at least say that the effect of periodontal disease treatment on reducing HbAlc levels in subjects with diabetes has promise. There is such great variability among patients in the studies to date that it appears that some diabetic subjects had little change in glycemic control while others had major improvement. Nonetheless, it is very clear that periodontal health is a major goal for subjects with diabetes (Mealey & Oates 2006).

Last, the evidence for the effect of periodontal intervention on bacterial pneumonia shows promise. There are a number of studies which examine the effect of treating oral infection in reducing the risk of pneumonia in high-risk populations. DeRiso and colleagues (1996) studied subjects admitted to a surgical intensive care unit. When subjects received a chlorhexidine rinse twice a day compared to control subjects receiving a placebo rinse, the incidence of pneumonia was reduced 60% in the chlorhexidine treated group compared to the control group. Fourrier and colleagues (2000) found a similar 60% reduction in pneumonia with the use of a 0.2% chlorhexidine gel.

In a landmark study, Yoneyama and co-workers (2002) examined the role of supervised toothbrushing plus providone–iodine on the incidence of pneumonia in a group of elders living in nursing homes in Japan. When these subjects had their mouths cleaned, with supervision, there was a 39% reduction in pneumonia over a 2-year period compared to the control group. Recent reviews of the evidence clearly indicate that when bacterial plaque is reduced in the mouth in at-risk subjects, the risk of pneumonia is reduced. These findings are limited at present to special-care populations. Little evidence exists that poor oral hygiene and periodontal disease increase the risk for community-acquired pneumonia (Azarpazhooh & Leake 2006; Scannapieco *et al*. 2003b).

Dentistry has come a long way since 1900 when Willoughby Miller and William Hunter proclaimed that oral disease caused most systemic disease. A century later we are developing a scientifically based understanding of how in fact periodontitis may be a risk for certain systemic diseases. As these more recent observations are confirmed and clarified, dentistry will have a new responsibility in caring for patients who may develop or who have periodontitis. It is no longer just teeth that are at risk.

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Chapter 22

The Periodontal Abscess

Mariano Sanz, David Herrera, and Arie J. van Winkelhoff

Introduction

Odontogenic abscesses include a broad group of acute infections that originate from the tooth and/or the periodontium. Such abscesses are associated with an array of symptoms, including a localized purulent inflammation in the periodontal tissues that causes pain and swelling. Abscesses are one of the main causes for patients to seek emergency care in the dental clinic. Depending on the origin of the infection the lesions can be classified as periapical, periodontal, and pericoronary abscesses.

Classification

Different classifications have been suggested for periodontal abscesses: chronic or acute; single or multiple; gingival or periodontal; occurring in the supporting periodontal tissues or in the gingiva. A classification has been proposed (Meng 1999) and includes *gingival abscesses* (in previously healthy sites and caused by impactation of foreign bodies), *periodontal abscesses* (either acute or chronic, in relation to a periodontal pocket), and *pericoronal abscesses* (at incompletely erupted teeth). This classification was included at the revised classification system for periodontal diseases developed at *The International Workshop for a Classification of Periodontal Diseases and Conditions* organized by the American Academy of Periodontology in 1999, and for the first time, periodontal abscesses were included as an independent entity.

The most rational classification of periodontal abscesses is, however, the one based on its aetiology. Depending on the cause of the acute infectious process, two types of abscesses may occur:

- *Periodontitis-related abscess*, when the acute infection originates from bacteria present at the subgingival biofilm in a deepened periodontal pocket
- *Non-periodontitis-related abscess*, when the acute infection originates from bacteria originating from another local source, such as a foreign body impaction or from alterations in the integrity of the root leading to bacteria colonization.

In a periodontitis patient a periodontal abscess represents a period of active tissue breakdown and is the result of an extension of the infection into the still intact periodontal tissues. This abscess formation is usually due to the marginal closure of a deep periodontal pocket and lack of proper drainage. Therefore, the existence of deep, tortuous pockets and deep concavities associated with furcation lesions favors the development of these acute conditions. Once the acute inflammatory process is started, there is a local accumulation of neutrophils, formation of pus, and tissue breakdown. The retention of pus in the pocket may further compromise the drainage and the lesion may progress rapidly.

There are different mechanisms behind the formation of a *periodontitis-related abscess*:

- *Exacerbation of a chronic lesion*. Such abscesses may develop in a deepened periodontal pocket without any obvious external influence, and may occur in: (a) an untreated periodontitis patient, or (b) as a recurrent infection during supportive periodontal therapy.
- *Post-therapy periodontal abscesses*. There are various reasons why an abscess may occur during the course of active therapy:
  - Post-scaling periodontal abscess (Dello Russo 1985). When these lesions occur immediately after scaling or after a routine professional prophylaxis they are usually related to the presence of small fragments of remaining calculus that obstruct the pocket entrance once the oedema in the gingiva has disappeared (Dello Russo 1985; Carranza 1990). This type of

abscess formation can also occur when small fragments of calculus have been forced into the deep, previously uninflamed portion of the periodontal tissues (Dello Russo 1985).

- Post-surgery periodontal abscess. When an abscess occurs immediately following periodontal surgery, it is often the result of an incomplete removal of subgingival calculus or to the presence of foreign bodies in the periodontal tissues, such as sutures, regenerative devices, or periodontal pack (Garrett *et al.* 1997).
- Post-antibiotic periodontal abscess. Treatment with systemic antibiotics without subgingival debridement in patients with advanced periodontitis may also cause abscess formation (Helovuo & Paunio 1989; Helovuo *et al.* 1993; Topoll *et al.* 1990). In such patients, the subgingival biofilm may protect the residing bacteria from the action of the antibiotic, resulting in a super-infection leading to an acute process with the ensuing inflammation and tissue destruction. Helovuo *et al.* (1993) followed patients with untreated periodontitis who were given broad-spectrum antibiotics (penicillin, erythromycin) for non-oral reasons. They showed that 42% of these patients developed marginal abscesses within 4 weeks of antibiotic therapy.

Non-periodontitis-related abscess formation may also occur in relation to a periodontal pocket, but in such cases, there is always an external local factor that explains the acute inflammatory process. Such factors may include:

- Impaction of foreign body in the gingival sulcus or periodontal pocket (Gillette & Van House 1980; Abrams & Kopczyk 1983). It may be related to oral hygiene practices (toothbrush, toothpicks, etc.) (Gillette & Van House 1980; Abrams & Kopczyk 1983), orthodontic devices, food particles, etc.
- Root morphology alterations. In this instance local anatomic factors, such as an invaginated root (Chen *et al.* 1990), a fissured root (Goose 1981), an external root resorption, root tears (Haney *et al.* 1992; Ishikawa *et al.* 1996) or iatrogenic endodontic perforations (Abrams *et al.* 1992), may be the cause of the abscess formation.

Prevalence

The prevalence of periodontal abscesses was studied in emergency dental clinics (Ahl *et al.* 1986; Galego-Feal *et al.* 1996), in general dental clinics (Lewis *et al.* 1990), in periodontitis patients before treatment (Gray *et al.* 1994), and in periodontitis patients during supportive periodontal therapy (SPT) (Kaldahl *et al.* 1996; McLeod *et al.* 1997).

Among all dental conditions in need of emergency treatment, periodontal abscesses represent between 8% and 14% (Ahl *et al.* 1986; Galego-Feal *et al.* 1996). Gray *et al.* (1994) monitored periodontal patients in a military clinic and found that periodontal abscesses had a prevalence of 27.5%. In this population, 13.5% of the patients undergoing active periodontal treatment had experienced abscess formation, while untreated patients showed a higher figure, 59.7%. McLeod *et al.* (1997) followed 114 patients in SPT and identified 42 patients (27.5%) that had suffered from acute episodes of periodontal abscess.

In a prospective longitudinal treatment study, by Kaldahl *et al.* (1996), the occurrence of periodontal abscesses during 7 years of periodontal maintenance was also studied. From the 51 patients included, 27 abscesses were detected. Twenty-three of the abscesses occurred at teeth in quadrants treated only by coronal scaling, three in areas treated by root planing, and only one in areas treated by surgical therapy. Sixteen out of 27 abscess sites had an initial probing pocket depth >6 mm, while in eight sites the probing depth was 5–6 mm.

Abscesses often occur in molar sites, representing more than 50% of all sites affected by abscess formation (Smith & Davies 1986; McLeod *et al.* 1997; Herrera *et al.* 2000a). The most likely reason for this high prevalence of abscesses in molars could be presence of pockets involving the furcation and the complex anatomy and root morphology of such teeth. However, in a recently published study in Colombian patients, the lower anterior incisors were the most frequently affected teeth (Jaramillo *et al.* 2005).

The occurrence of a periodontal abscess may be important not only due to its relatively high prevalence, but also on how these acute infections may influence the prognosis of the affected teeth. Since abscesses sometimes develop during SPT in teeth with remaining deep periodontal pockets and a reduced periodontal support, the additional periodontal destruction occurring during the acute periodontal process may be the main indication for its extraction (Chace & Low 1993; McLeod *et al.* 1997).

Pathogenesis and histopathology

The periodontal abscess lesion contains bacteria, bacterial products, inflammatory cells, tissue breakdown products, and serum. The precise pathogenesis of this lesion is still obscure. It is hypothesized that the occlusion of the periodontal pocket lumen, due to trauma or tissue tightening, will prevent drainage and result in extension of the infection from the pocket into the soft tissues of the pocket wall, resulting in the formation of the abscess. The entry of bacteria into the soft tissue pocket wall could be the event that initiates the formation of a periodontal abscess, however it is the accumulation of leukocytes and the formation of an acute inflammatory infiltrate what will be the main cause of the connective tissue

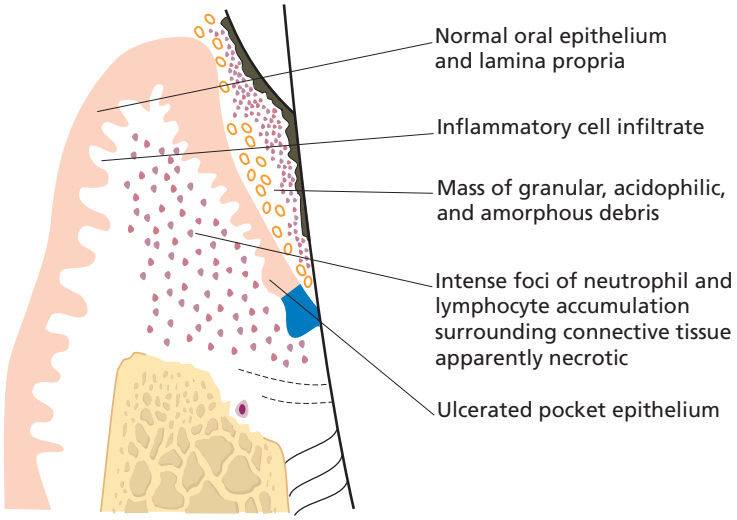

Fig. 22-1 Schematic drawing showing the histopathology of a periodontal abscess.

destruction, encapsulation of the bacterial mass, and formation of pus. The inflammatory cells and their extracellular enzymes are, therefore, the main cause of this destruction of connective tissue. Both the lowered tissue resistance and the virulence and number of bacteria will determine the course of this acute infection.

The histopathology of this lesion demonstrates, in its first phases, the central area of the abscess filled with neutrophils, in close vicinity with remains of tissue destruction and soft tissue debris. At a later stage, a pyogenic membrane, composed of macrophages and neutrophils, is organized. The rate of tissue destruction within the lesion will depend on the growth of bacteria inside the foci and their virulence, as well as on the local pH. An acidic environment will favor the activity of lysosomal enzymes and promote tissue destruction (DeWitt *et al.* 1985).

De Witt *et al*. (1985) studied biopsies sampled from 12 abscesses. The biopsies were taken immediately apical to the centre of the abscess and processed for histologic examination. They observed that the sites examined had a normal oral epithelium and lamina propria, but an inflammatory cell infiltrate resided lateral to the pocket epithelium. There were foci of neutrophil and lymphocyte accumulations in areas characterized by massive tissue destruction and a mass of granular, acidophilic, and amorphous debris present in the pocket (Fig. 22-1). Gram-negative bacteria were seen invading both the pocket epithelium and the compromised connective tissue in seven out of nine biopsies evaluated by electron microscopy.

Microbiology

In review articles and textbooks it is usually cited that that purulent oral infections are polymicrobial, and mainly caused by endogenous bacteria (Tabaqhali 1988). However, very few studies have investigated the specific microbiota of periodontal abscesses. Newman & Sims (1979) studied nine abscesses and found that 63.1% of the microbiota was comprised of strict anaerobes. Topoll *et al.* (1990) analysed 20 abscesses in 10 patients who had taken antibiotics prior to the study. They reported that 59.5% of the microbiota was made up of strict anaerobes. Herrera *et al*. (2000a) reported that 45.1% of the bacteria in the abscess material included anaerobes.

These studies have shown that the microbiota of periodontal abscess is not different from the microbiota of chronic periodontitis lesions. This microflora is polymicrobial and dominated by non-motile, Gram-negative, strict anaerobic, rod-shaped species. From this group, *Porphyromonas gingivalis* is probably the most virulent and relevant microorganism. The occurrence of *P. gingivalis* in periodontal abscesses ranges from 50–100% (Newman & Sims 1979; van Winkelhoff *et al.* 1985; Topoll *et al.* 1990; Hafström *et al.* 1994; Herrera *et al.* 2000a; Jaramillo *et al.* 2005). Using a polymerase chain reaction technique, Ashimoto *et al*. (1998) found *P. gingivalis* in all of the seven cases of abscesses they investigated. Other anaerobic species that are usually found include *Prevotella intermedia*, *Prevotella melaninogenica*, *Fusobacterium nucleatum*, and *Tannerella forsythia*. Spirochetes (*Treponema* species) are also found in most cases (Ashimoto *et al.* 1998). The majority of the Gram-negative anaerobic species are non-fermentative and display moderate to strong proteolytic activity. Strict anaerobic, Gram-positive bacterial species in periodontal abscesses include *Micromonas micros*, *Actinomyces* spp., and *Bifidobacterium* spp. Facultative anaerobic Gram-negative bacteria that can be isolated from periodontal abscesses include *Campylobacter* spp., *Capnocytophaga* spp., and *Aggregatibacter actinomycetemcomitans* (Hafström *et al.* 1994). The presence of Gram-negative enteric rods has also been reported (Jaramillo *et al.* 2005).

Diagnosis

The diagnosis of a periodontal abscess should be based on the overall evaluation and interpretation of

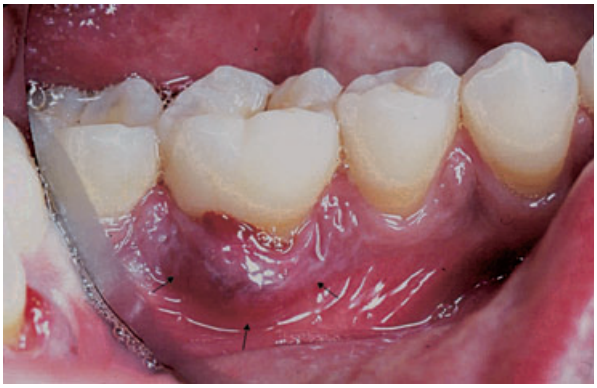

Fig. 22-2 Periodontal abscess associated with a lower right first molar. Observe the association between the abscess formation and the furcation lesion in this molar.

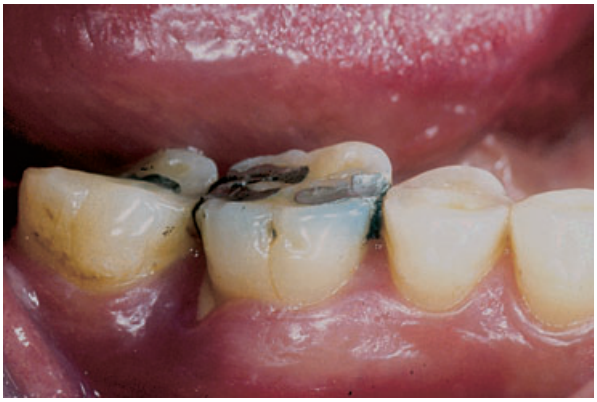

Fig. 22-4 Periodontal abscess associated with a lower right first molar. Observe the spontaneous suppuration expressed through the gingival margin.

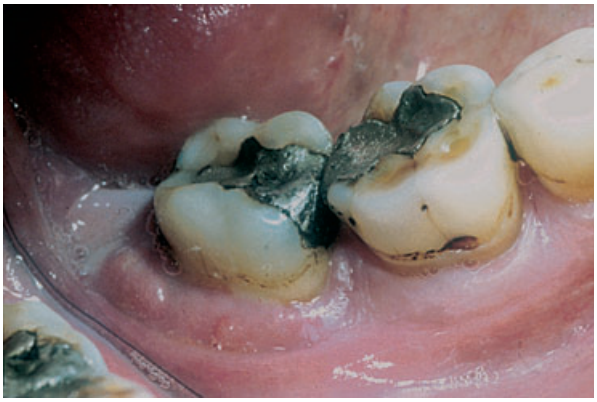

Fig. 22-3 Periodontal abscess associated with a mandibular second molar. There is diffuse swelling affecting all the buccal surface of the molar.

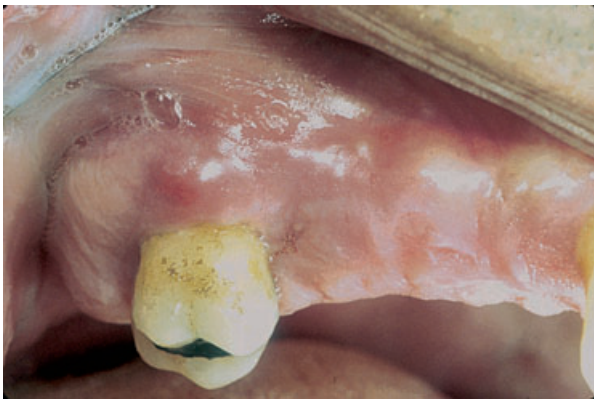

Fig. 22-5 Periodontal abscess associated with an upper right third molar. This lesion is associated with tooth extrusion and mobility.

the patient´s chief complaint, together with the clinical and radiological signs found during the oral examination (Corbet 2004).

The most prominent symptom of a periodontal abscess is the presence of an ovoid elevation of the gingival tissues along the lateral side of the root (Fig. 22-2). Abscesses located deep in the periodontium may be more difficult to identify by this swelling of the soft tissue, and may present as diffuse swellings or simply as a red area (Fig. 22-3). Another common finding is suppuration, either from a fistula or, most commonly, from the pocket (Fig. 22-4). This suppuration may be spontaneous or occur after applying pressure on the outer surface of the gingiva.

The clinical symptoms usually include pain (from light discomfort to severe pain), tenderness of the gingiva, swelling, and sensitivity to percussion of the affected tooth. Other related symptoms are tooth elevation and increased tooth mobility (Fig. 22-5).

During the periodontal examination, the abscess is usually found at a site with a deep periodontal pocket. Signs associated with periodontitis such as bleeding on probing, suppuration and sometimes increased tooth mobility are also present (Smith & Davies 1986; Hafström *et al.* 1994; Herrera *et al.* 2000a). The radiographic examination may reveal either a normal appearance of the interdental bone or evident bone loss, ranging from just a widening of the periodontal ligament space to pronounced bone loss involving most of the affected root (Fig. 22-6).

In some patients the occurrence of a periodontal abscess may be associated with elevated body temperature, malaise, and regional lymphadenopathy (Smith & Davies 1986; Carranza 1990; Ibbott *et al.* 1993; Herrera *et al.* 2000a). Herrera *et al.* (2000a) reported laboratory data from blood and urine in patients immediately after the diagnosis of a periodontal abscess and reported that in 30% of the patients there was an elevated number of blood leukocytes. The absolute number of blood neutrophils and monocytes was also increased in 20–40% of the patients.

Differential diagnosis

The differential diagnosis of periodontal abscesses should always be made with other abscesses that can occur in the oral cavity. Acute infections, such as periapical abscesses, lateral periapical cysts, vertical root fractures, endo-periodontal abscesses, may have a similar appearance and symptomatology as a periodontal abscess, although with a clearly different

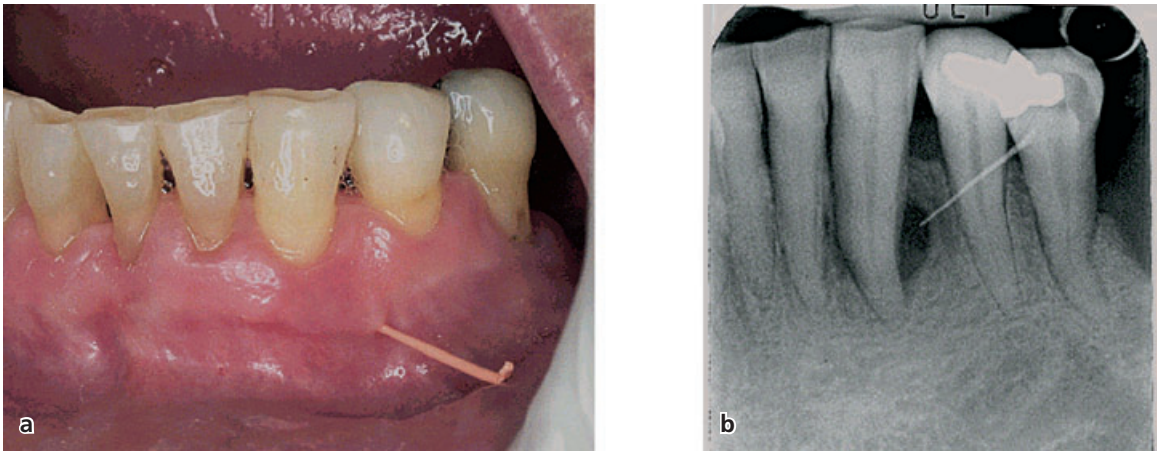

Fig. 22-6 (a) Periodontal abscess associated with a lower left canine. The fistulous tract opening is demonstrated with a gutta-percha point. (b) Radiologic image of the lower canine from (a). The differentiation from a periapical abscess was by the positive tooth vitality and absence of caries or restoration in the canine and the presence of a deep periodontal pocket in the lingual aspect of this tooth.

aetiology. Signs and symptoms indicating a more likely periodontal origin include: a history of periodontal disease or previous periodontal therapy; clinical signs of deep periodontal pockets releasing pus; frequently a vital pulp response; and radiographic findings of crestal bone loss, frequently associated with angular bone defects and furcations. On the contrary signs and symptoms indicating a more likely periapical (endodontal) origin will include: a history of caries, restorative or endodontic therapy; clinical signs of questionable or lack of response to pulp tests; presence of advanced caries lesions or restorations and the presence of a sinus tract; the radiographic findings will usually evidence the presence of a periapical radiolucency associated with either a carious or restored tooth or an endodontically treated tooth showing more or less endodontic filling or endodontic or post perforations.

Other lesions may appear in the oral cavity with a similar appearance as a periodontal abscess. Parrish *et al.* (1989) described three cases of osteomyelitis in periodontitis patients, initially diagnosed as periodontal abscesses. Different tumors may also have the appearance of a periodontal abscess. Such tumors include gingival squamous cell carcinoma (Torabinejad & Rick 1980; Kirkham *et al.* 1985), a metastatic carcinoma from pancreatic origin (Selden *et al.* 1998), a metastatic head and neck cancer (Elkhoury *et al.* 2004), and an eosinophilic granuloma diagnosed by rapid bone destruction after periodontal therapy (Girdler 1991). In cases where the abscess does not respond to conventional therapy, a biopsy and pathologic diagnosis are recommended (see also Chapter 16).

Treatment

The treatment of the periodontal abscess usually includes two stages: (1) the management of the acute lesion, and (2) the appropriate treatment of the original and/or residual lesion, once the emergency situation has been controlled.

For the treatment of the acute lesion, different alternatives have been proposed ranging from: (1) incision and drainage, (2) scaling and root planing, (3) periodontal surgery, and (4) the use of different systemically administered antibiotics. Some authors have recommended a pure mechanical treatment with either surgical drainage through the pocket, or scaling and planing of the root surface and compression and debridement of the soft tissue wall (Ahl *et al.* 1986; Ammons 1996). This mechanical therapy may cause irreversible damage to healthy periodontal tissues adjacent to the lesion. Such damage may particularly occur when the swelling is diffuse or is associated with marked tissue tension. In order to avoid this damage to healthy periodontal tissue other authors recommend the use of systemically administered antibiotics as the only initial treatment in abscesses with marked swelling, tension, and pain. In such instances, once the acute condition has receded, mechanical debridement, including root planing, should be performed.

The clinical evidence of the efficacy of these different therapeutic approaches is scarce, since only few clinical studies have assessed the efficacy of abscess therapy. Smith and Davies (1986) studied 62 abscesses in 55 patients. Their proposed treatment included incision, drainage, and systemic metronidazole (200 mg, tid for 5 days) and after the acute phase, regular periodontal treatment. Hafström *et al.* (1994) recommended supragingival debridement, together with systemic tetracycline therapy for 2 weeks, and reported good clinical outcomes when drainage and irrigation were added to the protocol. Similar good results were obtained in a controlled parallel study in which two systemic antibiotic regimes (amoxicillin/clavulanate, 500 + 125 mg, tid for 8 days; and azithromycin, 500 mg, once per day for 3 days) were used as the only treatment during the phase of initial

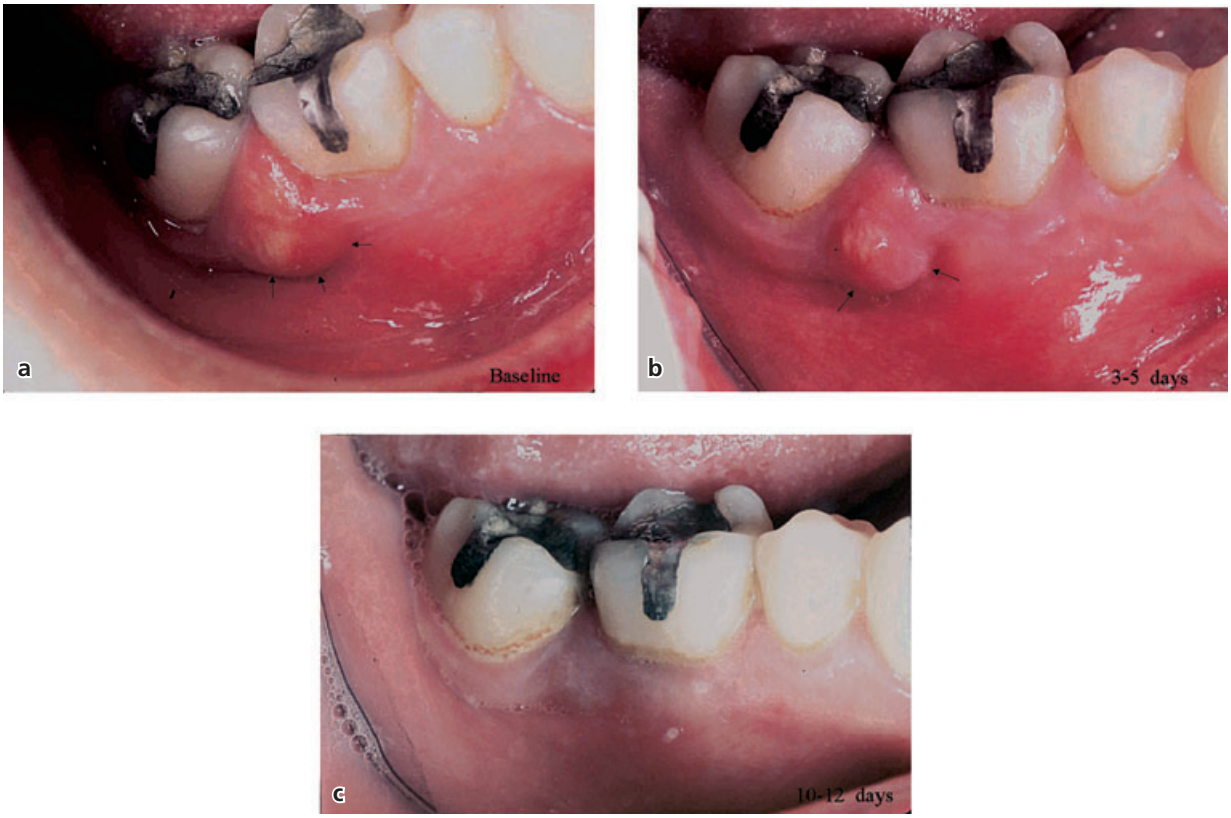

Fig. 22-7 (a) Treatment of a periodontal abscess with systemic antibiotics (azithromycin, 500 mg for 3 days) without any mechanical therapy. Baseline situation. (b) 5 days after antibiotic therapy. (c) 12 days after antibiotic therapy, just before the final periodontal instrumentation.

therapy. This was followed by regular periodontal treatment once the acute phase was resolved (Herrera *et al.* 2000b). The study showed that the short-term clinical outcome with the use of both antibiotics regimens was successful and the infectious process and abscess symptomatology was controlled just by using systemic antibiotics without concomitant or prior debridement (Fig. 22-7). There was a rapid reduction of the pain, significant resolution of the oedema, redness, and swelling, and the suppuration almost entirely disappeared. Periodontal outcome measurements, such as bleeding and periodontal probing depth, were also significantly reduced. Short-term microbiological results demonstrated a reduction of the microbiota in the abscess, as well as the number of selected periodontal pathogens (Herrera *et al.* 2000b). However, none of the antibiotic therapies were able to resolve the infection entirely. This implies that mechanical debridement, sometimes including a surgical approach, is an essential measure in the definitive treatment of this lesion. Moreover, two different studies have provided information on the antibiotic susceptibility profiles of periodontal pathogens isolated from periodontal abscesses and have reported the presence of resistant strains (Herrera *et al.* 2000b; Jaramillo *et al.* 2005).

Table 22-1 shows a number of different antibiotics that may be used in the treatment of a periodontal abscess. Doses and regimes recommended may differ between different countries. In principle, a high dose of the antibiotic delivered during a short period of time, is recommended. If the patient is recovering properly, the antibiotic should not be given for more than a 5-day period.

Complications

Tooth loss

Periodontal abscesses have been suggested as the main cause for tooth extraction during the phase of supportive periodontal therapy (SPT) (Chace & Low 1993). A tooth with a history of repeated abscess formation is considered to be a tooth with a questionable prognosis (Becker *et al.* 1984). In a retrospective study, 45% of teeth with periodontal abscesses in a SPT population were extracted (McLeod *et al.* 1997). Another retrospective study including 455 of teeth with a questionable prognosis showed that 55 (12%) were lost after a mean of 8.8 years, and that the main reason for tooth extraction was periodontal abscess formation (Chace & Low 1993). Smith and Davies (1986) evaluated 62 teeth with abscesses; 14 (22.6%) teeth were extracted as initial therapy, and 9 (14.5%) after the acute phase. Out of the 22 teeth treated and subsequently monitored, 14 had to be extracted during the following 3 years.

Table 22-1 Antimicrobial agents that may be used in the treatment of periodontal abscesses

Antimicrobial agent	Effective against	Properties
Penicillin V	Streptococci, some strict anaerobes	Poorly absorbed, affected by β-lactamases, bactericidal
Amoxicillin	Most Gram-positive oral species, many Gram-negative	Well absorbed, affected by β-lactamases but can be protected by clavulanic acid, bactericidal
Cephalexin	Anaerobes, streptococci, strict anaerobes, facultative	Well absorbed, affected by β-lactamases, not against methicillin-resistant staphylococci, bactericidal
Ceftibuten	Gram-negative rods, broad-spectrum against Gram-negative and Gram-positive bacteria	Resistant to most β-lactamases, bactericidal, not effective against staphylococci, pseudomonads
Clindamycin	Gram-positive cocci including staphylococci	Bacteriostatic or bactericidal depending on local concentration and susceptibility of the pathogen, drug of choice in case of rapid local spread
Metronidazole	Gram-positive and Gram-negative anaerobes	Well absorbed, not effective against facultative bacteria, bactericidal
Azithromycin	Most anaerobes, Gram-positive and negative bacteria, many strict anaerobes	Good tissue concentration, bacteriostatic for most pathogens

Dissemination of the infection

A number of publications, mainly case reports, have described different systemic infections in different parts of the body, in which the suspected source of infection was a periodontal abscess. Two possible sources of dissemination have been described:

- Dissemination of the bacteria inside the tissues during therapy. A case of pulmonary actinomycosis was related to the treatment of a periodontal abscess, which was ultrasonically scaled 1 month earlier (Suzuki & Delisle 1984). A case of brain abscess was observed in a healthy patient with a periodontal abscess who was treated with drainage and curettage without systemic antibiotic 2 weeks earlier. The microbiology of the lesions demonstrated, among other bacteria, *Prevotella melaninogenica* and other *Bacteroides* sp. (Gallaguer *et al.* 1981). A retrospective study on total knee arthroplasty infections (Waldman *et al.* 1997) discovered that 9 out of 74 infections had been previously treated for an oral infection, including the drainage of a periodontal abscess.
- Bacterial dissemination through the blood stream due to bacteremia from an untreated abscess. Cellulitis in breast cancer patients have been reported following gingivitis or an abscess (Manian 1997), due to transient bacteremia and reduced host defenses (radiation therapy and axillary dissection). A periodontal abscess was associated with the development of a cervical necrotizing fasciitis (Chan & McGurk 1997). A necrotizing cavernositis was thought to be related to a severe periodontal infection, including three periodontal abscesses (Pearle & Wendel 1993).

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Chapter 23

Lesions of Endodontic Origin

Gunnar Bergenholtz and Domenico Ricucci

Introduction

In the study of pathogenesis and causality of periodontal disease processes, lesions of endodontic origin are significant as they frequently extend and manifest themselves in the attachment apparatus. Not only do these lesions produce signs and symptoms of inflammation in apical areas of teeth, they may also induce tissue destruction along the lateral aspects of roots and in furcations of two- and multirooted teeth. In either instance, the lesions are maintained by noxious elements that derive from the pulpal space along openings to the periodontal tissues. Channels connecting the two tissue compartments include foramina at the apex and lateral ramifications termed accessory canals.

Microorganisms residing in necrotic areas of a more or less broken down pulp usually maintain these lesions. Lesions of endodontic origin may also appear or prevail following endodontic treatment. In these cases, treatment measures, aimed at either preventing the establishment of a root canal infection or getting rid of an already manifest infection, have been unsuccessful. As root canal infections have been assumed to have an impact on both the progression of periodontitis and the potential to achieve optimal results of periodontal therapy, the first part of this chapter describes the specific features and dynamic events that are associated with lesions of the pulp and the manner by which they may interfere with the periodontium.

The fact that the periodontium and the dental pulp are anatomically interconnected also implies that exchange of noxious agents may also occur in the opposite direction, that is from the external environment to the pulp. A prerequisite for this is that those communication pathways that are normally secured by healthy periodontal tissue have been uncovered. This will occur as periodontal disease advances. The lesion of the pulp that may follow may involve both pain and tissue destruction. Resorptive processes and treatment measures aimed at managing periodontal disease enhance this potential as the accompanying exposure of dentinal tubules, by loss of cementum, establishes yet another passage across the body of the tooth structure. In fact, a common complication to periodontitis and periodontal therapy is an ailment commonly termed root dentin hypersensitivity, a condition associated with the direct exposure of root dentin to the oral environment (Gillam & Orchardson 2006).

The second part of this chapter is concerned with the consequences for the vital pulp of root surface exposure by periodontal disease and periodontal therapy. It also covers aspects of the mechanisms and management of root dentin hypersensitivity.

Disease processes of the dental pulp

Causes

The dental pulp is normally well protected from injurious influences by an intact hard tissue encasement and by a healthy periodontium. The healthy condition of the pulp, however, is regularly challenged under clinical conditions. While some adverse influences are of minor significance and cause only negligible tissue injury and minimal discomfort to the

patient, others threaten the pulp's vital functions and can result in infectious complications, with effects both locally and systemically. Lesions of the pulp may have either a direct infectious background or may be induced by non-infectious injury. Both causes will be covered here in some detail.

Of non-infectious impairments, accidental trauma causing rupture of the neurovascular supply at the apex and major internal bleeding represents a distinct threat to the vitality of the pulp. Hence, concussions, sub-luxations, and various forms of tooth displacements may result in widespread ischemia leading to complete necrosis of the tissue. As the potential for tissue regeneration is slim in the fully developed tooth (Kristerson & Andreasen 1984), such pulp tissue necrosis, although not primarily infected, acts as a target for microbial invasion. The infecting microorganisms usually originate from the oral cavity. Following their penetration of cracks in the enamel and the dentinal tubules, multiplication in the necrotic pulp results in the development of inflammatory lesions of the periodontal tissues (Bergenholtz 1974; Sundqvist 1976).

Most pulpal conditions are initiated and maintained by infectious elements that access the pulp following loss of hard tissue integrity. Tooth destruction by caries is by far the most common source of bacterial exposure and is especially threatening when the lesion has reached the vicinity of the pulp tissue proper (see further below). Also fractures of teeth and dental restorative work bring an inherent risk for detrimental bacterial effects, should a restoration fail to seal completely the defect in the tooth substance (see review by Bergenholtz 2000). Most risky are extensive restorative works like full coverage crowns, which often require substantial sacrifice of healthy tooth tissue. Clearly in the short term, before the permanent restoration is cemented, the tissue exposure is subject to bacterial leakage along the margins of the temporary restoration, especially if it is poorly adapted to the remaining tooth substance. Yet, even though the pulp may have survived the initial stress of the cutting trauma and the leakage of bacterial elements, the injury induced usually results in considerable repair phenomena (scars). Such tissue changes involve hard tissue depositions and soft tissue fibrosis, which occur at the expense of vascularity and nerve tissue support (Bender & Seltzer 1972). Tissue alterations of this nature logically result in impaired immune defense function and, thus, reduce the potential for the pulp to resist future bacterial challenges.

Clinical follow-ups of teeth supplied with single crowns or included as abutments in bridge works have indeed demonstrated that pulp tissue necrosis is not a rare complication and may affect 10–20% of the observed teeth over a 10–15-year period (Bergenholtz & Nyman 1984; Karlsson 1986; Saunders & Saunders 1998; Cheung *et al*. 2005). In fact, the incidence of loss of pulpal vitality has been reported to increase over the course of time (Bergenholtz & Nyman 1984; Cheung *et al*. 2005). A similar increasing rate of pulpal infections has also been reported for young permanent teeth suffering traumatic ischemic injuries where pulps have been partly or completely replaced by hard tissue repair (Jacobsen & Kerekes 1977; Robertson *et al*. 1998).

Conclusion

Injurious elements that may put the vital functions of the pulp at risk include deep caries, accidental trauma, and dental restorative procedures. A single insult, such as a traumatic injury, may cause an immediate breakdown of the tissue by severing the neurovascular supply. In other instances tissue breakdown is preceded by a direct bacterial exposure or following tissue repair to non-infectious and infectious insults.

Progression and dynamic events

Although any injury may have serious implications for the vitality of the pulp, its ability to withstand insults, especially of a microbial nature, is far better if an intervening layer of dentin remains than if the tissue is directly exposed through the hard tissue barrier. In the former case even a thin dentin wall, although permeable, usually allows the pulp to mount an appropriate inflammatory response to offset bacterial threats. The common observation that the pulp rarely suffers breakdown underneath a caries lesion confined to dentin is strong evidence of the pulp's defense potential (Reeves & Stanley 1966; Massler 1967; Kamal *et al*. 1997; see also review by Björndal & Mjör 2001). The mechanisms involved relate both to innate and adaptive immune responses (Hahn *et al*. 2003; Dommisch *et al*. 2005; Durand *et al*. 2006; for a review see also Jontell *et al*. 1997) as well as to changes in dentin that constrict its permeability (for reviews see Pashley 1996; Bergenholtz 2000).

Experimental evidence to this effect derives from observations in both humans (Lundy & Stanley 1969; Warfvinge & Bergenholtz 1986) and animals (Lervik & Mjör 1977; Warfvinge & Bergenholtz 1986; Taylor *et al*. 1988). In some of these studies test cavities were prepared deep into dentin and were left unrestored to the oral environment (Lundy & Stanley 1969; Taylor *et al*. 1988). In other experimental series, similar cavities were challenged with soft carious dentin (Mjör & Tronstad 1972; Lervik & Mjör 1977) or components of dental plaque bacteria (Bergenholtz & Lindhe 1975; Warfvinge & Bergenholtz 1986). Reflecting the permeability of dentin to microbial elements, inflammatory sequels consisting of increased vascular permeability, migration of polymorphonuclear leukocytes (PMNs) (Bergenholtz & Lindhe 1975; Warfvinge & Bergenholtz 1986), and nerve fiber sproutings (Taylor *et al*. 1988) rapidly emerged in the pulp adjacent to the exposed dentinal tubules. The

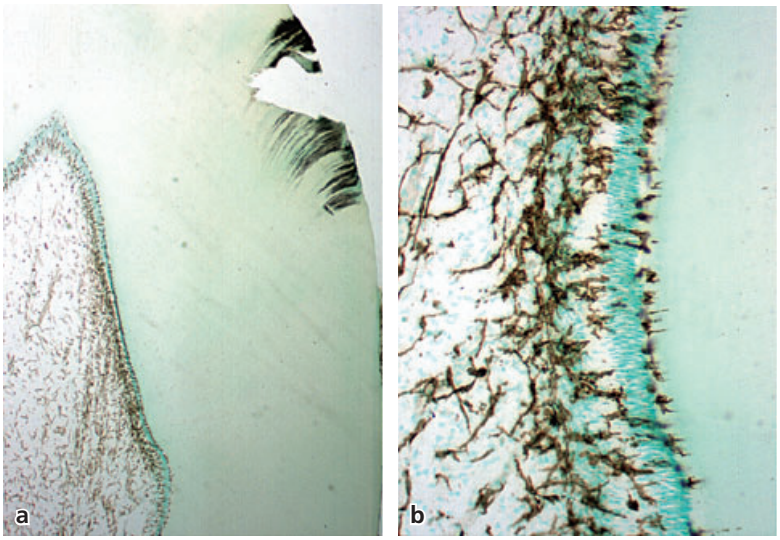

Fig. 23-1 (a) Defense response of a human dental pulp to superficial caries in dentin (defect and dark stain at upper right hand corner) as represented by increased accumulation of Class II molecule-expressing cells of a dendritic morphology. (b) Extensions of cytoplasmatic processes into the dentinal tubules are numerous. Images kindly provided by Dr. Takashi Okiji.

adapative immune defense is also activated at very early stages as indicated by an increased presence of antigen-presenting cells (Jontell *et al*. 1997). Indeed, dendritic cells appear soon in an area of the pulp next to both cavity preparations (Ohshima *et al*. 1995) and superficial caries (Kamal *et al*. 1997) (Fig. 23-1). Yet, over the course of time, these responses subside and reparative dentin and soft tissue repair emerge, along with a reduction of immunocompetent cells, at the site of the previous inflammatory event (Lundy & Stanley 1969; Lervik & Mjör 1977; Warfvinge & Bergenholtz 1986; Kamal *et al* 1997). In the experiments involving unrestored human teeth (Lundy & Stanley 1969), patients experienced pain and increased sensitivity of the exposed dentin along with the initial inflammatory episode. As repair and healing progressed the pain symptoms disappeared.

An important point is that although inflammatory responses develop rapidly and early to bacterial challenges, microorganisms *per se* are rarely able to penetrate the dentinal barrier and enter the pulp tissue, so long as it retains vital functions. Staining for bacteria in the histologic analysis of Lundy and Stanley (1969), for example, revealed that in no case, observed after 2–240 days, were organisms traced in the pulp tissue proper, while the exposed dentinal tubules were invaded to a varying extent. This finding once again demonstrates that dentin and pulp in concert are able to oppose bacterial threats.

By contrast, direct exposure of the pulp to the oral environment puts its vital functions at risk as bacteria in the oral cavity now may gain direct access to the tissue. Even a minuscule exposure is critical, unless properly treated, as there is little self-healing capacity by virtue of epithelium that can bridge the defect. Defense mechanisms may therefore prevent bacterial invasion of the pulpal space for only a limited period of time.

Three clinical cases, displayed in Figs. 23-2 to 23-4, demonstrate how pulpal inflammatory processes may typically develop and progress to the adjoining periodontal tissues. In these cases, caries has advanced to expose the tissue at an earlier point in time.

In the first example (Fig. 23-2) an inflammatory lesion is present at the site where caries has exposed the pulpal tissue. A rather thick layer of reparative dentine has formed at the roof of the pulp chamber next to the exposure indicating a repair response to previous irritation (Fig. 23-2a). Note that, except for the lesion area, the pulp displays normal tissue morphology with intact odontoblast layers lining the periphery of the tissue. Bacteria have accumulated (blue stains in dentin) near the exposure site (Fig. 23-2c). The high magnification in Fig. 23-2d reveals numerous bacterial profiles in the pulp as well, where they are opposed by infiltrating PMNs in the lesion area. In this particular case the inflammatory process was clearly localized and both radiographic (Fig. 23-2a) and histologic examination gave no indication of interference with the periodontium.

A more advanced pulpal lesion is demonstrated in Fig. 23-3, where the inflammatory response to the distally located caries process in the lower molar has extended to the furcation area along a wide accessory canal (23-3b). Intrafurcal alveolar bone is resorbed and has been replaced by inflammatory tissue displaying proliferating epithelium (23-3c). There is also an apical radiolucency at the distal root, while the apical region of the mesial root seems unaffected (23-3a).

A third case (Fig. 23-4) shows necrosis of the coronal pulp following what has obviously been a rather long-standing caries process in a lower first molar. There are radiographic signs of apical periodontitis on both the distal and the mesial roots and a widened periodontal ligament space in the furcation (Fig. 23-4A). At the mesial aspect of the tooth, gingival tissue has proliferated into the pulp chamber (Fig. 23-4B). Figure 23-4C displays an area of the pulpal space at the entrance of the distal root canal,

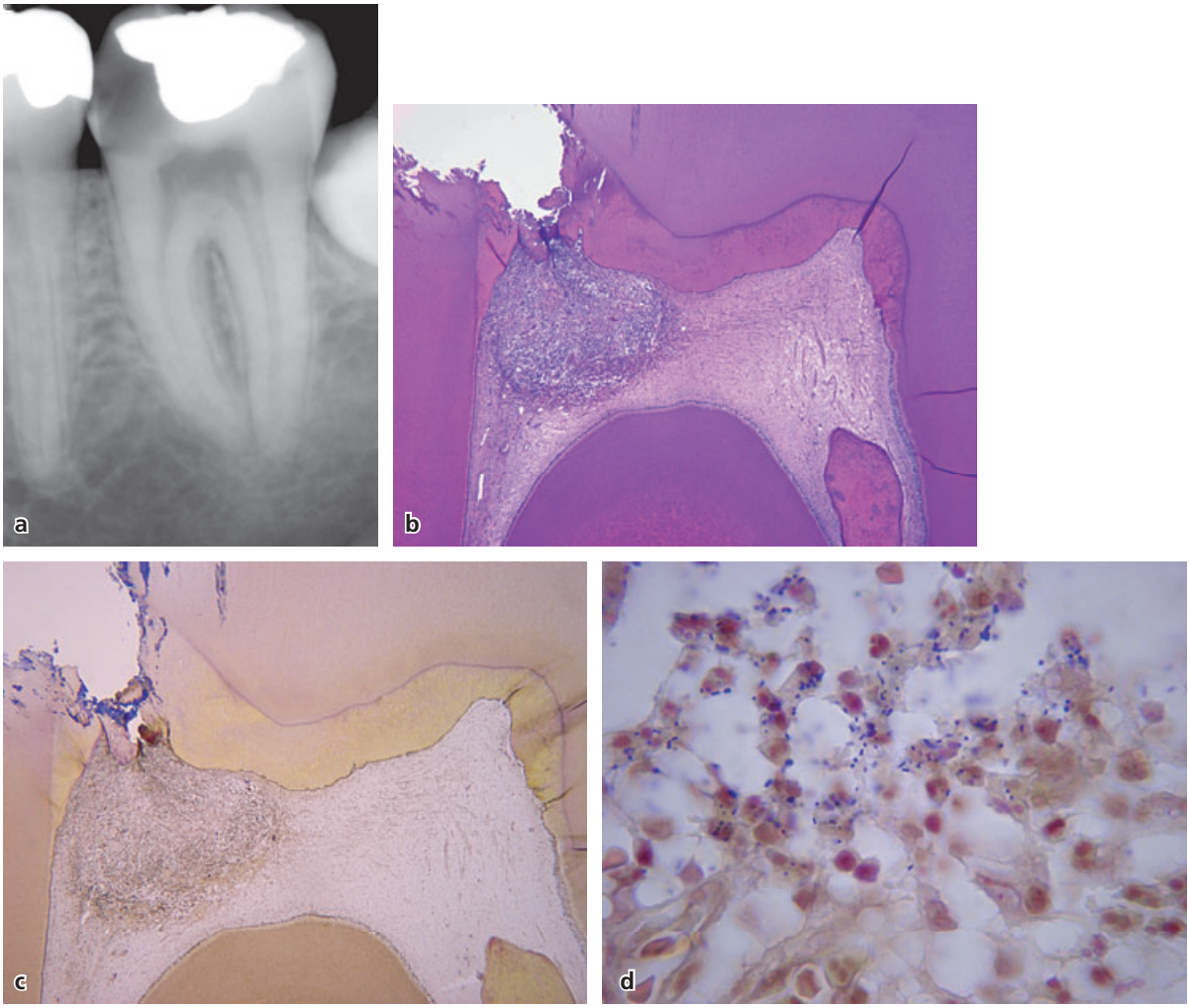

Fig. 23-2 (a) Second lower molar from a 30-year-old man with deep caries at the mesial aspect. Before extraction of the tooth the patient had presented with typical signs of pulpitis including percussion sensitivity and radiating pain. (b) A localized inflammatory response is present in the pulp adjacent to the site of caries penetration without spreading. In a section stained for bacteria (c) organisms are seen at the exposure site (blue stain) as well as in the inflammatory tissue lesion *per se* (d) (see also text).

where the pulp is necrotic and where bacterial organisms have aggregated on the canal walls in a biofilm structure. Further down in the middle portion of the root, numerous PMNs meet the bacterial front and are engaged in phagocytic activities (Fig. 23-4D and inset). In more apical portions of the canal, numerous widened blood vessels are seen along with an infiltrated pulp connective tissue (Fig. 23-4E). The most apical portion of the pulp shows normal tissue structure (Fig. 23-4G), which also applies to the soft tissue attached to the root tip (Fig. 23-4F and inset) representing the apical radiolucency at the distal root in Fig. 23-4A.

Conclusion

The cases selected demonstrate an important function of the inflammatory defense in general that also applies to the dental pulp, which is to confine infectious elements and limit spread to other body compartments. The cases also demonstrate that a pulpal lesion has its prime focus at the source of the bacterial exposure. Hence, it is only following extension due to breakdown of the pulp and advancement of the bacterial front that periodontal tissue involvement is imminent. In some cases this may occur at a rather early stage of the pulp tissue lesion if an accessory canal is open to the marginal periodontium such as in the case in Fig. 23-3. In the absence of accessory canals extensive breakdown of the pulp is first required before the periodontal tissues may become engaged.

Accessory canals

Accessory canals are lateral ramifications off the root canal system that connect the neurovascular system of the pulp with that of the periodontal ligament. Such anastomoses are formed during the early phases of tooth development, but may become blocked or reduced in width during the completion of root formation. Patent communications of varying sizes, numbers and locations, however, may remain in the fully developed tooth and serve as additional

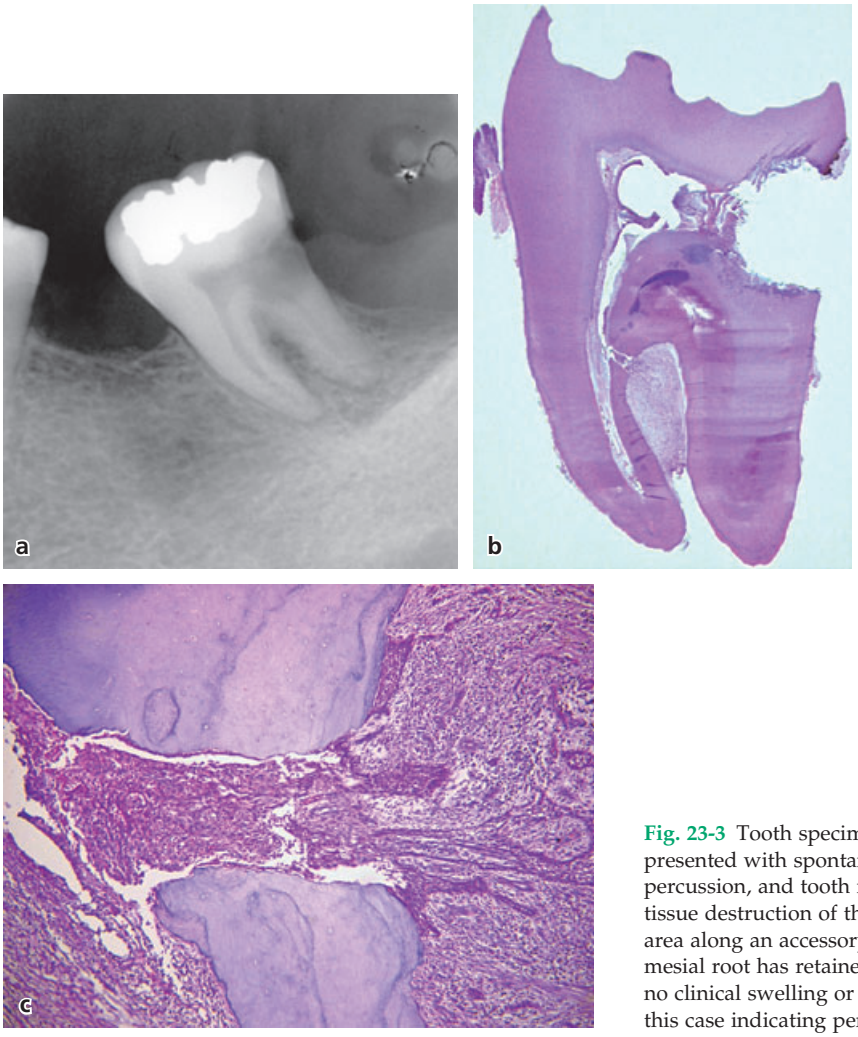

Fig. 23-3 Tooth specimen of a 48-year-old man, who presented with spontaneous pain, pain on mastication, percussion, and tooth mobility. An extensive inflammatory tissue destruction of the coronal pulp extends into the furcal area along an accessory canal. More apically, the pulp of the mesial root has retained normal tissue structures. There was no clinical swelling or remarkable pocket probing depth in this case indicating periodontal involvement (see text).

pathways for the neurovascular supply of the pulp beyond that of the main apical foramen.

Accessory canals can be observed in all groups of teeth. In fact, careful examinations of large numbers of extracted teeth, rendered transparent and injected with contrasting medium in the pulp chamber to allow three-dimensional visualizations, have revealed accessory canals in cervical and middle-root areas as well as in the apical root portions (DeDeus 1975; Vertucci 1984). Clearly the majority is found apically, whereas the prevalence tapers off in the middle and cervical root segments (DeDeus 1975; Vertucci 1984). In a study of 1140 extracted human teeth from adult subjects, De Deus (1975) reported accessory canals in 27% of the examined teeth. These canals were distributed at various levels of the root as depicted in Fig. 23-5.

Molars harbor accessory canals more frequently than premolars and anterior teeth. Patent canals are especially common in the furcation areas, where they have been found in between 20% and 60% of examined teeth (Lowman *et al*. 1973; Vertucci & Williams 1974; Gutmann 1978; Vertucci 1984). Vertucci (2005) has distinguished between different directions of entry by which accessory canals go into the furcation of mandibular molars. In some cases they run more or less vertically from the pulpal chamber. They may also extend off either root canal in a horizontal direction of which 80% derive from the distal root canal (Vertucci 2005) (Fig. 23-6).

When accessory canals do occur, the potential dissemination of inflammatogenic elements from a diseased pulp to the periodontium is obvious. There is no documentation yet available to indicate how often such lesions develop. Although clinical observations demonstrate occurrence (Figs. 23-3, 23-7, 23-8), the rate at which endodontic lesions appear in the marginal periodontium from accessory and furcation canals seems to be low, as indicated by lack of reports of this being a significant clinical problem. It is to be expected that the wider accessory canals are, the greater is the likelihood for overt lesions to develop. Diameters of furcation canals in mandibular molars for example have been reported to vary from just a few microns to 720 microns (Vertucci 2005). Consequently, thin accessory canals, with the potential to mediate some release of infectious substances, may not cause more than a minor periodontal reaction that goes clinically undetected.

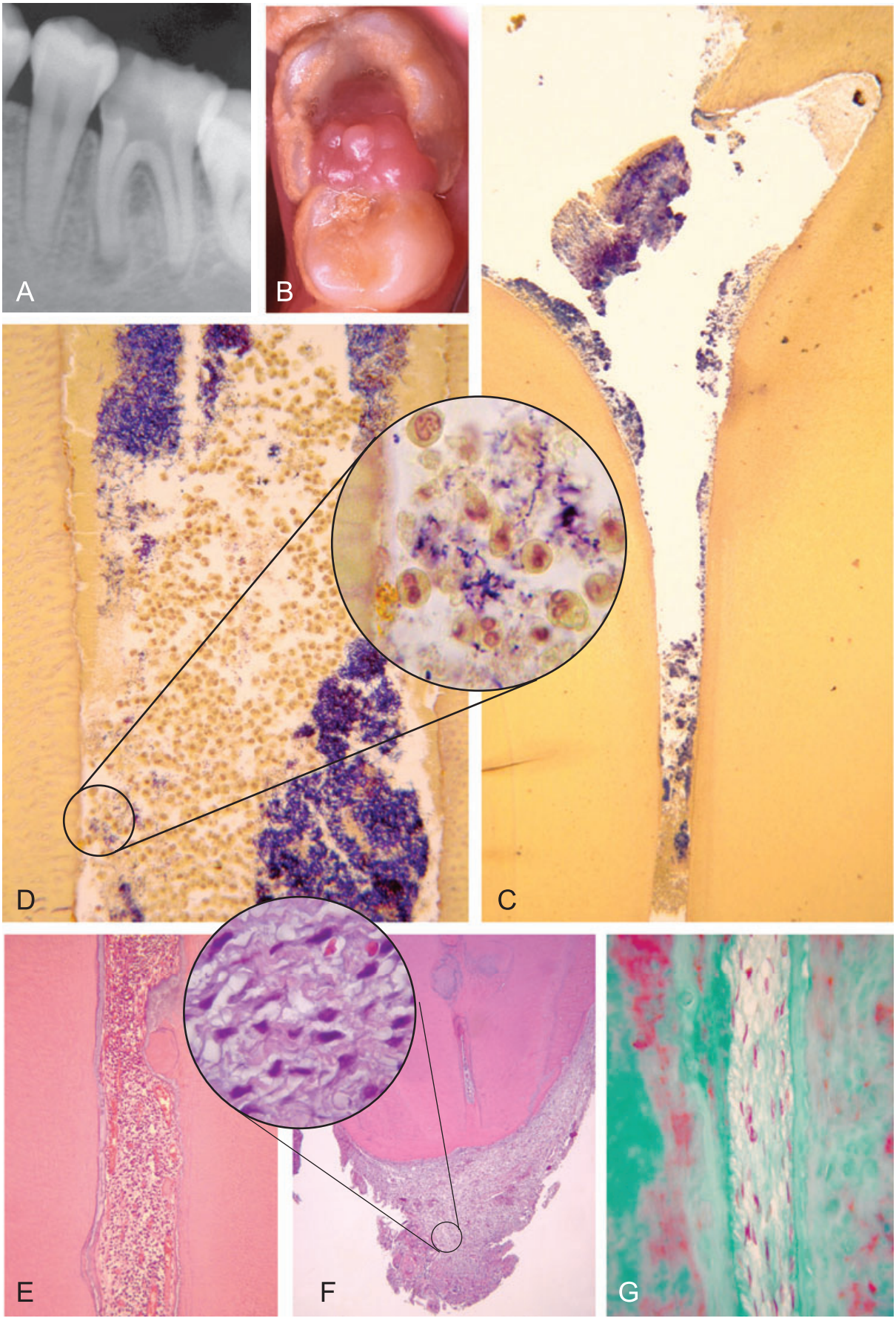

Fig. 23-4 Tooth specimen of a 19-year-old female with extensive caries in a 1st lower molar that has led to partial pulp tissue breakdown, bacterial invasion, and establishment of an inflammatory defense line inside the pulpal space (see text). From Ricucci & Bergenholtz (2004), images appeared in *Endodontic Topics* 2004, **8**, 68–67.

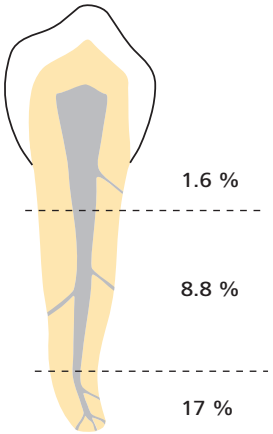

Fig. 23-5 Frequency of accessory canals at different levels of the root. The data are average values obtained from DeDeus (1975). Observations were made after teeth had been rendered transparent and the root canal system filled with India ink. The figures given for the coronal portion include those of bi- and trifurcations of two- and multi-rooted teeth.

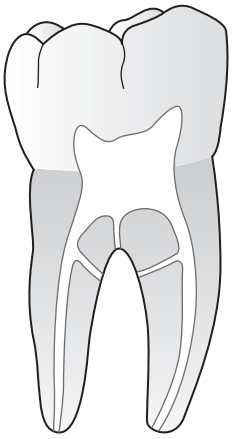

Fig. 23-6 Furcal canals of two- and multirooted teeth, when present, may extend into the periodontium from the pulpal space either in a horizontal or vertical direction or both. Drawing adapted from Vertucci (2005).

Conclusion

Although they occur, the large majority of teeth lack accessory canals in their cervical and middle root regions. This fact may explain why pulpal inflammatory lesions rarely are seen extended to the marginal periodontium. Most often they become centered around root apices only. When present with a diameter similar to that of the apical foramen, accessory canals can certainly mediate lesions of endodontic origin in the marginal periodontium. In endodontically treated teeth iatrogenic root perforations, carried out in conjunction with root canal instrumentation or post preparations, may serve as yet another pathway for dissemination of noxious elements to the periodontium (see Chapter 40).

Periodontal tissue lesions to root canal infection

The ultimate outcome of an inflammatory breakdown of the pulp is microbial take over of the pulpal space (Fig. 23-9). As host defense mechanisms are unable to reach far into root canals of necrotic pulps in order to combat the infection and pave the way for regeneration of pulpal tissue, an inflammatory defense zone is established in the periodontal tissues at exits of accessory canals and apical foramina. Hence, lesions of this nature remain as chronic processes unless subjected to treatment. Because the inflammatory process most frequently becomes positioned near root apices, the term apical periodontitis is commonly employed. As lesions may also develop along the lateral aspects of roots, the expression endodontic lesion will be used throughout this text to denote a periodontal lesion in any position that is sustained by noxious elements of endodontic origin.

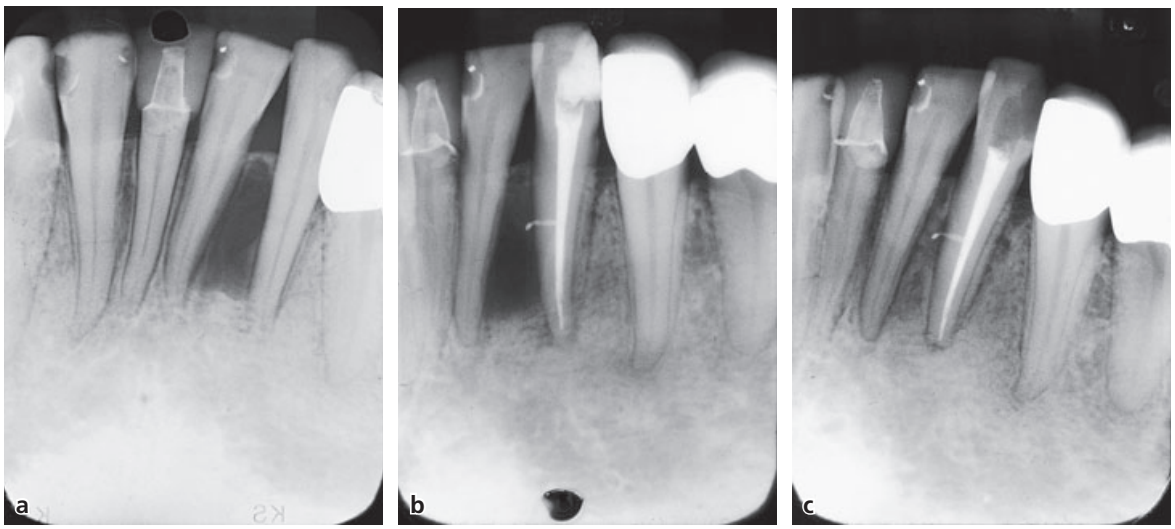

Fig. 23-7 (a) A lateral, alveolar bone destruction is observed between the roots of teeth #31 and #32. (b) The lesion in this case turned out to be associated with an accessory canal (filled in conjunction with the root filling procedure) emanating from an infected root canal in tooth #32. (c) Two-year recall of the endodontic treatment demonstrates near complete resolution of the bone lesion. Courtesy of Dr. Conrad Jacobsson.

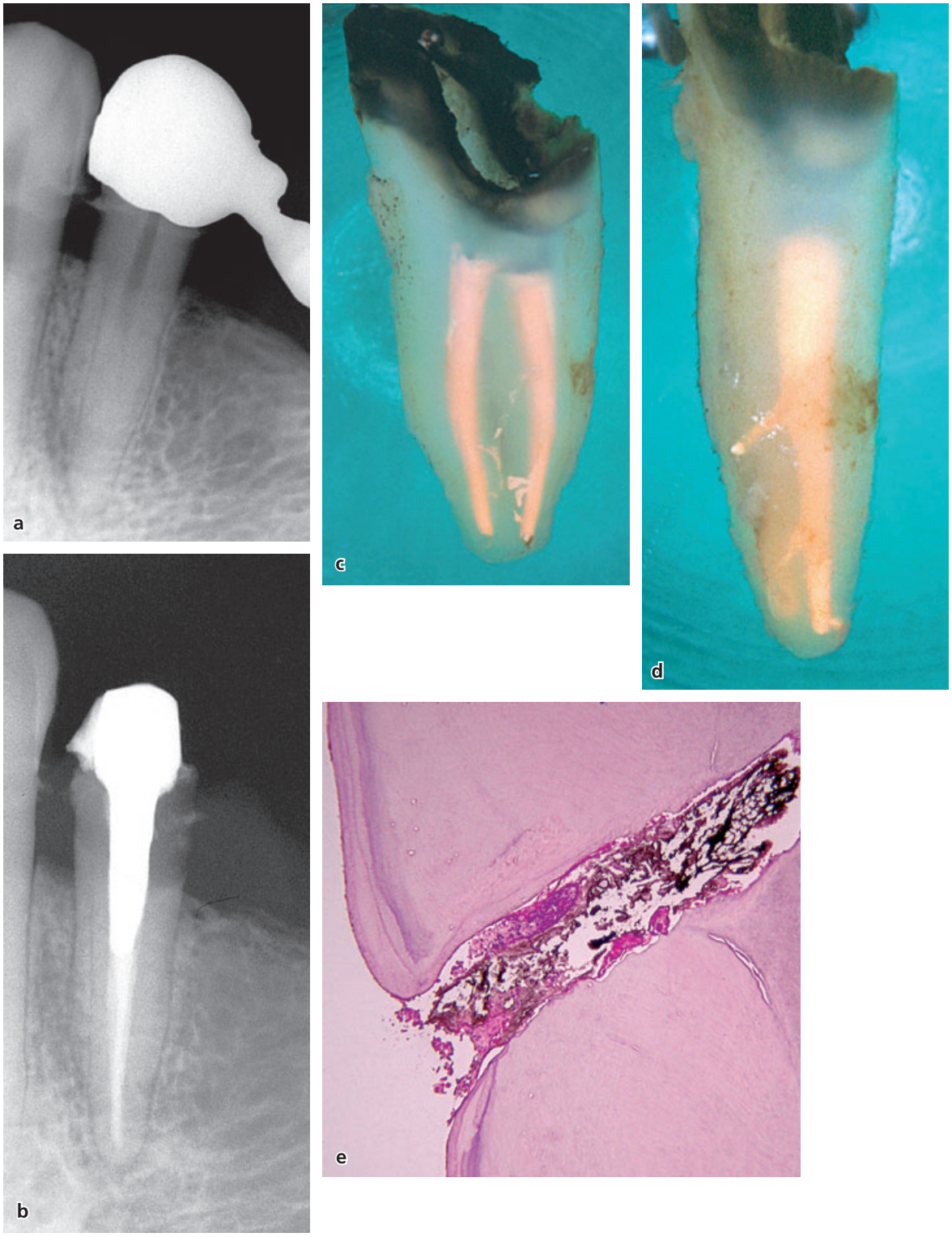

Fig. 23-8 Radiographs of a lower premolar molar; (a) prior to endodontic treatment, (b) prior to extraction due to extensive caries 11 years after endodontic treatment. (c, d) Cleared specimens show numerous accessory canals filled with root filling material. (e) Histologic examination shows that accessory canals are only partially filled (black material interspersed with inflammatory tissue).

The bacterial organisms that are able to initiate and maintain endodontic lesions have been studied in great detail over the years, primarily by sampling infected root canals followed by laboratory processing and phenotypic identification. The purpose of such studies has been to identify organisms that are prevalent and which can be linked to more or less aggressive forms of apical periodontitis (see below). In recent years molecular identification methods, including the polymerase chain reaction (PCR), have been used to supplement the picture (for reviews see Siqueira & Rocas 2005a; Spratt 2004). Indeed it has

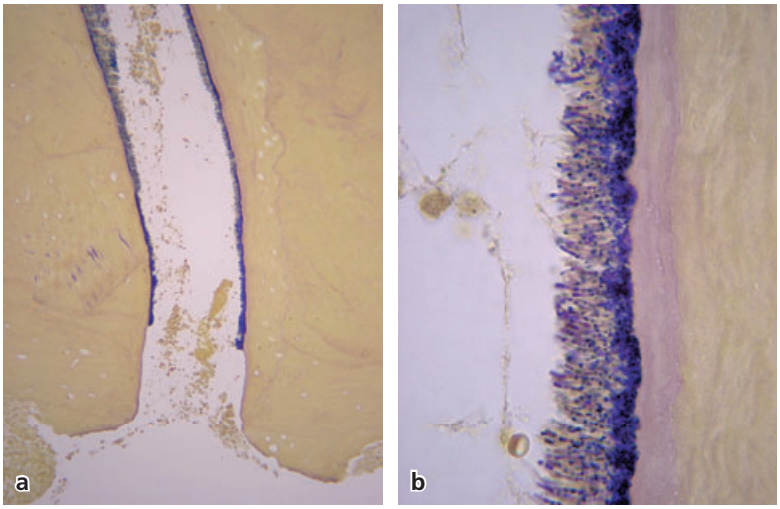

Fig. 23-9 (a) Tooth specimen with complete absence of pulp tissue. (b) Filaments and coccoid organisms are seen attached in a biofilm to the root canal walls. From Dr Ricucci's collection, images previously published by Svensäter & Bergenholtz (2004).

been demonstrated that many more species are involved than previously anticipated and the concept that only a limited group of 20–30 common isolates are associated with these lesions is currently being reassessed (Siqueria & Rocas 2005a,b; Siqueria *et al.* 2005). Yet, the microbiota in primary endodontic infections show features similar to that of deep periodontal pockets (Kerekes & Olsen 1990) and anaerobes usually have a dominant role. Spirochetes (Dahle *et al*. 1996; Rocas & Siqueria 2005; Foschi *et al*. 2005) and fungi (Waltimo *et al*. 1997; Peciuliene *et al*. 2001; Egan *et al*. 2002) may also reside in infected root canals and may contribute to the maintenance of these lesions. By contrast persistent infections subsequent to endodontic treatments seem less dominated by anaerobes and cultivation studies have demonstrated high prevalences of Gram-positive facultatives (Molander *et al*. 1998; Sundqvist *et al*. 1998; Chavez de Paz *et al*. 2003; Gomes *et al*. 2004; Forschi *et al*. 2005).

Although not comprehensively studied, root canal infections most likely involve attachment of bacterial organisms to the root canal walls and the development of microbial communities in biofilms (Fig. 23-9) (Svensäter & Bergenholtz 2004). Organization in biofilms affords these organisms better protection against host defense mechanisms in comparison to their planktonic counterparts, but they are detached from such sites and dispersed for colonization at other body sites. Root canal bacteria usually have limited potential to survive in the periodontal tissue lesion *per se* although bacterial organisms can be found in acute abscesses (Oguntebi *et al*. 1982; Williams *et al*. 1983; Lewis *et al*. 1986). It should also be mentioned that case reports have indicated that *Actinomyces*-related species occasionally may invade the tissue lesion and aggregate in clusters or nests that elude host tissue elimination (Sundqvist & Reuterving 1980; Happonen *et al*. 1986). Yet in most instances bacteria are confined to the root canal space (Nair 1987). While the front line may be established at the orifice of the canal (Fig. 23-10), the host tissue–bacterial interface zone usually becomes localized well inside the root canal exits (Nair 1987) (Fig. 23-11). In what may be a rare situation (Siqueira & Lopes 2001), bacterial organisms in primary endodontic infections may overcome the host defense and aggregate as a biofilm on the outer root surface (Lomcali *et al*. 1996) (Fig. 23-12). Such structures have also been observed on root ends of teeth which have not responded favorably to endodontic treatment (Tronstad *et al*. 1990).

The shape and character of the periodontal tissue response to a root canal infection may vary. Often lesions assume a limited and stable extension around root apices and/or at orifices of accessory canals. The inflammatory process may then remain unchanged in size for years, although cyst transformation can result in substantial destruction of alveolar bone (Fig. 23-13). However, the initial expansion of an emerging lesion or acute exacerbation of a chronic lesion, can result in rapid and extensive destruction of the attachment apparatus. In certain cases the periodontal tissue support can be lost to an extent that the gingival sulcus is involved, from where drainage of pus occurs to the oral environment (Fig. 23-14). Such an apical marginal communication along the root surface may later become a permanent pathway for pus that will be released periodically along what is simply a fistulous tract.

The character of the infecting microbiota, its metabolic activity, and the virulence factors it produces, together with the capacity of the host defense to confine and neutralize the bacterial elements, are important parameters that decide the course of the inflammatory process. Hence, growing and multiplying organisms with capacities to invade the periodontal tissues and evade host defense mechanisms mediate acute manifestations of endodontic lesions. Single organisms are normally unable to cause these lesions, which are maintained by groups of organisms; virulent strains of *Porphyromonas*, *Prevotella*, *Fusobacterium* and *Peptostreptococcus* spp. have been implicated by culture studies (Dahlén 2002). Recent

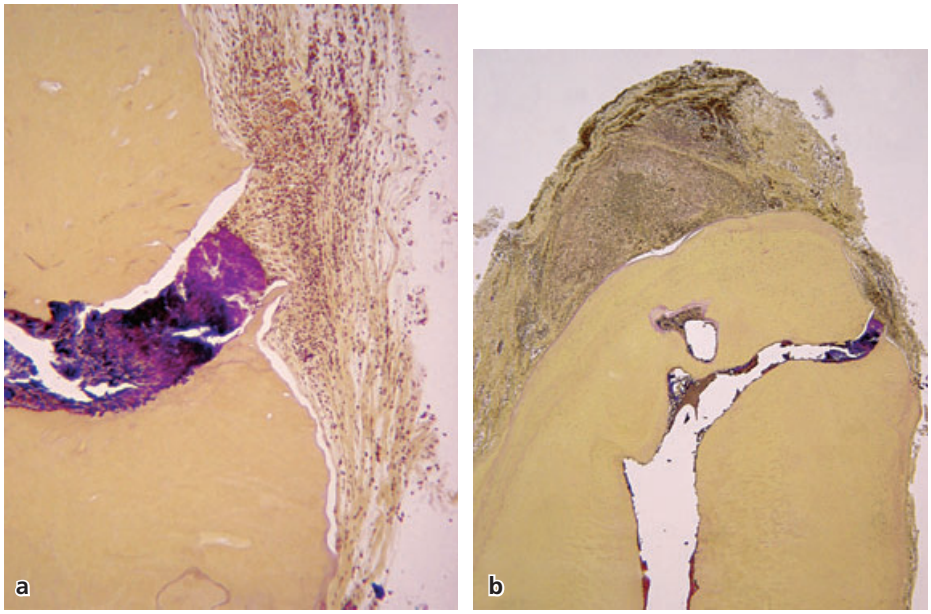

Fig. 23-10 (a) Demonstration of bacterial front (blue stain) near the root canal exit of a root tip with attached periapical tissue lesion (low magnification in (b)). From Ricucci & Bergenholtz (2004).

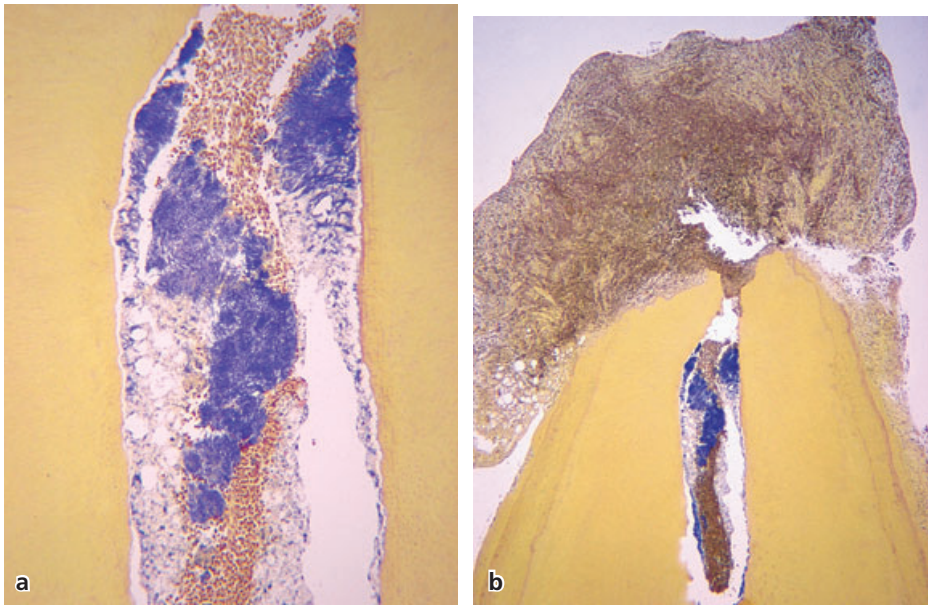

Fig. 23-11 (a) Display of bacterial masses (blue stain) attached to the walls of a root canal well inside the apical foramen. A band of inflammatory cells appear to be in combat with the infection. (b) A low magnification overview of the root with attached periapical tissue lesion. From Ricucci & Bergenholtz (2004).

reports utilizing PCR methodology have inferred that a variety of other species, unrecognized by culture, may be of prime importance (Rocas & Siqueria 2005; Sakamoto *et al*. 2006). Given the recent surge in use of molecular methods to map the structure of the endodontic microbiota, it is likely that, in the future, a clearer understanding will be gained of the key organisms which cause acute manifestations of endodontic infections.

The endodontic microbiota associated with asymptomatic lesions is apparently less aggressive. This condition is likely to be linked to the harsh nutritional supply that usually prevails in root canals and which puts the organisms in a low state of metabolic activity. Nutrients are available primarily from tissue components of the necrotic pulp. In the absence of inflammatory exudate entering the root canal along apical foramina and accessory canals, organisms will consequently have little drive to grow, multiply, and invade the periodontal tissue compartment. When this condition of relative starvation is broken by increase of the nutritional supply, an acute endodontic lesion may occur. Suppressed virulent strains can then be revived and become the dominant organisms

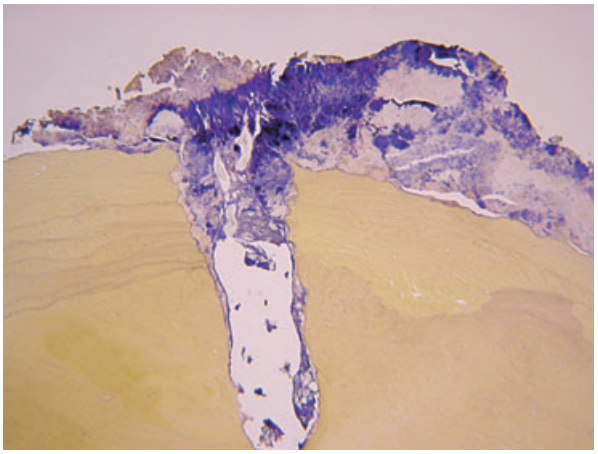

Fig. 23-12 Accumulation of bacterial mass (blue stain) at the external root surface of a tooth with an infected necrotic pulp. From Ricucci & Bergenholtz (2004).

at the expense of the less virulent members of the microbial community. Consequently, acute exacerbations of asymptomatic endodontic lesions may occur, for example, when saliva and gingival exudates gain access to the root canal space following a direct exposure of root canals to the oral environment. Similarly during endodontic treatment, inadvertent enlargement of the apical foramen increases the passageway for protein-rich inflammatory exudate into the root canal space.

While acute manifestations of endodontic lesions are characterized by expanding bone resorption, exudation and influx of phagocytic cells, a balanced host–parasite relationship will be established sooner or later (Stashenko 1990; Nair 1997; Stashenko *et al*. 1998). Microscopically, the established lesion is characterized by a richly vascularized granulation tissue, which is infiltrated, to a varying degree, by inflammatory cells (Fig. 23-15). PMNs play a most

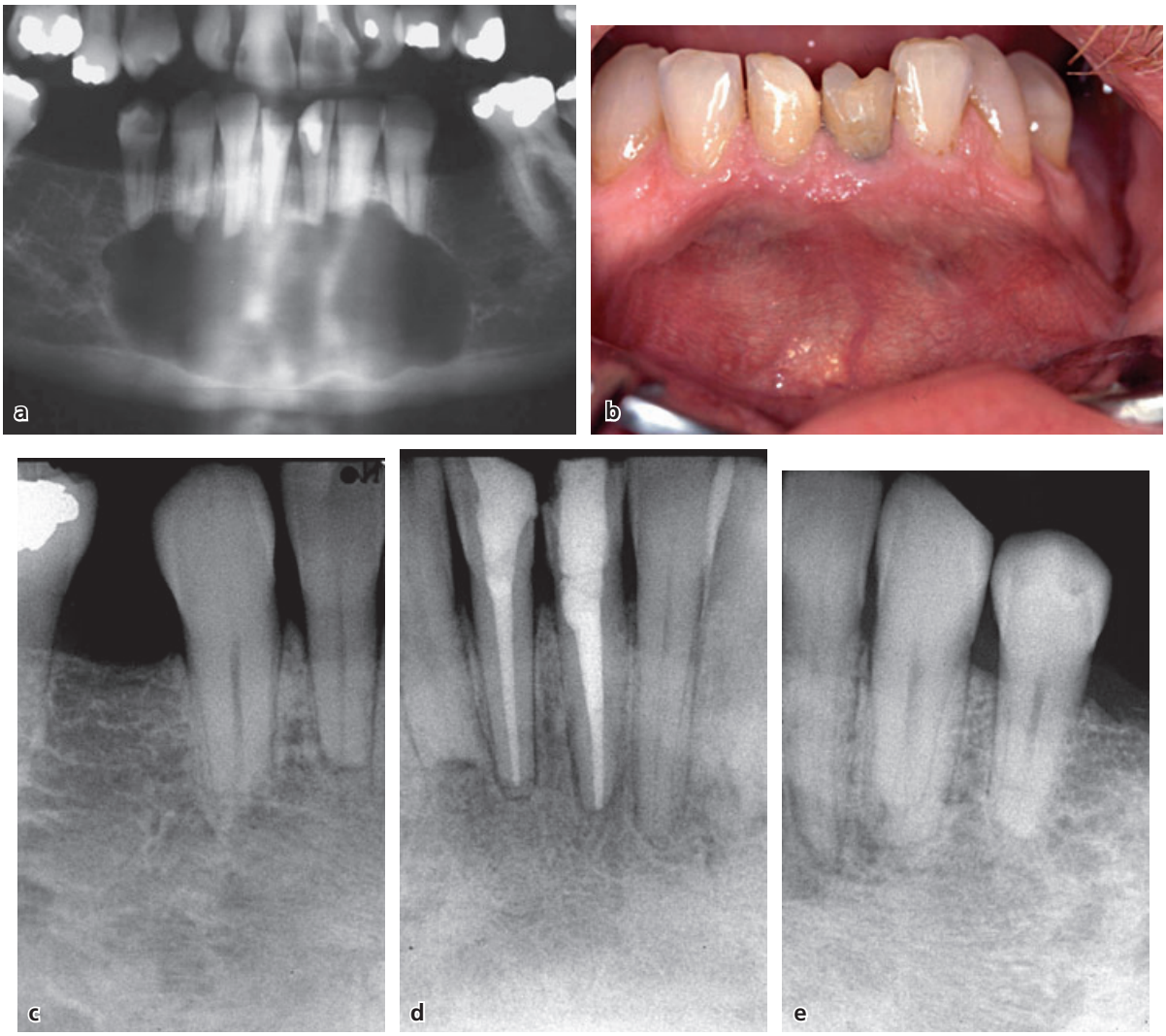

Fig. 23-13 Extensive destruction of alveolar bone as a result of cyst transformation of a periapical lesion emanating from tooth #31. (a) Note root resorption of neighboring teeth. (b) Buccal protrusion of the process was non-painful to palpation. All teeth responded vital to pulp testing except for the root filled teeth #31 and #41. The latter tooth, however, had a vital pulp as revealed on accessing the root canal. Treatment, carried out in collaboration with Dr. Ulf Lekholm, included placement of an oburator for drainage, decompression, and saline irrigation of the cyst cavity over 6 months. Following its reduction, teeth #31 and #41 received completion of endodontic treatment and a residue of the process was excised surgically. (c–e) Complete resolution of the process 10 months post surgery.

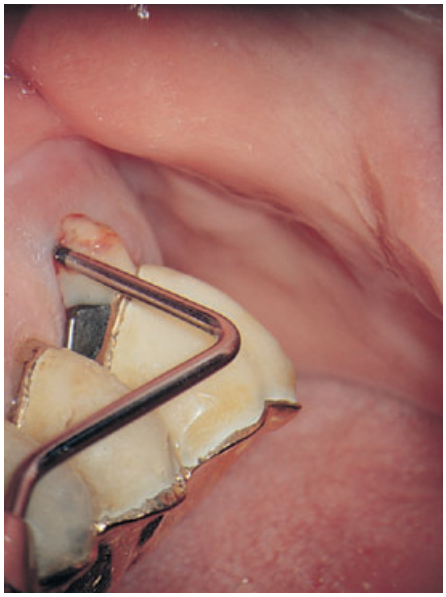

Fig. 23-14 Drainage of pus upon periodontal probing from a lesion of endodontic origin associated with an upper molar.

important role in confining the infection to the pulpal space (Stashenko *et al*. 1995) and constitute an important cellular front line (Fig. 23-11). The remainder of the lesion will be composed of a mixed cellular response (Fig. 23-15c) typical of a longstanding infectious process where various immunocompetent cells (*viz.* dendritic cells, macrophages, T and B cells) are prevalent (Torabinejad & Kettering 1985; Babal *et al*. 1987; Okiji *et al*. 1994; Stashenko *et al*. 1998; Marton & Kiss 2000). With increasing distances from the root canal apertures, the established lesion harbors a decreasing number of inflammatory cells and an increasing amount of fibrovascular elements representing attempts at repair. More peripherally there is a much stronger expression of fibroblastic activity and formation of new vessels. In the most peripheral portions of the lesion, a collagen-rich connective tissue normally separates it from the surrounding bone tissue (Bergenholtz *et al*. 1983) (Fig. 23-15a,d).

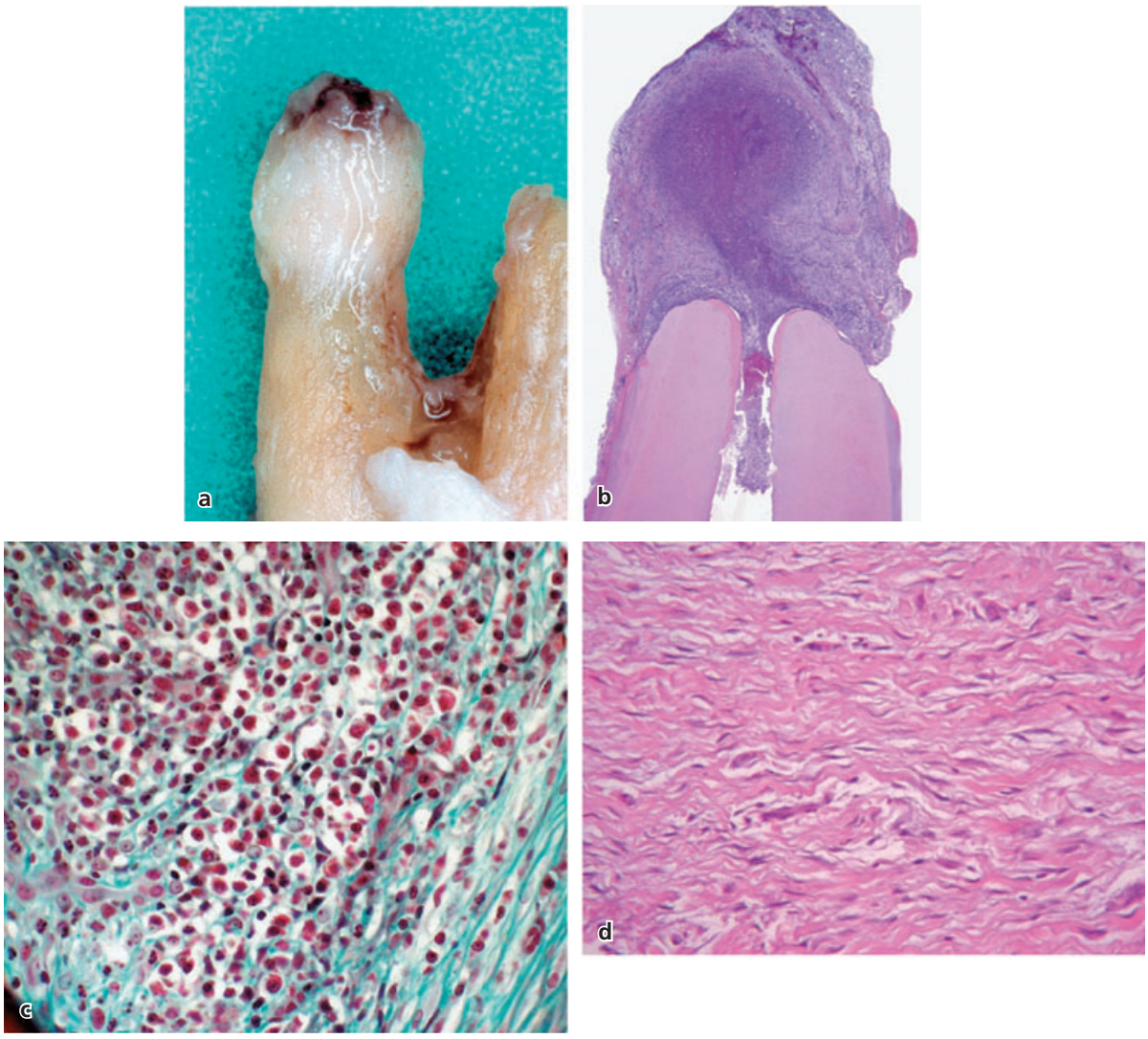

Fig. 23-15 Series of images demonstrating features of apical inflammatory lesions caused by root canal infection. (a) A soft lesion attached to the tip of the palatal root of an extracted upper molar. (b) The longitudinally cut tissue section through the root tip shows an overview of the lesion. The outer collagen-rich connective tissue confines the soft tissue lesion and attaches it to the root surface. (c) A typical mixed inflammatory cell infiltrate at the center of a lesion. (d) In the most peripheral portion the connective of an established lesion is rich in collagen and devoid of inflammatory cells. Microphotograph in (c) is from an apical lesion in a monkey.

In non-symptomatic endodontic lesions, the relative distribution of cellular and tissue elements may show great variation and some, but far from every lesion, may also contain proliferating epithelial cells (Nair 1997). The origin of epithelial strands is thought to be the epithelial rests of Malassez (Ten Cate 1972) that are stimulated to divide and proliferate by the release of pro-inflammatory cytokines and growth factors during the process of inflammation (Thesleff 1987; Lin *et al*. 1996; Suzuki *et al*. 2002). In the lesion, they appear to take a random course, but sometimes they may also attach to the root surface (Fig. 23-16) and eventually block the root canal exit for bacterial advancement into the periapical tissue compartment (Nair & Schroeder 1985). Their contribution to periodontal pocket formation upon an endodontic lesion, developing in close proximity to the epithelial sulcus of the marginal periodontium, remains obscure.

Conclusion

Inflammatory processes of the periodontium associated with necrotic dental pulps have an infectious etiology similar to periodontal disease. An essential difference between the two disease entities is their different source of infection. While periodontal disease is maintained by bacterial accumulations in the dentogingival region, endodontic lesions are directed towards infectious elements released from the pulpal space. The bacterial organisms in endodontic infections are usually confined to the root canal space. They may also be found in the soft tissue lesion *per se* either as clusters or as bacterial aggregations on the external root surface. Endodontic lesions rarely involve the marginal periodontium, unless abscessed. Cyst transformation may occur but even then marginal involvement is not common. In its established form, the endodontic lesion is clearly localized and constitutes an immunologically active protection zone which is important in preventing the dissemination of endodontic pathogens to the surrounding tissues (Stashenko 1990).

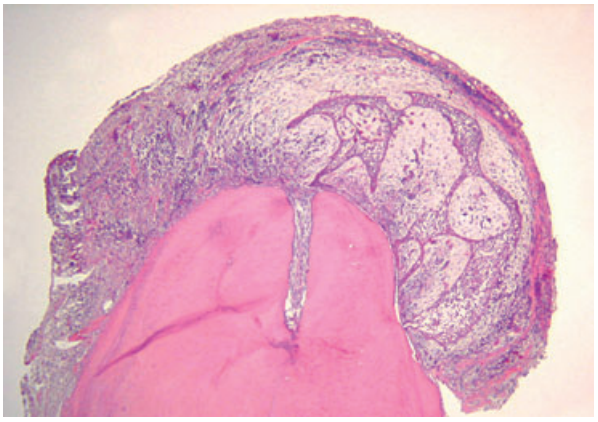

Fig. 23-16 Display of a periapical inflammatory process with proliferating epithelium partially attached to the root surface.

Effects of periodontal disease and periodontal therapy on the condition of the pulp

Influences of periodontal disease

The formation of bacterial plaque on detached root surfaces following periodontal disease has the potential to induce inflammation in the pulp along the very same pathways as an endodontic infection can affect the periodontium in the opposite direction. Thus, bacterial products and substances released by the inflammatory process in the periodontium may gain access to the pulp via exposed accessory canals and apical foramina, as well as dentinal tubules.

A clear association between progressive periodontal disease and pulpal involvement, however, does not exist. While inflammatory alterations as well as localized inflammatory cell infiltrates and necrosis of pulp tissue have been observed adjacent to accessory canals in teeth exposed by periodontal disease (Seltzer *et al*. 1963; Rubach & Mitchell 1965), a number of clinical studies has failed to confirm a direct relationship between progression of periodontitis and pulp tissue changes (Mazur & Massler 1964; Czarnecki & Schilder 1979; Torabinejad & Kiger 1985). In the cases in these studies, the pulp was observed to remain fully functional without overt inflammatory changes even though the periodontal tissue breakdown was severe. As already pointed out, an important reason for the lack of pulp tissue involvement, is that patent accessory canals are not invariably present and especially not in the cervical root portions. Another is that cementum obviously exerts protection. It is only when the cementum layer has been damaged, by, for example, instrumentation in periodontal therapy, wear from tooth cleaning, external root resorption, and root surface caries, that dentinal tubules can serve as pathways for microbial elements to the pulp (Figs. 23-17 to 23-19).

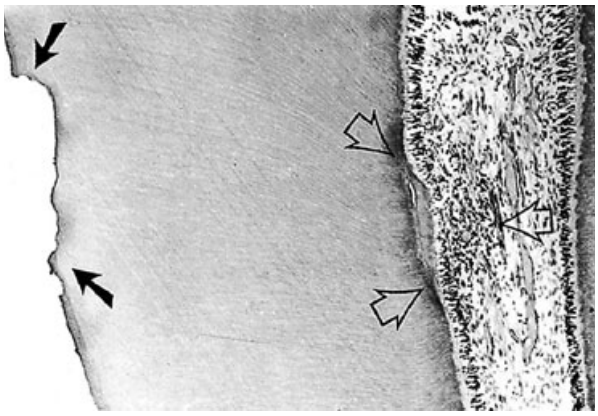

Fig. 23-17 Histologic section of a monkey tooth exposed to experimental periodontal tissue breakdown. Beneath resorptive defects in the external root surface a minor inflammatory cell infiltrate and a small rim of reparative dentin have been formed in the pulp. From Bergenholtz & Lindhe (1978).

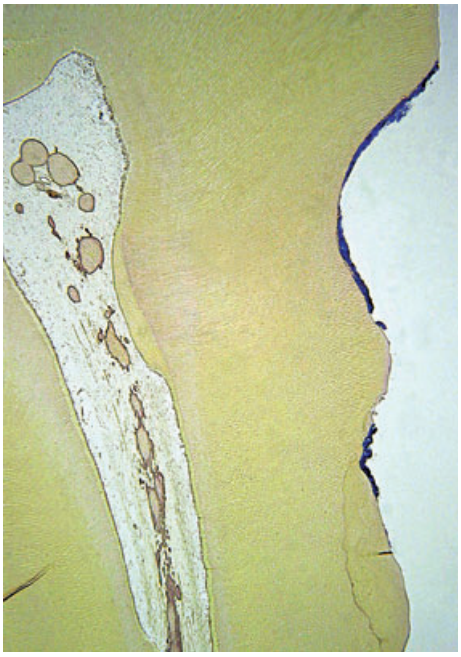

Fig. 23-18 Histologic section of a human tooth with bacterial accumulations on the external root surface. There are obvious defects in the root surface. Pulp tissue is minimally affected, however, except for numerous mineralization processes both in the tissue proper and at the inner root canal wall.

The fact that tissue changes develop infrequently and even so only locally in the pulp of teeth subjected to periodontitis was underscored by an experimental study in monkeys (Bergenholtz & Lindhe 1978). Following a ligature-induced breakdown of the attachment apparatus, it was found that the majority of the root specimens examined (70%) exhibited no inflammatory changes, despite the fact that approximately 30–40% of the periodontal attachment was lost. The remaining roots (30%) displayed only small inflammatory cell infiltrates and/or formations of reparative dentin in the pulp subjacent to root areas exposed by the periodontal tissue destruction. These tissue changes were associated with root surface resorption (Fig. 23-17), supporting the view that dentinal tubules have to be uncovered before external irritants can be transmitted to the pulp. Consequently, the lack of correlation found in clinical observations between periodontal disease and pulp tissue alterations, may simply depend on the fact that few open pathways exist to the pulp in many periodontally involved teeth. Furthermore, as described above, once the dentin/pulp complex has been exposed to bacterial elements, repair and healing will often be instituted

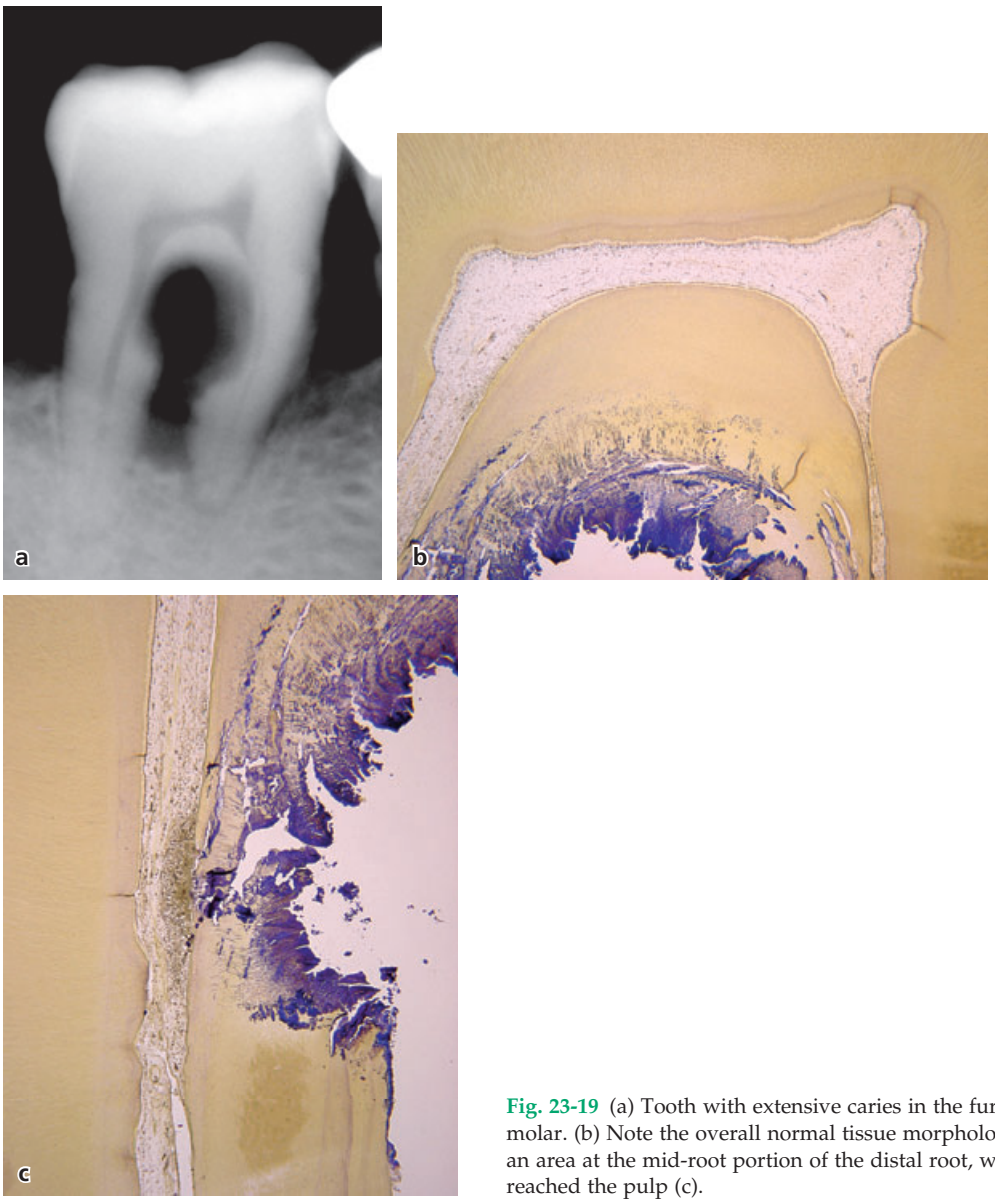

Fig. 23-19 (a) Tooth with extensive caries in the furcation region of a lower molar. (b) Note the overall normal tissue morphology of the pulp except for an area at the mid-root portion of the distal root, where caries process has reached the pulp (c).

soon after the initial inflammatory events, leaving the remaining tissue unaffected.

In the study by Bergenholtz and Lindhe (1978), destructive periodontal disease was produced experimentally during a comparatively short period (5–7 months), while in humans a similar degree of destruction of periodontal tissue normally requires several years. It has been reported that the pulp of teeth with longstanding periodontal disease develops fibrosis and various forms of intra-pulpal mineralizations (Bender & Seltzer 1972; Lantelme *et al*. 1976) (Fig. 23-18). If there is an association, it seems reasonable to assume that tissue changes of this nature represent the accumulated response of the pulp to the relatively weak, but repeatedly occurring, insults to the tissue over time, for example by microbial elements reaching the pulp over root surface exposures. Nonetheless the pulp can obviously remain healthy for as long as periodontal disease has not arrived at a terminal stage, when plaque accumulation and associated inflammatory lesions interfere with the neurovascular supply of the tissue through the main apical foramen (Fig. 23-20).

Conclusion

Available documentation suggests that the vital functions of the pulp are rarely threatened by periodontal disease influences. In teeth with moderate breakdown of the attachment apparatus, the pulp usually remains healthy. Breakdown of the pulp presumably does not occur until the periodontal disease process has reached a terminal stage, i.e. when plaque and the periodontal inflammatory process have progressed to the main apical foramina, whereby a retrograde destructive inflammatory pulpal lesion is initiated (Langeland *et al*. 1974) (Fig. 23-20). Consequently, as long as the blood supply through the apical foramen remains intact, the pulp is usually capable of withstanding injurious elements released by the lesion in the periodontium.

Influence of periodontal treatment measures on the pulp

Pocket/root debridement in periodontal therapy by hand instrumentation (scaling and root planing, S/RP) or ultrasonics is indispensable in the treatment of periodontal disease. However, this treatment is associated with a number of undesired side effects. Except for recession of gingival tissues resulting in exposures of root surfaces, the instrumentation *per se* may also inadvertently remove root cementum and the superficial parts of dentin. Thereby a large number of dentinal tubules will become exposed to the oral environment as treated root surfaces are normally left unprotected. Subsequent contact with microbial elements in the oral cavity is potentially harmful to the pulp as bacterial invasion of the exposed dentinal tubules may occur (Adriaens *et al*. 1988). While localized inflammatory lesions may be initiated in the pulp, the experimental study by Bergenholtz and Lindhe (1978) did not observe increased incidence of pulpal lesions in teeth subjected to S/RP in comparison to non-treated teeth subjected to periodontal tissue breakdown alone. In the study, root surfaces denuded of root cementum were left open to the oral environment for up to 30 days. The finding that plaque accumulation on root dentin exposed by one session of S/RP does not seriously threaten the vitality of the pulp has been confirmed in similarly designed experimental studies (Nilvéus & Selvig 1983; Hattler & Listgarten 1984). Yet, root dentin hypersensitivity may follow such treatment measures, causing an uncomfortable problem which is difficult to manage (see below).

During the maintenance phase of periodontal therapy, there are reasons to restrict repeated instrumentations, as some additional dentin always will be removed. Such therapy can result in weakening of the tooth structure and also in extensive reparative dentin formation in the pulp (Fig. 23-21).

Conclusion

Results of clinical observations and animal experiments support the view that pocket/root debridement procedures normally do not threaten the vitality of the pulp. Localized inflammatory alterations may occur adjacent to instrumented root surfaces followed by tissue repair in the form of hard tissue depositions on the root canal walls.

Root dentin hypersensitivity

Symptoms and incidence

Patients who have received pocket/root debridement in periodontal therapy may frequently experience sensitivity of the treated teeth to evaporative, tactile, thermal, and osmotic stimuli (Fischer *et al*. 1991; Kontturi-Närhi 1993; Chabanski *et al*. 1996; Tammaro *et al*. 2000; for review see Gillam & Orchardson 2006). Usually, the symptoms, when they occur, develop and peak during the first week, and then subside or disappear within the subsequent weeks; they are, although uncomfortable, most often a temporary and sustainable problem (Schuurs *et al*. 1995; Chabanski *et al* 1996; Gillam *et al*. 1999; Fardal *et al*. 2002). Occasionally, the condition may become a chronic pain problem and may persist for months or years. Patients appear to be especially at risk after periodontal surgery. In a comprehensive questionnaire survey, severe painful symptoms were reported to prevail in 26% of the subjects 6 months to 5 years after the completion of treatment, while 16%, treated non-surgically, reported pain symptoms (Kontturi-Närhi 1993). In a clinical trial comprising 35 patients, Tammaro *et al*. (2000) observed that the incidence of sensitive teeth increased following non-surgical

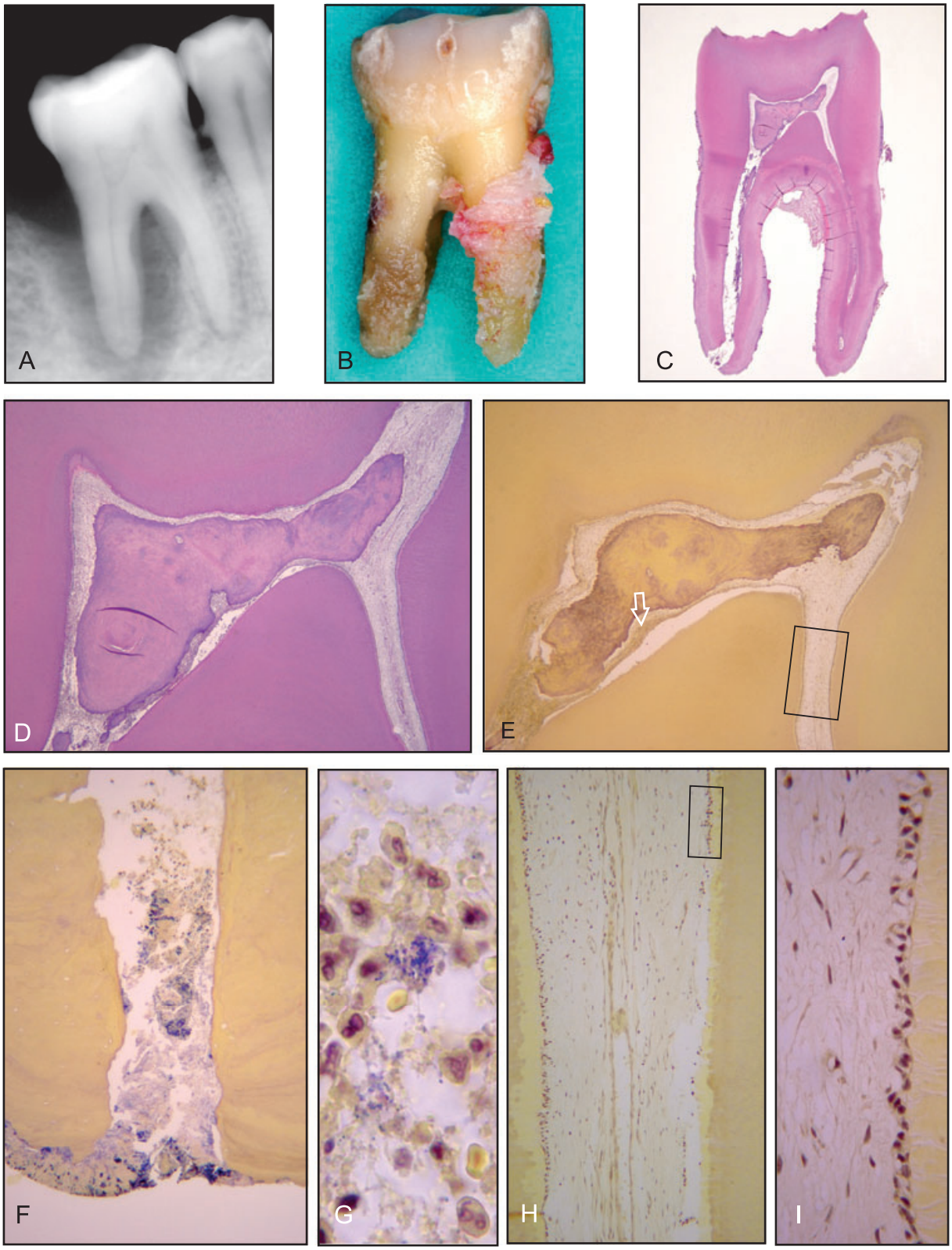

Fig. 23-20 (A) Extensive periodontal tissue breakdown circumscribing the distal root of a lower molar. (B, F) Plaque and calculus cover the root surface to the apical foramen. (C–G) The pulp is necrotic and infected all the way to the extensive hard tissue deposition in the coronal pulp (to arrow in E). Microphotographs enlarging marked area in (E) (H, I) indicate that the pulp tissue of the mesial root is completely unaffected and displays normal tissue morphology. Tooth responded vital to pulp testing.

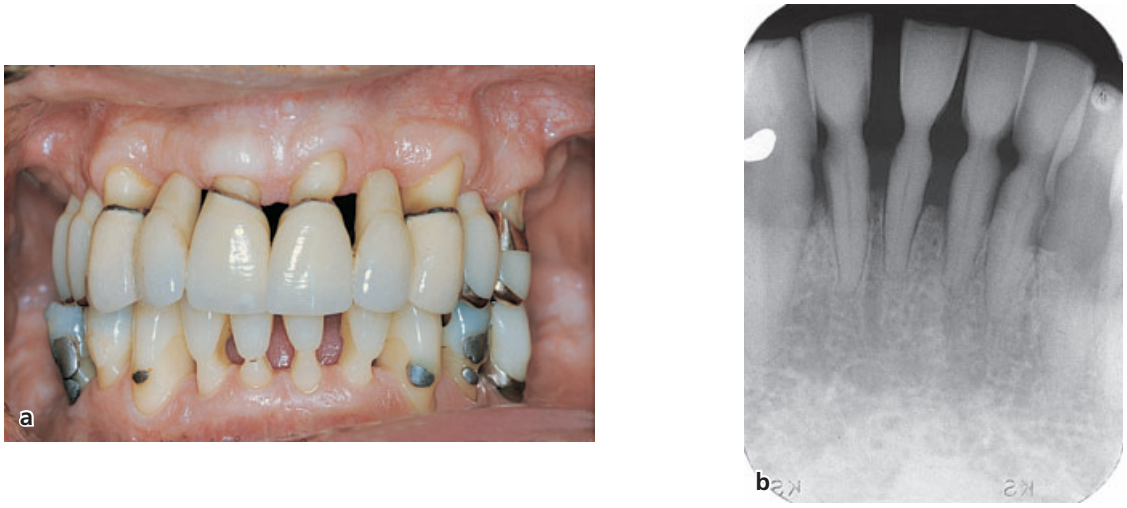

Fig. 23-21 (a) Clinical photograph of a patient, who has been in the maintenance phase for periodontal disease. While there are excellent gingival conditions and no pocket probing depths, there is substantial loss of cervical root dentin. (b) One of the lower incisors later had a horizontal fracture, but without a pulpal exposure due to fill of reparative dentin in the coronal portion of the pulp chamber. Courtesy of Dr. Sture Nyman.

periodontal instrumentation in comparison to non-instrumented teeth after initiating a self-performed oral hygiene program in patients with moderate to advanced periodontal disease. While affecting a majority of the patients, pain was generally reported to be minor. Only a few teeth in a small number of the patients developed highly sensitive root surfaces.

The main initial symptom is sharp pain of rapid onset that disappears once the stimulus is removed. In more severe, long-standing cases, shorter or longer periods of lingering, dull or aching pain may be provoked. These symptoms of a pulpitis character may not only be localized to the tooth (teeth) in question but to both quadrants of the jaw. Even a minimal contact with a toothbrush may elicit intense pain – a condition which is not only uncomfortable but one that is likely to hinder proper oral hygiene measures.

Mechanisms

The painful condition has been given many names, including dentine sensitivity, cervical dentine hypersensitivity, root dentine sensitivity, and root dentine hypersensitivity, reflecting some of the confusion that still exists regarding its etiologic background (Gillam & Orchardson 2006). The fact that root surfaces become sensitive to a variety of externally derived stimuli after periodontal instrumentation is not surprising as dentinal tubules become uncovered to the oral environment and subject to hydrodynamic forces. Hence, a variety of pain-evoking stimuli including evaporative, tactile, thermal, and osmotic stimuli may elicit sudden fluid shifts in the exposed tubules, thereby inducing a painful sensation according to the hydrodynamic theory of dentin sensitivity (Brännström 1966; Pashley 1996). This mechanism alone can certainly explain the sensitivity patients experience immediately after the instrumentation procedure and during a short period afterwards, while it does not make clear why the symptoms increase over time and why pain may prevail in certain patients and in certain teeth.

The increase in pain intensity may have one or both of the following two explanations. Firstly, the smear layer formed on the root surface by the S/RP procedure will be dissolved within a few days (Kerns *et al*. 1991). This in turn will increase the hydraulic conductance of the involved dentinal tubules (Pashley 1996) and thus decrease the peripheral resistance to fluid flow across dentin. Thereby pain sensations are more readily evoked. Secondly, open dentinal tubules serve as pathways for diffusive transport of bacterial elements in the oral cavity to the pulp, which may cause a localized inflammatory pulpal response (Bergenholtz & Lindhe 1975, 1978). Indeed, experiments in dogs have shown that dentin exposures left unprotected greatly enhance the sensitivity of responding nerve fibers (Närhi *et al*. 1994). A large number of intradental A-delta fibers, normally inactive, then become able to respond (Närhi *et al*. 1996). It has furthermore been shown that the receptive field of each individual fiber gets wider (Närhi *et al*. 1996). In addition, sprouting of new terminal branches from pulpal axons may occur in the area subjacent to the root surface defect (Taylor *et al*. 1988). As already stated, sprouting of nerves is a temporary event and will subside if inflammation disappears; a feature which is consistent with their involvement in root dentin hypersensitivity (Byers & Närhi 1999). In other words, an essential component of the increasing root sensitivity patients experience after an instrumentation procedure is likely to be related to a peripheral sensitization of pulpal nociceptors leading to what is termed primary hyperalgesia.

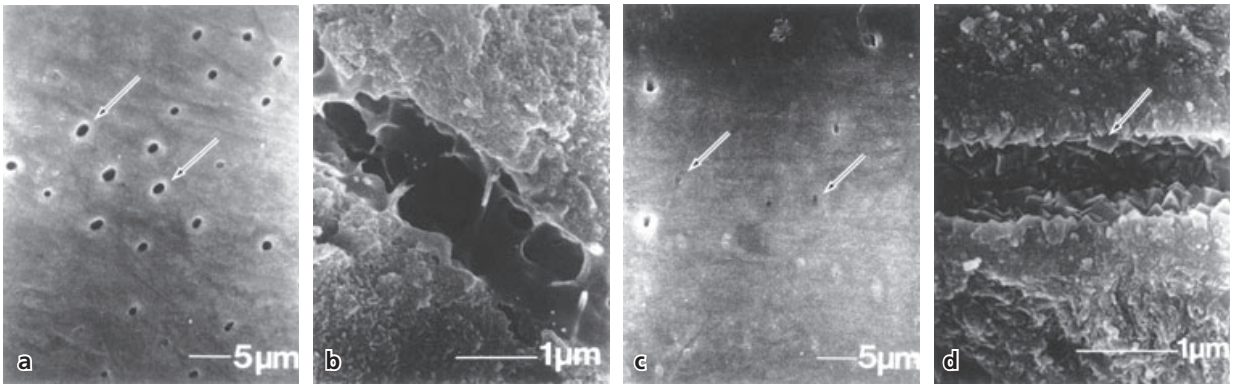

Fig. 23-22 Scanning electron microscopic images of root surface biopsies of hypersensitive (a, b) and of non-sensitive root dentin areas of human teeth (c, d). Numerous wide tubular apertures are seen in (a). These tubules show no evidence of hard tissue deposition after being opened longitudinally (b). By contrast, most tubules are occluded in (c) and below the surface rhombohedral crystals of from 0.1–0.3 µm are present. Images kindly provided by Dr. Masahiro Yoshiyama and published with permission of the *Journal of Dental Research*.

The fact that root dentin hypersensitivity often disappears a few weeks after the instrumentation procedure is best explained by the development of a natural occlusion of the exposed dentinal tubules. The deposition of mineral crystals in the tubular lumen may play an important role (Yoshiyama *et al*. 1989, 1990) (Fig. 23-22), firstly by inactivating the hydrodynamic mechanism for dentinal pain and secondly, by restricting the potential for an inward diffusion of bacterial elements to the pulp. The observation of few open tubules in non-sensitive root dentin (Hiatt & Johansen 1972; Absi *et al*. 1987; Yoshiyama *et al*. 1989; Cuenin *et al*. 1991; Oyama & Matsumoto 1991; Kontturi-Närhi 1993), while hypersensitive root areas show large numbers of tubular apertures on their surfaces (Absi *et al*. 1987; Yoshiyama *et al*. 1989; Cuenin *et al*. 1991; Oyama & Matsumoto 1991; Kontturi-Närhi 1993), supports this view.

The fact that only certain individuals become seriously affected may be related to local factors in the oral cavity, as well as to the level of the subjects' pain perception. Certain dietary factors, in particular fruit juices, yoghurt, and wines, have been implicated in the causation of root dentin hypersensitivity (Addy *et al*. 1987). By their acidity and ability to etch dentin these substances may dissolve the occlusions of the dentinal tubules or prevent them from forming. It needs be recognized that pain is not only an expression of injury and noxious stimuli, but also a psychobiologic phenomenon having both a physiologic and psychologic basis for its perception and reaction to it. Indeed, a variety of emotional elements may influence the subjective interpretation of pain. Anxiety, fear, and depression are factors that are known to affect pain perception as well as the subject's ability to identify coping methods (Eli 2003).

An important consideration in the deliberation of the mechanisms behind enhanced and lingering pain symptoms of root dentin hypersensitivity is the potential of central nervous system sensitization (for review see Sessle 2006). It is now well documented that frequent and repeated pain stimulations result in structural and functional changes that allow the brain to respond more rapidly and more effectively to the same stimuli. Such an increase of the excitability of central neurons has a downside in that pain may continue as a memory function even if the peripheral cause has been eliminated. Thus, it is possible that central sensitization phenomena explain failure of treatment attempts in some patients.

Principles for management

In patients suffering from severe root dentin hypersensitivity, active treatment is urgent. However, the methods presently available provide an unpredictable remedy and at best only temporary relief is attained (Ikola 2001; Gillam & Orchardson 2006). Since tubular patency of the exposed dentin seems to play a crucial role in the pathogenesis of root dentin hypersensitivity most procedures hitherto attempted are logically aimed at inducing blockage of the peripheral openings. Some agents commonly employed, primarily for dentist-applied treatment, act by causing an astringent or coagulating effect on the tubular content. Such chemicals include strontium chloride, sodium monofluorophosphate, sodium fluoride, calcium hypophosphate, calcium hydroxide, potassium nitrate, potassium oxalates, glutaraldehyde, ferric oxalate, and stannous fluoride. Other methods aim to produce a physical block for example by the use of grafting procedures and laser applications (for reviews see Zappa 1994; Gangarosa 1994; Ikola 2001; Gillam & Orchardson 2006).

There may be several explanations why such treatments sometimes fail to remedy the problem. One is likely to be of a technical nature in that it is often difficult to attain a completely dry dentin surface during the application of, for example, an astringent solution. Hence, the release of gingival fluid from the sulcus is not easily restrained by compressed air or other methods. Consequently, upon application of

the agent, protein from the gingival exudate might primarily be brought to coagulation rather than the tubular content. The precipitate is then easily removed upon subsequent tooth cleaning measures leaving the tubules unoccluded. Most agents furthermore may only cause a superficial block that may be dissolved over the course of time. Also topical applications do not address the pain mechanisms associated with either peripheral or central sensitization of nociceptors. Agents able to decrease the excitability of intradental nerves have, therefore, been proposed based on the assumption that potassium ions released from formulations containing potassium salts (e.g. chlorides, nitrates, citrate, and oxalates) may penetrate dentinal tubules and temper intradental nerve activity (Markowitz & Kim 1992; Orchardson & Peacock 1994). Toothpastes with potassium-containing preparations as active ingredients have indeed shown promise in clinical trials by giving better relief of pain in selected teeth in comparison to toothpastes without active substance (Sowinski *et al*. 2001; Wara-Aswapati *et al*. 2005). Experiments employing electrophysiological recordings in dogs, however, have shown that the effect of topical application of potassium salt is weak and becomes abolished after irrigation (Ikola 2001). More research appears necessary to confirm a clear treatment effect of potassium salts in gels, mouthwashes, and toothpastes (Orchardson & Gillam 2000). This also applies to any other treatment mode. It needs be recognized that demonstrating a significant treatment effect of a given compound in clinical trials is fraught with several difficulties. One is to assemble a sufficient number of patients that are reasonably identical in terms of duration and level of pain. Another is that the pain condition may go into natural remission at any time. A large placebo effect also operates in studies of this nature (Holland *et al.* 1997; Yates *et al*. 1998; Orchardson & Gillam 2000).

Any treatment approach to root dentin hypersensitivity should be preceded by a careful analysis of conditions that may be the cause of, or contributory to, the symptoms. Cracked teeth including cusp fractures, fractured or leaky restorations, caries, as well as a variety of other exposures of dentin to the oral environment may cause pulpal pain sensations to the very same stimuli which elicit root dentin hypersensitivity. An area of exposed dentin may be more sensitive if there is irritation of the pulp from other areas of the tooth, for example from the margin of a restoration that is not sealed from the oral environment (Närhi *et al*. 1994). Particular care should be taken to eliminate traumatic occlusion to alleviate any activation of pulpal nociceptors. Furthermore, dietary counseling should be given to patients who admit excessive consumption of citrus fruits, apples, or any other food or drinks that are acidic in nature.

Self-performed plaque control is important for the prevention and treatment of root dentin hypersensitivity. It has been observed clinically that, with time, teeth in patients with excellent oral hygiene habits develop hard, smooth, and insensitive root surfaces. Electron microscopic examination of the dentin of such root surfaces has revealed that mineral deposits obliterate the tubular openings (Hiatt & Johansen 1972). However, when severe symptoms of root hypersensitivity have emerged, it is difficult to motivate the patient to maintain the degree of plaque control that is necessary to allow for a natural occlusion of the dentinal tubules. In such situations, an agent which has a capacity to block the tubular openings, may be beneficial at least temporarily, so that proper oral hygiene measures can be reinforced. In severe cases, where no remedy is achieved with any advice or treatment approach, pulpectomy and root filling are a last resort.

Any pain treatment should take into consideration the potential of preventing the condition from emerging in the first place. However, no well proven protocol has as yet been established whereby root dentine hypersensitivity can be effectively prevented. Attempts to block the exposed dentinal tubules immediately following S/RP should be an obvious approach. In fact a couple of placebo-controlled studies have shown promise in that significantly fewer sensitive teeth were attained subsequent to instrumentation when 6% ferric oxalate (Wang *et al*. 1993) and 3% potassium oxalate (Pillon *et al*. 2004) were applied topically. The long-term outcome of such procedures awaits confirmation.

Conclusion

Root dentin hypersensitivity frequently develops as an uncomfortable and sometimes difficult ailment to treat subsequent to scaling and root planing procedures in periodontal therapy. Although the exact mechanism is not well established, the condition is clearly related to open dentinal tubules that allow hydrodynamic mechanisms to elicit painful sensations upon external stimulation. Both peripheral and central sensitizations are likely to contribute to the more intense and lingering pain symptoms some patients experience after root dentin exposure.

Diagnosis and treatment planning should consider contributory etiologic factors including over-consumption of acidic food items. Root dentin hypersensitivity should also be checked against other conditions causing similar pain symptoms and rule out cracked teeth, leaky restoration margins, caries in the tooth or in neighboring teeth, as well as trauma from occlusion. A large number of treatment methods are available for both in-office and over-the-counter applications. Some aim to block tubular patency of the exposed root dentin and others attempt to decrease excitability of intradental nerves for reduced pain transmission. Unpredictable treatment results are to be expected and only temporary relief may be attained.

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Part 7: Peri-implant Pathology

Chapter 24

Peri-implant Mucositis and Peri-implantitis

Tord Berglundh, Jan Lindhe, and Niklaus P. Lang

Definitions

Peri-implant disease

Inflammatory processes in the tissues surrounding an implant (Albrektsson & Isidor 1994).

Peri-implant mucositis

Reversible inflammatory process in the soft tissues surrounding a functioning implant.

Peri-implantitis

Inflammatory process additionally characterized by loss of peri-implant bone.

See Fig. 24-1.

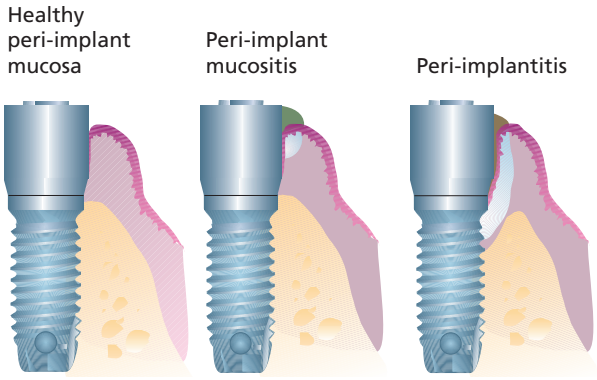

Fig. 24-1 Schematic drawing illustrating healthy peri-implant mucosa, peri-implant mucositis, and peri-implantitis.

Ridge mucosa

The edentulous, hard tissue portion of the alveolar process is covered by a mucosa that is about 2–4 mm thick (see also Chapter 3). The mucosa is lined by a keratinized epithelium and is comprised of a connective tissue that is rich in fibroblasts, collagen fibers, and vascular structures (e.g. Türk 1965; Krajicek *et al*. 1984; Liljenberg *et al*. 1996). The connective tissue is continuous with the cortical bone crest via the periosteum. A few scattered inflammatory cells can be observed adjacent to the basement membrane in the connective tissue papillae between the rete pegs of the epithelium.

Peri-implant mucosa

Following implant installation, a transmucosal passage is formed around the abutment portion of the device. The ridge mucosa at such sites adapts to the new functional demands and a peri-implant mucosa becomes established. The mucosa surrounding implants and the gingiva surrounding teeth have many features in common. Both types of tissues are lined with a keratinized oral epithelium; at clinically healthy sites this is continuous with a thin non-keratinized barrier or junctional epithelium that faces the implant or the tooth surface. In the connective tissue immediately lateral to these thin epithelial linings small infiltrates of inflammatory cells (neutrophils, macrophages, T cells, B cells) are frequently seen (Liljenberg *et al*. 1997). The inflammatory cells represent the host's defense against bacterial products and hence they may be considered as one important component of the biological seal that separates the peri-implant and periodontal attachment tissues from the oral cavity (see also Chapters 3 and 11).

Peri-implant mucositis

Clinical features

The clinical features of peri-implant mucositis are in many respects similar to those of in gingivitis at teeth and include classical symptoms of inflammation, such as swelling and redness (see Chapter 17). Differences in the morphology of the peri-implant mucosa and the lack of light transmission through the metal of the device, however, may mask visible signs of inflammation. Assessment of peri-implant mucositis must therefore always include assessment of bleeding following probing (Fig. 24-2).

Prevalence

Bleeding on probing (BoP) is a good discriminating indicator of peri-implant mucositis. The prevalence of this disease remains difficult to estimate since data on BoP at implants are infrequently reported (Berglundh *et al*. 2002). In a study on 25 subjects treated with implant-supported fixed prosthesis, Lekholm *et al*. (1986) reported that BoP occurred at 80% of the implants. Roos-Jansåker *et al*. (2006a,b,c) examined 987 implants in 216 patients and reported that more than 73% of all implants exhibited BoP. Higher frequencies of BoP at implants were presented by Fransson *et al*. (2007) in a study on 82 subjects. It was reported that BoP occurred in more than 90% of implant sites.

Histopathology

Response to early plaque formation

The response of the gingiva and the peri-implant mucosa to early and more long-standing periods of plaque formation was analyzed both in studies in man and in experiments in animals. Pontoriero *et al*. (1994) engaged 20 partially edentulous human subjects in a clinical "Experimental gingivitis in man" (Löe *et al*. 1965) study. All subjects had been treated for advanced periodontal disease and thereafter had been restored with implants in one or several segments of the dentition. During a 6-month period following the prosthetic rehabilitation, the subjects were enrolled in a meticulous maintenance program that included regularly repeated supportive measures. A baseline examination was subsequently performed including assessment of plaque, soft tissue inflammation, probing pocket depth (PPD), soft tissue recession, and composition of oral biofilms. The participants refrained from all oral hygiene measures for 3 weeks. It was observed that during this interval plaque build-up (amount and composition) and the soft tissue response to the microbial challenge, e.g. inflammation and PPD change, developed in a similar manner in the tooth and implant segments of the dentition.

Zitzmann *et al*. (2001) studied the response to plaque formation in the soft tissues at implant and tooth sites in humans. Twelve subjects with healthy periodontal and peri-implant conditions were asked to refrain from tooth/implant cleaning for a period of 3 weeks (Fig. 24-3). Clinical examinations were performed and soft tissue biopsies were harvested prior to and at the end of the plaque accumulation period. The tissues were examined using histologic techniques. It was demonstrated that plaque build-up was associated with clinical signs of soft tissue inflammation. Furthermore, the initially minute lesions in the gingiva and in the peri-implant mucosa markedly increased in size after 3 weeks of plaque build-up: from 0.03 mm^2 at baseline to 0.3 mm^2 (gingiva) and 0.2 mm^2 (peri-implant mucosa). In addition, the proportion of B cells and neutrophils increased more in the lesion in the gingiva than in its counterpart in the peri-implant mucosa.

Experimental model

In a carefully supervised experiment in the dog, Berglundh *et al*. (1992) compared the reaction of the gingiva and the peri-implant mucosa to 3 weeks of *de novo* plaque formation. The mandibular premolars in one side of the mandible were extracted, leaving the premolars on the contralateral side as controls. After 3 months of socket healing, implants were inserted in the edentulous ridge. The animals were placed in a plaque-control program to allow for ideal healing of the mucosa at the implants and to prevent

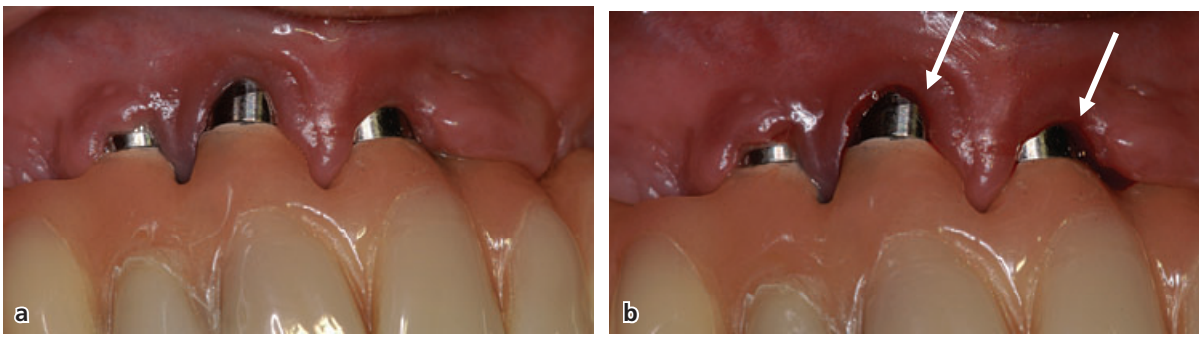

Fig. 24-2 (a) Clinical symptoms of peri-implant mucositis including varying signs of redness and swelling. (b) Probing resulted in bleeding from the margin of the mucosa.

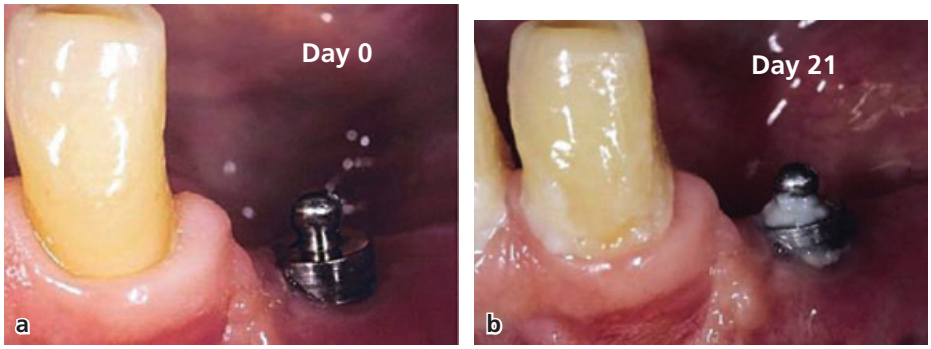

Fig. 24-3 (a) Clinical photograph from sites with healthy gingiva and peri-implant mucosa. (b) The sites illustrated in (a) following 3 weeks of plaque formation.

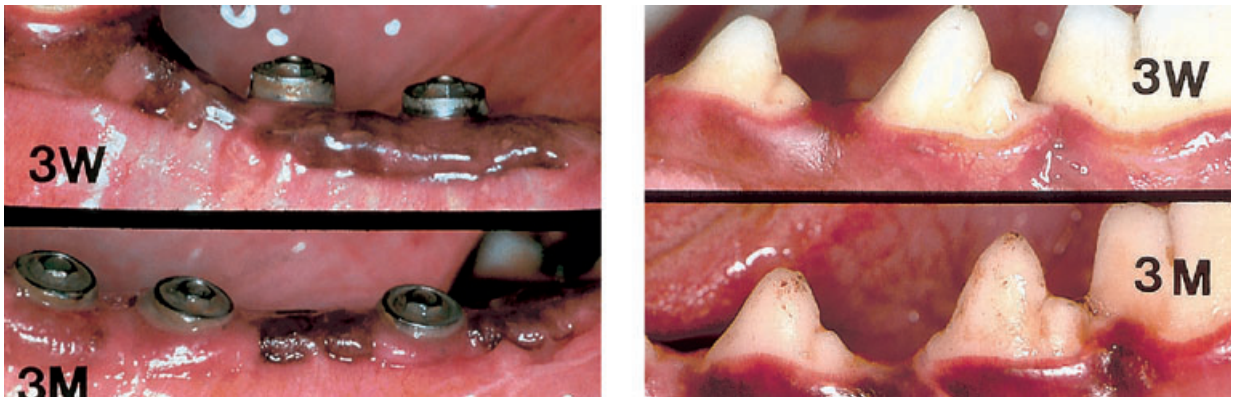

Fig. 24-4 A clinical view illustrating 3 weeks (3 W) and 3 months (3 M) of undisturbed plaque formation on the implants and the teeth of a beagle dog.

gingivitis from occurring in the tooth segments of the dentition. After this healing period, the dogs were examined and samples from the minute biofilms that were present on the implant and the tooth surfaces were harvested. The plaque-control program was terminated and the animals given a soft diet, that allowed gross plaque formation. Re-examinations, including clinical assessment (Fig. 24-4), sampling of plaque from teeth and implants as well as biopsy, were performed after 3 weeks.

During the course of the study, it was observed that similar amounts of plaque formed on the tooth and implant segments of the dentition. The composition of the two developing plaques was also similar. It was therefore concluded that early microbial colonization on titanium implants followed the same pattern as that on teeth (Leonhardt *et al.* 1992).

Both the gingiva and the peri-implant mucosa responded to this microbial colonization with the establishment of overt inflammatory lesions, i.e. infiltrates of leukocytes in the connective tissue. The lesions in the gingiva and in the peri-implant mucosa were matched both with respect to size and location. Hence, both lesions were consistently found in the marginal portion of the soft tissues and between the keratinized oral epithelium and the junctional or barrier epithelium (Fig. 24-2).

Response to long-standing plaque formation

With increasing duration of plaque build-up (3 months) in the dog model described above, the lesions in the peri-implant mucosa seemed to have expanded and to have progressed further "apically" while the gingival lesions remained unchanged (Ericsson *et al.* 1992) (Fig. 24-5). Furthermore, the lesion in the peri-implant mucosa contained a much smaller number of fibroblasts than the corresponding infiltrate in the gingiva. In any inflammatory lesion of long standing, periods of breakdown and periods of repair interchange. It was suggested, therefore, that in the gingival lesion, the amount of tissue breakdown that occurred during the 3 month interval was more or less fully compensated by tissue build-up that took place during a subsequent phase of repair. In the lesion within the peri-implant mucosa, the tissue breakdown was not fully recovered by reparative events. This reduced build-up may have been the reason for the resulting additional propagation and spread of the lesion in the peri-implant mucosa.

In a similar dog experiment Abrahamsson *et al.* (1998) studied soft tissue lesions after 5 months of plaque formation at three different implant systems. They observed that the response of the peri-implant mucosa to long-standing plaque formation appeared

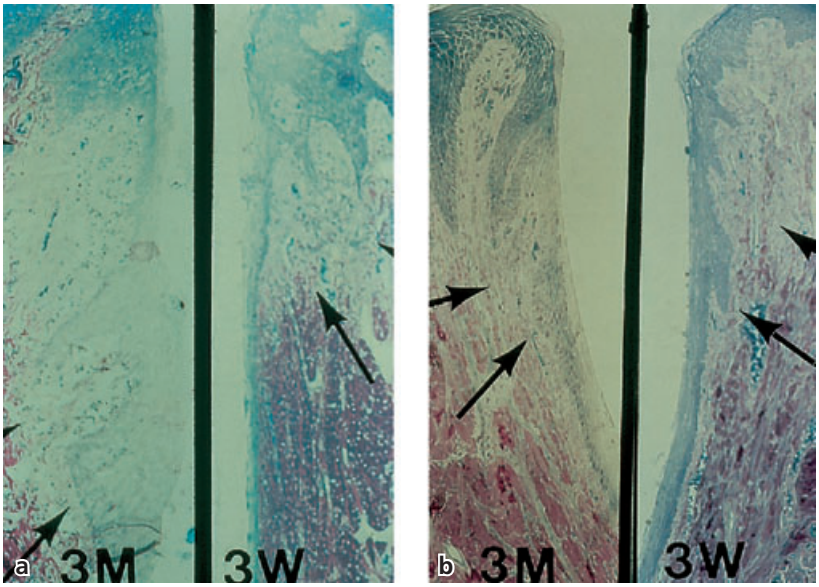

Fig. 24-5 Microphotographs illustrating the establishment of inflammatory cell infiltrates (ICT) in the peri-implant mucosa (a) and the gingiva (b) (3 W = 3 weeks; 3 M = 3 months). Note, in the microphotographs representing 3 months, the infiltrate in the peri-implant mucosa extends much deeper into the tissue than is the case in the gingiva.

to be independent of the implant system that harbored the biofilm.

Peri-implantitis

Clinical features

Peri-implantitis represents a clinical condition that includes the presence of (1) an inflammatory lesion in the peri-implant mucosa and (2) loss of peri-implant bone. The assessment of the diagnosis *peri-implantitis* must consequently require detection of both bleeding on probing (BoP) as well as bone loss in radiographs. Peri-implantitis initially affects the marginal part of the peri-implant tissues and the implant may remain stable and in function for varying periods of time. Implant mobility is therefore not an essential symptom for peri-implantitis but may occur in a final stage of disease progression and indicates complete loss of integration.

As pointed out for the clinical characteristics of peri-implant mucositis, various factors such as the morphology of the peri-implant mucosa and position of the implant may also influence the clinical appearance of inflammation in peri-implantitis. Probing is therefore a prerequisite in the examination of peri-implant tissues and should include assessment of both BoP and probing pocket depth (PPD).

The clinical appearance of peri-implantitis may, hence, vary and may not always be associated with overt signs of pathology. Two different cases are illustrated in Figs. 24-6 and 24-7. While plaque and calculus together with clinical signs of inflammation are present in the case in Fig. 24-6, the case in Fig. 24-7a does not reveal such symptoms. Probing the site in Fig. 24-7a, however, resulted in a PPD of about 10 mm and BoP (Fig. 24-7b).

Crater-formed defects around implants are frequently found in radiographs obtained from sites with peri-implantitis (Fig. 24-8). Bone loss in such

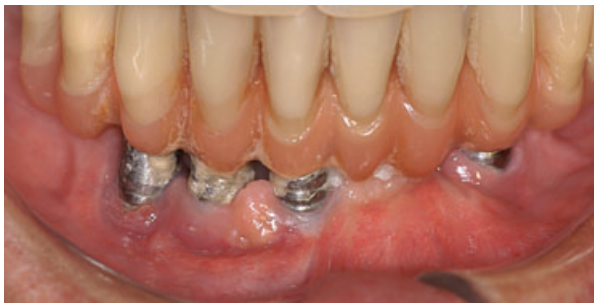

Fig. 24-6 Clinical symptoms of peri-implantitis. Note the large amounts of plaque and calculus and visible signs of inflammation in the peri-implant mucosa.

sites appears also to be symmetric, i.e. similar amount of bone loss occur at mesial, distal, buccal, and lingual aspects of the implants. On the other hand, the morphology of the osseous defect may vary depending on the horizontal dimension of the alveolar ridge. Thus, in sites where the buccal–lingual width of the ridge exceeds that of the peri-implantitis lesion, a buccal and lingual bone wall may remain. Conversely, in sites with a narrow ridge the buccal and lingual bone will be resorbed and lost during progression of peri-implantitis.

Conclusion

Symptoms of peri-implantitis relate to the infectious/inflammatory nature of the lesion. Thus, there is radiographic evidence of bone loss and the bone loss often has the shape of a crater. Swelling and redness of the mucosa as well as bleeding on gentle probing occur. Suppuration is also a frequent finding. The implant may remain stable over long periods.

Prevalence

Previous estimates of the prevalence of peri-implantitis were based on reports describing varying

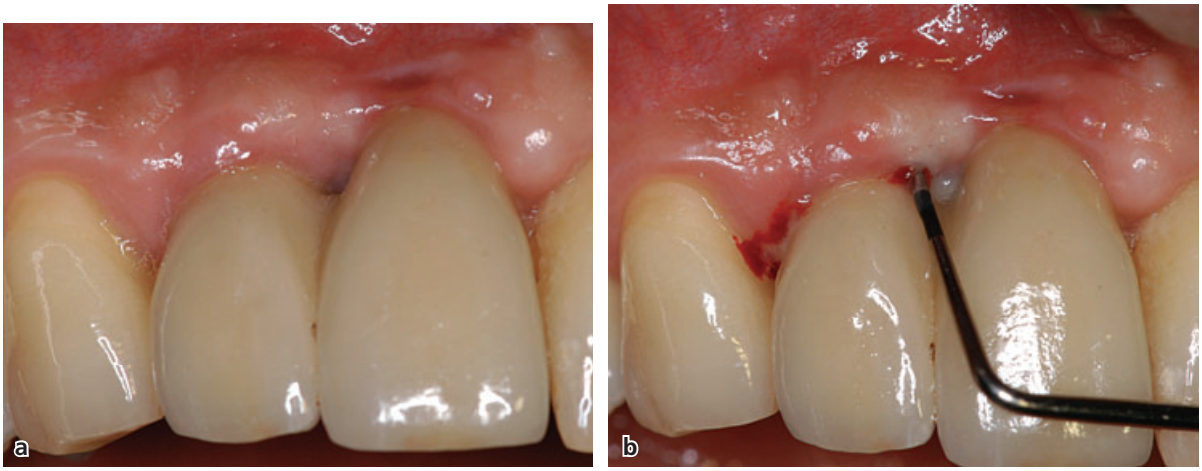

Fig. 24-7 Clinical photograph from two implant-supported crowns in the lateral (12) and central (11) incisor positions. (a) No or minor signs of inflammation in the surrounding mucosa. (b) Probing resulted in bleeding and suppuration from the implant site in the lateral incisor position.

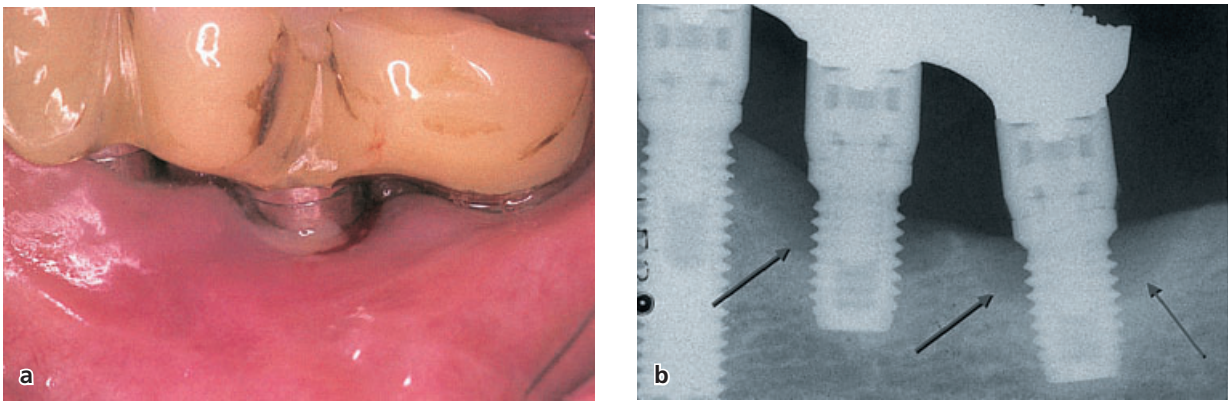

Fig. 24-8 Clinical (a) and radiographic (b) characteristics of two implant sites with peri-implantitis in the left side of the mandible. Note the presence of swelling and suppuration in the peri-implant mucosa (a) and the crater-formed bone destruction around the implants in the radiograph (arrows) (b).

frequencies of implant failures that were associated with high plaque scores or severe signs of inflammation (van Steenberge *et al*. 1993; Weyant & Burt 1993; Weyant 1994; Esposito *et al*. 1998). Other criteria were used by Mombelli and Lang (1998) and Brägger *et al*. (2001) and it was suggested that the prevalence of peri-implantitis may vary between 5 and 10% among implants.

The difficulty of retrieving information on the prevalence of peri-implantitis was confirmed in a systematic review by Berglundh *et al*. (2002). They evaluated the incidence of biologic and technical complications in implant therapy reported in prospective longitudinal studies of at least 5 years. From the 1310 titles and abstracts provided by the search in databases, 159 studies were selected for full-text analysis, out of which 51 studies were used for meta-analysis. Implant loss was the most frequently reported type of complication, while information regarding peri-implantitis and pronounced bone loss was only provided in 40–50% of the studies. The limited information on the incidence of peri-implantitis was explained by the fact that the term peri-implantitis, with the definition by Albrektsson and Isidor (1994) referred to above, was included in only a few studies. The inability to use information on the incidence of peri-implantitis and the occurrence of pronounced bone loss at implants was also due to the lack of data describing frequency distributions of various probing depths and amount of radiographic bone loss.

It is important to use appropriate terms in clinical reports to avoid confusion. Peri-implantitis is a clinical condition and should not be mistaken for implant failure. If left untreated, however, peri-implantitis may progress and lead to implant loss. The term failure should thus be avoided and terms referring to peri-implant disease (peri-implant mucositis and peri-implantitis) should be used for implants in function. Implant loss is consequently the term to use for implants that were lost or removed. In a consensus report from the 4th European Workshop on Periodontology, Lang *et al*. (2002) suggested that authors should avoid the terms implant success and failure

and report data on implant survival in combination with incidence of complications. It was also recommended that data should be provided on a subject basis. The majority of publications in implant dentistry, however, describe results based on number or proportions of implants. This information is of limited value for the clinician and, hence, data that relate the outcome of treatment for the patient under examination should be required.

Recently subject-based data on peri-implantitis were presented. Fransson *et al*. (2005) evaluated the prevalence of subjects with progressive bone loss at implants with a function time of at least 5 years. Radiographs of 1346 patients who had attended annual follow-up visits at the Brånemark Clinic, Göteborg, Sweden were retrieved. 662 subjects fulfilled the inclusion criteria. Implants that had suffered bone loss amounting to three or more threads of an implant were identified. Progressive bone loss at implants in the study was defined as bone loss occurring between the 1-year examination and the 5 or more years of follow-up examination. It was reported that 27.8% (184) of the 662 included subjects had one or more implants with "progressive" bone loss. A logistic regression analysis revealed that the individuals in this group carried a significantly larger number of implants than the subjects in whom no implants with progressive loss were detected (6 vs. 4.8). Furthermore, >30% of the subjects in the group with progressive bone loss had three or more identified implants and about 33% of all such implants in this group exhibited extensive bone loss. Out of the total 3413 implants included in the study, 423 implants (12.4%) demonstrated progressive bone loss. Fransson *et al*. (2005) concluded that the prevalence of progressive bone loss at implants assessed from subject-based data is higher than that evaluated from implant-based data. In a subsequent clinical study Fransson *et al*. (2007) reported that about 94% of the implants with "progressive" bone loss exhibited BoP. Thus, according to the definition of peri-implantitis presented in this chapter, the findings in the study by Fransson *et al*. (2005) suggest that the prevalence of subjects with peri-implantitis within this implant population was about 28%.

Roos-Jansåker *et al*. (2006b) examined 216 implant-treated patients (Brånemark System®) after 9–14 years of function and reported that 16% of the subjects and 6.6% of the implants had peri-implantitis. Roos-Jansåker *et al*. (2006b), however, used a modified definition of peri-implantitis and suggested that a certain amount of bone loss (≥1.8 mm compared with the 1-year data) together with the finding of BoP was required for the diagnosis *peri-implantitis*. It should be pointed out, however, that the prevalence of implants with peri-implantitis in the study by Roos-Jansåker *et al*. (2006b) would be >43% if normal criteria for peri-implantitis, i.e. bone loss and BoP, were applied.

Conclusion

The majority of clinical studies reported in the literature did not provide sufficient data on the prevalence of peri-implant mucositis and peri-implantitis. Results from recent publications, however, indicate that both peri-implant mucositis and peri-implantitis are common disorders. The prevalence of subjects with peri-implantitis in more recent studies varied between 25 and 45%.

Histopathology

Microscopic examinations of tissues harvested from peri-implantitis sites in humans consistently revealed that the mucosa contained large inflammatory cell infiltrates. Sanz *et al*. (1991) analyzed soft tissue biopsies from six patients with peri-implantitis and reported that 65% of the connective tissue portion was occupied by an inflammatory lesion. Piattelli *et al*. (1998) described some pathological features of tissues harvested from 230 retrieved implants. It was reported that at sites where implants were removed due to peri-implantitis, "an inflammatory infiltrate, composed of macrophages, lymphocytes and plasma cells, was found in the connective tissue around the implants". In a study including 12 human peri-implantitis lesions, Berglundh *et al*. (2004) found that the mucosa contained very large lesions in which numerous plasma cells, lymphocytes, and macrophages were present (Fig. 24-9). It was furthermore observed that the inflammatory cell infiltrate consistently extended to an area apical to the pocket epithelium and that the apical part of the soft tissue lesion frequently reached the bone tissue. Berglundh *et al*. (2004) also reported that numerous neutrophil granulocytes (PMN cells) were present in the lesions. Such cells occurred not only in the pocket epithelium and associated areas of the lesions, but also in perivascular compartments in the center of the infiltrate, i.e. distant from the implant surface. In the apical part of the lesion the inflamed connective tissue appeared to be in direct contact with the biofilm on the implant surface. Gualini and Berglundh (2003) included six subjects in a study and used immunohistochemical techniques to analyze the composition of peri-implantitis. PMN cells were found in large numbers in the central portions of the infiltrate. This finding was in agreement with observations made by Hultin *et al*. (2002). They analyzed the exudate that could be harvested from implant sites in 17 patients with peri-implantitis and reported the presence of large numbers of PMN cells.

Experimental models

In order to study the ability of the peri-implant mucosa to respond to long-standing plaque exposure and to manage the associated inflammatory lesions, an experimental periodontitis/peri-implantitis model was developed in the dog (Lindhe *et al*. 1992) and in

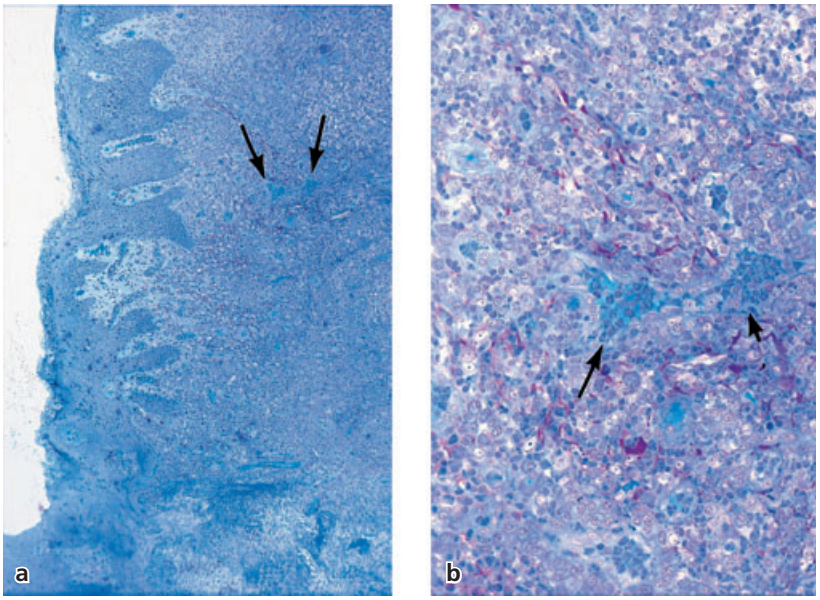

Fig. 24-9 (a) Microphotograph illustrating a human peri-implantitis lesion. Note the large inflammatory infiltrate lateral to the pocket epithelium. The implant was positioned to the left. (b) Arrows indicate vascular units illustrated in a larger magnification.

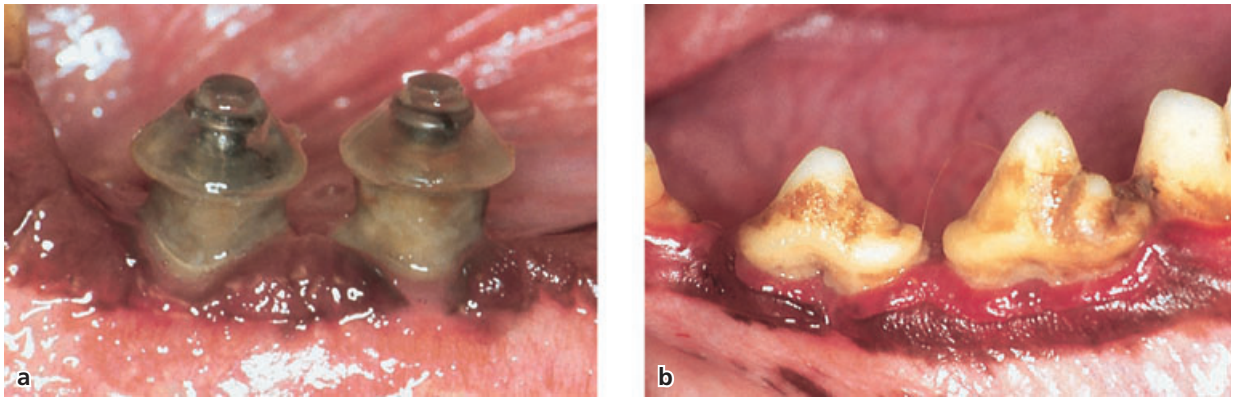

Fig. 24-10 (a) A clinical view describing features of experimental peri-implantitis in the beagle dog. (b) A clinical view describing features of experimental periodontitis in the beagle dog.

the monkey (Lang *et al*. 1993; Schou *et al*. 1993). Although the experiments had somewhat varying design, the outcome of the studies was almost identical and, hence, only the result from the dog model will be reported.

In the *dog model*, the premolars were extracted in one side of the mandible, fixtures (Brånemark system®) were inserted and abutment connection performed 3 months later as described above (Berglundh *et al*. 1991). During the healing phase a strict plaque control regimen was maintained and healthy tissue conditions were thereby established in all tooth and implant sites to be monitored. On a given day, the periodontitis and peri-implantitis lesions were induced. This was accomplished by (1) terminating the plaque control regimen and (2) placing cotton floss ligatures around the neck of both the premolar teeth and the implants. The ligatures were forced into a position apical to the soft tissue margins. A "pocket" between the tooth/gingiva and implant/mucosa was thereby created, a submarginal microbiota rapidly formed, and inflammatory lesions developed in the neighboring tissues. Radiographs obtained after 6 weeks of the experiment revealed that a substantial amount of bone tissue had been lost at both teeth and implant sites. The ligatures were removed. After another 4 weeks, the animals were re-examined (Fig. 24-10), radiographs obtained, bacteria sampled, and biopsies of tooth and implant sites harvested.

It was observed that the plaque that had formed in the deep "pockets" was similar at tooth and implant sites and was dominated by Gram-negative and anaerobic species (Leonhardt *et al*. 1992). This observation is consistent with findings indicating that, in humans, the microbiota at teeth and implants has many features in common but also that the microbiota at healthy and diseased sites – tooth sites as well as implant sites – is very different. Thus, implants and teeth that are surrounded by healthy soft tissues are associated with biofilms including small amounts of Gram-positive coccoid cells and rods. Sites with extensive periodontal and peri-implant inflammation harbor biofilms with large numbers of

Gram-negative anaerobic bacteria (for review see Mombelli 1999).

The histopathologic examination of the biopsy samples from the dog study (Lindhe *et al*. 1992) revealed that there were marked differences in the size and location of the inflammatory lesions of the two sites. Thus, while the lesions in the periodontal sites (Fig. 24-11) were consistently separated from the alveolar bone by a zone, about 1 mm high, of uninflamed connective tissue, the lesion in the peri-implant tissue in most situations extended into and involved the marrow spaces of the alveolar bone. It was concluded that the pattern of spread of inflammation was different in periodontal and peri-implant tissues. The lesions in plaque-associated periodontitis were limited to the connective tissue, while in the peri-implant tissues the lesions extended to the alveolar bone (Fig. 24-12).

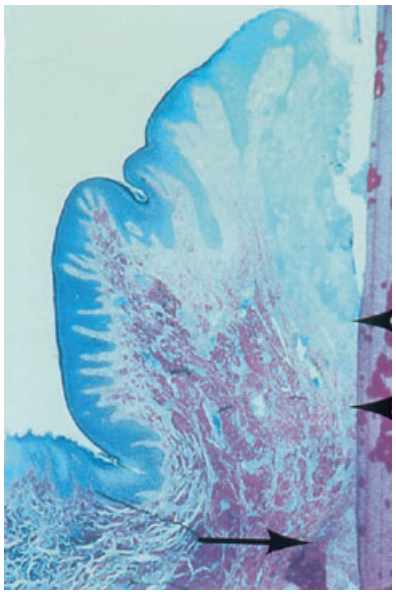

Fig. 24-11 Microphotograph (buccal–lingual section) illustrating a periodontitis lesion. Note the apical extension of the infiltrate (arrow) but also the presence of a zone of normal connective tissue between the infiltrate and the bone crest (arrow).

It was suggested that the peri-implant tissues, in variance with the periodontal tissues, are poorly organized to resolve progressive, plaque-associated lesions. The validity of this conclusion was substantiated in subsequent studies (Marinello *et al*. 1995; Ericsson *et al*. 1996; Persson *et al*. 1996; Gotfredsen *et al*. 2002), using similar models but allowing for different periods of tissue breakdown.

It was also reported that peri-implantitis lesions, which initially were experimentally induced by ligatures as reported above, could spontaneously progress after the removal of the ligatures. Thus, Zitzmann *et al*. (2004) prepared 21 sites with ligature-induced experimental peri-implantitis in five Labrador dogs. After the lesions had become established, the ligatures were removed and the sites were monitored for an additional 12-month interval. It was observed that in 16 sites the aggressive peri-implantitis conditions persisted and caused continuous bone loss. In the remaining five sites, however, the lesions became encapsulated and no further breakdown of peri-implant bone took place. Using a similar model, Berglundh *et al*. (2007) evaluated progression of peri-implantitis at implants with different surface roughness. Experimental peri-implantitis was induced at implants with either a sandblasted acid-etched surface (SLA) or a polished surface. The ligatures were removed when about 40% of the height of the supporting bone had been lost and plaque accumulation continued during an additional 5 months. It was reported that following ligature removal the progression of bone loss was larger at SLA than at

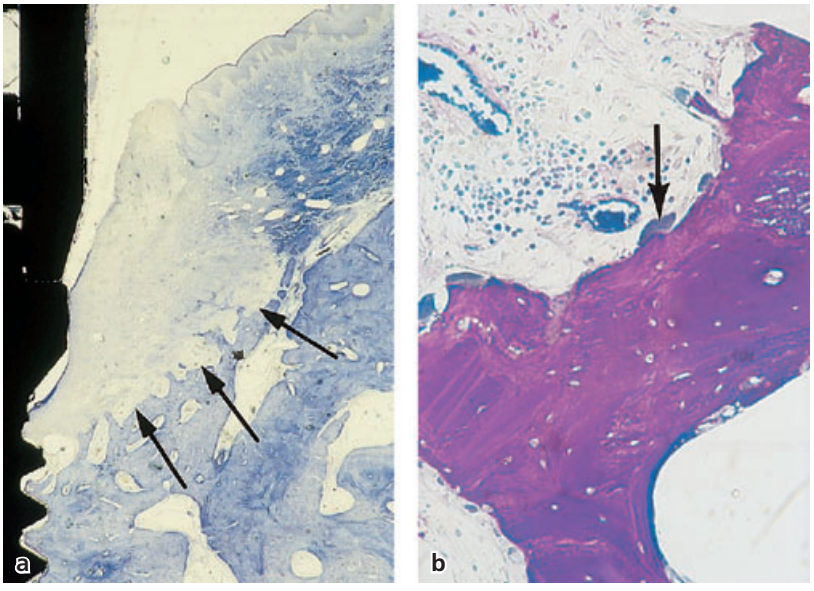

Fig. 24-12 (a) Ground section illustrating a peri-implantitis lesion. The implant is positioned to the left and the apical portions of the infiltrate (arrows) extend into contact with the bone. (b) Close-up of (a) illustrating the presence of inflammatory cells and osteoclasts (arrow) on the bone surface.

polished sites. The histologic examination revealed that both bone loss and the size of the inflammatory lesion in the connective tissue were larger in SLA than in polished implant sites. The area of plaque was also larger at implants with a SLA surface than at implants with a polished surface. It was concluded that the progression of peri-implantitis, if left untreated, is more pronounced at implants with a moderately rough surface than at implants with a polished surface.

Conclusion

Peri-implantitis lesions are poorly encapsulated, extend to the marginal bone tissue and may, if they are allowed to progress, lead to the loss of the implant. The large numbers of neutrophils in the peri-implantitis lesion and the absence of an epithelial lining between the lesion and the biofilm, indicate that the peri-implantitis lesions have features that are different from those of periodontitis lesions. Progression of peri-implantitis is more pronounced at implants with rough than at smooth surfaces.

Summary

Studies in man and experiments in animals have documented that *de novo* formation of a biofilm on the implant surface initiates a host response that involves the establishment of an inflammatory lesion in the peri-implant mucosa (peri-implant mucositis). This lesion is initially located in the connective tissue immediately lateral to the barrier epithelium and is, in many respects, similar to that which develops in the gingiva when plaque forms on adjacent tooth surfaces. In the continued presence of a submarginal biofilm, the lesion in the marginal mucosa around implants may occasionally spread in an "apical" direction to involve the hard tissue, compromise osseointegration, cause varying degrees of marginal bone loss (peri-implantitis), and eventually the loss of the implant.

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Part 8: Tissue Regeneration

Chapter 25

Concepts in Periodontal Tissue Regeneration

Thorkild Karring and Jan Lindhe

Introduction

At risk assessment in periodontal patients, the presence of sites with a residual pocket depth ≥6 mm after active treatment plays a significant role in predicting future periodontal destruction (Haffajee *et al*. 1991; Grbic & Lamster 1992; Claffey & Egelberg 1995). Thus, an important goal of periodontal therapy is to obtain a reduced pocket depth after treatment in order to prevent further disease progression. Usually, this goal can be accomplished by non-surgical therapy in patients with moderate periodontitis, whereas in severe cases, particularly in the presence of intrabony defects and furcations, the treatment must be supplemented with periodontal surgery. A fundamental objective of periodontal surgery is to provide access for proper instrumentation and cleaning of the root surface; in addition, most surgical procedures result in the elimination or the reduction of the soft tissue component of the periodontal pocket. Generally, the elimination of deep pockets is achieved by gingivectomy or apical displacement of raised tissue flaps, sometimes associated with bone contouring. In recent years, however, the use of regenerative procedures aimed at restoring the lost periodontal support has become more common.

Periodontal treatment, both surgical and non-surgical, results in recession of the gingival margin after healing (Isidor *et al*. 1984). In severe cases of periodontitis, this may lead to poor esthetics in the front areas of the dentition, in particular when applying surgical procedures including bone contouring for the eradication of bone defects. Treatment of such cases without bone contouring, on the other hand, may result in residual pockets inaccessible to proper cleaning during post-treatment maintenance. These problems can be avoided or reduced by applying regenerative surgical procedures by which the lost periodontal attachment in the bone defects can be restored. Thus, the indication of applying regenerative periodontal therapy is often based on esthetic considerations, besides the fact that the function or long-term prognosis of the treated teeth may be improved.

Localized gingival recession and root exposure may represent an esthetic problem to the patient, and it is often associated with root sensitivity. Such a situation is an indication to apply regenerative periodontal therapy to obtain root coverage in order to improve esthetics and reduce root sensitivity. Successful root coverage implies regeneration of the attachment apparatus on the exposed root surface including cementum with inserting collagen fibers, as well as an esthetically acceptable restoration of the anatomy of the mucogingival complex.

Another indication for regenerative periodontal therapy is furcation-involved teeth. The furcation area is often inaccessible to adequate instrumentation and frequently the roots present concavities and furrows which make proper cleaning of the area after resective surgery impossible. Considering the long-term results and complications reported following

treatment of furcation involvements by traditional resective therapy (Hamp *et al*. 1975; Bühler 1988), it is reasonable to anticipate that the long-term prognosis of furcation-involved teeth can be improved considerably by successful regenerative periodontal therapy.

Case reports also exist demonstrating that "hopeless" teeth with deep vertical defects, increased tooth mobility or through-and-through furcations can be successfully treated with regenerative periodontal therapy (Gottlow *et al*. 1986). However, controlled clinical trials or serial case reports presenting a reasonable predictability of treating such advanced cases are not available.

Regenerative periodontal surgery

Regenerative periodontal therapy comprises procedures which are specially designed to restore those parts of the tooth-supporting apparatus which have been lost due to periodontitis. Regeneration is defined as a reproduction or reconstruction of a lost or injured part in such a way that the architecture and function of the lost or injured tissues are completely restored (Glossary of Periodontal Terms, 1992). This means that the attachment of the tooth has been regenerated when new cementum with inserting collagen fibers has formed on the detached root surface, while regeneration of the periodontal supporting apparatus (periodontium) also includes re-growth of the alveolar bone. Procedures aimed at restoring lost periodontal support have also been described as "reattachment" or "new attachment" procedures.

The term "reattachment" was used to describe the regeneration of a fibrous attachment to a root surface surgically or mechanically deprived of its periodontal ligament tissue, whereas the term "new attachment" was preferred in the situation where the fibrous attachment was restored on a root surface deprived of its connective tissue attachment due to the progression of periodontitis. Research findings, however, indicate that there is no difference regarding the possibility of restoring a connective tissue attachment, whether this has been lost because of periodontal disease or mechanically removed (Nyman *et al*. 1982; Isidor *et al*. 1985). Therefore, it was suggested that the term "new attachment" should be used to describe the formation of new cementum with inserting collagen fibers on a root surface deprived of its periodontal ligament tissue, whether or not this has occurred because of periodontal disease or by mechanical means, and that the term "reattachment" should be confined to describing the reunion of surrounding soft tissue and a root surface with preserved periodontal ligament tissue (Isidor *et al*. 1985).

Periodontal regeneration has been reported following a variety of surgical approaches involving root surface biomodification, often combined with coronally advanced flap procedures, the placement of bone grafts or bone substitute implants, or the use of organic or synthetic barrier membranes (guided tissue regeneration). However, many cases that clinically are considered successful, including cases with significant regrowth of alveolar bone, may histologically show an epithelial lining along the treated root surface instead of deposition of new cementum (Listgarten & Rosenberg 1979).

Successful regeneration is assessed by periodontal probing, radiographic analysis, direct measurements of new bone, and histology. Although histology remains the ultimative standard in assessing true periodontal regeneration, periodontal probing, direct bone measurements, and radiographic measurements of osseous changes are used in the majority of studies of regenerative therapy (Reddy & Jeffcoat 1999).

At the American Academy of Periodontology World Workshop in Periodontics in 1996, the fulfillment of the following criteria was required in order for a periodontal regenerative procedure to be considered as a therapy which can encourage regeneration:

- Human histologic specimens demonstrating formation of new cementum, periodontal ligament, and bone coronal to a notch indicating the apical extension of the periodontitis-affected root surface.
- Controlled human clinical trials demonstrating improved clinical probing attachment and bone.
- Controlled animal histologic studies demonstrating formation of new cementum, periodontal ligament, and bone.

In addition, however, it seems reasonable to require that a regenerative procedure is based on a biological concept which can explain why the treatment results in periodontal regeneration on the basis of current knowledge about periodontal wound healing.

Periodontal wound healing

Regeneration of the periodontium must include the formation of new cementum with inserting collagen fibers on the previously periodontitis-involved root surfaces and the regrowth of the alveolar bone. However, whether regrowth of alveolar bone should always be considered a requirement for success following regenerative periodontal surgery is a matter of discussion. The basis for this discussion is that a fibrous attachment may exist without opposing bone in a normal dentition, not affected by periodontitis, in the presence of bone dehiscenses and fenestrations (see Fig. 1-74).

In 1976, Melcher suggested in a review paper that the type of cell which repopulates the root surface after periodontal surgery determines the nature of the attachment that will form. After flap surgery the

curetted root surface may be repopulated by four different types of cell (Fig. 25-1):

1. Epithelial cells
2. Cells derived from the gingival connective tissue
3. Cells derived from the bone
4. Cells derived from the periodontal ligament.

Previously, in most attempts to restore lost tooth support, particular attention was directed towards the regeneration of the alveolar bone. An investigation was carried out in dogs in order to examine the relationship between the re-establishment of a connective tissue attachment to the root surface and the regrowth of alveolar bone (Nyman & Karring 1979). After elevation of mucoperiostal flaps, the marginal 5–7 mm of the buccal alveolar bone of each experimental tooth was removed (Fig. 25-2). During this procedure, care was taken to minimize the mechanical injury to the connective tissue attachment on the root surface. Prior to flap closure, a notch, serving as a landmark for the histologic measurements, was prepared in the root surface at the level of the surgically reduced bone crest. After 8 months of healing, the animals were sacrificed. Histologic analysis demonstrated that although a connective tissue attachment was re-established consistently on the roots, the amount of bone regeneration varied widely. In some roots, bone regrowth was negligible (Fig. 25-3), whereas in others the bone had regenerated to its normal level. These results demonstrated that the amount of bone regrowth is unrelated to the re-establishment of a connective tissue attachment.

Another experiment was carried out in monkeys (Lindhe *et al*. 1984), in order to examine whether the presence of bone may stimulate the formation of a new connective tissue attachment. Mandibular and maxillary incisors were extracted and re-implanted

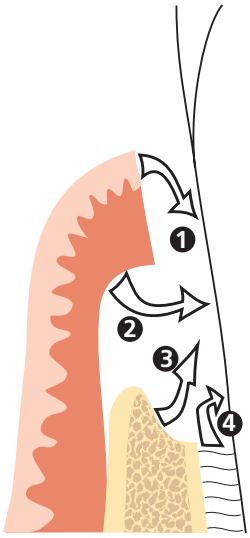

Fig. 25-1 Following flap surgery, the curetted root surface may be repopulated by (1) epithelial cells, (2) gingival connective tissue cells, (3) bone cells, or (4) periodontal ligament cells.

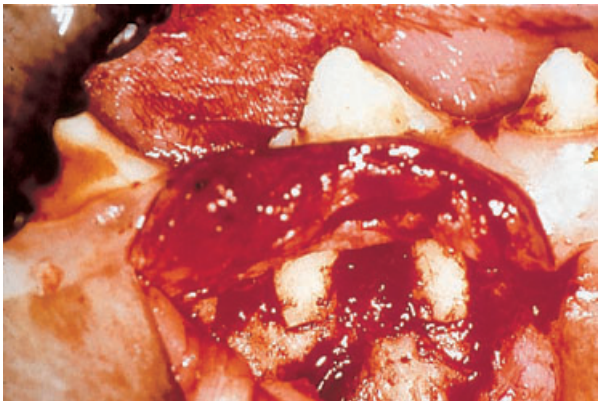

Fig. 25-2 Following flap elevation, the buccal bone, including a part of the inter-radicular and interproximal alveolar bone, is removed without injuring the connective tissue attachment on the root surface.

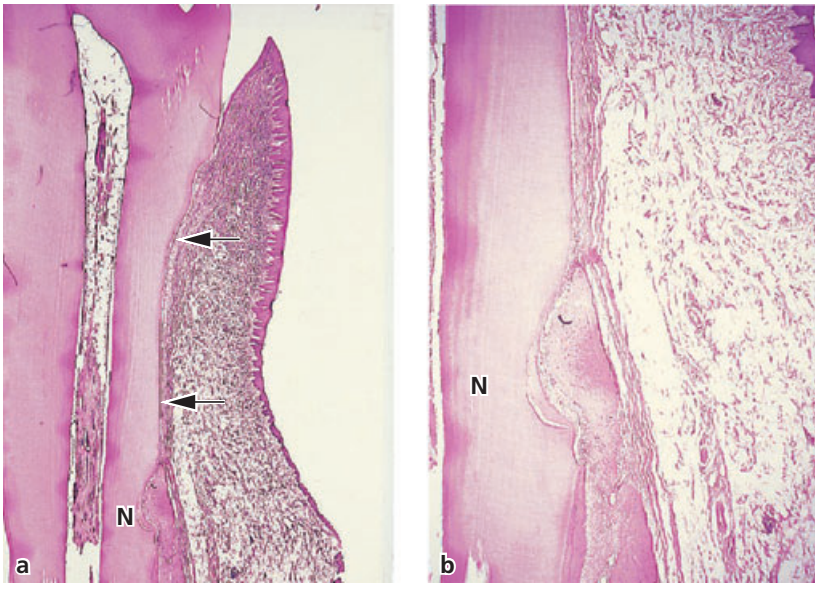

Fig. 25-3 (a) Microphotograph of specimen 8 months following bone removal. A connective tissue attachment is re-established (arrows). Bone regeneration is negligible and is confined to the notch (N) in the root surface. (b) Higher magnification of the newly formed bone in the notch area (N).

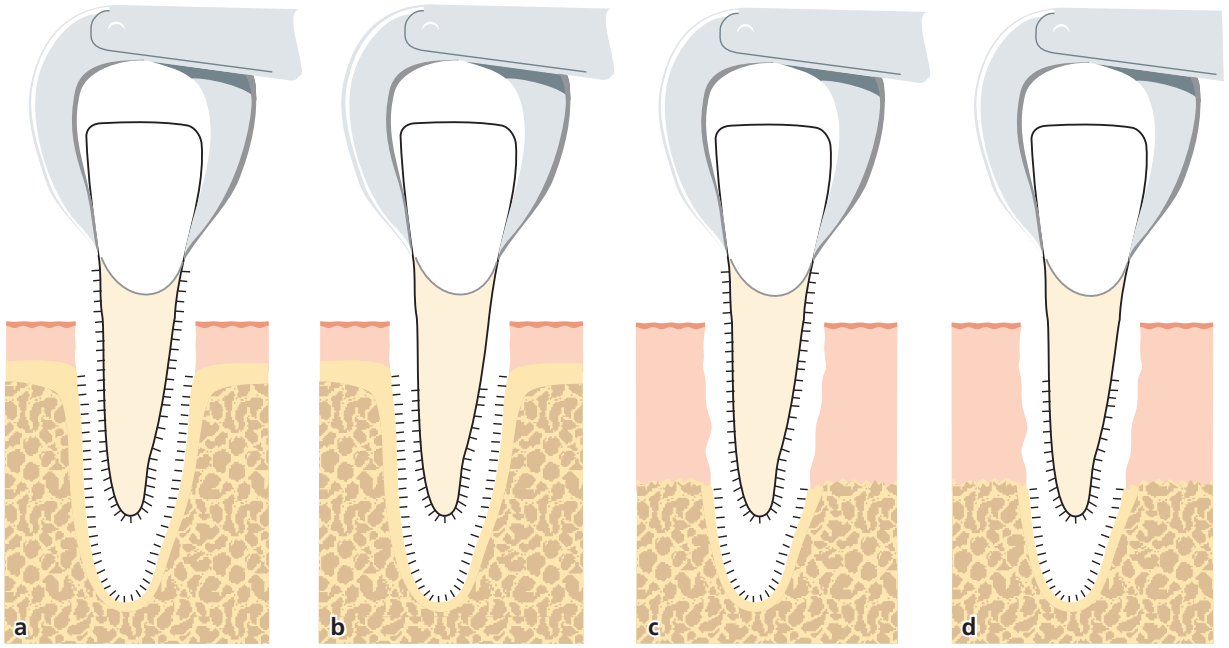

Fig. 25-4 Schematic drawing showing the four experimental conditions (a–d) under which experimental teeth were extracted and re-implanted in their own sockets.

in their own sockets under the following four experimental conditions (Fig. 25-4):

1. Non-root-planed teeth were re-implanted into sockets with normal bone height.
2. Teeth, root planed in their coronal portion, were re-implanted into sockets with normal bone height.
3. Non-root-planed teeth were re-implanted into sockets with a reduced bone height.
4. Teeth, root planed in their coronal portion, were re-implanted into sockets with reduced bone height.

Histologic examination after 6 months of healing revealed that a fibrous reunion was established in areas where the periodontal connective tissue attachment was retained at the time of re-implantation. However, in areas, where the periodontal ligament tissue was removed, the epithelium had always migrated to the apical extension of root instrumentation (Fig. 25-5). These results of healing occurred irrespective of the presence or absence of bone, indicating that the establishment of a connective tissue attachment is unrelated to the presence of alveolar bone.

Using orthodontic appliances, Karring *et al*. (1982) tilted maxillary second and third incisors in labial direction in dogs. Subsequently, these teeth were moved back to their original position. During the same period the contralateral incisors were moved to a labially deviated position. The orthodontic appliances were then used to retain the teeth in these positions for a period of 5 months before sacrifice of the animals. Histologic analysis demonstrated that in all experimental teeth, the apical termination of the junctional epithelium was at the cemento-enamel junction. In the teeth which were retained in their labially displaced position, the level of the alveolar bone was reduced to a position about 4.5 mm apical to the cemento-enamel junction (Fig. 25-6a), while in the teeth which were moved back to their original position, the alveolar bone crest was located at a normal level relative to the cemento-enamel junction (Fig. 25-6b). This experiment demonstrated that bone resorption or bone regeneration may be induced by orthodontic forces on teeth with a pristine connective tissue attachment. The experiments described above indicate that the re-establishment of a connective tissue attachment to the root surface and the regeneration of the alveolar bone are not related to each other.

The use of bone grafts in regenerative periodontal therapy is based on the assumption that the promotion of bone regrowth may also induce cells in the bone to produce a new cementum layer with inserting collagen fibers on previously periodontitis-involved root surfaces. However, histologic studies in both humans and animals have demonstrated that grafting procedures often result in healing with a long junctional epithelium rather than a new connective tissue attachment (Caton & Zander 1976; Listgarten & Rosenberg 1979; Moscow *et al*. 1979).

Ellegaard *et al*. (1973, 1974, 1975, 1976) and Nielsen *et al*. (1980) reported that grafting materials in periodontal bony defects may be:

1. Osteoproliferative (osteogenetic), which means that new bone is formed by bone-forming cells contained in the grafted material.
2. Osteoconductive, which means that the grafted material does not contribute to new bone forma-

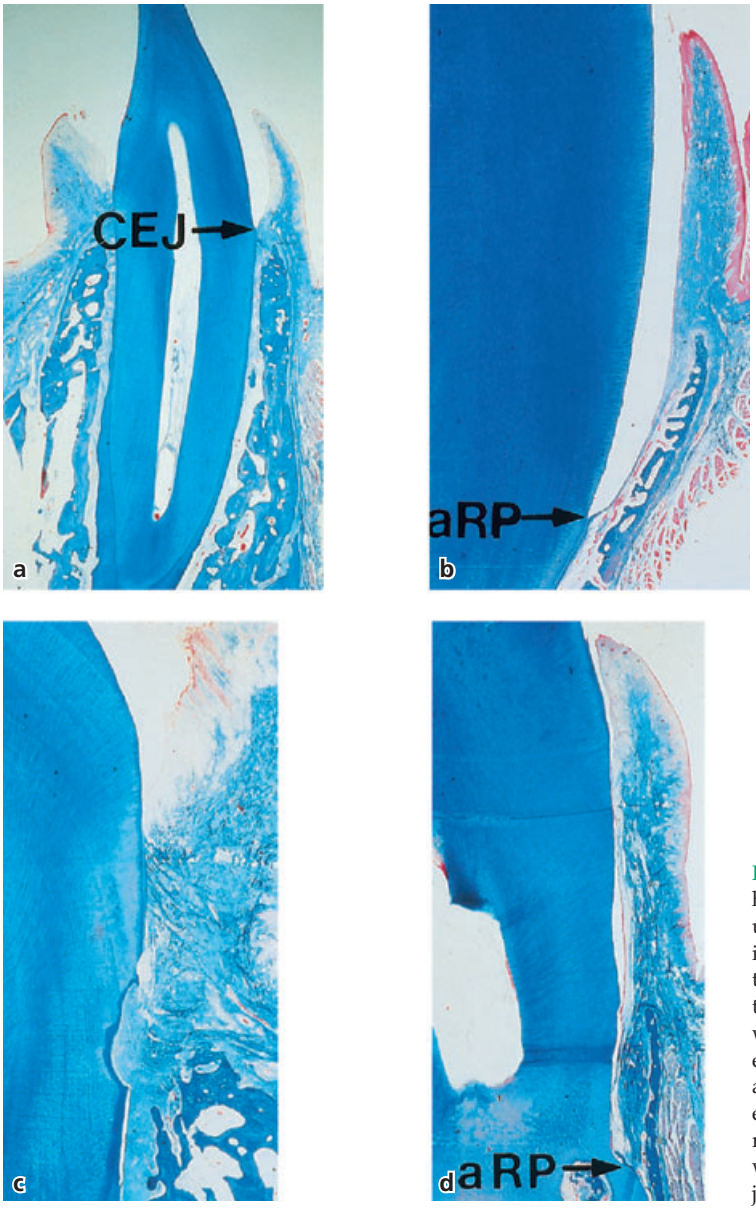

Fig. 25-5 Microphotographs showing the histological features after 6 months of healing, under the four experimental conditions (a–d) illustrated in Fig. 25-4. The teeth in (b) and (d) are those root planed in their coronal portion, and the teeth (a) and (b) are those re-implanted in sockets with normal bone height. A fibrous reunion was established in areas where the connective tissue attachment was retained (a and c) while the epithelium has migrated to the apical extension of root instrumentation (a RP) where the attachment was removed (b and d). CEJ = cemento-enamel junction.

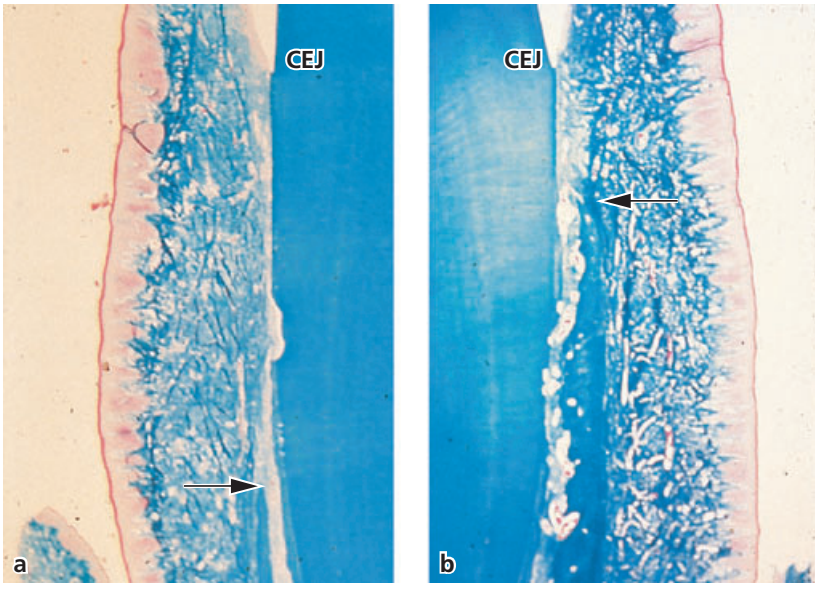

Fig. 25-6 Microphotograph of a tooth retained in its labially displaced position (a) and a tooth (b) moved back to its original position. The level of alveolar bone (arrow) is reduced in (a) while it has regenerated to its normal level (arrow) in (b). The apical termination of the junctional epithelium is at the cemento-enamel junction (CEJ) in both situations.

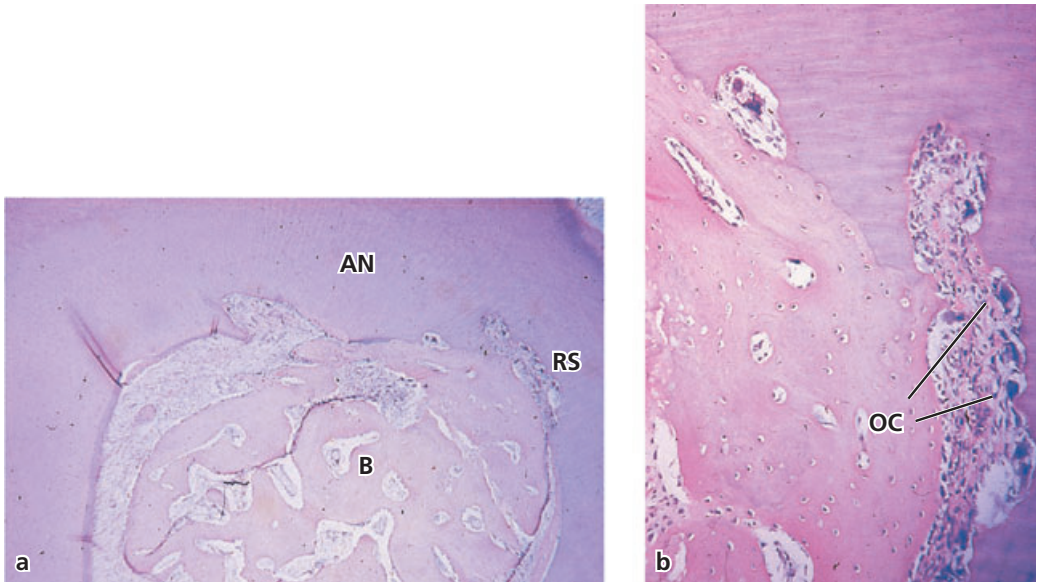

Fig. 25-7 (a) Microphotograph of furcation 6 weeks after grafting with iliac crest marrow. The furcation is completely filled with bone (B), but ankylosis (AN) and root resorption (RS) can be seen. (b) Higher magnification of the area in (a) showing ankylosis and resorption. OC = osteoclasts.

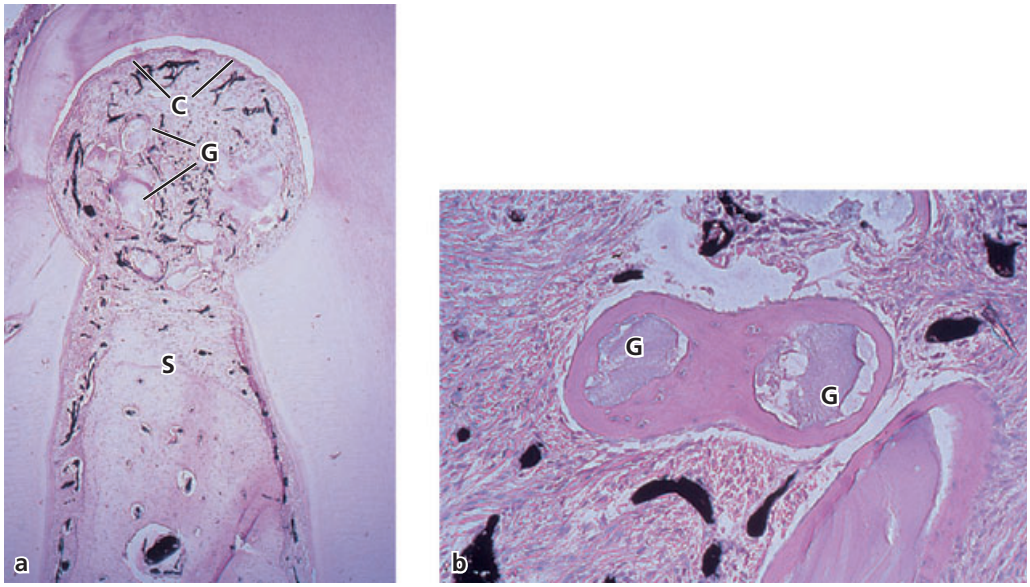

Fig. 25-8 (a) Microphotograph of a healed bifurcation defect following transplantation of non-vital bone grafts. The grafts (G) have not been reached by bone formation from the interradicular septum (S), but occur as isolated particles surrounded by "cementum". Cementum (C) and new connective tissue attachment formation have taken place along the entire circumference of the bifurcation. (b) High magnification of isolated bone grafts (G) with newly formed "cementum" on the surface.

tion *per se* but serves as scaffold for bone formation originating from adjacent host bone.

3. Osteoinductive, which means that bone formation is induced in the surrounding soft tissue immediately adjacent to the grafted material.

These studies, where various types of bone graft were placed in intrabony defects or inter-radicular lesions, revealed that cells survived transplantation only in iliac bone marrow grafts. Transplantation of iliac bone marrow grafts almost consistently resulted in bone fill in the experimental defects, but healing was frequently accompanied by ankylosis and root resorption (Fig. 25-7). The iliac bone marrow grafts exerted an osteogeneic effect, and it was suggested that this was responsible for the induction of root resorption (Ellegaard *et al*. 1973, 1974). Jaw bone grafts and xenografts did not actively contribute to bone formation but served as a scaffold for bone regeneration (i.e. osteoconductive effect). Often, however, these bone grafts were not reached by the new bone growing out from the host bone, but occurred as isolated particles surrounded by a bone-like or cementum-like substance (Fig. 25-8). It was

found that the treated bifurcation defects became filled mainly with granulation tissue derived from the periodontal ligament (Fig. 25-9). The authors (Nielsen *et al*. 1980) suggested that this invasion of ligament tissue inhibited bone formation and that the new cementum on the root surface in the bifurcation defects, including the cementum-like substance observed around the implanted bone particles, was formed by periodontal ligament cells (Fig. 25-8). Thus, it appeared from these studies that the key cells in periodontal regeneration are periodontal ligament cells rather than bone cells.

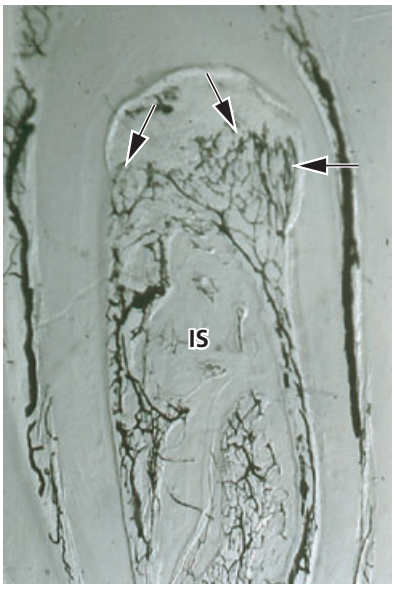

Fig. 25-9 Cleared specimen from a 1-week-old bifurcation defect treated with bone grafts. Judged from the course of the blood vessels, the granulation tissue in the defect has developed mainly from the periodontal ligament (arrows) and only to a minor extent from the inter-radicular septum (IS).

Regenerative capacity of bone cells

The ability of newly formed tissue originating from bone to produce a new connective tissue attachment was examined in a study by Karring *et al*. (1980). Roots of periodontitis-affected teeth were extracted and placed in surgically created sockets in edentulous areas of dogs. The implanted roots were covered with tissue flaps (submerged) and the results of healing were examined histologically after 3 months. A periodontal ligament was re-established in the apical portion of the re-implanted roots where, at the time of implantation, remnants of periodontal ligament tissue were preserved. In the coronal portion of the roots which were previously exposed to periodontitis and then scaled and planed, healing had consistently resulted in ankylosis and root resorption (Fig. 25-10). On the basis of this finding, it was concluded that tissue derived from bone lacks cells with the potential to produce a new connective tissue attachment.

Regenerative capacity of gingival connective tissue cells

Another experiment (Nyman *et al*. 1980) was carried out in order to examine the potential of gingival connective tissue to produce a new connective tissue attachment. The teeth were treated as described in the experiment above but were not transplanted into sockets. Instead they were placed in bone concavities prepared on the buccal aspect of the jaw and subsequently covered by tissue flaps. Thus, half the circumference of the roots was in contact with bone while the remaining part was facing the gingival connective tissue at the subsurface of the flaps. Histologic examination after 3 months of healing showed areas with periodontal ligament in the apical portion of the roots where, at the time of implantation,

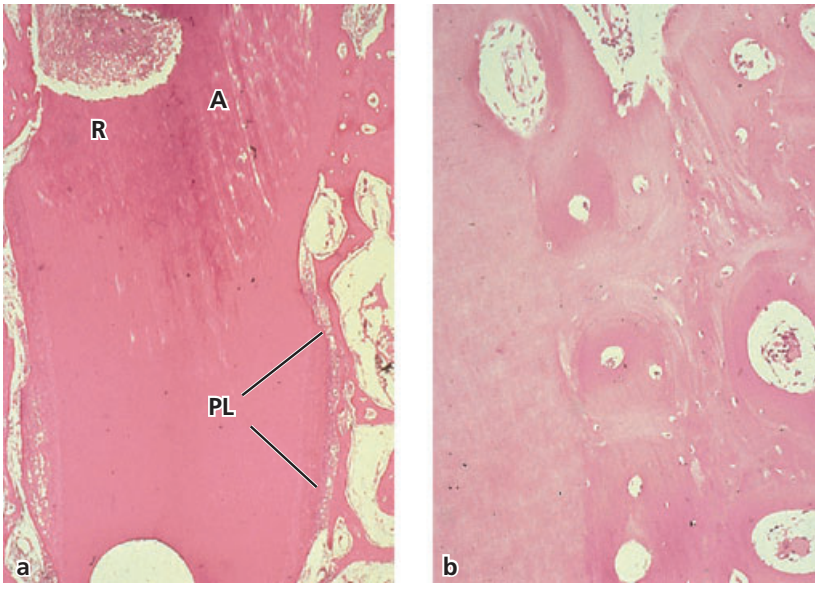

Fig. 25-10 (a) Microphotograph of a re-implanted root after 3 months of healing. A periodontal ligament (PL) has become re-established in the apical portion of the root whereas ankylosis (A) and root resorption (R) is the predominant feature in the coronal portion. (b) High magnification of the ankylosis seen in (a).

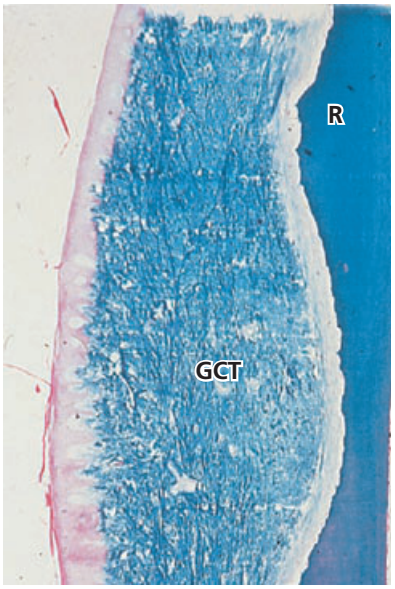

Fig. 25-11 Microphotograph of root (R) which has been re-implanted with its surface facing the gingival connective tissue (GCT). The surface exhibits extensive resorption.

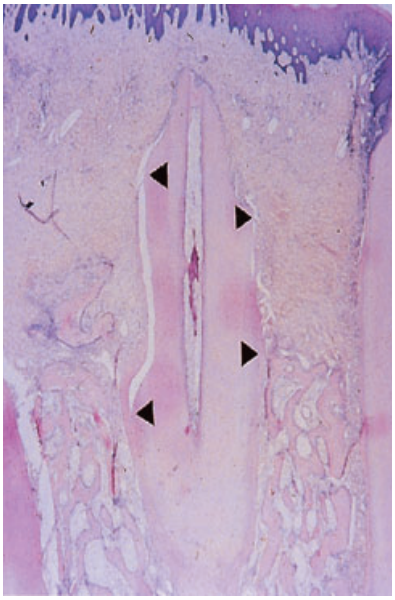

Fig. 25-12 Microphotograph showing new attachment formation (between the arrows) on a submerged root with a non-impaired periodontal ligament. Coronal to the cementum, root resorption is the predominant feature.

periodontal ligament tissue was preserved. In the coronal, previously exposed part of the roots, no signs of new connective tissue attachment were present. The root portion located in contact with gingival connective tissue demonstrated a connective tissue with fibers oriented parallel to the root surface and without attachment to the root. However, root resorption occurred at the majority of the surfaces (Fig. 25-11). On the basis of this result it was concluded that gingival connective tissue also lacks cells with the potential to produce a new connective tissue attachment.

Regenerative capacity of periodontal ligament cells

In the experiments described above, root resorption was also observed occasionally in the apical portion of the extracted and re-implanted roots (Karring *et al*. 1980; Nyman *et al*. 1980). It was suggested that this occurred because the periodontal ligament tissue retained on this part of the root had become injured during extraction, thereby allowing bone or gingival connective tissue to contact the root surface during healing and induce resorption. It was assumed that this damage of the retained periodontal ligament tissue had also restricted its potential of proliferating in the coronal direction along the root surface. Indeed, in a later study (Karring *et al*. 1985), where periodontitis-involved roots were retained in their sockets and subsequently submerged, significant amounts of new connective tissue attachment formed on the coronal portion of the roots (Fig. 25-12). The finding of new attachment only on the roots with a non-impaired periodontal ligament, but never on the extracted and re-implanted roots with an impaired ligament, indicates that periodontal ligament tissue contains cells with the potential to form a new connective tissue attachment on a detached root surface.

Active root resorption occurred consistently at the root surfaces above the coronal extension of new attachment (Fig. 25-12). It was suggested that this resorption was induced by gingival connective tissue which had proliferated apically from the covering tissue flap. Thus, only cells in the periodontal ligament seem capable of regenerating lost periodontal attachment.

The final evidence that the progenitor cells for new attachment formation reside in the periodontal ligament was provided in studies in which titanium dental implants were placed in contact with retained root tips whose periodontal ligament served as a source for cells which could populate the implant surface during healing (Buser *et al*. 1990a,b; Warrer *et al*. 1993). Microscopic analysis revealed that a distinct layer of cementum with inserting collagen fibers had formed on the surfaces of the implants (Fig. 25-13a), and that these fibers, often oriented perpendicularly to the surface, were embedded in the opposite bone (Fig. 25-13b). Control implants (Fig. 25-14) placed without contact with retained roots healed with the characteristic features of osseointegration (i.e. direct contact between bone and the implant surface).

Further proof of the ability of periodontal ligament cells to produce a new connective tissue attachment was recently provided by Parlar *et al*. (2005) using a novel and unique experimental model in dogs. After resection of the crowns of the canine teeth in the dogs, the roots were hollowed to a depth of 5 mm. leaving a thin dentinal wall. Slits were then

Fig. 25-13 (a) Microphotograph of a titanium implant placed in contact with retained root tips. A distinct cementum layer (arrows) and periodontal ligament (PL) in continuity with that on the roots (R) is visible on the implant surface. (b) High magnification in polarized light of the periodontal ligament formed around the implant seen in (a). A cementum layer (arrows) with Sharpey's fibers is present at the implant surface. Principal fibers, oriented perpendicular to the surface, are running across the ligament space (LS) and are inserting in the opposing bone (B) as in natural teeth (see Fig. 1-71).

Fig. 25-14 Microphotograph of a titanium implant placed without contact with retained roots (control). This implant has healed with a direct contact between the bone and the implant surface (osseointegration).

prepared in the cavity wall to create passages from this chamber to the surrounding periodontal ligament. A titanium implant was placed into the center of each chamber, and finally a collagen barrier was placed over the chamber before the roots were submerged. Histologic analysis after 4 months of healing revealed that a periodontal ligament, bone, and root cementum had formed between the implant and the dentinal wall of the chamber. Due to the invasion of periodontal ligament tissue through the slits into the chamber, cementum had formed on the implant as well as the dentinal wall, and a periodontal ligament was consistently interposed between the implant and the bone and between the bone and the dentinal wall. Thus, there is strong evidence that the progenitor cells for periodontal attachment formation reside in the periodontal ligament and not in the alveolar bone as previously assumed (Melcher *et al*. 1987).

Role of epithelium in periodontal wound healing

Some of the roots in the experiment described above (Karring *et al*. 1985) penetrated the covering mucosa at early stages of healing, thereby allowing the epithelium to grow apically along the root surface. The amount of new connective tissue attachment on these roots was considerably smaller than that formed on the roots which remained submerged throughout the study. This finding and those of other investigators (Moscow 1964; Kon *et al*. 1969; Proye & Polson 1982) indicate that the apical migration of epithelium reduces the coronal gain of attachment, evidently by preventing periodontal ligament cells from repopulating the root surface (Fig. 25-15).

Downgrowth of epithelium into the periodontal lesion has most likely occurred to a varying extent during healing following most flap and grafting procedures applied in regenerative periodontal therapy, which may explain the varying results reported. This view is supported by the results of the monkey study by Caton *et al*. (1980). These investigators examined healing in ligature-induced periodontal lesions following treatment with four different modalities of regenerative surgical procedures:

1. Root planing and soft tissue curettage
2. Widman flap surgery without bone grafting

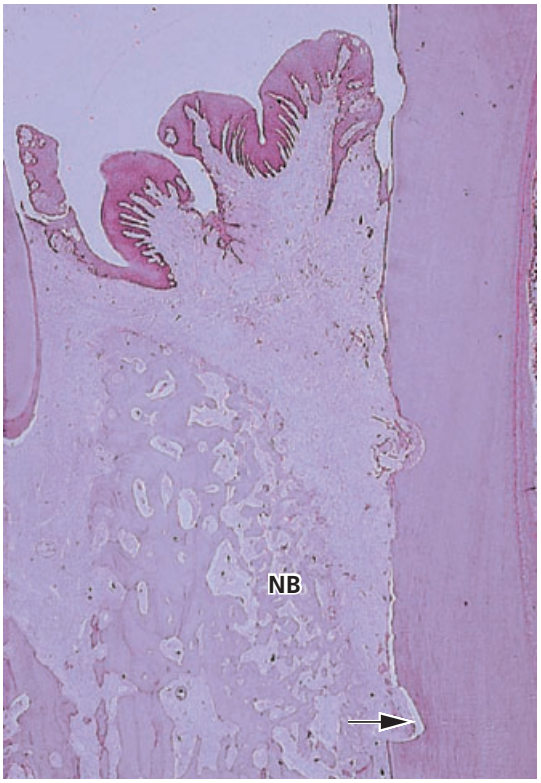

Fig. 25-15 Microphotograph illustrating an intrabony defect after regenerative treatment. New bone (NB) has formed in the defect but epithelium has migrated apically along the root surface to the notch (arrow) in the root surface indicating the bottom of the defect before treatment.

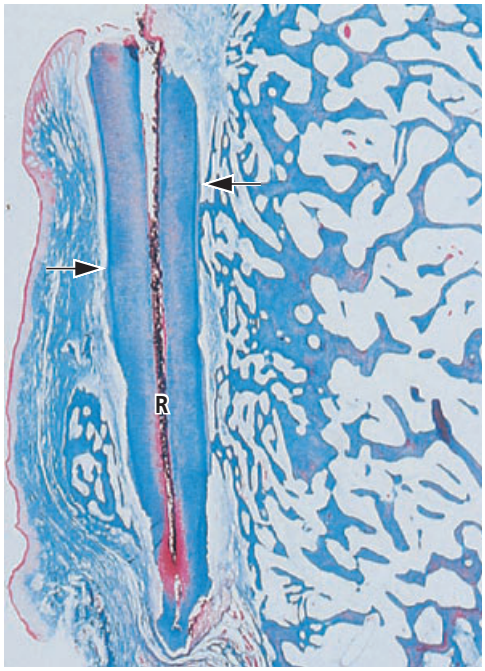

Fig. 25-16 Microphotograph of an implanted root (R) where epithelium was allowed to migrate into the wound after 2 weeks. The epithelium has migrated along the coronal, previously periodontitis-involved root surfaces down to the level indicated by the arrows. In the areas covered by epithelium, there are no signs of resorption. Apical to this level the root surfaces demonstrate root resorption.

3. Widman flap surgery with the placement of frozen autogeneous red bone marrow and cancellous bone
4. Beta-tricalcium phosphate in intrabony defects.

Healing following all treatment modalities resulted in the formation of a long junctional epithelium extending to or close to the same level as before treatment.

Root resorption

In the experimental studies described previously, granulation tissue, derived from gingival connective tissue or bone, produced root resorption when contacting the curetted root surface during healing following surgery (Karring *et al*. 1980, 1985; Nyman *et al*. 1980). It should be expected, therefore, that this phenomenon would occur as a frequent complication to periodontal surgery, particularly following those procedures which include the placement of grafting materials to stimulate bone formation. The reason why root resorption is rarely seen is most likely that post-operatively, the dentogingival epithelium migrates apically along the root surface, forming a protective barrier towards the root surface (Fig. 25-15). This view is supported by the results of an experimental study in monkeys (Karring *et al*. 1984) in which roots, which previously had been subjected to ligature-induced periodontitis, were extracted and re-implanted in contact with bone and connective tissue and covered with a tissue flap (submerged). After varying time intervals the submerged roots were exposed to the oral cavity by a second incision (wounding) through the covering mucosa, thereby permitting the epithelium to migrate into the wound. In specimens where the wounding occurred within 2 weeks (Fig. 25-16), the previously diseased part of the roots was covered by epithelium and showed no signs of resorption. With increasing intervals between implantation of the roots and the wounding, a steadily diminishing part of the diseased root surface was covered by epithelium, and root resorption and ankylosis became progressively pronounced (Fig. 25-17). This observation concurs with results presented by Björn *et al*. (1965) who treated 11 periodontally diseased teeth in seven human volunteers, using the submerging technique which prevented apical migration of the dentogingival epithelium. The authors reported that root resorption was indeed a common complication following this kind of therapy.

Regenerative concepts

One of the first methods used in attempts to obtain new attachment was scaling and root planing combined with soft tissue curettage (i.e. mechanical removal of the diseased root cementum and the pocket epithelium). Studies in humans (e.g. McCall 1926; Orban 1948; Beube 1952; Waerhaug 1952;

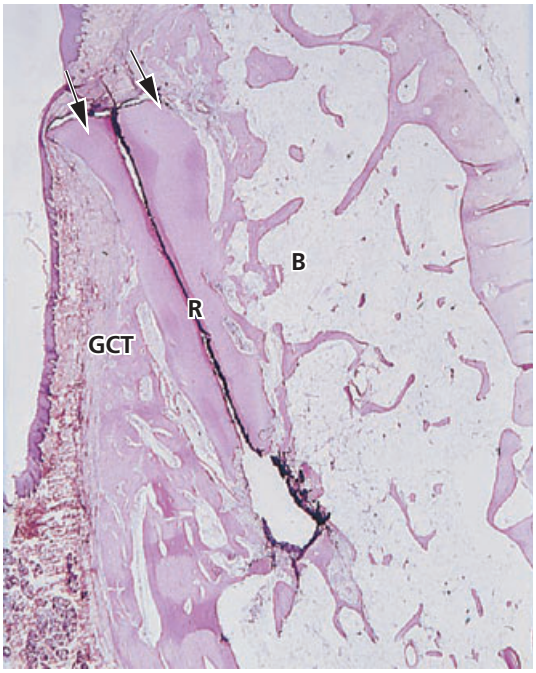

Fig. 25-17 Microphotograph of an implanted root (R) where epithelium was allowed to migrate into the wound after 4 weeks. The epithelium (arrows) covers only the coronal cut root surface. Extensive resorption is seen on the surface facing the gingival connective tissue (GCT) and resorption and ankylosis are seen on the surface facing the bone tissue (B).

Schaffer & Zander 1953; Carranza 1954, 1960) and in animals (e.g. Beube 1947; Ramfjord 1951; Kon *et al*. 1969) showed that this type of periodontal therapy resulted not only in the establishment of gingival health but also in a reduction of the initially recorded pocket depth. This decrease in the depth of the periodontal pocket was assumed to be partly the result of shrinkage of the initially inflamed gingiva, but partly also the effect of the formation of a new connective tissue attachment in the apical part of the pocket.

The possibility of obtaining new attachment became widely accepted with the work of Prichard (1957a,b), in which new attachment formation in intrabony periodontal lesions was reported as a predictable outcome of treatment. Seventeen cases were presented out of which four were subjected to a re-entry surgical procedure, revealing that these defects were filled with bone. The technique of Prichard (1957b, 1960) was only used for the treatment of three-wall intrabony defects, and the results obtained suggested that the morphology of the periodontal bony defect was essential for the establishment of a predictable prognosis. Goldman and Cohen (1958) introduced a classification of periodontal intrabony defects which was based on the number of osseous walls surrounding the defect, being either three-wall, two-wall or one-wall defects or a combination of such situations (Fig. 25-18).

The technique of Prichard (1957a,b, 1960) included the elevation of tissue flaps in order to get access to the defect. All granulation tissue in the defect was removed and the root surface was scaled and planed. In order to enhance regeneration of bone, small perforations were made with a bur at several sites of the bone walls. The flaps were sutured to accomplish complete coverage of the defect. Many clinical investigators have claimed that new attachment resulted following this type of treatment but there is little quantitative or qualitative documentation (Patur & Glickmann 1962; Wade 1962, 1966; Ellegaard & Löe 1971). Patur and Glickmann (1962) reported a clinical study including 24 intrabony defects treated according to the Prichard technique (1957a,b). The outcome was evaluated by comparing pre-operative and post-operative radiographs, measurements of the alveolar bone level adjacent to the root and study casts taken during operation and post-operatively after reflecting buccal and lingual flaps. The authors reported that new attachment had occurred in two-wall and three-wall intrabony defects but not in one-wall defects. Results from a study by Ellegaard and Löe (1971) comprising 191 defects in 24 patients with periodontal disease indicated that complete regeneration, determined radiographically and by periodontal probing, had occurred in around 70% of the three-wall defects, in 40% of the combined two-wall and three-wall defects, and in 45% of the two-wall defects.

In a later study by Rosling *et al*. (1976), 124 intrabony defects in 12 patients were treated by means of the modified Widman flap procedure (Ramfjord & Nissle 1974). Following treatment the patients were recalled twice per month for professional tooth cleaning. Re-examination performed clinically and on radiographs 2 years after therapy demonstrated bone fill-in of two-wall as well as three-wall defects. The authors suggested that this regrowth of bone was also associated with the formation of new connective tissue attachment and ascribed the successful healing mainly to the optimal standard of oral hygiene which was maintained in all patients during healing. A clinical study with almost identical results was presented by Polson & Heijl (1978). The results of several histologic studies in animals and humans, on the other hand, indicate that formation of new periodontal attachment is by no means predictable following subgingival curettage or flap surgery (Listgarten & Rosenberg 1979; Caton & Nyman 1980; Caton *et al*. 1980; Steiner *et al*. 1981; Stahl *et al*. 1983; Bowers *et al*. 1989a).

Grafting procedures

In a number of clinical trials and animal experiments, the flap approach was combined with the placement of bone grafts or implant materials into the curetted bony defects with the aim of stimulating periodontal regeneration. The various graft and

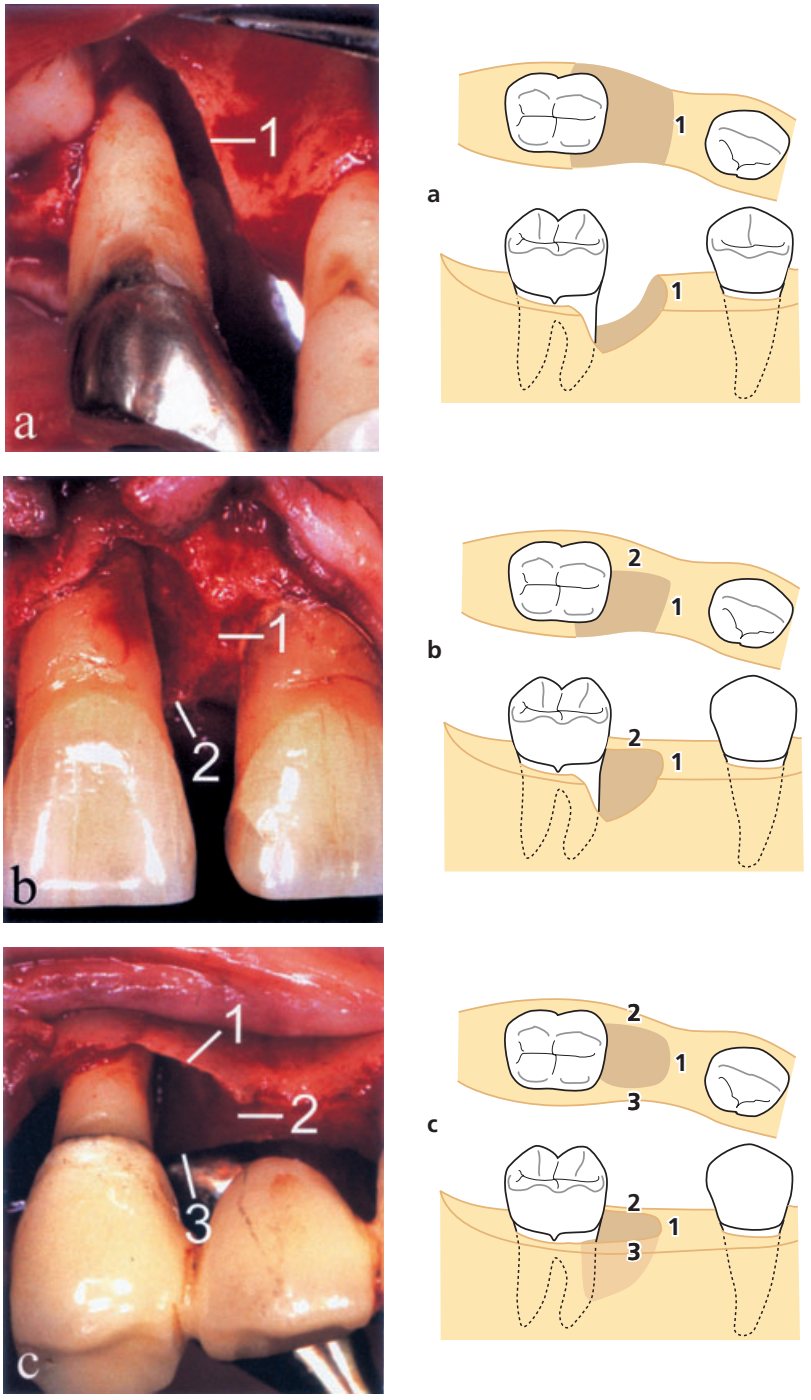

Fig. 25-18 Progression of periodontitis at a different rate on neighboring tooth surfaces results in the development of intrabony defects. Based on the number of surrounding bone walls such defects are classified as one-wall (a), two-wall (b) or three-wall (c) defects.

implant materials used so far can be placed into four categories:

1. *Autogenous grafts*: grafts transferred from one position to another within the same individual. This type of graft comprises (i) cortical bone or (ii) cancellous bone and marrow, and is harvested either from intraoral or extraoral donor sites.
2. *Allogeneic grafts*: grafts transferred between genetically dissimilar members of the same species. (i) Frozen cancellous bone and marrow, and (ii) freeze-dried bone have been used.
3. *Xenogeneic grafts*: grafts taken from a donor of another species.
4. *Alloplastic materials*: synthetic or inorganic implant materials which are used as substitutes for bone grafts.

The rationale behind the use of bone grafts or alloplastic materials is the assumption that both the regrowth of alveolar bone and the formation of new attachment would be stimulated because these materials may either (1) contain bone-forming cells (osteogenesis), or (2) serve as a scaffold for bone formation (osteoconduction), or because (3) the matrix of the bone grafts contains bone-inducing substances (osteoinduction) (Urist 1980; Brunsvold & Mellonig 1993). Such complete regeneration of the periodontal attach-

ment apparatus following grafting procedures would imply, however, that cells derived from bone possess the ability to form new cementum with inserting collagen fibers on a previously periodontitis-involved root surface (Melcher *et al*. 1987). This assumption is in conflict with current knowledge about the biology of periodontal wound healing, that repopulation of the detached root surface with cells from the periodontal ligament is the prerequisite for new attachment formation. This means that all therapeutic procedures involving the placement of bone grafts or bone substitute implants are based on a biologic concept which cannot explain how such treatment should result in regeneration of the periodontium.

The effect of using bone grafts or alloplastic materials for periodontal regeneration has mainly been examined in case reports, while histologic evidence of new attachment and controlled clinical studies is limited. The results from such reports vary and the documentation presented usually consists of pre-operative and post-operative probing attachment levels, radiographic interpretations or re-entry procedures.

Autogenous grafts

Autogenous grafts (autografts) may retain some cell viability and are considered to promote bone healing mainly through osteogenesis and/or osteoconduction. They are gradually resorbed and replaced by new viable bone. In addition, potential problems of histocompatibility and disease transmission are eliminated with autogenous grafts. Autogenous grafts can be harvested from intraoral or extraoral sites.

Intraoral autogenous grafts

Intraoral autogenous grafts obtained from edentulous areas of the jaw, healing extraction sites, maxillary tuberosities or the mandibular retromolar area were commonly used in periodontal regenerative surgery (Mann 1964; Ellegaard & Löe 1971; Rosenberg 1971a,b; Dragoo & Sullivan 1973a,b; Hiatt & Schallhorn 1973; Froum *et al*. 1983; Stahl *et al*. 1983). Generally cancellous bone is preferred as graft material but cortical bone, applied as small chips (Rosenberg *et al*. 1979), or mixed with blood prior to the placement in the defects (Robinson 1969; Froum *et al*. 1976), was also reported to be effective in producing regeneration in periodontal intrabony defects.

The effect of intraoral autogenous grafts has been evaluated in both animals and humans. In a study in monkeys, Rivault *et al*. (1971) observed that intrabony defects filled with intraoral autogenous bone chips mixed with blood (osseous coagulum) healed with new bone formation, but no more bone was found in such experimental defects than was observed in similar control defects treated with surgical curettage. Other studies in monkeys and dogs also failed to demonstrate significant differences in bone formation between grafted and non-grafted intrabony or furcation defects (Ellegaard *et al*. 1974; Coverly *et al*. 1975; Nilveus *et al*. 1978).

In clinical case series where intraoral autogenous grafts were used for the treatment of intrabony periodontal defects, a mean bone fill ranging from 3.0–3.5 mm was reported (Nabers & O'Leary 1965; Robinson 1969; Hiatt & Schallhorn 1973; Froum *et al*. 1975). Hiatt and Schallhorn (1973) treated 166 intrabony lesions with intraoral autogenous cancellous bone. They reported a mean increase in bone height of 3.5 mm, evaluated by clinical measurements. One-wall, two-wall, and three-wall defects were included, and the largest bone fill was observed in defects with the highest number of bone walls. A block section obtained from a patient treated in this study presented histologic evidence of new cementum, bone, and periodontal ligament formation. In controlled clinical studies, intraoral autogenous grafts were found superior to surgical debridement alone in terms of bone fill (Froum *et al*. 1976), or probing attachment (PAL) gain (Carraro *et al*. 1976) in two-wall defects. However, there are controlled studies that demonstrate more modest results regarding bone fill or PAL gain after intraoral grafting when compared to ungrafted controls (Ellegaard & Löe 1971; Renvert *et al*. 1985).

Ross and Cohen (1968) reported new bone and cementum formation in a human histologic specimen from an intrabony defect retrieved 8 months following debridement and placement of intraoral autogenous grafts. They also found that the grafts were without osteocytes and that the deposition of new alveolar bone had taken place around the grafts. Nabers *et al*. (1972) observed that new cementum and functionally oriented periodontal ligament fibers were present in half the length of a defect which was biopsied about 4.5 years after treatment with intraoral autogenous bone grafts. In other human histologic reports, bone fill and new attachment were observed coronal to reference notches placed on the treated roots at the apical termination of root planing (Hiatt *et al*. 1978) or at the most apical level of previously existing calculus (Froum *et al*. 1983; Stahl *et al*. 1983). Other investigators, however, observed an epithelial lining which occupied a varying portion of the previously diseased part of the root (Hawley & Miller 1975; Listgarten & Rosenberg 1979; Moscow *et al*. 1979). The results from these studies and those from a recent meta-analysis (Trombelli 2005) indicate that the treatment of periodontal osseous defects with intraoral bone grafts may result in periodontal regeneration, but not predictably.

Extraoral autogenous grafts

Schallhorn (1967, 1968) introduced the use of autogeneous hip marrow grafts (iliac crest marrow) in the treatment of furcation and intrabony defects. Later several studies were published demonstrating the osteogenic potentials of this material (Schallhorn *et al*. 1970; Schallhorn & Hiatt 1972; Patur 1974; Froum

et al. 1975), and as much as 3–4 mm gain in crestal bone was reported following the treatment of intrabony defects with hip marrow grafts. The effect of iliac crest marrow and of intraoral cancellous bone grafts in one-wall, two-wall, and three-wall bony defects in humans was evaluated by Patur (1974). He reported that bone fill occurred to a varying extent with both types of graft. The amount of bone fill in one-wall bony defects was larger with iliac crest marrow than with cancellous bone or when no grafts were used. Some defects within all three groups showed bone fill, and no difference was observed between the control defects and those treated with intraoral cancellous bone grafts. The author stated that even with fresh iliac crest marrow, bone regeneration is variable and unpredictable.

Healing of inter-radicular and intrabony lesions following placement of iliac crest marrow was evaluated in monkeys by Ellegaard *et al*. (1973, 1974). Regeneration occurred more frequently with the use of grafts, but iliac crest marrow frequently resulted in ankylosis and root resorption (Fig. 25-19).

Histologic evidence of periodontal regeneration in humans following the use of iliac crest marrow grafts was provided by Dragoo and Sullivan (1973a,b). At 8 months following therapy a mature periodontal ligament was present at the grafted sites and about 2 mm supracrestal new attachment had also formed. Clinical evidence of root resorption was noted in seven of the 250 grafted sites.

Due to the morbidity associated with the donor site and the fact that root resorption sometimes results, iliac crest marrow grafts are not used in regenerative periodontal therapy today.

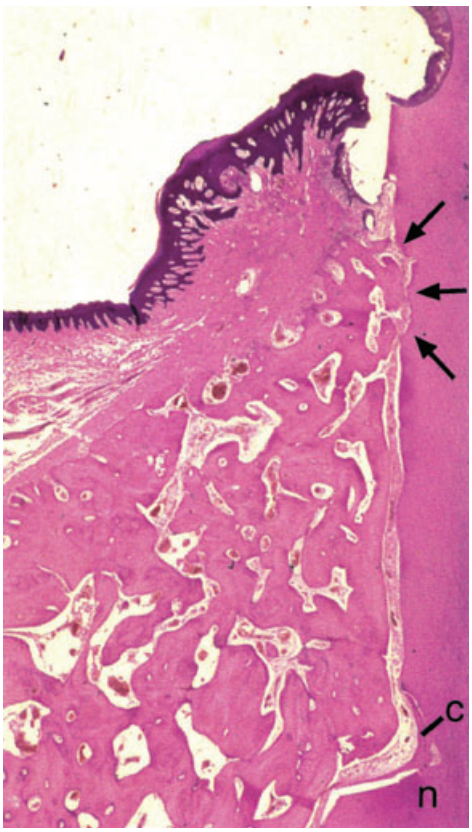

Fig. 25-19 Photomicrograph illustrating an intrabony defect 2 months following grafting with iliac crest marrow. The defect is completely filled with bone, but new cementum (c) is lacking on the root surface except for the most apical part (n) of the defect. Note that ankylosis and root resorption (arrows) are occurring in the coronal part of the defect.

Allogeneic grafts

Allogeneic grafts (allografts) were utilized in attempts to stimulate bone formation in intrabony defects in order to avoid the additional surgical insult associated with the use of autogenous grafts. However, the use of allogeneic grafts involves a certain risk regarding antigenicity, although the grafts are usually pretreated by freezing, radiation or chemicals in order to suppress foreign body reactions.

The types of allogeneic grafts used are frozen iliac cancellous bone and marrow, mineralized freeze-dried bone allogeneic grafts (FDBA), and decalcified freeze-dried alogeneic bone grafts (DFDBA). The need for cross matching to decrease the likelihood of graft rejection as well as the risk of disease transmission virtually eliminated the use of frozen iliac allogeneic grafts in periodontics.

FDBA is a mineralized bone graft, which loses cell viability through the manufacturing process and, therefore, is supposed to promote bone regeneration through osteoconduction/osteoinduction (Goldberg & Stevenson 1987). The freeze drying also markedly reduces the antigenicity of the material (Turner & Mellonig 1981; Quattlebaum *et al*. 1988). The efficacy of FDBA was evaluated in a study which included 89 clinicians (Mellonig 1991). At re-entry surgery it was found that 67% of the sites treated with FDBA alone and 78% of the sites treated with FDBA plus autogenous bone grafts demonstrated complete or more than 50% bone fill. Thus, FDBA plus autogenous bone appeared more effective than FDBA alone. In split-mouth studies where FDBA was combined with autogenous grafts or tetracycline powder (Sanders *et al*. 1983; Mabry *et al*. 1985), a defect fill of 60% and 80% of the initial lesion was reported. In a split-mouth study it was also shown that FDBA implantation had a similar effect on defect resolution as that achieved by DFDBA (Rummelhart *et al*. 1989) or granular porous hydroxyapatite (Barnett *et al*. 1989). However, the only controlled clinical trial comparing treatment of intrabony defects with FDBA implantation versus flap surgery failed to demonstrate any difference in terms of clinical attachment gain and bone fill between test and control sites at 1 year re-entry examination (Altiere *et al*. 1979). In addition, human histologic specimens demonstrated that implantation of FDBA in intrabony defects yielded no periodontal regeneration but resulted in a long epithelial attachment on the previously diseased root surface (Dragoo & Kaldahl 1983).

Several animal studies suggested that demineralization of a cortical bone allograft (DFDBA) enhances its osteogenic potential by exposing bone morphogenic proteins (BMPs) which presumably have the ability to induce host cells to differentiate into osteoblasts (Urist & Strates 1970; Mellonig *et al*. 1981). Several case reports presented clinical improvements and bone fill after implantation of DFDBA into intrabony defects (Quintero *et al*. 1982; Werbitt 1987; Fucini *et al*. 1993; Francis *et al*. 1995), and controlled clinical studies documented considerable gain of attachment and bone fill in sites treated with DFDBA as compared with non-grafted sites (Pearson *et al*. 1981; Mellonig 1984; Meadows *et al*. 1993). However, no statistical differences regarding attachment level changes and bone fill were found when comparing sites treated with FDBA and sites treated with DFDBA (Rummelhart *et al*. 1989).

Histologic evidence of regeneration following grafting with DFDBA was provided by Bowers *et al*. (1989b,c). Complete regeneration with new cementum, periodontal ligament, and bone amounting to 80% of the original defect depth was reported at sites treated with DFDBA, which was considerably more than that observed in defects treated with surgical debridement alone. However, animal experiments failed to confirm the regenerative potential of DFDBA grafting (Sonis *et al*. 1985; Caplanis *et al*. 1998).

The controversial results regarding the effect of DFDBA on the regeneration of periodontal intraosseous defects along with great differences in the osteoinductive potential (ranging from high to no osteoinductive effect) of commercially available DFDBA (Becker *et al*. 1994, 1995; Shigeyama *et al*. 1995; Schwartz *et al*. 1996; Garraway *et al*. 1998), and the (although minute) risk for disease transmission have raised concern about the clinical applicability of DFDBA. In EU countries, commercially available DFDBA is not granted a CE mark permitting distribution of the material within the community.

Xenogeneic grafts

The use of xenogeneic bone grafts (xenografts) in regenerative periodontal surgery was examined several years ago. Nielsen *et al*. (1981) treated 46 intrabony defects with Kielbone® (i.e. defatted and deproteinized ox bone) and another 46 defects with intraoral autogenous bone grafts. The results, which were evaluated by periodontal probing and radiographically, showed no difference between the amount of clinical gain of attachment and bone fill obtained in the two categories of defect. A study in monkeys also demonstrated that the two types of bone graft displayed similar histologic features and were frequently seen in the connective tissue of the healed defects as isolated bone particles surrounded by a cementum-like substance (Nielsen *et al*. 1980).

Recently, new processing and purification methods have been utilized which make it possible to remove all organic components from a bovine bone source and leave a non-organic bone matrix in an unchanged inorganic form (e.g. Bio-Oss®, Geistlich AG, Switzerland; Lubboc®/Laddec®, Ost Development SA, France; Endobone®, Biomet Inc. Dordrecht, The Netherlands; OsteoGraf®/N, DENTSPLY, Friadent CeraMed, Lakewood, CO, USA; Cerabone®, aap Implantate AG, Berlin, Germany). However, differences in the purification and manipulation methods of the bovine bone have lead to commercially available products with different chemical properties and possibly different biologic behavior. These materials are available in different particle sizes or as block grafts.

To date, no controlled human study has compared the effect of such graft materials in periodontal defects with flap surgery alone, but a clinical study has demonstrated that implantation of Bio-Oss® resulted in pocket reduction, gain of attachment, and bone fill in periodontal defects to the same extent as that of DFDBA (Richardson *et al*. 1999). There are, on the other hand, several controlled clinical studies reporting about the outcome of treatment of periodontal intrabony defects with Bio-Oss used as an adjunct to guided tissue regeneration (GTR). In one of these studies, including 124 patients, the combined treatment had an added benefit of 0.8 mm PAL gain over that with flap surgery alone (Tonetti *et al*. 2004). However, conflicting results have been reported following the combined Bio-Oss and GTR treatment of intrabony defects versus GTR alone. In a recent study, significantly more PAL gain was found after the combined treatment than after GTR treatment with a collagen membrane (5.1 mm versus 4.0 mm) (Paolantonio 2002), while in another study, the clinical improvements obtained following the two treatments were similar (Stavropoulos *et al*. 2003b). This latter finding is in agreement with the results of a recent systematic review evaluating various bone grafts and bone graft substitutes as adjuncts to GTR (Murphy & Gunsolley 2003). Studies in experimental animals have also failed to show an added effect of Bio-Oss combined with GTR (Carmagnola *et al*. 2002, 2003). However, human histology (Camelo *et al*. 1998; Nevins *et al*. 2003; Sculean *et al*. 2003) and a study in dogs (Clergeau *et al*. 1996) have suggested that the placement of bovine bone-derived biomaterials in periodontal bone defects may enhance both the regeneration of a new connective tissue attachment and bone. The results of several experimental studies in animals, on the other hand, have questioned whether Bio-Oss encourages bone formation (Stavropoulos *et al*. 2001, 2003a, 2004; Aghaloo *et al*. 2004; Cardaropoli *et al*. 2005). In fact, the results of some of these studies suggest that grafting of Bio-Oss may compromise bone formation.

The use of coral skeleton as a bone graft substitute was proposed some decades ago (Holmes 1979; Guillemin *et al*. 1987). Depending on the pretreatment procedure, the natural coral turns into

non-resorbable porous hydroxyapatite (e.g. Interpore 200, Interpore International, Irvine, US) or to a resorbable calcium carbonate (e.g. Biocoral, Inoteb, St Gonnery, France) skeleton (Nasr *et al*. 1999). Implantation of coralline porous hydroxyapatite in intrabony periodontal defects in humans produced more probing pocket depth reduction, clinical attachment gain, and defect fill than non-grafting (Kenney *et al*. 1985; Krejci *et al*. 1987; Yukna 1994; Mora & Ouhayoun 1995; Yukna & Yukna 1998), and similar results were found when compared with grafting of FDBA (Barnett *et al*. 1989). When porous hydroxyapatite was compared with DFDBA for the treatment of intraosseous defects, similar results were also obtained (Bowen *et al*. 1989), but another study reported clinical results in favor of this material (Oreamuno *et al*. 1990). However, both animal (West & Brustein 1985; Ettel *et al*. 1989) and human studies (Carranza *et al*. 1987; Stahl & Froum 1987) have provided only vague histologic evidence that grafting of natural coral may enhance the formation of true new attachment. In most cases, the graft particles were embedded in connective tissue with minimal bone formation.

Alloplastic materials

Alloplastic materials are synthetic, inorganic, biocompatible and/or bioactive bone graft substitutes which are claimed to promote bone healing through osteoconduction. There are four kinds of alloplastic materials, which are frequently used in regenerative periodontal surgery: hydroxyapatite (HA), beta-tricalcium phosphate (β-TCP), polymers, and bioactive glasses (bio-glasses).

Hydroxyapatite

The HA products used in periodontology are of two forms: a particulate non-resorbable ceramic form (e.g. Periograf®, Miter Inc., Warsaw, IN, US; Calcitite®, Calcitek Inc., San Diego, US) and a particulate, resorbable non-ceramic form (e.g. OsteoGraf/LD®, CeraMed Dental, Lakewood, CO, US). In controlled clinical studies, grafting of intrabony periodontal lesions with HA resulted in a PAL gain of 1.1–3.3 mm and also in a greater bone defect fill as compared with non-grafted surgically debrided controls (Meffert *et al*. 1985; Yukna *et al*. 1985, 1986, 1989; Galgut *et al*. 1992). In these studies, improvement of clinical parameters (i.e. PPD reduction and PAL gain) was more evident in the grafted sites than in the sites treated only with debridement, especially for initially deep defects. However, animal studies (Barney *et al*. 1986; Minabe *et al*. 1988; Wilson & Low 1992) and human histologic data (Froum *et al*. 1982; Moskow & Lubarr 1983; Ganeles *et al*. 1986; Sapkos 1986) showed that bone formation was limited and that a true new attachment was not formed consistently after grafting of intrabony periodontal defects with HA. The majority of the HA particles were embedded in connective tissue and new bone was only observed occasionally around particles in close proximity to host bone. A junctional epithelium lined the major part of the roots.

Beta-tricalcium phosphate (β-TCP)

β-TCP ($Ca_3(PO_4)_2$) (e.g. Synthograft®, Johnson and Johnson, New Brunswick, NJ, US) has been used in a series of case reports for the treatment of periodontal osseous lesions (Nery & Lynch 1978; Strub *et al*. 1979; Snyder *et al*. 1984; Baldock *et al*. 1985). After variable time intervals, a significant gain of bone was observed by means of re-entry or radiographs. However, there is no controlled study comparing the result of β-TCP grafting with that of open-flap debridement, and histologic data from animal (Levin *et al*. 1974; Barney *et al*. 1986) and human studies (Dragoo & Kaldahl 1983; Baldock *et al*. 1985; Bowers *et al*. 1986; Stahl & Froum 1986; Froum & Stahl 1987; Saffar *et al*. 1990) showed that β-TCP is rapidly resorbed or encapsulated by connective tissue, with minimal bone formation and no periodontal regeneration.

Polymers

There are two polymer materials that have been used as bone graft substitutes in the treatment of periodontal defects: a non-resorbable, calcium hydroxide coated co-polymer of polymethylmethacrylate (PMMA) and polyhydroxylethylmethacrylate (PHEMA), which is often referred to as HTR (hard tissue replacement) (e.g. HTR™, Bioplant Inc., New York, NY, US), and a resorbable polylactic acid (PLA) polymer (Driloc®, Osmed Corp., Costa Mesa, CA, US).

In controlled clinical studies, implantation of HTR polymer grafts in intrabony defects resulted in a defect fill of approximately 2 mm, representing about 60% of the initial defect depth, but the improved clinical response with grafting was not significantly better than that following solely flap operation (Yukna 1990; Shahmiri *et al*. 1992). Human histologic data from an experimental study (Plotzke *et al*. 1993), and from two case reports (Stahl *et al*. 1990b; Froum 1996) also revealed that grafting of osseous periodontal defects with HTR does not promote periodontal regeneration. The HTR particles were most frequently encapsulated by connective tissue with only scarce evidence of bone formation. Healing resulted in a long junctional epithelium along the root surface, and true new attachment formation was not observed.

When PLA particles were implanted into intrabony defects in humans and compared with DFDBA or surgically debrided controls, it was found that the healing results were less favorable than after flap operation alone, both in terms of clinical parameters (PPD and PAL gain), and in terms of bone fill (Meadows *et al*. 1993).

Bioactive glasses (bio-glasses)

Bio-glasses are composed of SiO_2, Na_2O, P_2O_5 and are resorbable or not resorbable depending on the relative proportion of these components. When bio-glasses are exposed to tissue fluids, a double layer of silica gel and calcium phosphate is formed on their surface. Through this layer the material promotes absorption and concentration of proteins used by osteoblasts to form extracellular bone matrix which theoretically may promote bone formation (Hench *et al*. 1972). Commercially available bio-glasses in particulate form, and theoretically resorbable, have been proposed for periodontal treatment (e.g. PerioGlass®, US Biomaterials Corp., Alachua, FL, US; BioGran®, Orthovita, Malvern, PA, US).

A human case report demonstrated that implantation of bio-glass in periodontal osseous defects resulted in a gain of clinical attachment of 2.0–5.3 mm and a radiographic bone fill of 3.5 mm, and in a controlled study, the treatment of intrabony defects with bio-glass also resulted in greater clinical improvements than surgical debridement alone (Froum *et al*. 1998). However, other controlled studies (Zamet *et al*. 1997) and split-mouth studies on grafting of intrabony defects with bio-glass (Ong *et al*. 1998) failed to demonstrate statistically significant better clinical results than surgery alone or DFDBA grafting (Lovelace *et al*. 1998). Although experimental studies in monkeys have suggested that bio-glass grafting of periodontal intrabony defects (Karatzas *et al*. 1999) may favor new cementum formation and inhibit epithelial downgrowth, there is no histologic evidence in humans that bio-glass may promote true periodontal regeneration. In a histologic evaluation of bio-glass implanted in intrabony defects in humans it was observed that, although clinically satisfactory results were produced, healing had most frequently occurred with a junctional epithelium along the previously diseased part of the root, and new cementum with inserting collagen fibers was found in only one out of five treated teeth. Bone formation was limited in all specimens (Nevins *et al*. 2000).

Evaluation of alloplastic materials

There are no controlled clinical studies demonstrating that grafting with tricalcium phosphate or polymers results in significant clinical improvements beyond that of flap surgery, whereas several reports have indicated that grafting with hydroxyapatite or bioactive glasses may produce more gain of attachment than open-flap debridement (Galgut *et al*. 1992; Zamet *et al*. 1997; Froum *et al*. 1998) or a gain similar to that obtained following grafting with DFDBA (Lovelace *et al*. 1998). Histologic evidence that the use of alloplastic or synthetic graft materials may lead to periodontal regeneration in humans is lacking, and animal experiments have failed to demonstrate regeneration of a functional periodontium following implantation of hydroxyapatite, tricalcium phosphate or polymers in periodontal lesions (Barney *et al*. 1986; Shahmiri *et al*. 1992). It was reported, however, that treatment with bioactive glasses in experimental animals produced significantly more bone fill and new attachment compared with that in non-grafted controls (Fetner *et al*. 1994; Karatzas *et al*. 1999) or in sites grafted with hydroxyapatite or tricalcium phosphate (Wilson & Low 1992). Although some bone formation has been reported following the use of alloplastic materials, there is no evidence that these materials may stimulate the formation of new cementum with inserting collagen fibers. At the 1996 American Academy of Periodontology World Workshop, it was concluded that synthetic graft materials function primarily as defect fillers.

Root surface biomodification

Much research has been directed to altering the periodontitis-involved root surface in a manner that will promote the formation of a new connective tissue attachment. Removal of bacterial deposits, calculus, and endotoxins from the cementum is generally considered essential for the formation of a new connective attachment (Garrett 1977). However, it was suggested by Stahl *et al*. (1972) that demineralization of the root surface, exposing the collagen of the dentin, would facilitate the deposition of cementum by inducing mesenchymal cells in the adjacent tissue to differentiate into cementoblasts. The biologic concept is that exposure of collagen fibers of the dentin matrix may facilitate adhesion of the blood clot to the root surface and thereby favor migration of the fibroblasts. However, it is doubtful whether this concept is in accordance with current knowledge about periodontal wound healing since there is no evidence that the exposure of collagen fibers of the dentin matrix may facilitate repopulation of the root surface with cells derived from the periodontal ligament. As mentioned previously, periodontal ligament cells are required for the accomplishment of a new connective tissue attachment.

Several studies using various animal models demonstrated an improved healing response histologically following citric acid and tetracycline root surface demineralization (Register & Burdick 1976; Crigger *et al*. 1978; Polson & Proye 1982; Claffey *et al*. 1987). However, in a study in dogs where naturally occurring furcations were treated with citric acid, several specimens demonstrated ankylosis and root resorption (Bogle *et al*. 1981). This finding corroborates that of Magnusson *et al*. (1985) in monkeys, where citric acid conditioning was evaluated in combination with coronally displaced tissue flaps after 6 months. These investigators found root resorption on 28 out of 40 surfaces examined and 21 of these also presented ankylosis.

New connective tissue attachment following citric acid demineralization of root surfaces has been demonstrated histologically in humans (Cole *et al*. 1980; Frank *et al*. 1983; Stahl *et al*. 1983; Stahl & Froum

1991a). Cole *et al*. (1980) showed histologic evidence of a new connective tissue attachment and bone formation coronal to reference notches placed in the apical extent of calculus identified on the root surface at the time of surgery. However, despite histologic evidence of regeneration following root surface biomodification with citric acid, results of controlled clinical trials failed to show any improvements in clinical conditions compared to controls not treated with acid (Moore *et al*. 1987; Fuentes *et al*. 1993).

In recent years, biomodification of the root surface with enamel matrix proteins (Emdogain®) during surgery and following demineralization with EDTA has been introduced to encourage periodontal regeneration. The biologic concept is that the application of enamel matrix proteins (amelogenins) may promote periodontal regeneration because it mimics events that took place during the development of the periodontal tissues (Hammarström 1997; Gestrelius *et al*. 2000). This view is based on the finding that the cells of the Hertwigs epithelial root sheath deposit enamel matrix proteins on the root surface prior to cementum formation and that these proteins are the initiating factor for the formation of cementum. The commercially available product, Emdogain®, a purified acid extract of porcine origin, contains enamel matrix derivatives (EMD), supposed to be able to promote periodontal regeneration. However, it is not quite clear how this concept is in accordance with current knowledge about periodontal wound healing since no evidence has been provided that it is cells derived from the periodontal ligament that are encouraged to repopulate the root surface after treatment. In fact, a study in dogs (Araùjo *et al*. 2003) where re-implanted roots that had been extracted and deprived of vital cementoblasts and subsequently treated with EMD failed to prevent ankylosis and root resorption, indicating that the root surfaces did not become repopulated with cells with the capacity to form cementum. A recent study in vitro has also failed to confirm that EMD has any significant effect on periodontal ligament cell proliferation (Chong *et al*. 2006).

In case series reports, 4–4.5 mm gain of clinical attachment, and about 70% bone fill in intrabony defects were reported following treatment with EMD (Heden *et al*. 1999; Heden 2000). In a multicenter clinical study involving 33 subjects with 34 paired intrabony defects, application of EMD resulted in larger amounts of PAL gain (2.2 mm) and statistically significantly more bone gain (2.6 mm) than open-flap debridement after 36 months, evaluated clinically and radiographically (Heijl *et al*. 1997). Similar results were reported in another split-mouth clinical trial (23 patients) published more recently (Froum *et al*. 2001). In that study a PPD reduction of 4.9 mm, a PAL gain of 4.3, and a bone gain of 3.8 mm (evaluated by re-entry surgery) were observed after EMD application in 53 intrabony defects. These values were statistically significantly larger than those obtained by flap surgery (2.2 mm, 2.7 mm, and 1.5 mm, respectively, in 31 defects).

In a more recent prospective multicenter randomized controlled clinical trial, the clinical outcomes of papilla preservation flap surgery (simplified papilla preservation flap, SPPF) with or without the application of enamel matrix proteins, were compared (Tonetti *et al*. 2002). A total of 83 test and 83 control patients with similar baseline periodontal conditions and defect characteristics were treated with either SPPF and Emdogain® or with SPPF alone. The test defects exhibited significantly more clinical attachment level (CAL) gain than the controls (3.1 ± 1.5 mm and 2.5 ± 1.5 mm, respectively).

When application of EMD was compared with GTR treatment, it was found that similar clinical improvements were obtained. In a randomized controlled clinical study, Pontoriero *et al*. (1999) compared EMD application with GTR with resorbable (two kinds: Guidor and Resolut) and non-resorbable (e-PTFE) membranes in intrabony defects. After 12 months, there were no significant differences among the groups, and EMD application resulted in a PPD reduction of 4.4 mm and a PAL gain of 2.9 mm, while the corresponding values from the membrane-treated sites (both GTR groups combined) were 4.5 mm and 3.1 mm, respectively. Silvestri *et al*. (2000) reported a PPD reduction of 4.8 mm and a PAL gain of 4.5 mm after EMD application in intrabony defects versus 5.9 mm and 4.8 mm, respectively, after GTR with non-resorbable membranes. Similar results were reported by other investigators (Sculean *et al*. 1999a,b; Silvestri *et al*. 2003; Sanz *et al*. 2004). There are studies indicating that following the application EMD in intrabony defects, clinical improvements can be achieved by the additional use of some bone graft materials (Zucchelli *et al*. 2003; Gurinsky *et al*. 2004; Trombelli *et al*. 2006), although others have failed to demonstrate a beneficial effect of this combined treatment (Sculean *et al*. 2005).

Histologic evidence of new cementum formation with inserting collagen fibers on a previously periodontitis-affected root surface and the formation of new alveolar bone in human specimens have been demonstrated following EMD treatment (Mellonig 1999; Sculean *et al*. 1999b). However, while in the study of Mellonig (1999) healing had occurred with acellular cementum on the root surface, the newly formed cementum in the study of Sculean *et al*. (1999b) displayed a predominantly cellular character. The ability of EMD to produce regeneration has been confirmed in controlled animal experiments (Fig. 25-20), following the treatment of intrabony, furcation, and dehiscence defects (Hammarström *et al*. 1997; Araújo & Lindhe 1998; Sculean *et al*. 2000). In a later study it was shown in monkeys that the combined application of EMD and autogenous bone grafts may improve periodontal regeneration in periodontal defects compared to flap surgery alone (Cochran *et al*. 2003).

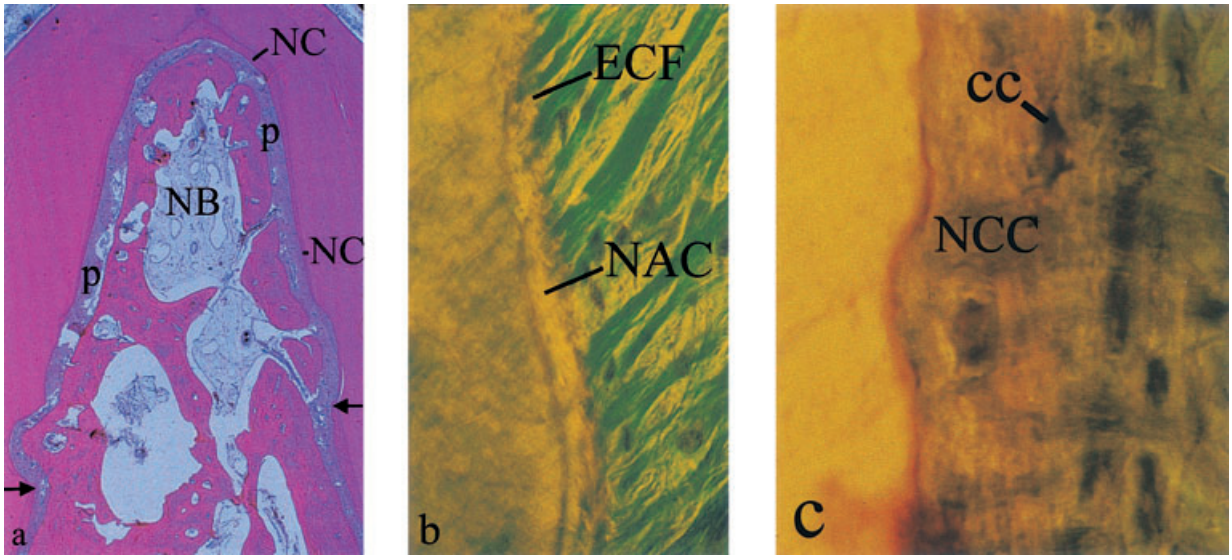

Fig. 25-20 (a) Photomicrograph of a grade III furcation defect in a dog following root surface biomodification with enamel matrix proteins and subsequently covered with a resorbable membrane. The defect has healed completely with bone (NB), a periodontal ligament (p) and new cementum (NC). The arrows indicate the apical extension of the lesion. (b) The cementum (NAC) formed on the root surface in the apical portion of the defect was acellular with inserting extrinsic collagen fibers (ECF) while (c) new cellular cementum (NCC) had formed in the coronal portion. cc = cells.

Growth regulatory factors for periodontal regeneration

Growth factor is a general term to denote a class of polypeptide hormones that stimulate a wide variety of cellular events such as proliferation, chemotaxis, differentiation, and production of extracellular matrix proteins (Terranova & Wikesjö 1987). Proliferation and migration of periodontal ligament cells and synthesis of extracellular matrix as well as differentiation of cementoblasts and osteoblasts is a prerequisite for obtaining periodontal regeneration. Therefore, it is conceivable that growth factors may represent a potential aid in attempts to encourage regeneration of the periodontium.

The effects of various growth factors were studied *in vitro*, and a significant regeneration potential of growth factors was also demonstrated in animal models. Lynch *et al*. (1989, 1991) examined the effect of placing a combination of platelet-derived growth factors (PDGF) and insulin-like growth factors (IGF) in naturally occurring periodontal defects in dogs. The control sites treated without growth factors healed with a long junctional epithelium and no new cementum or bone formation, while regeneration of a periodontal attachment apparatus occurred at the sites treated with growth factors. Similar results were reported by other investigators following application of a combination of PDGF and IGF in experimentally induced periodontal lesions in monkeys (Rutherford *et al*. 1992; Giannobile *et al*. 1994, 1996). One study examined the effect of PDGF and IGF in periodontal intrabony defects and grade II furcations in humans (Howell *et al*. 1997). At re-entry after 9 months, significantly increased bone fill was only observed at the furcation sites treated with growth factors. Considerable clinical improvements were also observed following a combined treatment of grade II furcations with GTR, a bone graft substitute and PDGF compared to open-flap debridement (Lekovic *et al*. 2003). It can be concluded that growth factors seem to have a positive effect on periodontal regeneration, but several important questions need to be resolved before this type of regenerative treatment can be used in humans (Graves & Cochran 1994).

Bone morphogenetic proteins (BMPs) are osteoinductive factors that may have the potential to stimulate mesenchymal cells to differentiate into bone-forming cells (Wozney *et al*. 1988). Sigurdsson *et al*. (1995) evaluated bone and cementum formation following regenerative periodontal surgery using recombinant human BMP in surgically created supraalveolar defects in dogs. Following application of BMP the flaps were advanced to submerge the teeth and sutured. Histologic analysis showed significantly more cementum formation and regrowth of alveolar bone on BMP-treated sites as compared to the controls. Significant amounts of bone regeneration in periodontal defects have also been reported by other investigators following application of BMPs combined with various carrier systems or space-providing devices in different animal models (Ripamonti *et al*. 1994; Selvig *et al*. 2002; Wikesjö *et al*. 2003a,b). Further experimentation is needed to evaluate a possible role of BMP in periodontal regeneration.

Guided tissue regeneration (GTR)

The experimental studies (Karring *et al*. 1980; Nyman *et al*. 1980; Buser *et al*. 1990a,b; Warrer *et al*. 1993) described previously have documented that the

progenitor cells for the formation of a new connective tissue attachment reside in the periodontal ligament. Consequently, it should be expected that a new connective tissue attachment would be predictably achieved if such cells populate the root surface during healing. This view was confirmed in a study in monkeys in which both gingival connective tissue and gingival epithelium were prevented from contacting the root surface during healing by the use of a barrier membrane (Gottlow *et al*. 1984). After reduction of the supporting tissues around selected experimental teeth, the root surfaces were exposed to plaque accumulation for 6 months. Soft tissue flaps were then raised and the exposed root surfaces were curetted. The crowns of the teeth were resected and the roots were submerged. However, prior to complete closure of the wound, a membrane was placed over the curetted root surfaces on one side of the jaws in order (1) to prevent gingival connective tissue contacting the root surface during healing, and (2) to provide a space for in-growth of periodontal ligament tissue. No membranes were placed over the contralateral roots. The histologic analysis after 3 months of healing demonstrated that the roots covered with membranes exhibited considerably more new attachment than the non-covered roots (Fig. 25-21). In four of the nine test roots, new cementum covered the entire length of the root. In all control specimens, the surface coronal to the newly formed cementum presented multinucleated cells and resorption cavities. In one control specimen virtually half the root was resorbed. Coronal regrowth of alveolar bone had occurred to a varying extent in test and control roots, and no relationship was found between the amount of new cementum formation and the degree of bone regrowth. The results of this study strongly suggested that the exclusion of epithelial and gingival connective tissue cells from the healing area by the use of a physical barrier may allow (guide) periodontal ligament cells to repopulate the detached root surface. This observation provided the basis for the clinical application of the treatment principle termed "guided tissue regeneration" (GTR). Thus. GTR treatment involves the placement of a physical barrier to ensure that the previous periodontitis-affected root surface becomes repopulated with cells from the periodontal ligament (Fig. 25-22).

Treatment of the first human tooth with GTR was reported by Nyman *et al*. (1982). Due to extensive periodontal destruction, the tooth was scheduled for extraction. This offered the possibility of obtaining histologic documentation of the result of the treatment. Following elevation of full thickness flaps, scaling of the root surface, and removal of all granulation tissue, an 11 mm deep periodontal lesion was ascertained. Prior to flap closure, a membrane was adjusted to cover parts of the detached root surfaces, the osseous defect, and parts of the surrounding bone. Histologic analysis after 3 months of healing revealed that new cementum with inserting collagen fibers had formed on the previously exposed root surface (Fig. 25-23). In a later study (Gottlow *et al*. 1986), 12 cases treated with GTR were evaluated clinically, and in five of these cases histologic documentation was also presented. The results showed that considerable but varying amounts of new connective tissue attachment had formed on the treated

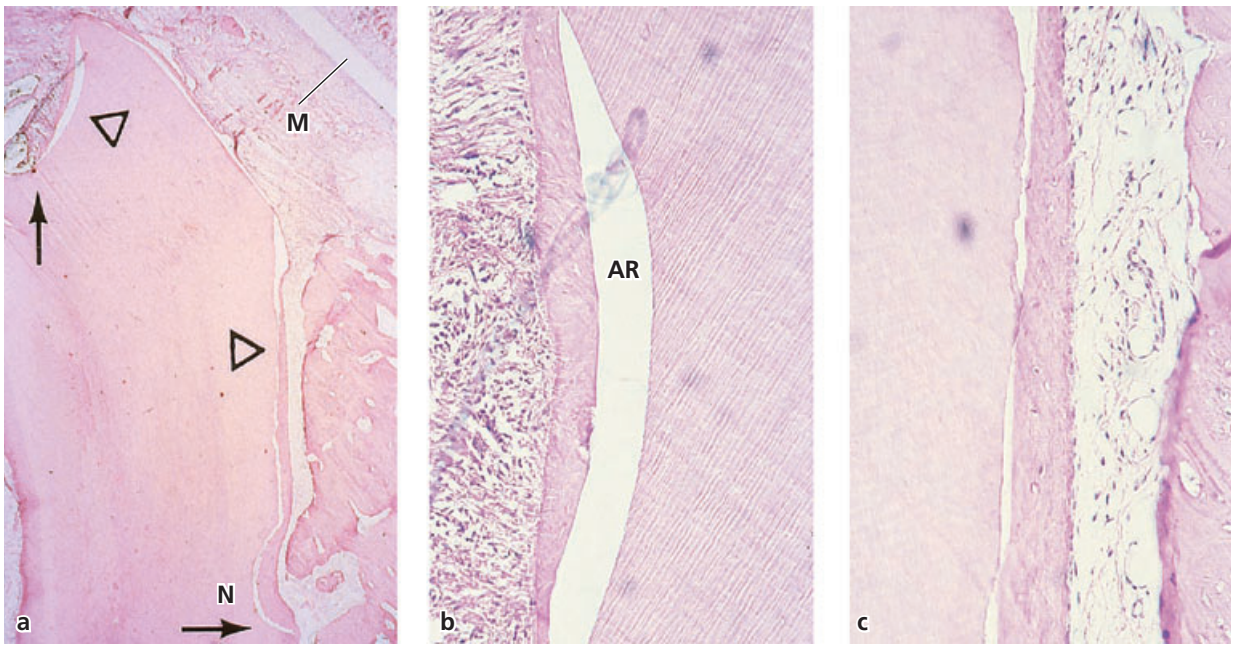

Fig. 25-21 (a) Microphotograph of membrane (M) covered root. Newly formed cementum is visible on the entire length of the buccal root surface coronal to the notch (N) and also on part of the coronal cut surface (arrow). (b, c) Higher magnifications of the areas at the upper and lower triangles in (a), showing that collagen fibers are inserted into the newly formed cementum. AR = artifact.

teeth. Frequently, however, bone formation was incomplete. The varying results were ascribed to factors such as the amount of remaining periodontal ligament, the morphology of the treated defect, technical difficulties regarding membrane placement, gingival recession, and bacterial contamination of the membrane and the wound during healing.

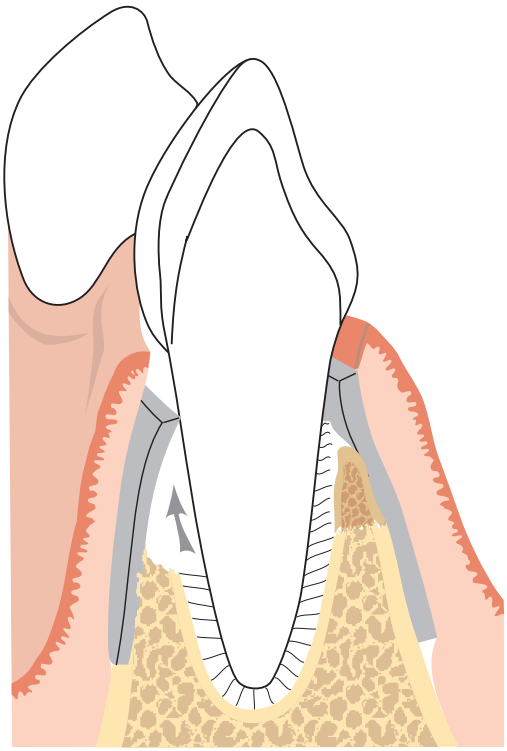

Fig. 25-22 Drawing illustrating the placement of the physical barrier which prevents the epithelium and gingival connective tissue from contacting the root surface during healing. At the same time the membrane allows cells from the periodontal ligament (arrow) to repopulate the previously periodontitis-involved root surface.

In the last decades, GTR has been applied in a number of clinical trials for the treatment of various periodontal defects such as intrabony defects (for review see Cortellini & Bowers 1995), furcation involvements (for review see Machtei & Schallhorn 1995; Karring & Cortellini 1999), and localized gingival recession defects (Pini-Prato *et al*. 1996). The efficiency of GTR in producing periodontal regeneration in these defects has been documented in animal studies (Gottlow *et al*. 1990; Araùjo *et al*. 1998; Laurell *et al*. 2006) and in several controlled clinical trials (see Chapter 43).

The clinical outcomes of GTR are most frequently evaluated by changes in clinical attachment levels (CAL), bone levels (BL), probing pocket depths (PPD), and the position of the gingival margin. In some of the studies on grade II and III furcations, horizontal changes in clinical attachment, bone level, and pocket depth were also measured. However, evidence of true regeneration of periodontal attachment can only be provided by histologic means.

Assessment of periodontal regeneration

In most studies on the effect of regenerative periodontal surgery, the outcomes are evaluated by probing attachment level measurements, radiographic analysis or re-entry operations. However, such methods do not provide proof of a true gain of attachment (i.e. formation of cementum with inserting collagen fibers coronal to the attachment level before treatment).

Periodontal probing

The inability of periodontal probing to determine accurately the coronal level of the connective tissue

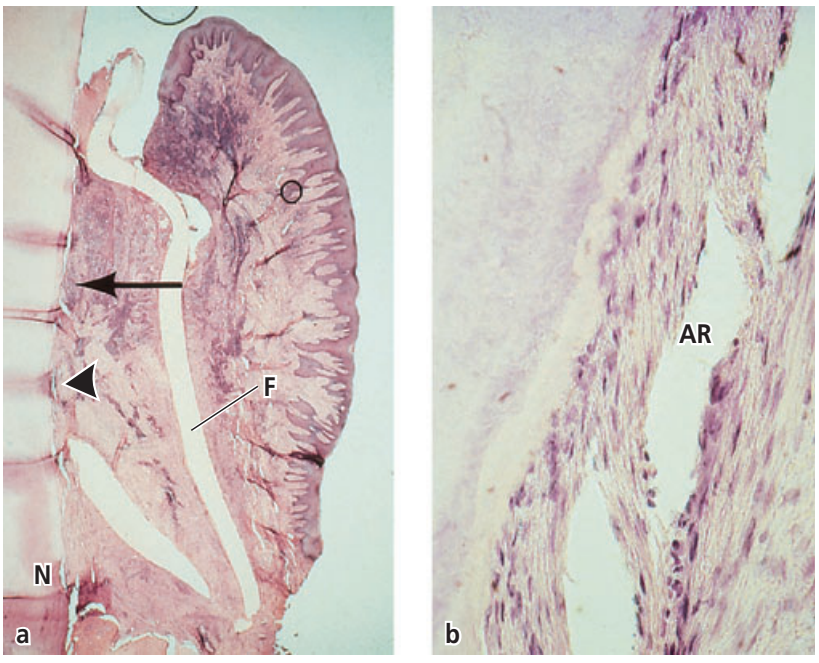

Fig. 25-23 (a) Microphotograph of a human tooth 3 months following GTR treatment using a Millipore filter (F). New cementum with inserting collagen fibers (about 5 mm) has formed from the notch (N) to the level of the arrow. Bone formation underneath the filter is lacking, probably due to the inflammatory infiltrate seen in the tissues adjacent to the filter. (b) Higher magnification of the area indicated by the arrowhead in (a) showing newly formed cementum with inserting collagen fibers. AR = artifact.

attachment has been demonstrated by several investigators (Listgarten *et al*. 1976; Armitage *et al*. 1977; Van der Velden & de Vries 1978). It is known from these studies that, in the inflamed periodontium, the probe does not stop precisely at the coronal level of the connective tissue attachment. Usually it penetrates 0.5 mm or more into the connective tissue, surpassing the transition between the apical extension of the dentogingival epithelium and the coronal level of connective tissue attachment. After therapy, when the inflammatory lesion is resolved, the probe tip tends to stop coronal to the apical termination of the epithelium. Following treatment of intrabony defects, new bone may form so close to the tooth surface that the probe cannot penetrate (Caton & Zander 1976). Thus, a gain of probing attachment level (PAL) following therapy does not necessarily mean that a true gain of connective tissue attachment was accomplished. More likely it is a reflection of improved health of the surrounding soft tissues which offer increased resistance to probe penetration.

Radiographic analysis and re-entry operations

Healing of intrabony defects following regenerative surgery is often documented by measurements made on radiographs obtained in a standardized and reproducible manner and/or assessed in conjunction with a re-entry operation. Analysis of radiographs before and after therapy and inspection of the treated area during a re-entry operation can certainly provide evidence of new bone formation. However, such "bone fill" does not prove formation of new root cementum with inserting collagen fibers (i.e. a new periodontal ligament). In fact, it was demonstrated by Caton and-Zander (1976) and Moscow *et al*. (1979) that despite the fact that bone regeneration had occurred adjacent to the root in intrabony defects, a junctional epithelium was interposed between the newly formed bone and the curetted root surface. This means that radiographic analysis and assessments of bone formation by re-entry operations are unreliable methods for the documentation of new attachment formation.

Histologic methods

In several studies healing is analyzed in histologic sections of block biopsies obtained after various forms of regenerative periodontal therapy. Histologic analysis is the only valid method to assess the formation of a true new attachment, but it requires that the location of the attachment level prior to therapy can be assessed with a reasonable accuracy. In a few studies histologic reference notches were placed in the apical extent of calculus deposits, identified on the root surface at the time of surgery (Cole *et al*. 1980; Bowers *et al*. 1989b,c). Usually, however, a reference is obtained by producing a notch in the root surface at the level of the reduced bone height. Although such a notch may not reflect the exact extent of the periodontitis-involved root surface prior to treatment, it is considered an adequate landmark for the assessment of new attachment (Isidor *et al*. 1985). It was also suggested that clinical signs of probing attachment gain and bone fill can be accepted as evidence of periodontal regeneration in the evaluation of GTR procedures (Lindhe & Echeverria 1994). This suggestion was based on evidence of a new attachment apparatus in histologic specimens from human biopsies harvested following GTR treatment (Nyman *et al*. 1982; Gottlow *et al*. 1986; Becker *et al*. 1987; Stahl *et al*. 1990a; Cortellini *et al*. 1993) and on the biologic concept of GTR (Karring *et al*. 1980, 1985, 1993; Nyman *et al*. 1980; Gottlow *et al*. 1984).

Conclusions

There is evidence that the progenitor cells for reformation of lost periodontal attachment are present in the periodontal ligament. Consequently, a periodontal regenerative procedure needs to encourage repopulation of the previous periodontitis-affected root surface with cells from the periodontal ligament.

GTR and conditioning of the root surface with enamel matrix proteins represent the best documented regenerative procedures for obtaining periodontal regeneration in periodontal lesions, although there is some uncertainty whether enamel matrix proteins in fact stimulate the proliferation of periodontal ligament cells.

Placement of bone grafts or bone substitute implants are based on a biologic concept which cannot explain how such treatment should result in regeneration of the periodontium. There are some studies indicating that bone grafting in periodontal intrabony defects may produce clinical improvements beyond that achieved with only flap surgery, but generally bone grafts or bone substitute implants are considered as primarily defect filler materials.

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Part 9: Examination Protocols

Chapter 26

Examination of Patients with Periodontal Diseases

Giovanni E. Salvi, Jan Lindhe, and Niklaus P. Lang

History of periodontal patients

The history of the patient is a revealing document as a basis for comprehensive treatment planning and understanding of the patient's needs, social and economic situation, as well as general medical conditions. In order to expedite history taking, a health questionnaire may be filled out by the patient prior to the initial examination. Such a questionnaire should be constructed in a way that the professional immediately realizes compromising or risk factors that may modify the treatment plan and, hence, may have to be discussed in detail with the patient during the initial visit. The assessment of the patient's history requires an evaluation of the following six aspects: (1) chief complaint, (2) social and family history, (3) dental history, (4) oral hygiene habits, (5) smoking history, and (6) medical history and medications.

Chief complaint and expectations

It is essential to realize the patient's needs and desires for treatment. If a patient has been referred for specific treatment, the extent of the desired treatment has to be defined and the referring dentist should be informed of the intentions for treatment.

Patients reporting independently, however, usually have specific desires and expectations regarding treatment outcomes. These may not be congruent with the true assessment of a professional with respect to the clinical situation. Optimal treatment results may only be achieved if the patient's demands are in balance with the objective evaluation of the disease and the projected treatment outcomes. Therefore, the patient's expectations have to be taken seriously and must be incorporated in the evaluation in harmony with the clinical situation.

Social and family history

Before assessing the clinical condition in detail, it is advantageous to elucidate the patient's social environment and to get a feeling for his/her priorities in life, including the attitude to dental care. Likewise, a family history may be important, especially with respect to aggressive forms of periodontitis.

Dental history

These aspects include an assessment of previous dental care and maintenance visits if not stated by a referring dentist. In this context, information regarding signs and symptoms of periodontitis noted by the patient, such as migration and increasing mobility of teeth, bleeding gums, food impaction, and difficulties in chewing have to be explored. Chewing comfort and the possible need for tooth replacement is determined.

Oral hygiene habits

In addition to the exploration of the patient's routine dental care, including frequency and duration of daily tooth brushing, knowledge about interdental cleansing devices and additional chemical supportive agents, and regular use of fluorides should be assessed.

Smoking history

Since cigarette smoking has been documented to be the second most important risk factor after inadequate plaque control (Kinane *et al*. 2006) in the etiology and pathogenesis of periodontal diseases, the importance of smoking counseling cannot be overestimated. Hence, determination of smoking status, including detailed information about exposure time and quantity, has to be gathered. Further aspects of smoking cessation programs are presented in Chapter 33.

Medical history and medications

General medical aspects may be extracted from the health questionnaire constructed to highlight the medical risk factors encountered for routine periodontal and/or implant therapy. The four major complexes of complications encountered in patients may be prevented by checking the medical history with respect to: (1) cardiovascular and circulatory risks, (2) bleeding disorders, (2) infective risks, and (4) allergic reactions. Further aspects are presented in Chapters 30 and 33.

In light of the increasing consumption of medications in the aging population, an accurate assessment of the patient's prescribed medications and their potential interactions and effects on therapeutic procedures has to be made. It may be necessary to contact the patient's physician for detailed information relevant to the planned dental treatment.

Signs and symptoms of periodontal diseases

Periodontal diseases are characterized by color and texture alterations of the gingiva, e.g. redness and swelling, as well as an increased tendency to bleeding upon probing in the gingival sulcus/pocket area (Fig. 26-1). In addition, the periodontal tissues may exhibit reduced resistance to probing perceived as increased probing depth and/or tissue recession. Advanced stages of periodontitis may also be associated with increased tooth mobility as well as drifting or flaring of teeth (Fig. 26-2).

In radiographs, periodontitis may be recognized by moderate to advanced loss of alveolar bone (Fig. 26-3). Bone loss is defined either as "horizontal" or "angular". If bone loss has progressed at similar rates in the dentition, the crestal contour of the remaining bone in the radiograph is even and defined as being "horizontal". In contrast, angular bony defects are the result of bone loss that developed at different rates around teeth/tooth surfaces and, hence, that type is defined as being "vertical" or "angular".

In a histological section, periodontitis is characterized by the presence of an inflammatory cell infiltrate within a 1–2 mm wide zone of the gingival connective tissue adjacent to the biofilm on the tooth (Fig. 26-4). Within the infiltrated area there is a pronounced loss of collagen. In more advanced forms of periodontitis, marked loss of connective tissue attachment to the root and apical downgrowth of the dentogingival epithelium along the root are important characteristics.

Results from clinical and animal research have demonstrated that chronic and aggressive forms of periodontal disease:

1. Affect individuals with various susceptibility at different rates (Löe *et al*. 1986)
2. Affect different parts of the dentition to a varying degree (Papapanou *et al*. 1988)
3. Are site specific in nature for a given area (Socransky *et al*. 1984)
4. Are sometimes progressive in character and, if left untreated, may result in tooth loss (Löe *et al*. 1986)
5. Can be arrested following proper therapy (Rosling *et al*. 2001).

For effective treatment planning, the location, topography, and extent of periodontal lesions must be recognized in all parts of the dentition. It is, therefore, mandatory to examine all sites of all teeth for the presence or absence of periodontal lesions. This, in turn, means that single-rooted teeth will have to be examined at least at four sites (e.g. mesial, buccal, distal, and oral) and multi-rooted teeth at least at six sites (e.g. mesio-buccal, buccal, disto-buccal, disto-oral, oral, and mesio-oral) with special attention to the furcation areas.

Since periodontitis includes inflammatory alterations of the gingiva and a progressive loss of periodontal attachment and alveolar bone, the comprehensive examination must include assessments describing such pathologic alterations. Figure 26-1 illustrates the clinical status of a 59-year-old patient diagnosed with advanced generalized chronic periodontitis. The examination procedures used to assess the location and extension of periodontal disease will be demonstrated by using this case as an example.

The gingiva

Clinical signs of gingivitis include changes in color and texture of the soft marginal gingival tissue and bleeding on probing.

Various index systems have been developed to describe gingivitis in epidemiologic and clinical research. They are discussed in Chapter 7. Even though the composition of the inflammatory infiltrate can only be identified in histologic sections, the correct clinical diagnosis for inflamed gingival tissue is made on the basis of the tendency to bleed on probing. The symptom "bleeding on probing" (BoP) to the bottom of the gingival sulcus/pocket is associ-

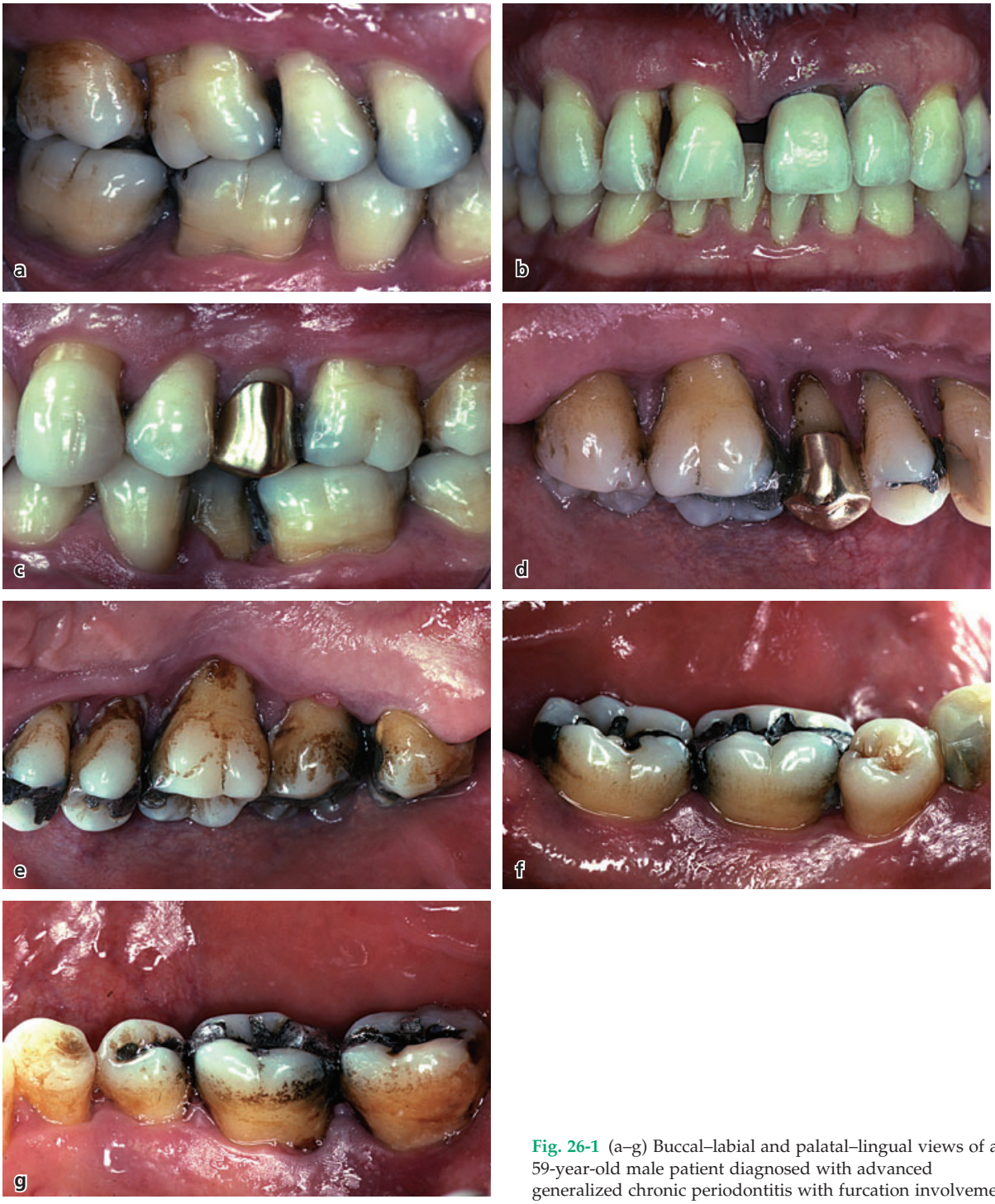

Fig. 26-1 (a–g) Buccal–labial and palatal–lingual views of a 59-year-old male patient diagnosed with advanced generalized chronic periodontitis with furcation involvement.

ated with the presence of an inflammatory cell infiltrate. The occurrence of such bleeding, especially in repeated examinations, is indicative for disease progression (Lang *et al*. 1986), although the predictive value of this single parameter remains rather low (i.e. 30%). On the other hand, the absence of bleeding on probing yields a high negative predictive value (i.e. 98.5%) and, hence, is an important indicator of periodontal stability (Lang *et al*. 1990; Joss *et al*. 1994).

Since trauma to the tissues provoked by probing should be avoided to assess the true vascular permeability changes associated with inflammation, a probing pressure of 0.25 N should be applied for assessing "bleeding on probing" (Lang *et al*. 1991; Karayiannis *et al*. 1992). The identification of the apical extent of the gingival lesion is made in conjunction with pocket probing depth (PPD) measurements. In sites where "shallow" pockets are present,

inflammatory lesions in the overt portion of the gingiva are distinguished by probing in the superficial marginal tissue. When the infiltrate is in sites with attachment loss, the inflammatory lesion in the apical part of the pocket must be identified by probing to the bottom of the deepened pocket.

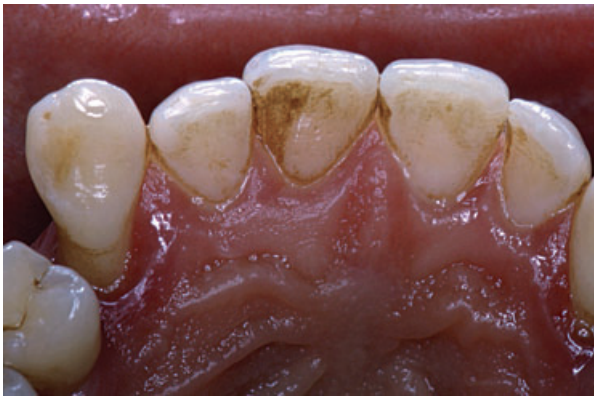

Fig. 26-2 Buccal migration of tooth 13 as a sign of advanced periodontitis.

Bleeding on probing (BoP)

A periodontal probe is inserted to the "bottom" of the gingival/periodontal pocket applying light force and is moved gently along the tooth (root) surface (Fig. 26-5). If bleeding is provoked by this instrumentation upon retrieval of the probe, the site examined is considered "bleeding on probing" (BoP)-positive and, hence, inflamed.

Figure 26-6 illustrates the chart used to identify BoP-positive sites in a dichotomous way at the initial examination. Each tooth in the chart is represented and each tooth surface is indicated by a triangle. The inner segments represent the palatal/lingual gingival units, the outer segments the buccal/labial units and the remaining fields the two approximal gingival units. The fields of the chart corresponding to the

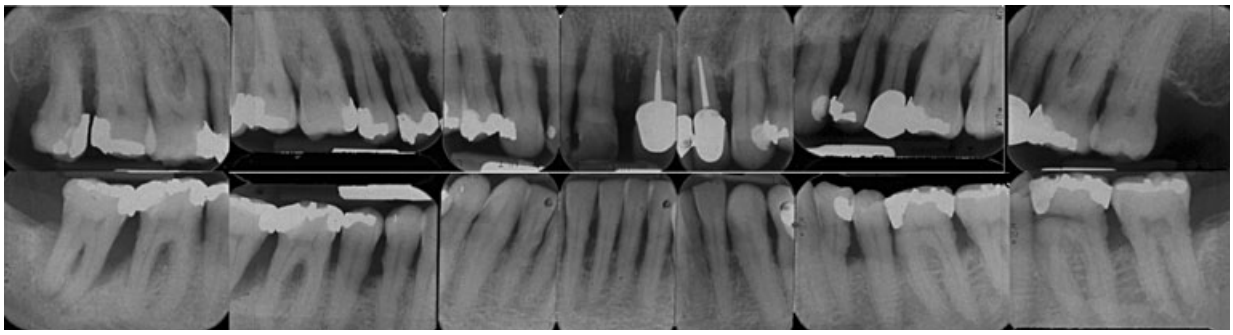

Fig. 26-3 Periapical radiographs of the patient presented in Fig. 26-1.

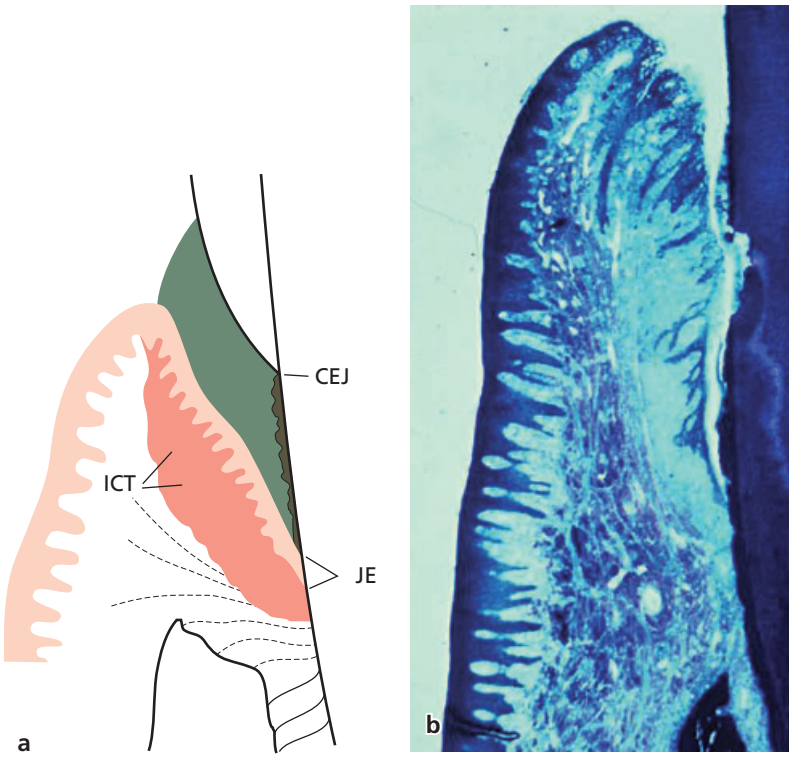

Fig. 26-4 Schematic drawing (a) and histologic section (b) illustrating the characteristics of periodontal disease. Note the zone of infiltrated connective tissue (ICT) lateral to the junctional epithelium (JE). CEJ = cemento-enamel junction; JE = junctional epithelium.

inflamed gingival units are marked in red. The mean BoP score (i.e. gingivitis) is given as a percentage. In the present example, 104 out of a total number of 116 gingival units bled on probing, amounting to a BoP percentage of 89%. This method of charting not only serves as a means of documenting areas of health and disease in the dentition but similar charting during the course of therapy or maintenance will disclose sites which become healthy or remain inflamed. The topographical pattern will also identify sites with consistent or repeated BoP at various observation periods.

The periodontal ligament and the root cementum

In order to evaluate the amount of tissue lost in periodontitis and also to identify the apical extension of the inflammatory lesion, the following parameters should be recorded:

1. Probing pocket depth (PPD)
2. Probing attachment level (PAL)
3. Furcation involvement (FI)
4. Tooth mobility (TM).

Assessment of probing pocket depth

The probing depth, i.e. the distance from the gingival margin to the bottom of the gingival sulcus/pocket, is measured to the nearest millimeter by means of a graduated periodontal probe with a standardized tip diameter of approximately 0.4–0.5 mm (Fig. 26-7). The pocket depth should be assessed at each surface of all teeth in the dentition. In the periodontal chart (Fig. 26-8), PPD <4 mm are indicated in black figures, while deeper PPD (i.e. ≥4 mm) are marked in red. This allows an immediate evaluation of diseased sites (i.e. red figures) both from an extent and severity point of view. The chart may be used for case presentation and discussion with the patient.

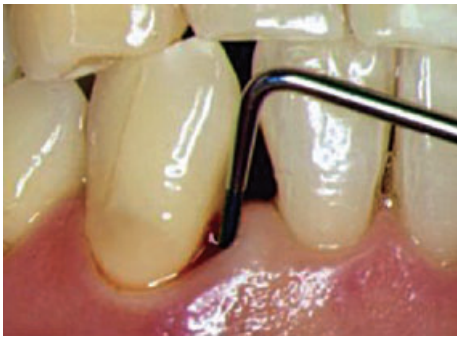

Fig. 26-5 Probing pocket depth (PPD) in conjunction with bleeding on probing (BoP). A graduated periodontal probe is inserted to the "bottom" of the gingival/periodontal pocket applying light force and is moved gently along the tooth (root) surface.

Results from pocket depth measurements will only give proper information regarding the extent of loss of probing attachment in rare situations (when the gingival margin coincides with the cemento-enamel junction, CEJ). For example, an inflammatory edema may cause swelling of the free gingiva resulting in coronal displacement of the gingival margin without a concomitant migration of the dentogingival epithelium to a level apical to the CEJ. In such a situation, a pocket depth exceeding 3–4 mm represents a "pseudopocket". In other situations, an obvious loss of periodontal attachment may have occurred without a concomitant increase of probing pocket depth. A situation of this kind is illustrated in Fig. 26-9, where multiple recessions of the gingiva can be seen. Hence, the assessment of the probing depth in relation to the CEJ is an indispensable parameter for the evaluation of the periodontal condition (i.e. PAL).

Assessment of probing attachment level

PAL may be assessed to the nearest millimeter by means of a graduated probe and expressed as the distance in millimeters from the CEJ to the bottom of the probeable gingival/periodontal pocket. The clinical assessment requires the measurement of the distance from the free gingival margin (FGM) to the CEJ for each tooth surface. After this recording, PAL may be calculated from the periodontal chart (i.e. PPD – distance CEJ to FGM). In cases with gingival recession, the distance FGM–CEJ turns negative and, hence, will be added to the PPD to determine PAL.

Errors inherent in periodontal probing

The distances recorded in a periodontal examination using a periodontal probe have generally been assumed to represent a fairly accurate estimate of the PPD or PAL at a given site. In other words, the tip of the periodontal probe has been assumed to identify the level of the most apical cells of the dentogingival (junctional epithelium) epithelium. Results from research, however, indicated that this is seldom the

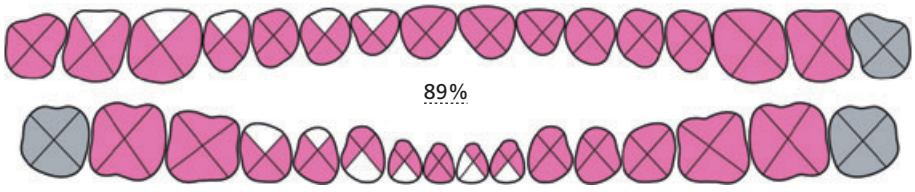

Fig. 26-6 Chart used to identify BoP-positive sites in a dichotomous way at the initial examination and during maintenance care.

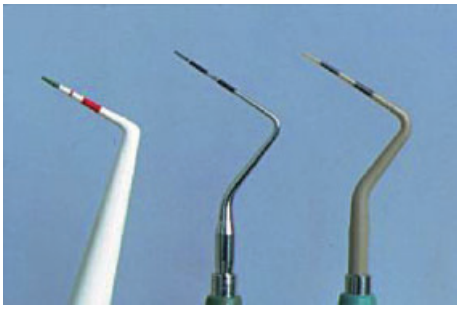

Fig. 26-7 Examples of graduated periodontal probes with a standardized tip diameter of approximately 0.4–0.5 mm.

case (Saglie *et al*. 1975; Listgarten *et al*. 1976; Armitage *et al*. 1977; Ezis & Burgett 1978; Spray *et al*. 1978; Robinson & Vitek 1979; van der Velden 1979; Magnusson & Listgarten 1980; Polson *et al*. 1980). A variety of factors influencing measurements made with periodontal probes include: (1) the thickness of the probe used, (2) angulation and positioning of the probe due to anatomic features such as the contour of the tooth surface, (3) the graduation scale of the periodontal probe, (4) the pressure applied on the instrument during probing, and (5) the degree of

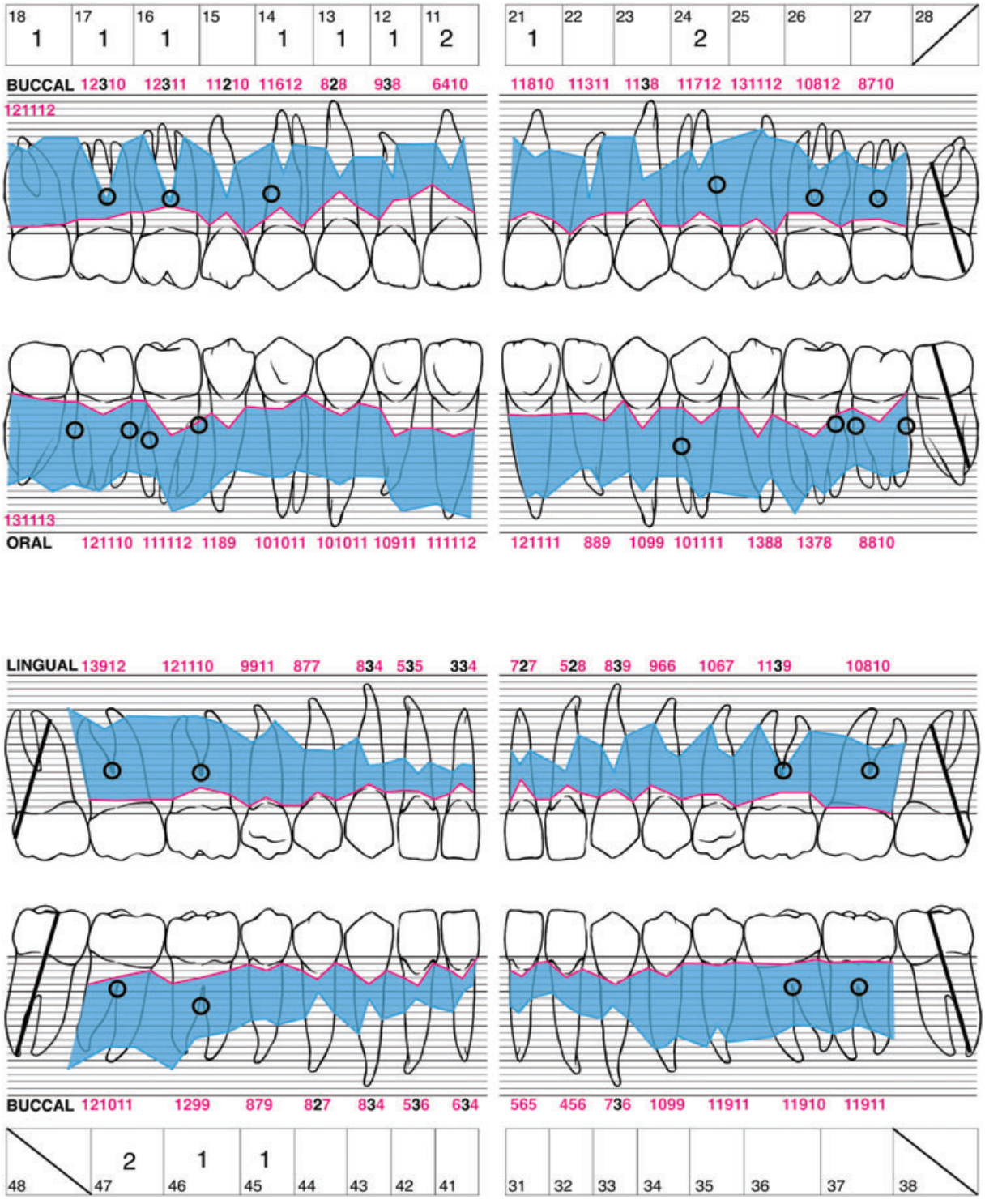

Fig. 26-8 Periodontal chart indicating PPD <4 mm in black figures and PPD ≥4 mm in red figures. This allows an immediate evaluation of diseased sites (i.e. red figures) both from an extent and severity point of view.

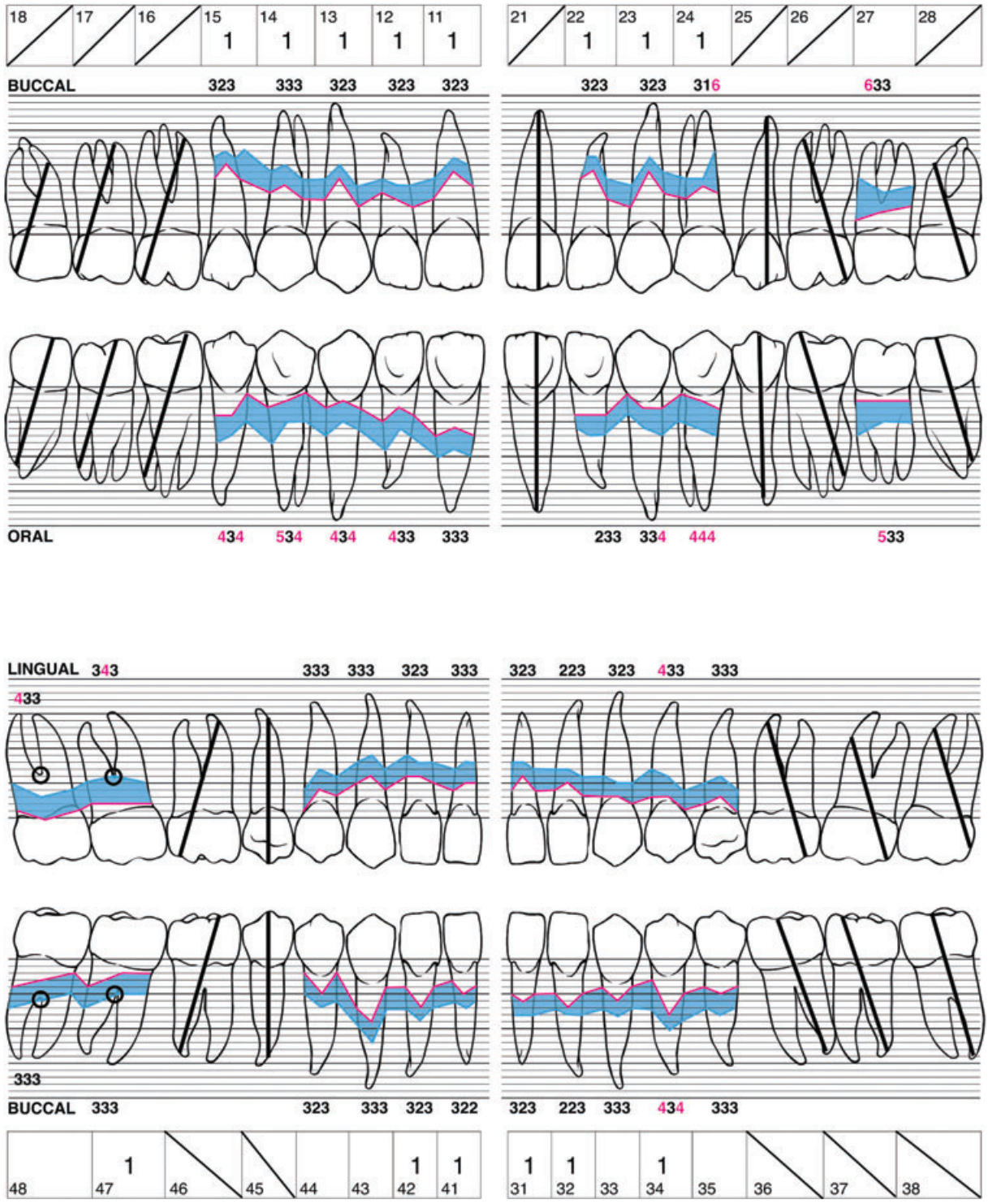

Fig. 26-9 Periodontal attachment loss has occurred without a concomitant increase of probing pocket depth. Multiple buccal/labial as well as palatal/lingual gingival recessions can be seen.

inflammatory cell infiltration in the soft tissue and accompanying loss of collagen. Therefore, a distinction should be made between the histologic and the clinical PPD to differentiate between the depth of the actual anatomic defect and the measurement recorded by the probe (Listgarten 1980).

Measurement errors depending on factors such as the thickness of the probe, the contour of the tooth surface, incorrect angulation, and the graduation scale of the probe can be reduced or avoided by the selection of a standardized instrument and careful management of the examination procedure. More difficult to avoid, however, are errors resulting from variations in probing force and the extent of inflammatory alterations of the periodontal tissues. As a rule, the greater the probing pressure applied, the deeper the penetration of the probe into the tissue. In this context, it should be realized that in investigations designed to disclose the pressure (force) used by different clinicians, the probing pressure was found to range from 0.03–1.3 N (Gabathuler & Hassell 1971; Hassell *et al*. 1973), and also, to differ by as

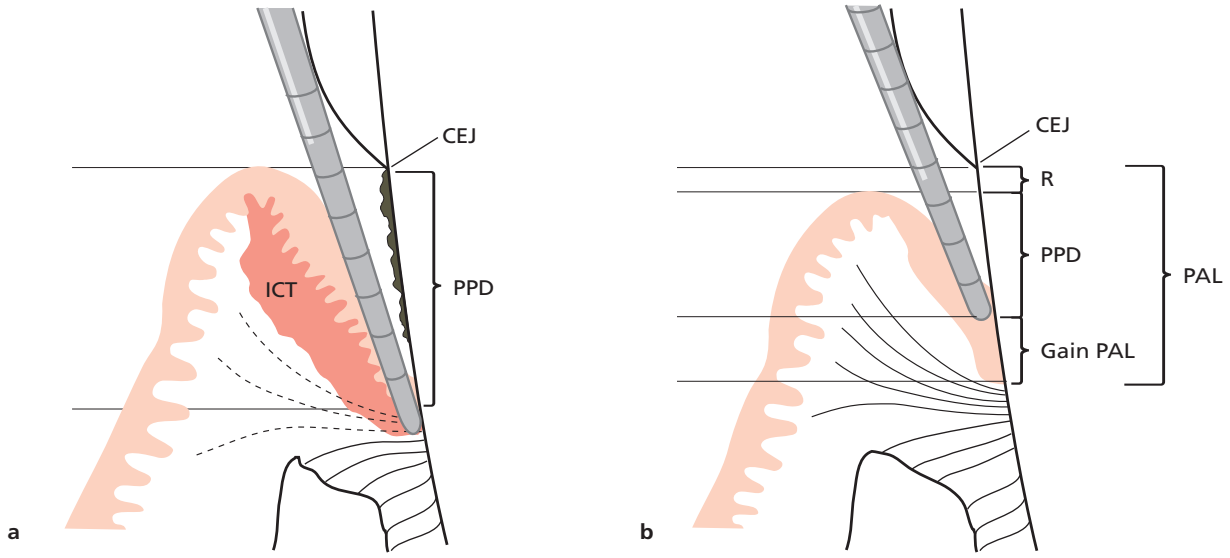

Fig. 26-10 (a) In the presence of an inflammatory cell infiltrate (ICT) in the connective tissue of the gingiva, the periodontal probe penetrates apically to the bottom of the histologic pocket. (b) Following successful periodontal therapy, the swelling is reduced and the connective tissue cell infiltrate is replaced by collagen. The periodontal probe fails to reach the apical part of the dentogingival epithelium. CEJ = cemento-enamel junction; PPD = probing pocket depth; PAL = probing attachment level; R = recession; Gain PAL = recorded false gain of attachment ("clinical attachment").

much as 2:1 for the same dentist from one examination to another. In order to exclude measurement errors related to the effect of variations in probing pressure, so-called pressure-sensitive probes have been developed. Such probes will enable the examiner to probe with a predetermined pressure (van der Velden & de Vries 1978; Vitek *et al*. 1979; Polson *et al*. 1980). However, over- and underestimation of the "true" PPD or PAL may also occur when this type of probing device is employed (Armitage *et al*. 1977; Robinson & Vitek 1979; Polson *et al*. 1980). Thus, when the connective tissue subjacent to the pocket epithelium is infiltrated by inflammatory cells (Fig. 26-10), the periodontal probe will most certainly penetrate beyond the apical termination of the dentogingival epithelium. This results in an overestimation of the "true" depth of the pocket. Conversely, when the inflammatory infiltrate decreases in size following successful periodontal treatment, and a concomitant deposition of new collagen occurs within the previously inflamed tissue area, the dentogingival tissue will become more resistant to penetration by the probe. The probe may now fail to reach the apical termination of the epithelium using the same probing pressure. This, in turn, results in an underestimation of the "true" PPD or PAL. The magnitude of the difference between the probing measurement and the histologic "true" pocket depth (Fig. 26-10) may range from fractions of a millimeter to a couple of millimeters (Listgarten 1980).

From this discussion it should be understood that reductions in PPD following periodontal treatment and/or gain of PAL, assessed by periodontal probing, do not necessarily indicate the formation of a new connective tissue attachment at the bottom of the previous lesion. Rather, such a change may merely represent a resolution of the inflammatory process and may thus occur without an accompanying histologic gain of attachment (Fig. 26-10). In this context it should be realized that the terms "probing pocket depth" (PPD) and "probing attachment level" (PAL) have replaced the previously used terms "pocket depth" and "gain and loss of attachment". Likewise, PAL is used in conjunction with "gain" and/or "loss" to indicate that changes in PAL have been assessed by clinical probing.

Current knowledge of the histopathology of periodontal lesions and healing thereof has thus resulted in an altered concept regarding the validity of periodontal probing. However, despite difficulties in interpreting the significance of PPD and PAL measurements, such determinations still give the clinician a useful estimate of the degree of disease involvement, and particularly so, when the information obtained is related to other findings of the examination procedure such as BoP and changes in alveolar bone height.

In recent years, periodontal probing procedures have been standardized to the extent that automated probing systems such as, e.g. the Florida Probe™, have been developed, yielding periodontal charts with PPD, PAL, BoP, furcation involvement (FI) and tooth mobility (TM) at one glance (Gibbs *et al*. 1988). Also, repeated examinations allow the comparison of parameters, and, hence, an assessment of the healing process (Fig. 26-11).

Assessment of furcation involvement

In the progression of periodontitis around multirooted teeth, the destructive process may involve the supporting structures of the furcation area (Fig.

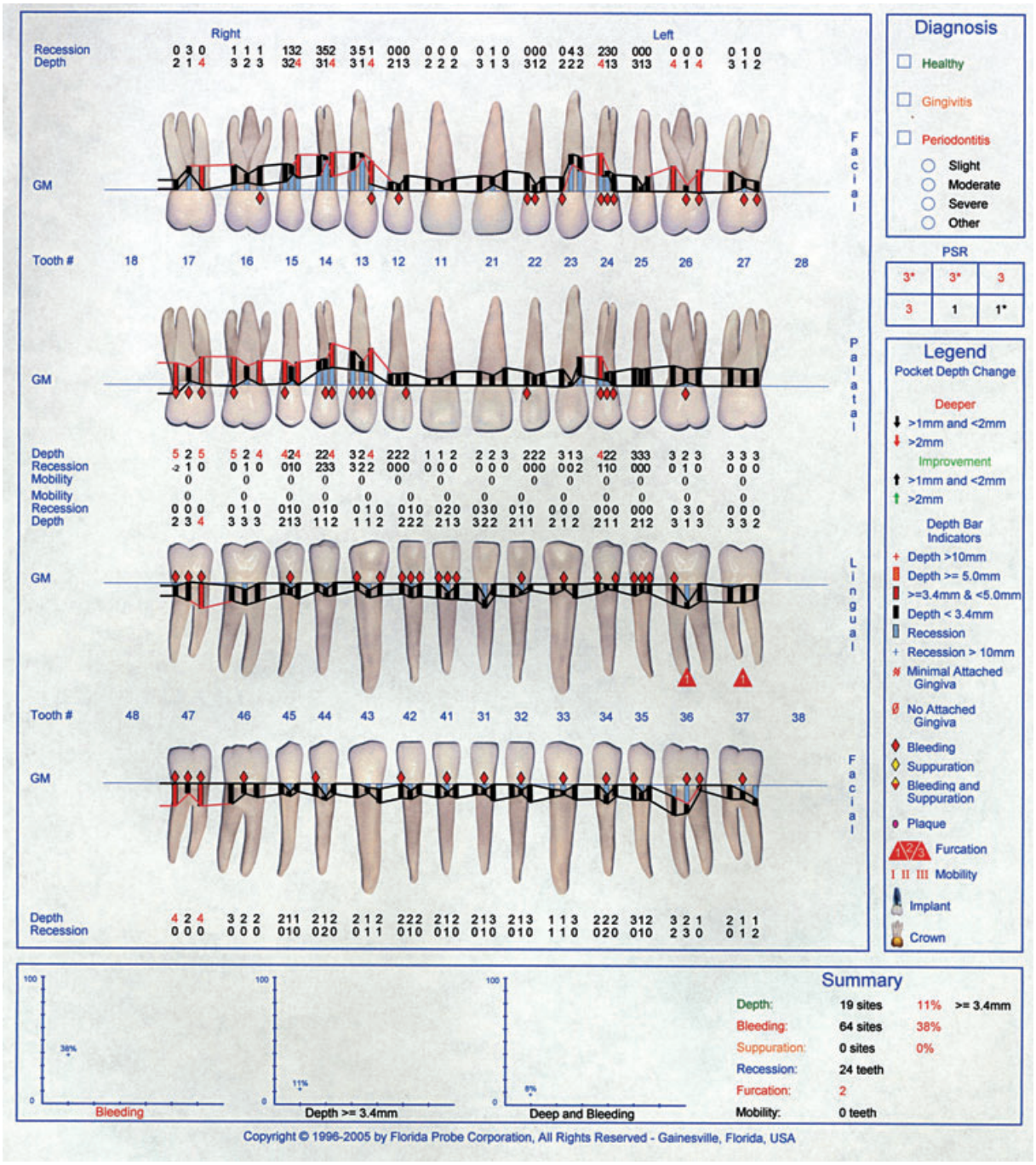

Fig. 26-11 Periodontal chart using an automated probing system (Florida Probe™). Reproduced with permission, © Copyright 1996–2005 Florida Probe Corporation.

26-12). In order to plan treatment for such involvement, a detailed and precise identification of the presence and extension of periodontal tissue breakdown within the furcation area is of importance for proper diagnosis.

Furcation involvement is assessed from all the entrances of possible periodontal lesions of multirooted teeth, i.e. buccal and/or lingual entrances of the mandibular molars. Maxillary molars and premolars are examined from the buccal, disto-palatal, and mesio-palatal entrances. Owing to the position of the first maxillary molars within the alveolar process, the furcation between the mesio-buccal and the palatal

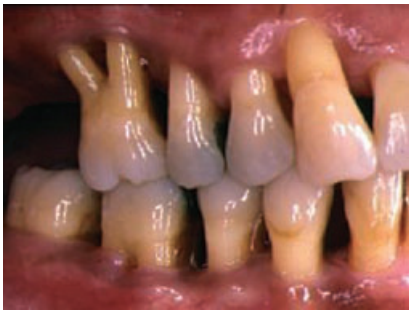

Fig. 26-12 Superficial (tooth 46) and deep (tooth 16) periodontal tissue destruction in the buccal furcation areas.

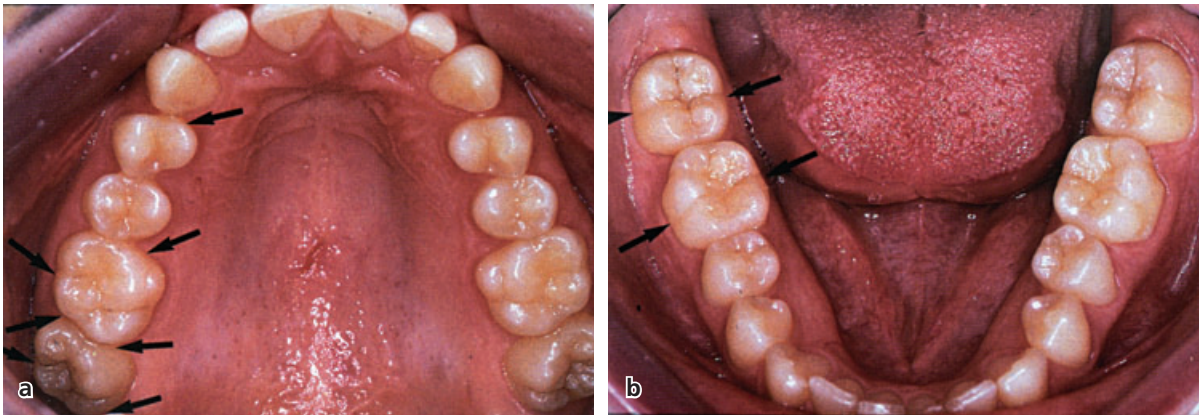

Fig. 26-13 (a,b) Anatomic locations for the assessment of furcation involvement (FI) in the maxilla and in the mandible.

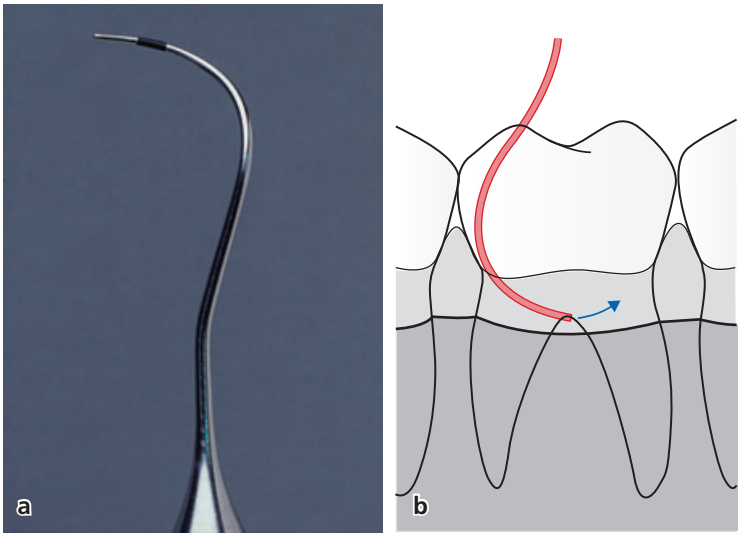

Fig. 26-14 (a,b) Furcation involvement (FI) is explored using a curved periodontal probe graduated at 3 mm (Nabers furcation probe).

roots is best explored from the palatal aspect (Fig. 26-13).

Furcation involvement is explored using a curved periodontal probe graduated at 3 mm (Nabers furcation probe) (Fig. 26-14). Depending on the penetration depth, the FI is classified as "superficial" or "deep":

- Horizontal probing depth ≤3 mm from one or two entrances is classified as a degree I FI.
- Horizontal probing depth >3 mm in at the most one furcation entrance and/or in combination with a degree I FI is classified as degree II FI.
- Horizontal probing depth >3 mm in two or more furcation entrances usually represents a "through-and-through" destruction of the supporting tissues in the furcation and is classified as degree III FI.

The FI degree is presented in the periodontal chart (Fig. 26-15) together with a description of which tooth surface the involvement has been identified on. A detailed discussion regarding the management

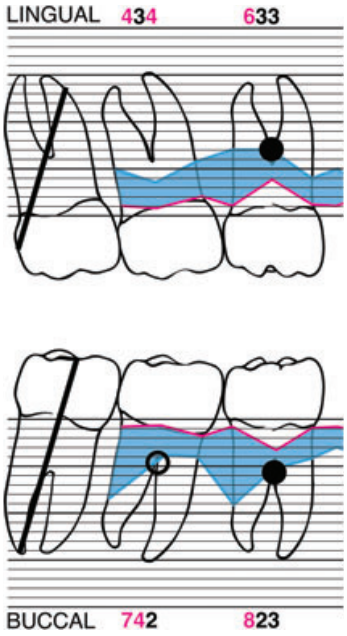

Fig. 26-15 The FI degree is illustrated in the periodontal chart. Open circles represent a superficial FI (i.e horizontal probe penetration ≤3 mm) whereas filled black circles represent a deep FI (i.e. horizontal probe penetration >3 mm).

of furcation-involved teeth is presented in Chapter 39.

Assessment of tooth mobility

The continuous loss of the supporting tissues during periodontal disease progression may result in increased tooth mobility. However, trauma from occlusion may also lead to increased tooth mobility. Therefore, the reason for increased tooth mobility as being the result of a widened periodontal ligament or a reduced height of the supporting tissues or a combination thereof should be elaborated. Increased tooth mobility may be classified according to Miller (1950).

- Degree 0: "physiological" mobility measured at the crown level. The tooth is mobile within the alveolus to approximately 0.1–0.2 mm in a horizontal direction.
- Degree 1: increased mobility of the crown of the tooth to at the most 1 mm in a horizontal direction.
- Degree 2: visually increased mobility of the crown of the tooth exceeding 1 mm in a horizontal direction.
- Degree 3: severe mobility of the crown of the tooth both in horizontal and vertical directions impinging on the function of the tooth.

It must be understood that plaque-associated periodontal disease is not the only cause of increased tooth mobility. For instance, overloading of teeth and trauma may result in tooth hypermobility. Increased tooth mobility can frequently also be observed in conjunction with periapical lesions or immediately following periodontal surgery. From a therapeutic point of view it is important, therefore, to assess not only the degree of increased tooth mobility but also the cause of the observed hypermobility (see Chapters 14 and 57).

All data collected in conjunction with measurements of PPD, PAL, as well as from the assessments of FI and tooth mobility are included in the periodontal chart (Fig. 26-8). The various teeth in this chart are denoted according to the two-digit system adopted by the FDI in 1970.

The alveolar bone

The height of the alveolar bone and the outline of the bony crest are examined in radiographs (Fig. 26-3). Radiographs provide information on the height and configuration of the interproximal alveolar bone. Obscuring structures such as roots of the teeth often make it difficult to identify the outline of the buccal and lingual alveolar bony crest. Analysis of radiographs must, therefore, be combined with a detailed evaluation of the periodontal chart in order to come up with a correct estimate concerning "horizontal" and "angular" bony defects.

Fig. 26-16 The use of a Rinn filmholder and a long-cone paralleling technique yield reproducible radiographs.

As opposed to the periodontal chart that represents a sensitive diagnostic estimate of the lesions, the radiographic analysis is a specific diagnostic test yielding few false-negative results and, hence, is confirmatory to the periodontal chart (Lang & Hill 1977).

To enable meaningful comparative analysis, a radiographic technique should be used which yields reproducible radiographs. In this context, a long-cone paralleling technique (Updegrave 1951) is recommended (Fig. 26-16).

Diagnosis of periodontal lesions

Based on the information regarding the condition of the various periodontal structures (i.e. the gingiva, the periodontal ligament, and the alveolar bone) which has been obtained through the comprehensive examination presented above, a classification of the patient as well as a diagnosis for each tooth regarding the periodontal conditions may be given (Table 26-1). Four different tooth-based diagnoses may be used:

- *Gingivitis*. This diagnosis is applied to teeth displaying bleeding on probing. The sulcus depth usually remains at levels of 1–3 mm irrespective of the level of clinical attachment. "Pseudopockets" may be present in cases of slightly increased probing depth without concomitant attachment and alveolar bone loss and presence/absence of bleeding on probing. The diagnosis of gingivitis usually characterizes lesions confined to the gingival margin.
- *Parodontitis superficialis* (mild–moderate periodontitis). Gingivitis in combination with attachment loss is termed "periodontitis". If the PPD does not exceed 6 mm, a diagnosis of mild–moderate

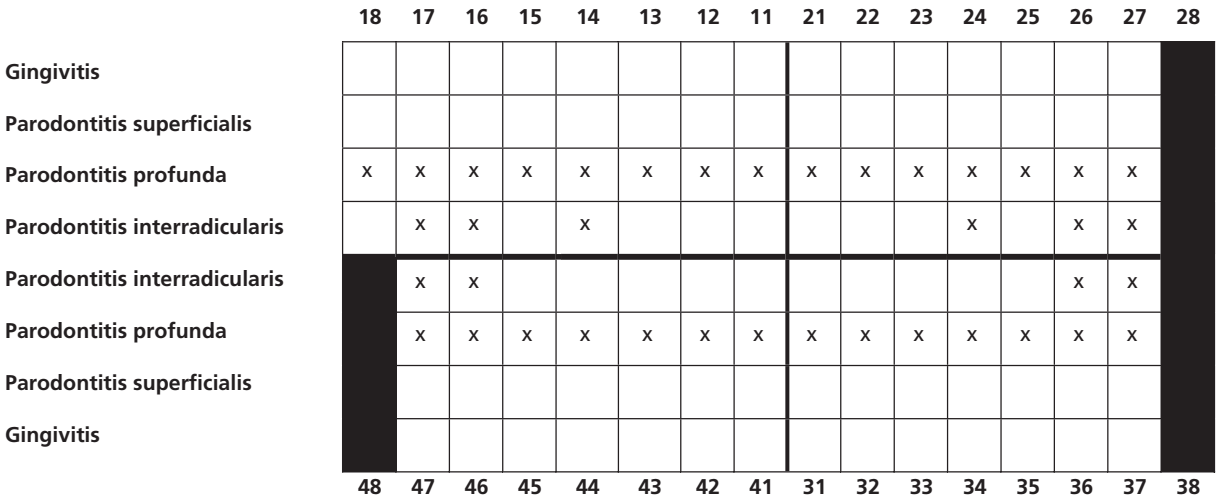

Fig. 26-17 Chart of the individual tooth diagnosis of the patient presented in Fig. 26-1.

Table 26-1 The diagnosis of the periodontal tissue conditions around each tooth in the dentition is given using main criteria (i.e. periodontal chart and radiographic analysis) and additional criteria (i.e. bleeding on probing)

Diagnosis	Main criteria	Additional criteria
Gingivitis	Bleeding on probing (BoP) No loss of PAL and alveolar bone PPD ≤3 mm Pseudopockets	
Parodontitis superficialis	PPD ≤5 mm, irrespective of the morphology of the periodontal lesion Angular and/or horizontal alveolar bone loss	Bleeding on probing (BoP)
Parodontitis profunda	PPD ≥6 mm, irrespective of the morphology of the periodontal lesion Angular and/or horizontal alveolar bone loss	Bleeding on probing (BoP)
Parodontitis interradicularis	Horizontal PPD ≤3 mm: superficial FI Horizontal PPD >3 mm: deep FI	Bleeding on probing (BoP)

periodontitis is given irrespective of the morphology of periodontal lesions. This diagnosis may, therefore, be applied to teeth with "horizontal" loss of supporting tissues, representing suprabony lesions, and/or to teeth with "angular" or "vertical" loss of supporting tissues, representing infrabony lesions. "Infrabony" lesions include "intrabony one-, two- and three-wall defects" as well as "craters" between two adjacent teeth.

- *Parodontitis profunda* (advanced periodontitis). If the PPD does exceeds 6 mm, a diagnosis of advanced periodontitis is given irrespective of the morphology of periodontal lesions. As for mild–moderate periodontitis, angular as well as horizontal alveolar bone loss are included in this diagnosis. The distinction between mild–moderate and advanced periodontitis is only based on increased PPD.
- *Parodontitis interradicularis* (periodontitis in the furcation area). Adjunctive diagnoses may be attributed to multi-rooted teeth with FI (see above): superficial FI if horizontal PPD ≤3 mm (parodontitis interradicularis superficialis) and deep FI for horizontal PPD >3 mm (parodontitis interradicularis profunda).

In the presence of necrotizing and/or ulcerative lesions, these terms may be added to tooth-related diagnoses of both gingivitis and periodontitis (Chapter 20). Acute lesions including gingival and periodontal abscesses are diagnosed as indicated in Chapter 22.

The various teeth of the patient whose clinical status is shown in Fig. 26-1, the radiographs in Fig. 26-3 and the periodontal chart in Fig. 26-8 have received the diagnoses described in Fig. 26-17.

Oral hygiene status

In conjunction with the examination of the periodontal tissues, the patient's oral hygiene practices must also be evaluated. Absence or presence of plaque on each tooth surface in the dentition is recorded in a dichotomous manner (O'Leary *et al*. 1972). The bacterial deposits may be stained with a disclosing solution to facilitate their detection. The presence of plaque is marked in appropriate fields in the plaque chart shown in Fig. 26-18. The mean plaque score for the dentition is given as a percentage in correspondence with the system used for BoP (Fig. 26-6).

Alterations with respect to the presence of plaque and gingival inflammation are illustrated in a simple

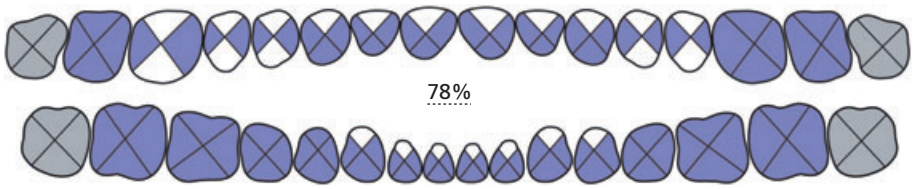

Fig. 26-18 The presence of bacterial deposits is marked in the appropriate fields in the plaque chart.

way by the repeated use of the combined BoP (Fig. 26-6) and plaque (Fig. 26-18) charts during the course of treatment. Repeated plaque recordings alone (Fig. 26-18) are predominantly indicated during the initial phase of periodontal therapy (i.e. infection control) and are used for improving self-performed plaque control. Repeated BoP charts alone (Fig. 26-6), on the other hand, are predominantly recommended during maintenance care.

Additional dental examinations

In addition to the assessment of plaque, retentive factors for plaque, such as supra- and subgingival calculus and defective margins of dental restorations, should also be identified. Furthermore, the assessment of tooth sensitivity is essential for comprehensive treatment planning. Sensitivity to percussion may indicate acute changes in pulp vitality and lead to emergency treatment prior to systematic periodontal therapy. It is obvious that a complete examination and assessment of the patient will have to include the search for carious lesions both clinically as well as radiographically.

Screening for functional disturbances may be performed using a short (i.e. 1/2 minute) test according to Shore (1963). In this test, harmonious function of the jaws with simultaneous palpation of the temporomandibular joints during opening, closing, and excursive movements is verified. Maximal mouth opening is assessed and finally, the lodge of the lateral pterygoid muscles is palpated for muscle tenderness. Further morphologic characteristics of the dentition as well as occlusal and articulating contacts may be identified.

Conclusion

The methods described above for the examination of patients with respect to periodontal disease provide a thorough analysis of the presence, extent and severity of the disease in the dentition. The classification of the patient and the correct diagnosis for each individual tooth should form the basis for a pretherapeutic prognosis and the treatment planning of the individual patient (see Chapter 31).

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Chapter 27

Examination of the Candidate for Implant Therapy

Hans-Peter Weber, Daniel Buser, and Urs C. Belser

Dental implants in periodontally compromised patients

Modern comprehensive dental care for patients with periodontally compromised dentitions has to include the consideration of dental implants. Since the initial description of osseointegration experimentally (Branemark *et al*. 1969; Schroeder *et al*. 1976, 1981), scientific evidence has been established through human clinical studies that dental implants will serve as long-term predictable anchors for fixed and removable prostheses in fully and partially edentulous patients and that patient satisfaction with dental implant therapy is high (Adell *et al*. 1990; Fritz 1996; Buser *et al*. 1997; Lindh *et al*. 1998; Moy *et al*. 2005; Pjetursson *et al*. 2005). Furthermore, substantial scientific and clinical evidence has become available to help the understanding of factors enhancing or compromising treatment success with regard to esthetic concerns (Belser *et al*. 2004a,b; Buser *et al*. 2004, 2006; Higginbottom *et al*. 2004; Martin *et al*. 2006). Overall, the pool of information on contributing factors enhancing or compromising treatment success with dental implants continues to grow and is becoming more and more valuable despite its diversity and scientific inconsistency. This is possible through a focused interpretation of the published information via systematic reviews.

The decision whether to use remaining natural teeth as abutments for conventional fixed prostheses or to add dental implants for the replacement of diseased natural teeth is influenced by a number of factors, such as location in the dental arches, strategic value and treatment prognosis for such teeth, subjective and objective need for tooth replacement, dimensions of the alveolar process, esthetic impact, as well as access for treatment. Indications for dental implants in the periodontally compromised dentition include the replacement of single or multiple "hopeless" or missing teeth within or as distal extensions to partially dentate maxillary and mandibular arches (Fig. 27-1).

In the edentulous jaw, implants supporting fixed or removable prostheses will more frequently be inserted in the anterior regions where there are more favorable alveolar bone dimensions and quality. In partially edentulous patients, implants are more likely indicated in posterior regions with less favorable anatomic conditions. The volume of the alveolar process may be substantially reduced, especially in dentitions where teeth have been lost due to periodontal disease (Fig. 27-2). This introduces a number of concerns related to the longevity of implant anchorage, function, and esthetics.

In the posterior areas of the jaw, such concerns may primarily be of biomechanical nature due to the resulting unfavorable "crown–root ratios" in the region of the greatest masticatory forces. Treatment alternatives include the use of multiple short implants splinted together with the fixed partial denture they support (Fig. 27-3), external or internal sinus floor elevation (Fig. 27-4), vertical ridge augmentation with various bone grafting techniques or distraction osteogenesis, nerve repositioning, distal extension

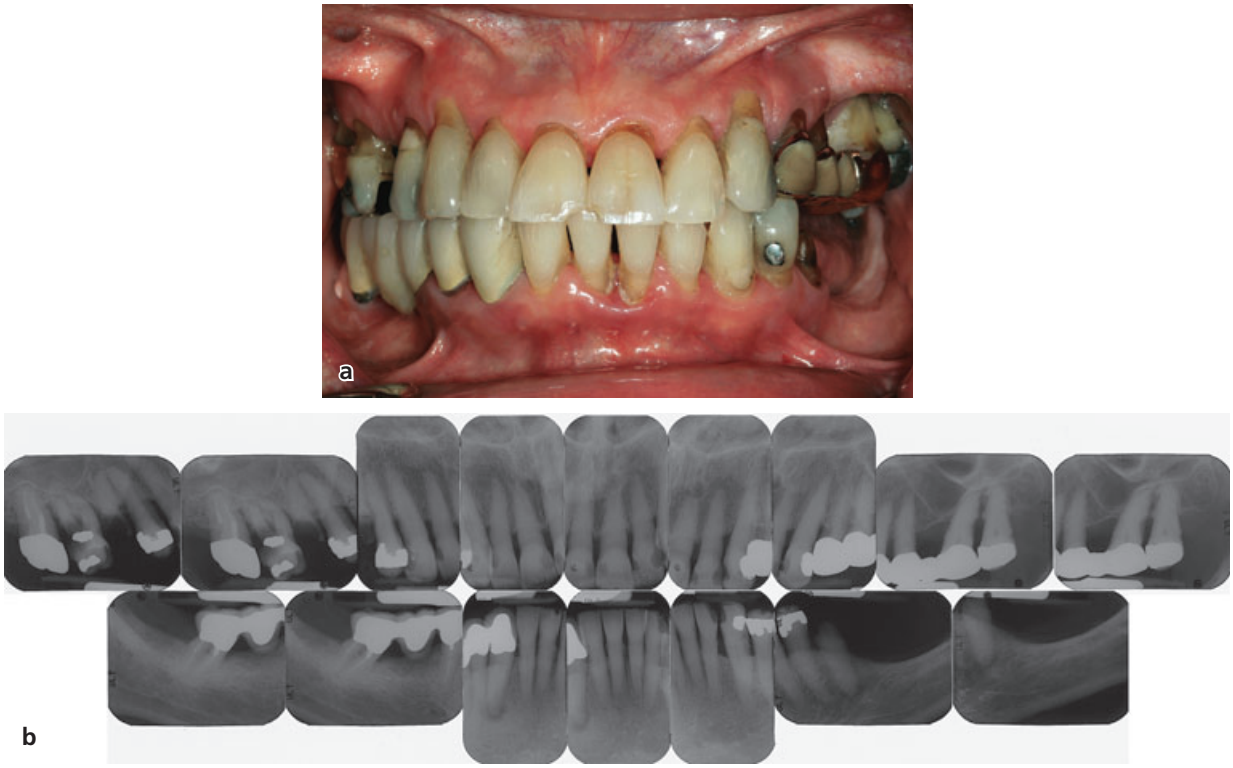


Fig. 27-1 (a) Intraoral image of a 77-year-old female patient with multiple dental problems including severe adult periodontitis after several years of neglect. At the initial examination on 12/6/06, the patient states that she does not want removable prostheses and asks for dental implants to replace the teeth, which may require extraction. (b) Full-mouth set of periapical radiographs of the same patient.

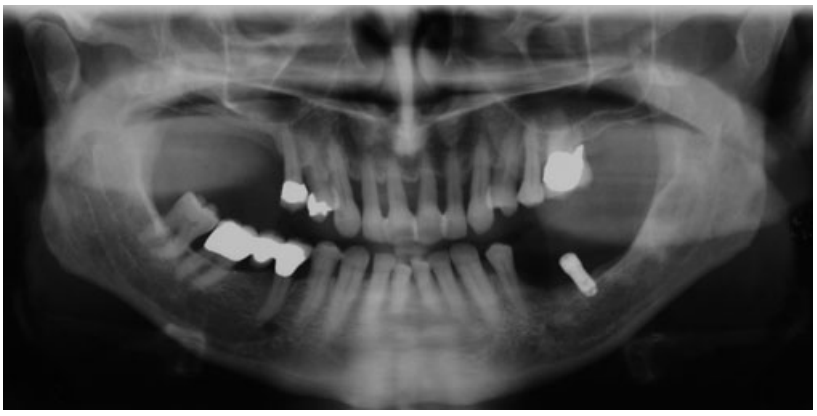
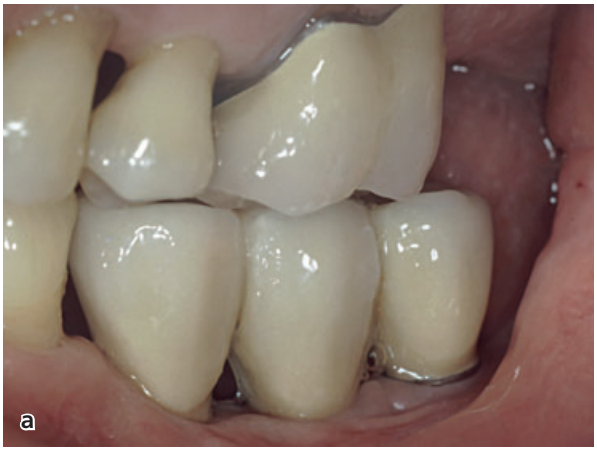


Fig. 27-2 Typical example of patient with reduced alveolar bone volume in the posterior areas of the upper right and lower left quadrant due to preceding severe periodontal bone loss. The lower left quadrant reveals a failed *alio loco* attempt for implant restoration of the lower left quadrant. According to the patient, one of the two short implants originally placed failed shortly after delivery of the fixed partial denture.

fixed prostheses anchored on remaining natural teeth or premolar occlusion without replacement of the failed molars (shortened dental arch concept) (Fig. 27-5).

Prior to the availability of dental implants and bone augmentation techniques for the replacement of posterior teeth lost to periodontal disease, cantilevered fixed partial dentures were a widely used alternative to extend dental arches distally where indicated and to spare the patient from removable partial dentures (Nyman and Lindhe 1976). Whereas this type of periodontal prosthesis performed admirably when designed and maintained properly (Fig. 27-5), the biological and biomechanical risks associated with such reconstructions have been shown to be considerable (Hammerle *et al*. 2000; Pjetursson *et al*. 2004). In the patient with advanced *generalized* periodontal disease and a lack of sufficient posterior bone volume for dental implants, the extraction of the remaining compromised anterior dentition for the purpose of placing implants in combination with cantilevered full-arch prostheses as originally described by Brånemark *et al*. (1985) may prognostically be the most favorable treatment approach (Adell *et al*. 1990).

This generally supportive evidence for implant therapy has to be weighed against the long-term performance of dental implants in patients with a history of periodontal disease. This issue has recently received increased attention in the peer-reviewed dental literature (Ellegaard *et al*. 1997; Baelum &



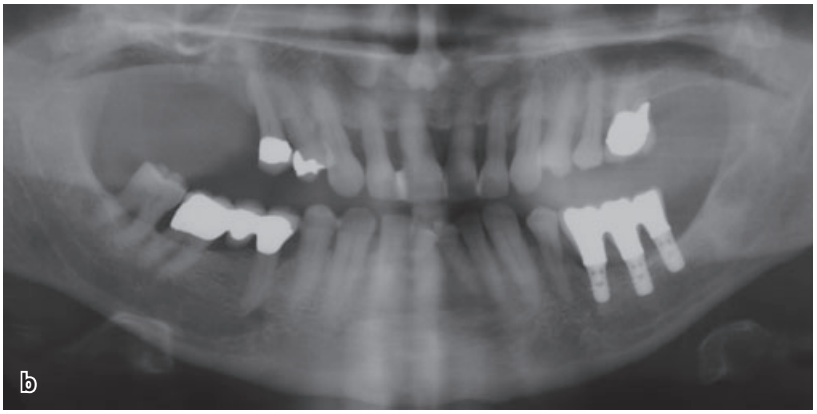
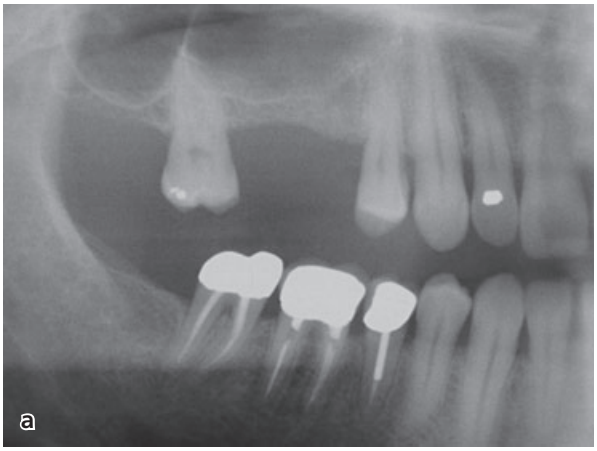


Fig. 27-3 (a) Intraoral clinical image of the same patient after prosthodontic reconstruction of the lower left quadrant with three short implants and a three-unit fixed partial denture. Note the resulting extensive crown heights. (b) Panoramic radiographic image of the implant restoration in the lower left quadrant using three 6 mm long implants. Five-year follow-up. The patient decided to wait with any prosthodontic treatment of the upper right quadrant, where a vertical ridge augmentation combined with external sinus elevation is required.



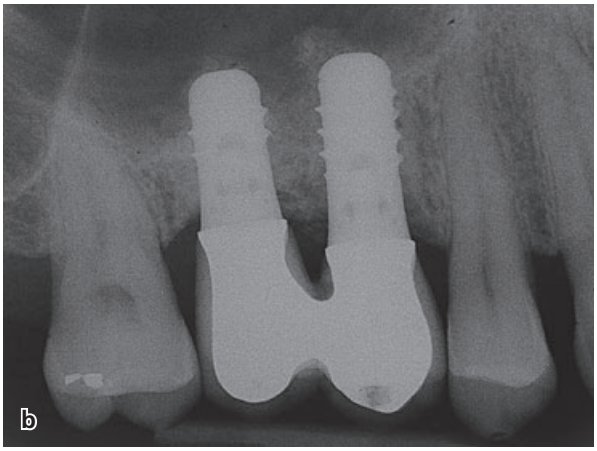


Fig. 27-4 (a) Reduced alveolar bone height in area of second premolar and first molar in the upper right quadrant. Teeth lost due to endodontic complications and periodontal disease combined. (b) Area restored with implant-supported, splinted restorations after internal sinus augmentation procedure at time of implant placement. Four-year follow-up.

Ellegaard 2004). Whereas after 5 years of function no difference was observed between implants in patients free of periodontal disease versus those with disease, a somewhat increased risk for peri-implantitis with bone loss and subsequent implant failure was found for certain implants after 10 years of follow-up. Despite this finding, the authors concluded that dental implants remain a good treatment alternative for patients with periodontal disease. In this context, the outcome with implants placed in sinus grafts in periodontitis patients was not different from subjects free of periodontal disease (Ellegaard *et al*. 2006).

A potential correlation of interleukin-1 (IL-1) gene polymorphism and susceptibility to severe periodontal disease has been reported by Kornman *et al*. (1997). Furthermore, the risk associated with IL-1 polymorphism, smoking and peri-implant bone loss was assessed in a study by Feloutzis *et al*. (2003). The results suggested that in heavy cigarette smokers, the presence of a functionally significant IL-1 gene complex polymorphism is associated with an increased risk for peri-implant bone loss following prosthetic reconstruction and during the supportive periodontal care phase of the treatment. More

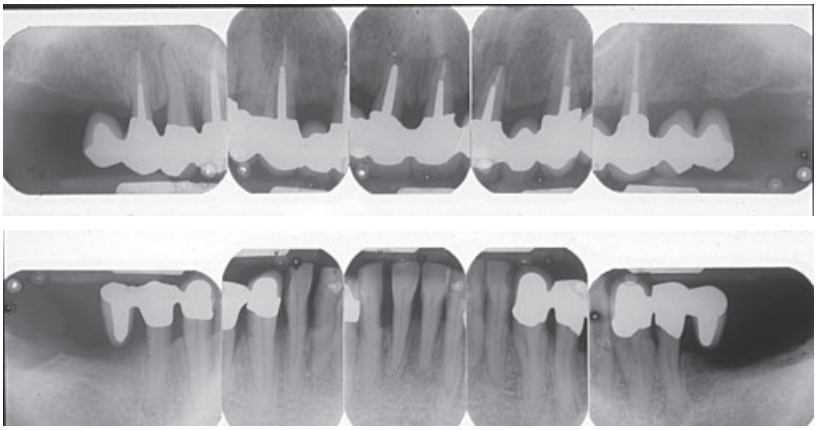


Fig. 27-5 Radiographic documentation of periodontal prostheses with distal cantilevers in all four quadrants as used prior to the availability of dental implants. The patient tolerated the shortened dental arches without difficulty.

recently, Laine *et al*. (2006) found that IL-1 gene polymorphism is associated with peri-implantitis (odds ratio = 2.6!). The authors conclude that this has to be considered a long-term risk factor for implant therapy.

In the anterior region, the loss of periodontal hard and soft tissues and the subsequent 'lengthening' of teeth brings along esthetic concerns, which can become complex, especially in patients with high expectations and smile lines as will be discussed later in this chapter. It is important to envision such problems and analyze local conditions carefully at the time of examination so that expected outcomes can be appropriately discussed with the patient prior to the initiation of therapy.

Patient history

Implant therapy is part of a comprehensive treatment plan. This is especially true for patients with a history of periodontal disease and tooth loss. An understanding of the patient's needs, social and economic background, general medical condition, etc., is a prerequisite for successful therapy. In order to expedite history taking, the patient should fill out a health questionnaire prior to the initial examination visit. As discussed in Chapter 26, such questionnaires are best constructed in a way that the professional immediately realizes compromising factors that may modify the treatment plan and may have to be discussed in detail with the patient during the initial visit or may require medical consultations to enable proper treatment planning. The assessment of the patient's history should include (1) chief complaint and expectations, (2) social and family history, (3) dental history, (4) motivation and compliance (e.g. oral hygiene), (5) habits (smoking, recreational drugs, bruxism), and (6) medical history and medications.

Chief complaint and expectations

To facilitate a successful treatment outcome, it is of critical importance to recognize and understand the patient's needs and desires for treatment. Patients usually have specific desires and expectations regarding treatment procedures and results. These may not be in tune with the attainable outcome projected by the clinician after assessment of the specific clinical situation. Optimal individual treatment results may only be achieved if the patient's demands are in balance with the objective evaluation of the condition and the projected treatment outcomes. Therefore, the patient's expectations have to be taken seriously and must be incorporated in the evaluation. A clear understanding of the patient's views is essential, especially in regard to dentofacial esthetics. Esthetic compromises need to be made often when implant restorations are performed in the periodontally compromised dentition because of the loss of hard and soft tissues. If a patient has been referred for specific treatment, the extent of the desired treatment has to be defined and the referring dentist informed of the intentions for treatment and the expectations regarding outcomes.

Social and family history

Before assessing the clinical condition in detail, it is helpful to interview the patient on her/his professional and social environment and on his/her priorities in life, especially when extensive, time-consuming, and costly dental treatment is envisioned as it is often the case with dental implant treatment. Likewise, a family history may reveal important clues with respect to time and cause of tooth loss, systemic or local diseases such as aggressive forms of periodontitis or other genetic predispositions, habits, compliance, and other behavioral aspects.

Dental history

It is important that previous dental care, including prophylaxis and maintenance, is explored with the patient if not stated by a referring dentist. As described in Chapter 26, information regarding cause of tooth loss, signs and symptoms of periodontitis noted by the patient such as migration and increasing mobility of teeth, bleeding gums, food impaction,

and difficulties in chewing have to be explored in this context. Patient comfort with regard to function and esthetics and the subjective need for tooth replacement is assessed at this time.

Motivation and compliance

In this part of the communication, an assessment is made of the patient's interest and motivation for extended and costly therapy. The patient's view on oral health, her/his last visit to a dentist and/or hygienist, frequency and regularity of visits to the dentist, and detailed information on home care procedures are helpful pieces of information in this regard.

Habits

Cigarette smoking has been shown to be a risk factor for implant failure (Bain & Moy 1993; Chuang *et al*. 2002; McDermott *et al*. 2003). In the patient with (severe) periodontal disease, smoking has to be of even greater concern when combined with IL-1 gene polymorphism as discussed earlier in this chapter (Feloutzis *et al*. 2003; Laine *et al*. 2006). The patient's smoking status including details on exposure time and quantity should be assessed as part of a comprehensive examination of the implant candidate. Furthermore, testing for IL-1 gene polymorphism is strongly recommended. In this context, the importance of smoking counseling cannot be overestimated. Further aspects of smoking cessation programs are presented in Chapter 33.

Whereas the scientific evidence for a correlation of bruxism and implant failure is lacking, prosthetic complications, such as fractures of the veneering material, appear to be more frequent. Reports in the literature support the value of including precautionary measures in the implant treatment plan such as the use of implants of sufficient length and diameter, splinting of multiple implants, and use of retrievable restorations and occlusal guards. Whereas early recognition of bruxism or clenching is beneficial for appropriate treatment planning (Lobbezoo *et al*. 2006), it often cannot be diagnosed at the outset of treatment.

Medical history and medications

A thorough review of the patient's medical history is important. Certain medical conditions may contraindicate dental implant therapy. Any condition which has the potential to negatively affect wound healing has to be considered at least a conditional contraindication. This includes chemotherapy and radiation therapy for the treatment of cancers, bisphosphonate therapy, antimetabolic therapy for the treatment of arthritis, uncontrolled diabetes, seriously impaired cardiovascular function, bleeding disorders including medication-induced anticoagulation, active drug addiction including alcohol, and heavy smoking. Patients with psychiatric conditions may not be good candidates for implant therapy. Such conditions are often difficult to identify at time of initial examination. If identified, these patients should be thoroughly examined by medical specialists before they are accepted for implant treatment (Hollender *et al*. 2003).

In light of the increasing need for medications in the aging population, an accurate assessment has to be made of the patient's prescribed and over-the-counter medications with their potential interactions and effects on therapeutic procedures. Most frequent in this context are anticoagulants, such as coumadin and aspirin. Also the need for antibiotic prophylaxis for dental surgical procedures should be recognized. Recently, the occurrence of ostoenecrosis of the jaw in patients on current long-term bisphosphonate therapy or a history thereof has been described. The occurrence of osteonecrosis has primarily been observed after oral surgical procedures in patients on long-term intravenous bisphosphonate therapy as used in the treatment of cancers, but has also been observed in patients taking oral drugs of this kind (Marx *et al*. 2005). According to the American Dental Association (online member information), the risk for osteonecrosis translates into about seven cases per year for every million people taking oral bisphosphonates. In the most recent article addressing this issue, Mortensen *et al*. (2007) conclude that the increasing number of reports about bisphosphonate-associated osteomyelitis and the difficulty in treating these patients require further investigation to identify those patients who are at increased risk. Also, the optimal and safe duration of treatment with bisphosphonates remains to be determined. Due to the existing uncertainty in this area, recognition of patients on bisphosphonate therapy, communication with the treating physician(s), and a risk:benefit assessment have to be made for such patients who are being considered for implant therapy.

In summary, while most of this medical information can be extracted from a health questionnaire as mentioned earlier (see example in Chapter 26), it is important for the clinician to ask specific questions related to the patient's answers in the questionnaire to clarify their potential impact on treatment with dental implants. In many instances it will be necessary to contact the patient's physician for detailed information relevant to the planned treatment. Further aspects are presented in Chapters 30 and 33.

Local examination

Extraoral

An extraoral examination should form part of any initial patient examination. The clinician should look for asymmetries, lesions or swellings of the head and

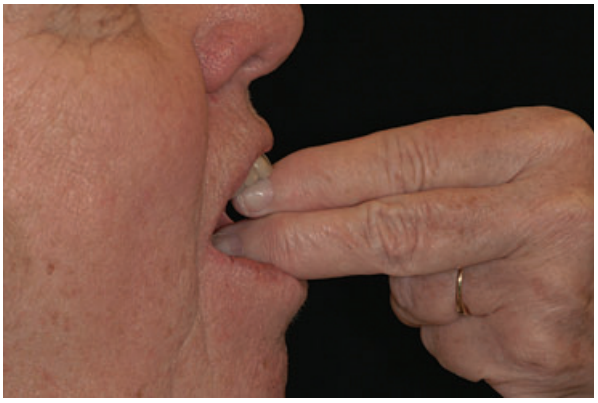


Fig. 27-6 Examination of patient's mouth-opening ability. The width of at least two of the patient's fingers placed vertically between upper and lower incisors is necessary to allow proper access for implant placement in posterior sites.

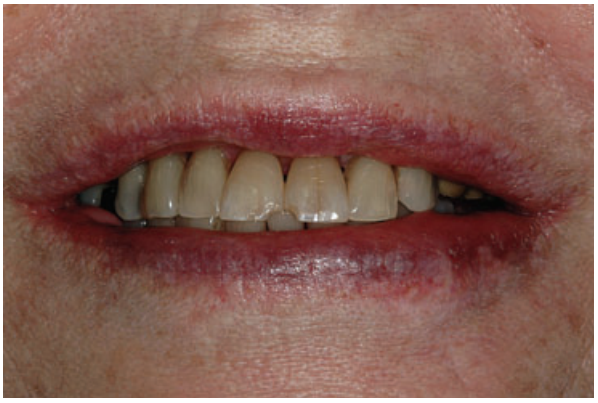


Fig. 27-7 Smile characteristics of patient introduced in Fig. 27-1.

neck areas. Observation of function and palpation of the head and neck musculature and temporomandibular joints are performed. Assessment of the opening amplitude of the mandible is especially important, since instrumentation involved with dental implant therapy requires that the patient is able to open sufficiently wide (Fig. 27-6). This is also the perfect time to take note of esthetic characteristics such as smile line, lip line, gingival line, and facial and dental midline (Fig. 27-7).

General intraoral examination

The general intraoral examination includes the assessment of the condition of soft and hard tissues of the oral cavity. This also entails a careful cancer screening. Soft or hard tissue lesions will most likely require treatment prior to the placement of dental implants. Pathological soft tissue conditions include herpetic stomatitis, candidiasis, prosthesis-induced stomatitis, tumors, hyperplasia, etc. Hard tissue pathologies, which most likely require treatment prior to implant therapy, include tooth impactions, bone cysts, root fragments, residual infections in the alveolar bone, e.g. caused by failed endodontic treatment, or tumors.

Dental hard tissues are equally carefully examined to determine the need for restorative treatment in the remaining dentition, most importantly those teeth directly adjacent to edentulous spaces. The need for restoration of the latter may influence the treatment plan in terms of choosing a conventional fixed partial denture over an implant-supported restoration to replace a missing tooth. Pathologies such as caries, fractures, attrition, abrasion, abfraction, tooth mobility, or tooth misalignment are noted. Existing restorations are recorded and deficiencies such as open margins, open contacts, or fractures identified. Testing for vitality of teeth, especially of those adjacent to potential implant sites, will point to possible endodontic pathologies, which should be treated prior to implant placement. The examination of periodontal tissues including the assessment of the patient's oral hygiene is described in detail in Chapter 26.

Finally, static and dynamic aspects of the patient's occlusion are determined, including the adequacy of the patient's vertical dimension of occlusion, maxillomandibular relationship (angle classification), overbite, overjet, stability in habitual occlusion, centric relation, slide in centric, and lateral and anterior excursive contacts (canine guidance, group function, anterior guidance).

Radiographic examination

The initial patient evaluation will include a radiographic survey. For the implant candidate with a history of periodontal disease and, hence, comprehensive treatment needs, a full-mouth set of periapical radiographs is needed to supplement the intraoral examination (Fig. 27-1b). A panoramic view will often be required as well, to reveal structures apical to the remaining teeth such as the infra-alveolar nerve canal, the mental foramina, the floor of the maxillary and nasal sinuses, and pathologic findings in the jaws (Fig. 27-8). Minimal radiographic bone height requirements for implant placement depend on a number of factors such as recommended implant length for a single implant restoration, single vs. multiple adjacent implants, jaw location, and ease and predictability of ridge augmentation in that location. For detailed planning of implant placement, additional radiographs such as occlusal views, cephalometric images, conventional or computer tomograms may be indicated. Implant-specific radiographic studies and their indications are described in Chapter 28, and treatment planning details are discussed in Chapter 32.

Implant-specific intraoral examination

Sites without esthetic implications

An implant-specific intraoral examination, emphasizing the local characteristics of potential implant

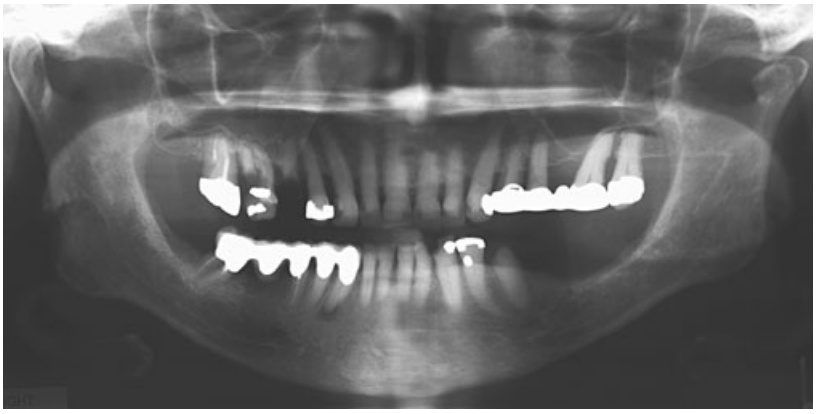


Fig. 27-8 Panoramic radiograph supporting the full-mouth radiographs shown in Fig. 27-1b.

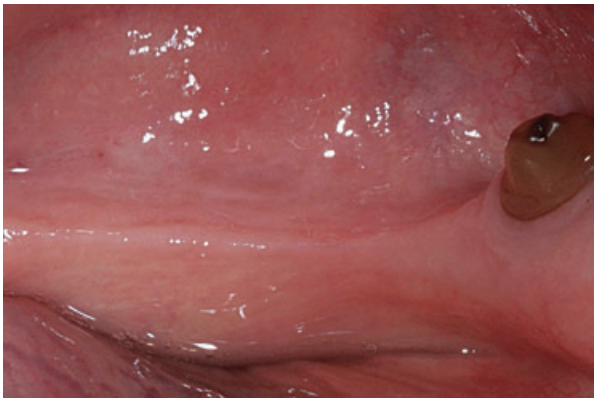


Fig. 27-9 Examination of alveolar ridge in lower left edentulous area. The ridge appears narrow in the area of the missing second premolar. Further radiographic information (lateral tomograms, computer tomograms) are recommended if dental implants are being considered.

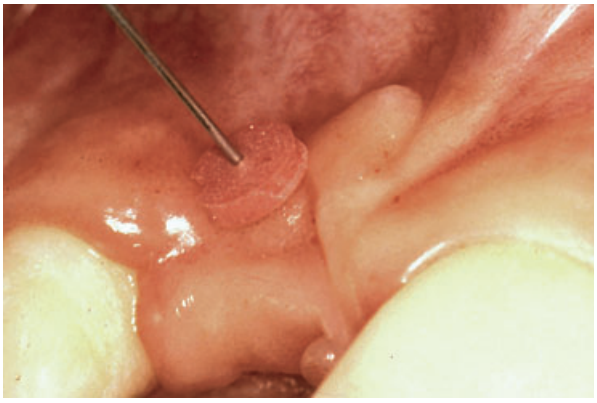


Fig. 27-10 Area of local soft tissue hyperplasia. Bone mapping is applied to explore the soft tissue thickness and the location of the underlying bone.

sites, is important. Different locations in the oral cavity have varying requirements in this regard, primarily due to differing esthetic impacts of implant treatment. They are, therefore, addressed separately in this text.

Although esthetic concerns are overall of lesser importance in mandibular and posterior maxillary sites, the evaluation of the condition of the local mucosa needs to be part of the examination in these areas as well. The clinical width and height of the alveolar process in potential implant areas is examined (Fig. 27-9). At the same time, pathologic changes are noted including mucosal hyperplasia or hypertrophy (Fig. 27-10). Probing of the local tissues may be indicated to assess tissue thickness and confirm the presence of sufficient alveolar bone. This can be done with a bone mapping procedure using a fine needle or explorer after local anesthesia has been applied (Fig. 27-10).

Besides the above, local assessment of sites with low esthetic impact consists primarily of a three-dimensional space assessment and evaluation of the condition of the adjacent teeth and their surrounding hard and soft tissues. A detailed and accurate space assessment is often difficult intraorally. Thus, it is strongly recommended to obtain diagnostic impressions and adequate bite records to produce articulator-mounted casts, on which these critical diagnostic steps can be properly performed, including a diagnostic tooth set-up or wax-up. This is especially important when multiple teeth need to be replaced (Fig. 27-11).

From a comprehensive restorative point of view, edentulous spaces to be restored with implant restorations should ideally have the mesio-distal width of the natural tooth (teeth) that would normally be there. In the patient with a history of periodontal disease, tooth movements occur frequently and space assessment becomes important. Orthodontic pretreatment may be desirable or even required (Fig. 27-12).

From the perspective of implant placement, a mesio-distal width of 7 mm will allow the insertion of a regular-platform or regular-neck implant (3.75–5 mm). For spaces only 5–6 mm wide, narrow-platform or narrow-neck implants of approximately 3.5 mm diameter are available. For single-tooth spaces larger than 7 mm, wide-platform or wide-neck implants with a platform diameter of 6–7 mm may be the choice.

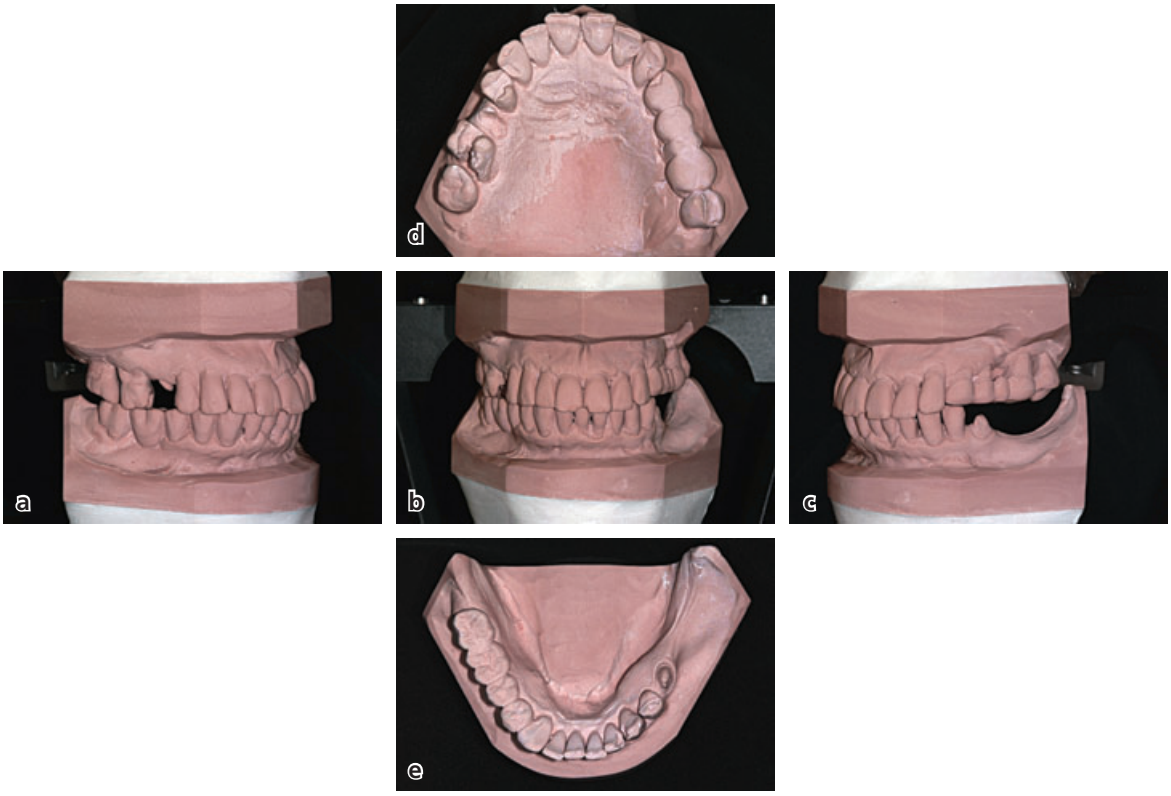


Fig. 27-11 Mounted diagnostic casts of patient introduced in Fig. 27-1: (a) right lateral view; (b) frontal view; (c) left lateral view; (d) maxillary occlusal view; (e) mandibular occlusal view.

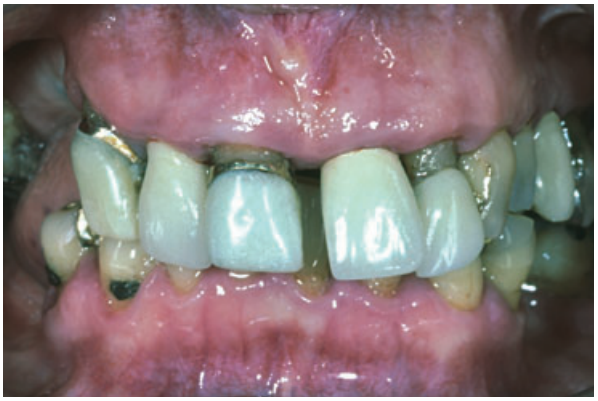


Fig. 27-12 Patient with severe periodontitis and resulting tooth movement in addition to pre-existing malocclusion.

It is important to note that wide-neck or -platform implants generally will also have a wider screw diameter. Thus, sufficient buccal–lingual bone width for the placement of a wider diameter implant is important so as to avoid perforation of the alveolar bone buccal or lingual to the implant. The buccolingual width of the alveolar process at an implant site is assessed either by bone mapping or cross-sectional radiographs (see Chapter 28).

A minimum vertical distance from the crestal mucosa of the potential implant site(s) to the opposing dentition is needed for implant restorations. This space requirement may vary depending on the design of the restoration, including the choice of abutments. As a general guideline, a vertical distance of at least 4 mm from the top of the mucosa to the opposing tooth (teeth) is required for straightforward implant placement and restoration. In the patient with tooth loss due to periodontal disease, this usually does not pose a problem. In contrast, due to concomitant bone loss, the distance is generally greater than the original height of a natural tooth (teeth) so that the potential esthetic and biomechanical impacts of the resulting overlong implant restoration have to be taken in consideration as documented earlier (Fig. 27-3).

Sites with esthetic implications

Definition of the problem

In the specific context of implant therapy in the *periodontally* compromised dentition with esthetic implications, which is primarily the anterior (maxillary) dentition, the local, implant-related examination will have to focus particularly on the esthetic consequences of periodontal disease in this area of the jaw. The most common visible sequels of generalized periodontal disease which may have a direct impact on esthetic appearance, depending on the patient's smile line, comprise (over-)long clinical crowns and flattening of the originally scalloped course of the gingival line, including loss of papillary tissue

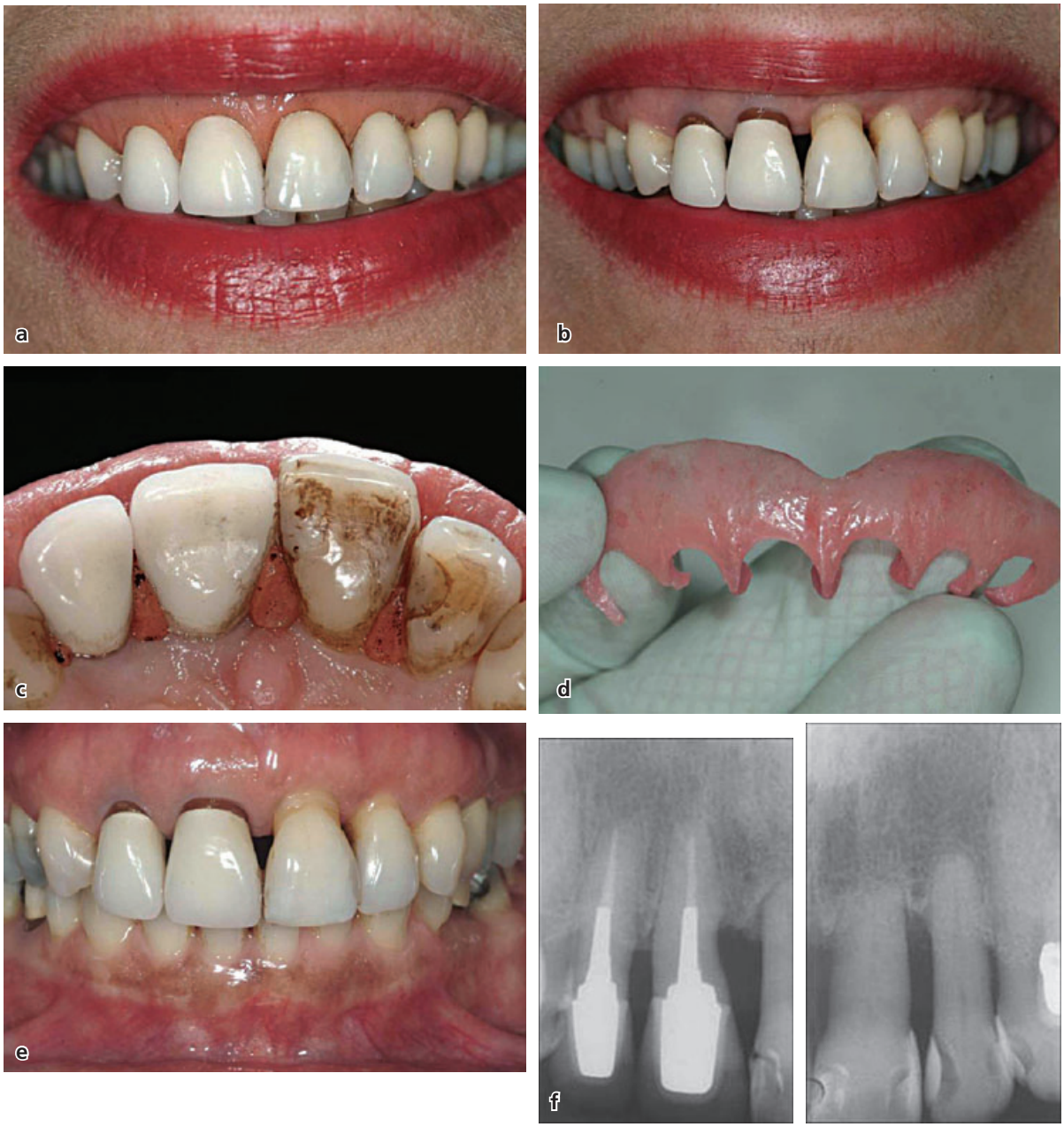


Fig. 27-13 (a) Frontal view of a 60-year-old female patient. During unforced smiling the transition between the clinical crowns and the artificial gingival epithesis is completely exposed. (b) The view without gingival epithesis displays long clinical crowns and open embrasures, both affecting the esthetic appearance. (c) The occlusal close-up view of the maxillary incisor region highlights the anchorage mechanism of the epithesis in the region of the open embrasures. (d) The gingival epithesis made of pink silicone is characterized by its regular scalloped occlusal course, compensating for the missing interproximal soft tissue. (e) The clinical view in centric occlusal reveals an average inter-arch relationship, but an altered length-to-width ratio of the clinical crowns of the four maxillary incisors as a consequence of periodontal tissue loss. (f) The corresponding radiographs document the advanced interproximal bone loss, indicating in particular that tooth #21 cannot be maintained.

leading to unsightly, "black interdental triangles". This is particularly pronounced in patients with an originally "*scalloped thin*" *gingival morphotype*, in contrast to a rather "*flat thick*" *phenotype* (Seibert & Lindhe 1989; Olsson & Lindhe 1991; Olsson *et al*. 1993). Not infrequently, vertical and/or lateral migration of teeth may also have occurred which, in turn, can significantly affect esthetic parameters. Furthermore, in case of more localized periodontal disease and loss of attachment, abrupt changes in vertical tissue height between neighboring teeth can be present.

The resulting major shortcomings from an esthetic point of view mainly consist of an altered length-to-width ratio of the involved clinical crowns (*long teeth syndrome*) on the one hand and of interdental spaces that are not completely filled-out with gingival tissue on the other hand (Fig. 27-13). The latter may not only affect esthetics, but also lead to food retention and phonetic disturbances. As a consequence,

reconstructive measures generally, and in implant therapy in particular, have not only to aim at a predictable and long-lasting functional rehabilitation, but need also to re-establish harmony from an esthetics and phonetics perspective. In general, fixed prosthodontic measures have somewhat limited potential of correcting length-to-width discrepancies of clinical crowns and to diminish open inter-proximal embrasures. Furthermore, the clinician should be aware of the additional specific limitations associated with current implant therapy (as described in Chapter 53), particularly when it comes to esthetic parameters, and therefore include this notion while proceeding to the local examination. In this context, the importance of assessing the height of the patient's smile line and his individual treatment expectations, should be once more underlined.

In the scope of this chapter and specifically addressing the local, pre-implant examination, two distinct clinical conditions can be theoretically encountered:

- One or several elements (teeth) of the anterior maxillary segment are periodontally compromised to such an extent (degree) that they can not be maintained and thus require replacement.
- One or several elements (teeth) of the anterior maxillary segment have already been lost due to periodontal disease.

This distinction is of importance, as the removal of a tooth consistently leads to horizontal and vertical tissue loss which includes soft and underlying bone tissue and which has been reported to vary between 2 and 3 mm vertically (Kois 1996; Araujo & Lindhe 2005; Araujo *et al*. 2005, 2006). This means that in the case of teeth still being present, but considered *irrational to treat*, an additional esthetic aggravation has to be expected. In this context, the beneficial potential of a slow orthodontic *"forced eruption"* procedure prior to tooth extraction, has to be mentioned (Salama & Salama 1993). Furthermore, as described in more detail in Chapter 53, one has to keep in mind that single-tooth replacement is significantly more predictable when it comes to long-term esthetic treatment outcome, than multiple adjacent implant restorations in the anterior maxilla (Belser *et al*. 2004a,b; Buser *et al*. 2004, 2006; Higginbottom *et al*. 2004). Clearly, single-tooth implant restorations benefit from tissue support provided by the adjacent natural teeth. As a consequence, the currently recommended *extraction strategy* for this area of the jaw should try to avoid, whenever feasible, ending up with *two-unit* tooth gaps. In other terms, one should either aim for *single-tooth gaps* or, if this is not possible, for *more extended edentulous segments* (three or more missing adjacent teeth). The latter concept, on the one hand, permits one to replace part of the missing teeth with pontics and thus benefit from their inherent superior esthetics (eventually enhanced by connective tissue grafting procedures), and, on the other hand, to avoid adjacent implant restorations.

Table 27-1 Elements of the local, implant-specific examination of the periodontally compromised dentition in the esthetic zone

- Patient's smile line (high, medium, low)
- Periodontal examination (including gingival index, plaque index, probing pocket depth, clinical attachment level, bleeding on probing, width of the keratinized mucosa, gingival recessions, tooth mobility, tooth migrations)
- Inter-proximal bone height (as assessed on radiographs)
- Bone anatomy of the existing and/or anticipated (in case of inevitable tooth extractions) edentulous ridge
- Soft tissue anatomy (course of the gingival line in relation to the cemento-enamel junction of existing teeth and/or the osseous ridge)
- Gingival phenotype ("flat thick" vs. "scalloped thin")
- Shape of anatomic tooth crowns ("square" vs. "triangular")
- Length-to-width ratio of clinical crowns
- Overbite, overjet, malposition of teeth, occlusal parafunctions (wear facets, bruxism)
- Restorative/endodontic status of remaining teeth
- Width of existing and/or prospective edentulous spaces (single-tooth vs. multiple-unit gaps; identification of edentulous spaces that do not correspond to the volume of the respective missing teeth)

Clinical and radiographic examination

A structured comprehensive examination of the periodontally compromised anterior maxillary dentition (Table 27-1) should logically start with the assessment of the height of the patient's smile line. This will immediately indicate if the major esthetic shortcomings associated with an implant rehabilitation under such conditions, i.e. *long clinical crowns and open embrasures*, will become visible during unforced smiling. The examination will then focus on the detailed periodontal status, aiming at determining the prognosis of each individual unit of the respective dentition from a primarily periodontal perspective. As it is anticipated in the scope of this chapter that either one or several teeth cannot be maintained for periodontal reasons, or that one or several teeth have already been lost due to periodontal disease, the examination will have to assess whether implant therapy represents the adequate treatment solution or not. This means that additional parameters, directly related to implant therapy, have to be included in the examination process. These parameters comprise the localization of interproximal bone height assessed on radiographs, the bone anatomy of the existing or prospective (after additional tooth extractions) edentulous ridge, the course of the gingival (mucosal) line in relation to the cemento-enamel junction, as well as the width of the edentulous spaces. Furthermore, the general shape of the anatomic crowns (square or triangular) and the length-

to-width ratio of the clinical crowns have to be assessed. Finally, the restorative and endodontic status of the remaining teeth and the overall occlusal conditions such as overbite, overjet, and the presence of occlusal parafunctions (wear facets, bruxism) have to be registered. In other words, all additional information which refers directly to implant therapy (e.g. bone volume) is a prerequisite for the decision-making process, to determine if implant therapy is feasible under these specific circumstances.

Patient-specific risk assessment

Summarizing the above mentioned aspects of a comprehensive preoperative examination, an individual risk profile is recommended for every candidate for implant therapy. Two different risk assessment forms are routinely used by the authors when examining potential implant patients, one for implant sites without esthetic priority, generally those in the mandible or in the posterior maxilla depending on the patient's smile profile, and a more detailed version for sites where esthetic aspects play a dominant role, primarily those in the (anterior) maxilla.

Risk assessment for sites without esthetic implications

The risk assessment in partially edentulous patients without or with low objective and subjective esthetic concerns is less complex. It should include the patient's health status, periodontal disease susceptibility, smoking history, interleukin-1 phenotype, history of bruxism, patient compliance including oral hygiene, and presence and type of alveolar bone deficiencies at potential implants sites (Table 27-2). In most patients, it takes less than 5 minutes to complete the proposed risk assessment form. Utilizing the obtained information, each implant candidate is categorized as low, medium or high risk. In patients with a 'high risk' mark in multiple areas, the appropriateness of implant therapy must be questioned. For example, heavy smokers with advanced or refractory periodontal disease and a positive IL-1 test have to be considered overall high risk when extended bone augmentation procedures are needed to enable sufficient bony implant anchorage. It is important to discuss the individual risk situation with the patient prior to therapy and obtain the patient's consent based on the given circumstances.

Risk assessment for sites with esthetic implications

Risk assessment for implant sites with esthetic importance is much more detailed and complex. The risk assessment form contains additional surgical and prosthetic parameters, which are critical for an esthetic treatment outcome (Table 27-3). These parameters have been outlined in detail by Martin *et al*. (2006) in the first ITI Treatment Guide. In periodontally compromised patients, clinicians are often confronted with medium- to high-risk situations, since vertical bone and soft tissue deficiencies are a frequent clinical finding.

Conclusion

Modern comprehensive dental care for patients with a periodontally compromised dentition has to include the consideration of dental implants. Implant-assisted replacement of teeth that are missing or need to be extracted due to periodontal disease is an overall predictable treatment alternative in this type patient. A meticulous comprehensive examination of implant candidates is crucial and should include a patient and indication-specific risk assessment to achieve favorable short- and long-term treatment outcomes with regard to function and esthetics.

Table 27-2 Risk assessment for patients/sites without esthetic treatment implications

	Low risk	Medium risk	High risk
Health status (see Medical history and medications)	Normal wound healing		Conditions with potential for impaired wound healing
Periodontal disease susceptibility	Gingivitis	Mild to moderate chronic periodontitis	Severe or refractory periodontitis
Smoking	Non-smoking	<10 cigarettes per day	≥10 cigarettes per day
IL-1 gene phenotype	Negative		Positive
Bruxism	No		Yes
Compliance including oral hygiene	Good	Fair	Poor
Bone deficiency at implant site	None	Horizontal deficiency	Vertical deficiency

Table 27-3 Risk assessment for patients/sites with esthetic treatment implications

	Low risk	Medium risk	High risk
Health status (see Medical history and medications)	Normal wound healing		Conditions with potential for impaired wound healing
Periodontal disease susceptibility	Gingivitis	Mild to moderate chronic periodontitis	Severe or refractory periodontitis
Smoking	Non-smoking	<10 cigarettes per day	≥10 cigarettes per day
IL-1 gene phenotype	Negative		Positive
Bruxism	No		Yes
Patient's esthetic demand	Low	Medium	High
Lip line	Low	Medium	High
Gingival biotype	Thick, low scalloped	Medium thick, medium scalloped	Thin, highly scalloped
Shape of tooth crown	Rectangular		Triangular
Bone level at adjacent teeth	≤5 mm to contact point	5.5–6.5 mm to contact point	≥7 mm to contact point
Local infection at implant site	None	Chronic	Acute
Restorative status of neighboring teeth	Virgin		Restored
Width of edentulous space	One tooth ≥7 mm* One tooth ≥5.5 mm**	One tooth <7 mm* One tooth <5.5 mm**	Two teeth and more
Soft tissue anatomy	Intact soft tissues		Soft tissue defect
Bone deficiency at implant site	No bone deficiency	Horizontal bone deficiency	Vertical bone deficiency

* For regular neck/regular platform implants.
** For narrow neck/narrow platform implants.

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Chapter 28

Radiographic Examination of the Implant Patient

Hans-Göran Gröndahl and Kerstin Gröndahl

Introduction

In 1965, Brånemark installed the first dental implants made of titanium in the mandible of a 35-year-old male who, due to a cleft palate and loss of most of his teeth, could neither speak nor eat properly (Brånemark *et al*. 2005). The era of osseointegration, as a means to restore oral function compromised as a result of missing teeth, had begun.

The foundation for the use of titanium as the metal of choice for prostheses placed in the bone was laid many years earlier. In 1940, Bothe, Beaton and Davenport published the results of a study in which they had inserted pegs of different metals, among them titanium, in cat femurs. They found that "... the response to titanium was as good as, if not better, than that to the non-corrosive alloys in that there was more tendency for the bone to fuse with it". In 1951, Leventhal inserted screws made of titanium into the femurs of rats. He describes that "At the end of six weeks, the screws were slightly tighter than when originally put in; at twelve weeks the screws were more difficult to remove; and at the end of sixteen weeks, the screws were so tight that in one specimen the femur was fractured when an attempt was made to remove the screw". He continues: "In the past, the use of some prostheses has not become popular because it has been felt that these would remain separate from the bone and eventually loosen. Since titanium adheres to bone, it may prove to be an ideal metal for such prostheses".

Brånemark realized that screw-shaped titanium implants placed in the human jawbone could serve as substitutes for teeth that had been lost or never developed. In 1977, results from a 10-year study period were published (Brånemark *et al*. 1977) that demonstrated the clinical usefulness of what would become known as osseointegrated implants.

In the beginning of the osseointegration era limited numbers of people, and practically only those with no teeth left, were treated with dental implants. Gradually the indications were widened until partially edentulous and the patient missing just a single tooth also became candidates for implant treatment. From having been a treatment modality offered by a small number of specialists, it has emerged as a treatment mode provided by more and more dentists worldwide. It seems to grow exponentially and many more years probably remain before the vertex of its diffusion curve has been reached (Fig. 28-1a).

From a radiological point of view this must give us pause because it means that more people will undergo more extensive radiographic examination than people who receive conventional prosthetic treatment do. Consequently, we must try to use radiographic methods that do not unnecessarily increase the radiation burden to the population whilst providing us with all the information that is necessary for successful long-term treatment results.

In this chapter we will show how radiographic examinations for implant treatment purposes can be made so that they yield all necessary information at a reasonable cost both in terms of radiation dosage and economical resources. We will, in other words, adhere to the very important principle in radiography, the ALARA principle. This states that all radiographic information should be obtained with radiation doses that are As Low As Reasonably

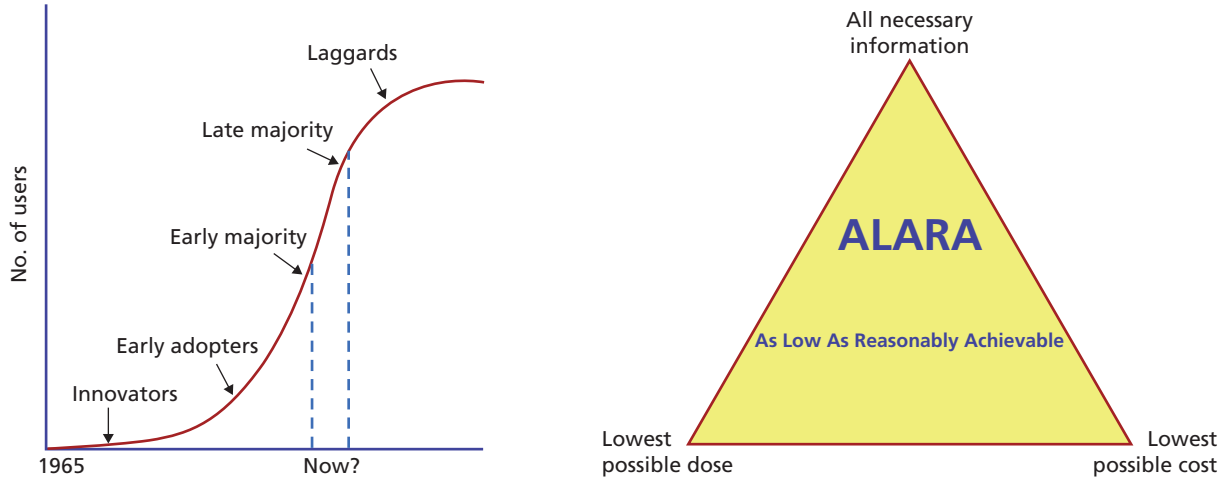

Fig. 28-1 (a, b) With the increasing use of implant treatment, it becomes increasingly important to adhere to the ALARA principle and keep radiation doses and monetary costs as low as possible.

Achievable. This principle may well be broadened so that it is also understood as stating that the monetary costs should be as low as reasonably achievable (Fig. 28-1b).

Radiographic examination for implant planning purposes – general aspects

The clinical vs. the radiologic examination

Too often a distinction is made between the clinical and the radiographic examination. The latter depends on the former and a meticulous clinical examination, including a thorough patient history, is the foundation upon which any radiologic examination must be based. Without it one can neither decide whether radiographic information is necessary, nor where and how it must be sought. The clinical examiner, whether or not he or she plans to make the radiographic examination her/himself, or refer the patient to a radiologist, thereby plays a decisive role when it comes to keeping radiation doses as low as reasonably achievable whilst obtaining the radiographic information that is necessary for a successful treatment planning. According to the International Commission on Radiation Protection, ICRP 60 (1991) all radiographic examinations should be justified and optimized. It is the clinical need of radiographic information that can make the radiographic examination justified. It is then the responsibility of the person, who will plan and perform the latter, to make certain that it will be made optimally.

What is the necessary radiographic information?

Before any radiographic technique can be chosen for any type of clinical problem one needs to clarify what radiographic information that is needed to enable a proper diagnosis and treatment plan. As regards the prospective implant patient, the necessary radiographic information is that which allows the clinician to determine:

- Whether implant treatment is the treatment option that offers the best long-term prognosis
- Whether pathological conditions are present in the jaws or remaining teeth that must be taken into account before implant treatment can be contemplated
- Where and how implants can be placed so that they have the best possibilities to become integrated with the surrounding bone and the associated crown/bridge can come into best clinical use
- How to place the implant(s) so that the surgical procedure becomes as safe as possible and the risk for post-operative failures as small as possible

A pre-operative radiographic examination is essential for all implant patients but how much of the jawbones that need to be examined and in what way will vary from patient to patient. Therefore, different radiographic techniques have to be used for different patients.

The pre-operative radiographic examination has several roles to play in respect to the clinician's needs. More specifically, the clinician needs to know the height of the bone that can be used for implant placement. One must then bear in mind that the bone height that can be used for implant placement is not necessarily the same as the total bone height (Fig. 28-2). The bone must also preferably be of a width which allows the implant to be surrounded by bone around its entire circumference. It is not only the available height that is of interest. When planning for implants to be placed adjacent to teeth or other implants one should try to ensure that they do not become positioned too close to each other (Fig. 28-3). Hence, the horizontal dimension of a potential implant site also needs to be assessed. When an

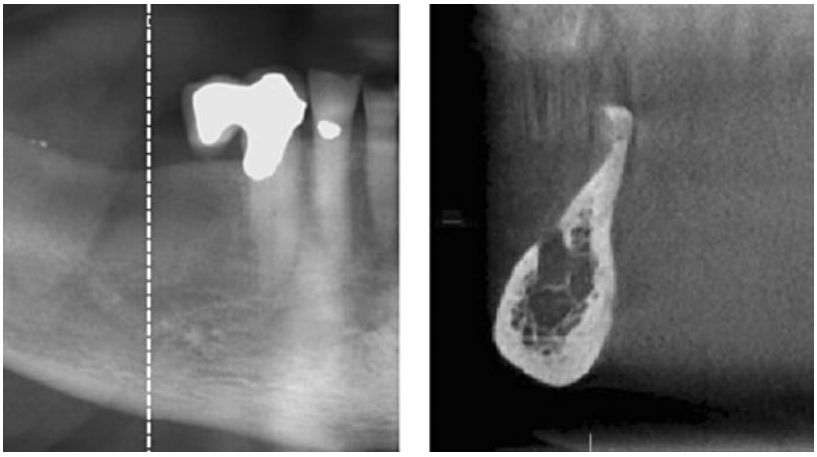

Fig. 28-2 An apparent height, as seen in the cropped panoramic image to the left, does not necessarily correspond to a bone volume useful for implant placement, as revealed by a tomogram (right image) representing a layer indicated by the dotted line.

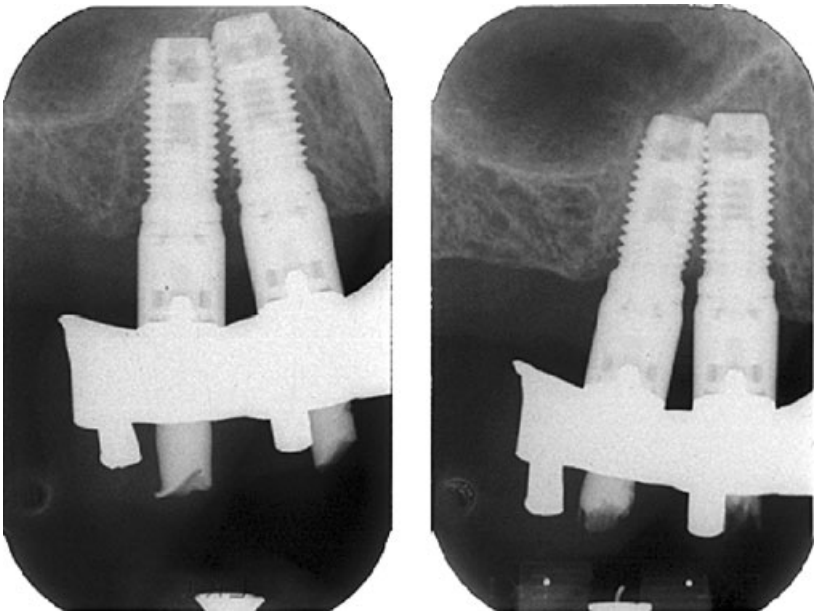

Fig. 28-3 Two implants placed very close to each other. A control radiograph taken 1 year after bridge connection (on right) demonstrates, by the thin radiolucent lines around the implants, that they have not become integrated with the surrounding bone.

implant will be placed adjacent to a tooth one should make certain that it does not become inserted too close to the tooth. Should this happen there is an increased risk of bone loss at the adjacent tooth or implant at least in the immediate period after implant surgery (Esposito *et al*. 1993; Andersson *et al*. 1995; Cardaropoli *et al*. 2003).

It is of great importance that the implant can be placed so that it will remain stable during the healing phase. The marginal bone crest may be used as a supporting bone cuff and a bony border in which the "apical" part of the implant can be placed will render some support. This can also be provided by the lingual and/or buccal cortical bone plate(s). The lower borders of the nasal cavity and the maxillary sinuses can give support to an implant (Fig. 28-4), but the upper border of the mandibular canal must not be used as anchorage of the implant tip (Worthington 2004).

A crucial aspect is that which concerns the location of anatomic structures that must not be damaged during implant surgery. In the lower jaw the mandibular canal, with its nerve bundle and blood vessels, is the most important. In the upper jaw placement of the implants so that they come in conflict with the nasopalatine canals should be avoided.

To make the placing of the implant(s) as safe a procedure as possible the radiographic examination must also enable a description of the outer contours of the jawbones so that, for example, tilting of the alveolar bone as well as the presence and depth of bony fossae will be observed and accounted for.

From the above it can be concluded that it is important to evaluate different aspects of the bone in which one intends to place an implant and that accurate and precise measurements of different distances are essential.

The pre-operative radiographic examination serves more purposes than those described above. When implants are to be placed in jaws with remaining teeth, the condition of those and their surrounding bone must be thoroughly evaluated. Inflammatory lesions in the vicinity of an implant site may compromise the implant treatment result. Careful assessment of the remaining teeth may also lead to the choice of an alternative treatment modality. The pre-operative radiographic examination thus serves to:

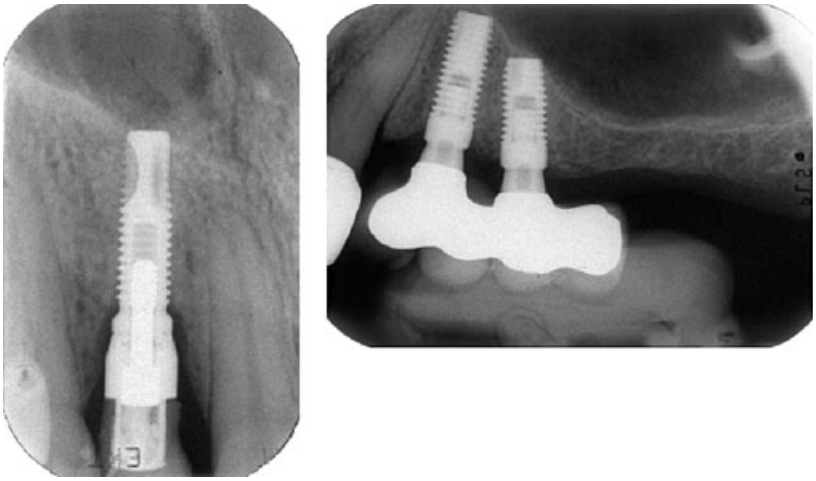

Fig. 28-4 The lower border of the nasal cavity and the maxillary sinus can provide support to an implant.

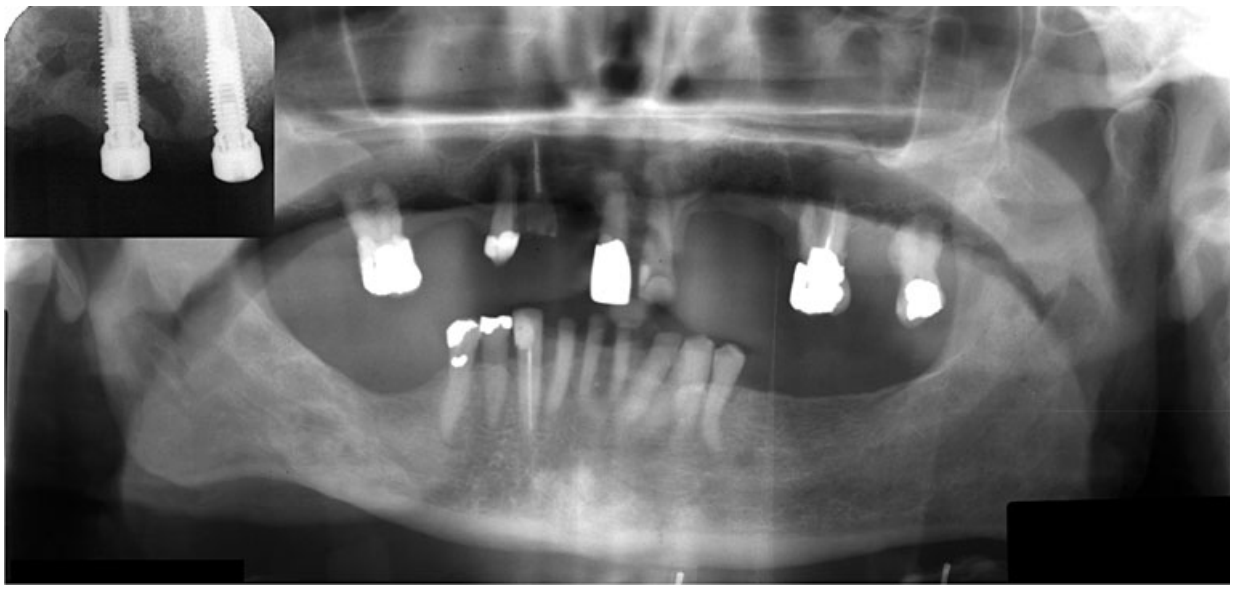

Fig. 28-5 A panoramic image of poor quality can give rise to serious problems. In this one it was not noticed that the bone in the upper right anterior region was not suitable for implant placement. Nevertheless, implants were placed (see inlay in upper left corner), soon to be lost.

- Ascertain that implant treatment is an appropriate treatment given the condition of the remaining teeth
- Make certain that bone height and width are sufficient for implant placement
- Provide measurements so that implants can be inserted without damaging neighboring structures
- Make implant insertion a safe procedure.

Needless to say, none of these objectives can be obtained without a radiographic examination of the best possible quality.

Radiographic methods for obtaining the information required for implant planning

In this chapter we will not discuss the examination of totally edentulous patients, only of those who have lost one or several teeth in jaws where some teeth still remain. As already mentioned one must then take into account the conditions of the remaining teeth in order not to jeopardize the implant treatment. A comprehensive examination, clinical as well as radiologic, of the dentition should therefore be made prior to a decision about where and how to insert implants. Depending upon the result of the clinical examination, the primary radiographic examination can be made with a combination of panoramic and intraoral radiography or by one or the other. One should not hesitate to take intraoral radiographs in regions where the panoramic radiograph has not been able to provide a clear view of the anatomic structures.

An adage well worth remembering, when determining whether an image is good enough for diagnosis and treatment planning, is that optimal diagnostic quality is only present when all diagnostically important structures are clearly visualized. Figure 28-5 illustrates a case when a panoramic radiograph was considered of good enough quality to be used for implant planning purposes. However, implants were lost, even before being subjected to

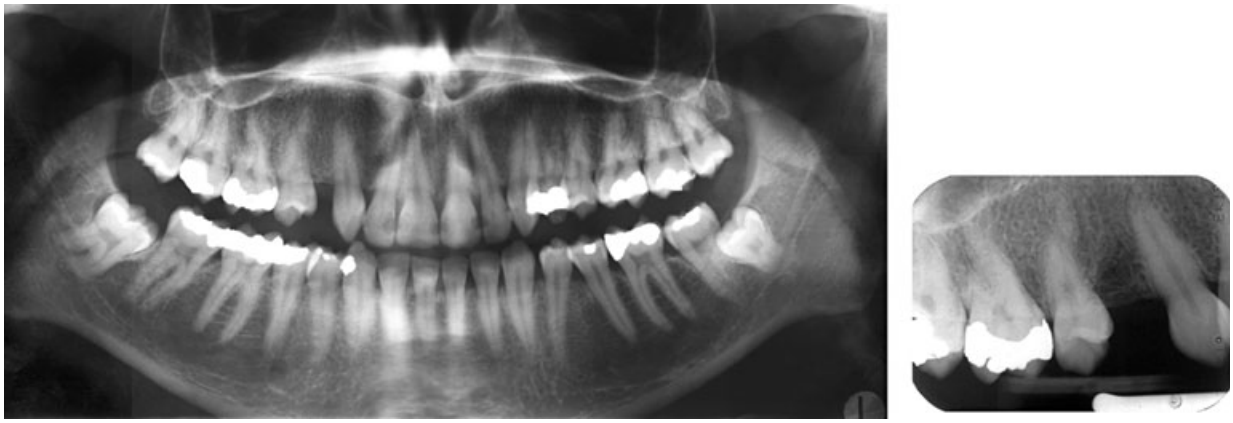

Fig. 28-6 Horizontal distortions are common in panoramic radiographs, especially in the upper premolar area, and give a false impression of available horizontal bone dimensions. Compare the distance between the second premolar and the cuspid in the two images.

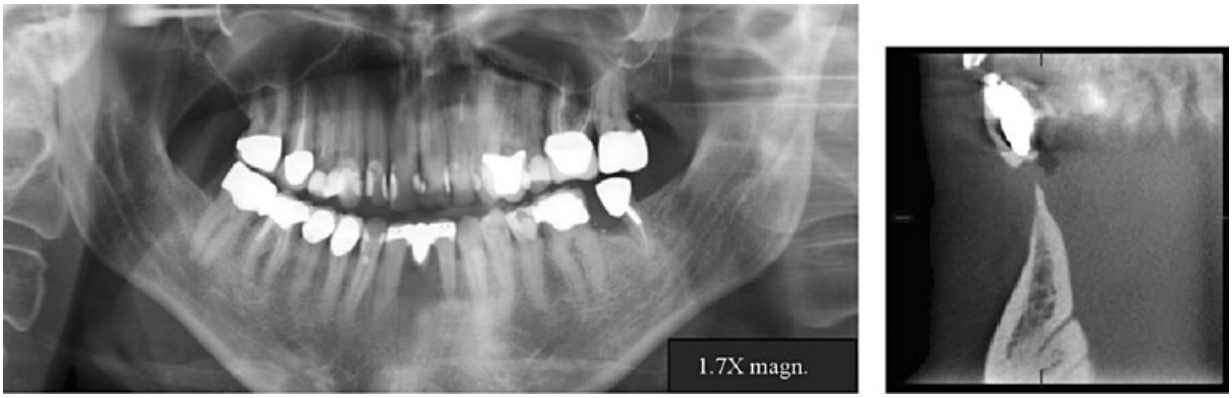

Fig. 28-7 The panoramic radiograph does not provide information about the width of the alveolar bone. A sagittal tomographic image reveals the true conditions in the lower anterior region.

occlusal loads, due to the poor bone conditions in the region that could have been observed had a better pre-operative radiographic examination been made.

Intraoral radiography should be performed according to the paralleling technique and radiographs taken so that there will be some overlapping between adjacent image fields. Most teeth will then be seen from two different angulations allowing for a better appreciation of the location of different structures.

Panoramic radiography may seem easy to perform but is a technique where many mistakes are made, not least in patient positioning. Panoramic radiographs taken on incorrectly positioned patients may provide a severely distorted view of the patient's jaws (Tronje 1982). This can cause large overlapping of neighboring teeth that can prevent a proper diagnosis. In regions where teeth are present the distortions are evident due to the overlapping of tooth surfaces (Fig. 28-6). In edentulous areas, however, distortions may not be that apparent which can lead to misjudgement of distances within the jaws. The panoramic technique can be used to provide a quick estimate of the bone height. A tomographic examination needs to be carried out in many cases to determine whether it is sufficient for implant placement (Fig. 28-7). The magnification in panoramic images varies between different types of panoramic machines. Some units also permit various types of radiographic images to be taken, that differ in magnification. It is thus important that one makes certain what magnification is indicated in the image to be evaluated.

Tomography can be used to obtain cross-sectional images, that is, images that are perpendicular to the curvature of the jawbones in the intended implant site. This is the best way in which to assess the width of the jawbone, and thereby the height available for implant placement, as well as other important aspects of the jawbone anatomy. Equipment for tomographic examinations shows much more variation than does that for panoramic and intraoral radiography. Widely different imaging principles are used resulting in different types of images.

The implant treatment spectrum varies from the single implant case to that where large parts of the facial skeleton are missing, and making an implant-anchored facial prosthesis necessary. Ideally, a clinic for oral and maxillofacial radiology is therefore equipped with a spectrum of X-ray machines for tomography capable of satisfying different demands

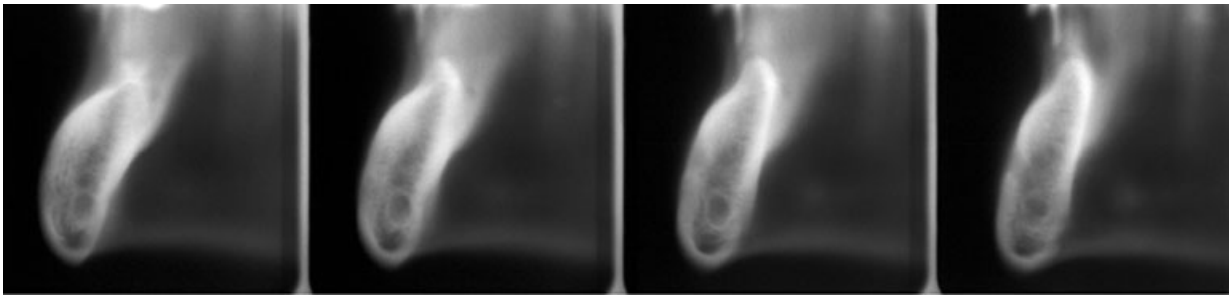

Fig. 28-8 Conventional spiral tomography of the lower jaw. Contiguous, 4 mm wide slices with the most anterior one taken in the region of the mental foramen (image to far right) that serves as an anatomic landmark.

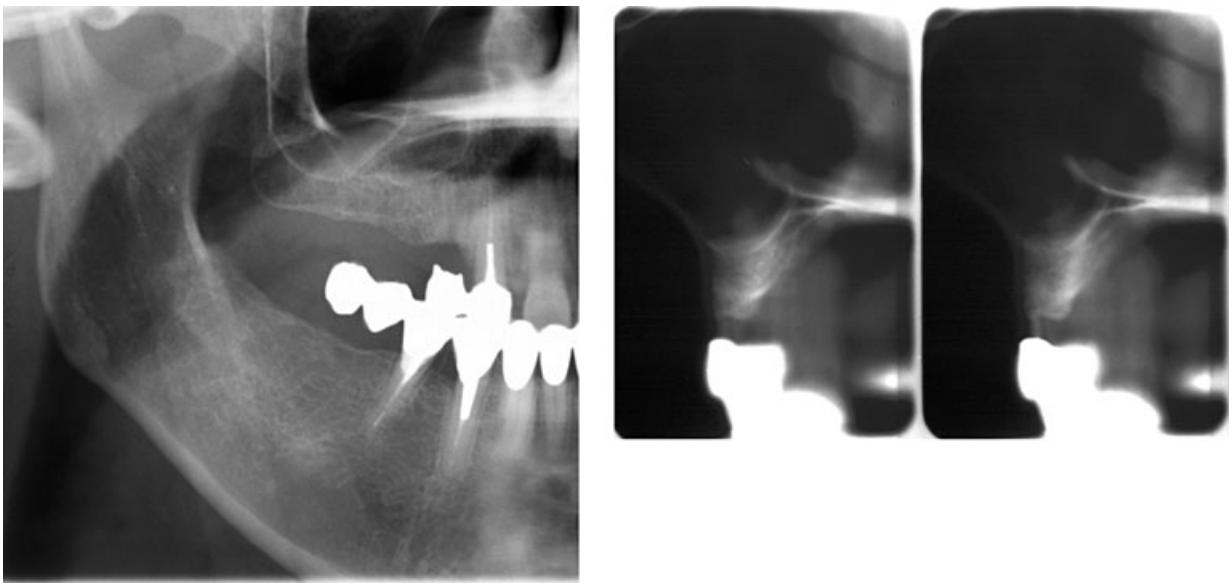

Fig. 28-9 By selecting just a few tomographic layers the dose can be minimized. Images taken distal to the upper right cuspid (see cropped) panoramic image.

and providing high-quality tomographic examinations. There is a difference between what different machines are best suited for. Three main groups of tomographic techniques are used for pre-implant tomography: motion (conventional) tomography, computed tomography (CT), and digital volume tomography (DVT), also known as cone beam CT. This is not the place to present these techniques in any detail but a little will be said about each of them as it relates to the examination of the implant patient.

Conventional tomography as applied for dental purposes underwent a profound development in the end of the 1980s when tomographic X-ray machines dedicated for the examination of the jawbones entered the market. Units such as the Scanora (Soredex Co, Helsinki, Finland) later to be followed by Cranex Tome from the same company meant that, most of the time, a comprehensive pre-implant examination of the patient could be made in the same unit and with the patient in the same position (Gröndahl *et al*. 1996, 2003). From a panoramic image one determines where in the jaw(s) one needs information that can only be found in cross-sectional, tomographic images. The tomographic examination of the selected region is then accomplished by means of a synchronized, spiral, movement of the X-ray tube and the detector (film or image plate) permitting image layers of 2–4 mm width to be obtained containing a minimum of spurious contours from adjacent structures.

One to four images of contiguous tomographic layers can be taken during the same examination, that is, without changing patient position or detector. They will then appear on the same film, or within the same digital image frame (Fig. 28-8). By selecting just a few layers to be exposed, radiation doses can be minimized (Fig. 28-9).

By means of multimodality units, conventional spiral tomography provides the possibility of tomographic examinations of limited regions selected from a panoramic view of the entire jaw or a part of it. It has the advantage of being done with a small unit that can also be used for many other radiographic examinations of the oromaxillofacial regions. Spiral tomography can be made with film or image plates but not with CCD or CMOS solid-state detectors: these are not yet available for use with the dental multimodality-type of X-ray machines.

Computed tomography is widely used for pre-implant tomography, often because other techniques are not available (Ekestubbe *et al*. 1997). In the overwhelming majority of cases a stack of axial tomographic layer images is first taken. The height of the stack should be such that it covers a distance from just outside the marginal bone crest down to and including the base of the mandible or, for the upper jaw, up to and including the hard palate. In the upper jaw the slices should be parallel to the hard palate, in the lower jaw to the base of the mandible (Fig. 28-10). The information in the axial slices can be used for image reformatting so that cross-sectional views of the jawbone will be displayed (Fig. 28-11). These are perpendicular to a curve corresponding to the shape of the jaw as seen in a representative axial view.

Computed tomography is easily performed but can also be associated with high radiation doses (Dula *et al*. 1996, 1997; Frederiksen *et al*. 1995; BouSerhal *et al*. 2001). Doses can, however, be significantly reduced by adhering to so-called low-dose protocols which are well suited for studies where the primary interest lies in examining bony structures (Ekestubbe *et al*. 1996, 1999). When using computed tomography it is also important that the height of the examined volume is kept as small as possible. Computed tomography is not ideal for tomographic examinations of partially dentate patients. This is because the volume of diagnostic interest, even when the height of the exposed volume is small, constitutes only a small fraction of the latter. Exposing as small a volume as diagnostically feasible is one of the best ways of adhering to the ALARA principle. Should several edentulous regions within the same jaw need to be tomographically examined, computed tomography may be justified (Buser *et al*. 2002).

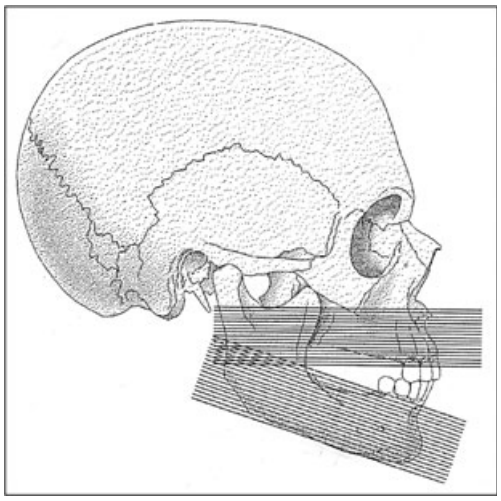

Fig. 28-10 Orientation of the axial tomographic slices differs between jaws. The height of the stack should be kept to a minimum.

Digital volume tomography (*DVT*) is becoming exceedingly popular as a tool for maxillofacial imaging not least for pre-implant planning purposes. With the midpoint of the region of interest as a centre, the X-ray tube moves along the periphery of a circle, on the other side of which is positioned the detector. During this movement a cone-shaped X-ray beam, the diameter of which differs between different types of equipment, exposes the region of interest either continuously or in short bursts. From the X-ray detector a signal is sent to a computer where the electronic signal is converted into a digital one. Based on this information images can be reconstructed so that layer images (axial, sagittal, and coronal) of the exposed volume will appear on the screen. It is possible to travel in either direction within the volume so that the entire volume can be easily searched. Many DVT units make it possible to display curved layers of varying width so that something similar to a conventional panoramic view, although with thinner layer thickness, is obtained.

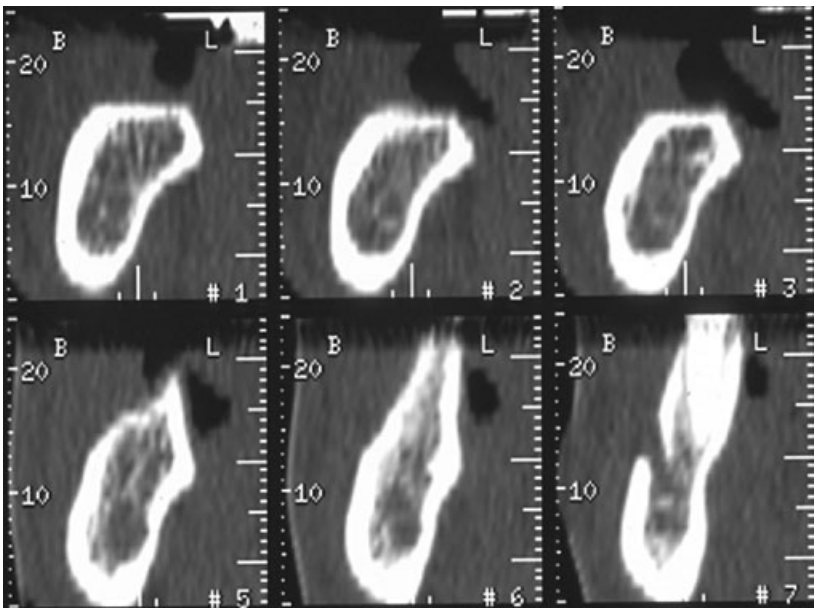

Fig. 28-11 Some reformatted cross-sectional images from the right side of the mandible.

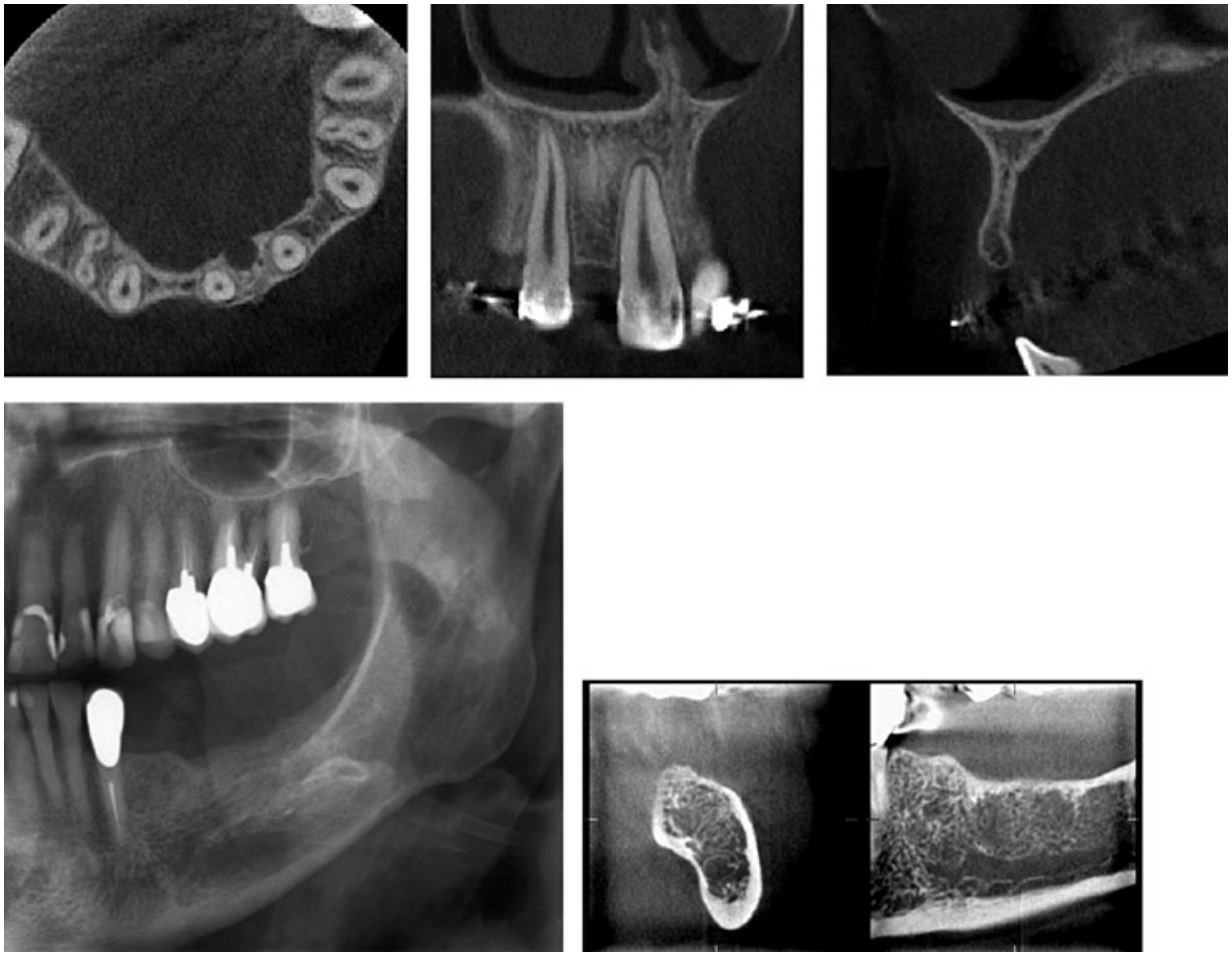

Fig. 28-12 Images (except the panoramic view) taken with 3DX Accuitomo DVT unit (J. Morita Co., Kyoto, Japan). The upper row images show the conditions in the right upper lateral incisor region. In the lower row the coronal and the sagittal tomographic images show the mandibular canal that is barely visible in the panoramic image.

Equipment for digital volume tomography comes in many different shapes (Frederiksen 2004), and they vary with regard to size of the volume that can be examined, geometric resolution, ease of use etc. They also differ as regards the radiation dose to the patient due to, above all, differences in volume size, resolution, and type of detector (Ludlow *et al*. 2006). Digital volume tomography could very well become the technique with which most partially dentate patients in need of implant treatment will be examined. The examination is easily done and radiation doses can be kept low, especially when machines that permit different sized volumes are used. An excellent way of reducing radiation dose is to expose the smallest possible volume. An advantage with digital volume tomography is its applicability in many areas of clinical dentistry. Figures 28-12 and 28-13 provide examples of images taken with DVT units.

Realizing that far from everybody has access to a wide spectrum of X-ray machines we will present various types of commonly seen cases. We will describe how they can be radiographically examined by means of different techniques but not include the totally edentulous patient or the patient in need of facial prosthetic constructions.

Radiographic examination for implant planning purposes – upper jaw examination

Depending upon where in the upper jaw implant treatment is to be planned one must take different anatomic factors into account. A common denominator is of course that the width and height of the bone must be evaluated. The available height depends on the bucco-palatal width of the bone because, ideally, the implant should be covered by bone both on its buccal and palatal aspects. The length of implants that can be used thus depends on the distance between the inferior border of the nasal cavity, or the maxillary sinus, and that part of the alveolar bone where it is sufficiently wide for implant placement (Fig. 28-14). When implants are to be placed in the vicinity of the midline one must evaluate the width of the incisive foramen and the nasopalatine canal. One must assess the height and width of the alveolar bone on the buccal and distal side of these structures to determine whether and where an implant can be placed (Fig. 28-15).

In the upper frontal region it is not uncommon for a single tooth be missing as a result of previous

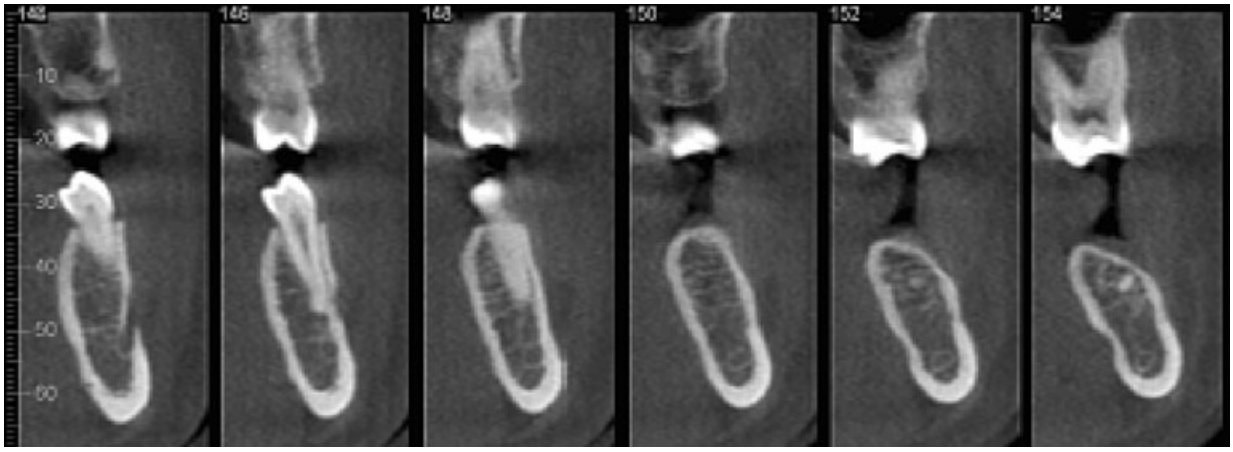

Fig. 28-13 Lower jaw tomography performed by i-CAT cone beam CT machine (Imaging Sciences International, Hatfield, PA, USA). Courtesy of Dr. Allan Farman, University of Louisville, Kentucky, USA.

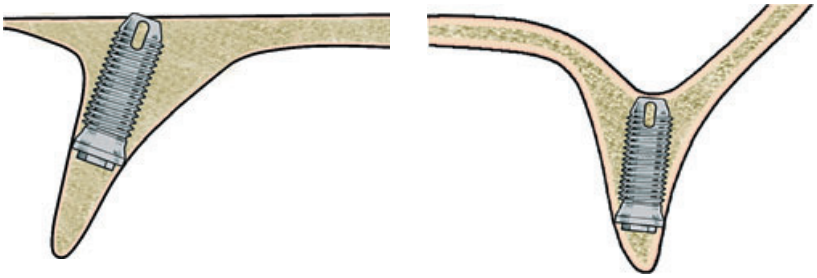

Fig. 28-14 The height of the bone available for implant placement depends on its width. It may therefore be less than the height as it appears in e.g. intraoral or panoramic radiographs.

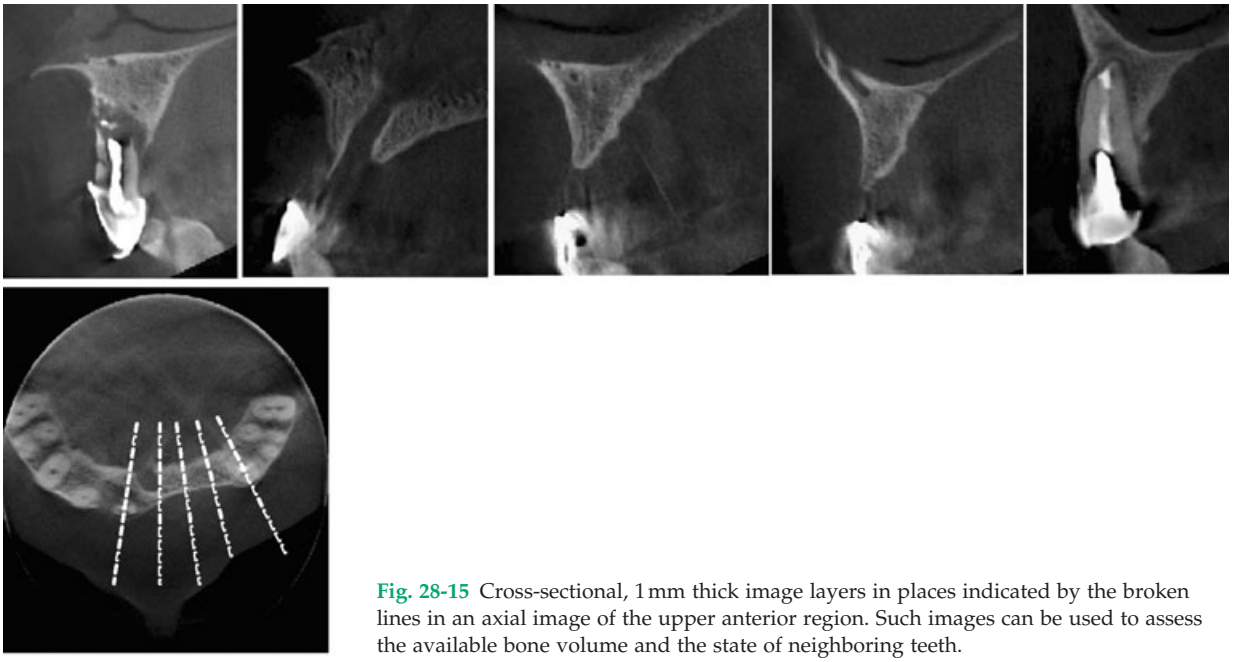

Fig. 28-15 Cross-sectional, 1 mm thick image layers in places indicated by the broken lines in an axial image of the upper anterior region. Such images can be used to assess the available bone volume and the state of neighboring teeth.

trauma. In these cases the radiographic examination can be done in a simple, yet comprehensive, way by one or two intraoral radiographs and a single tomographic image (Fig. 28-16).

Should the available bone lack the dimensions needed for the placement of an implant, the patient may be willing to accept that bone augmentation is performed to provide for sufficient height and width of the bone. In the latter case tomographic images will be of help when determining exactly where the bone is of less than sufficient width or height and the extent to which it needs to be augmented. Tomographic images can also be used to observe the results after healing (Figs. 28-17 and 28-18).

In areas where teeth have been extracted and it is uncertain how much of the alveolus has become

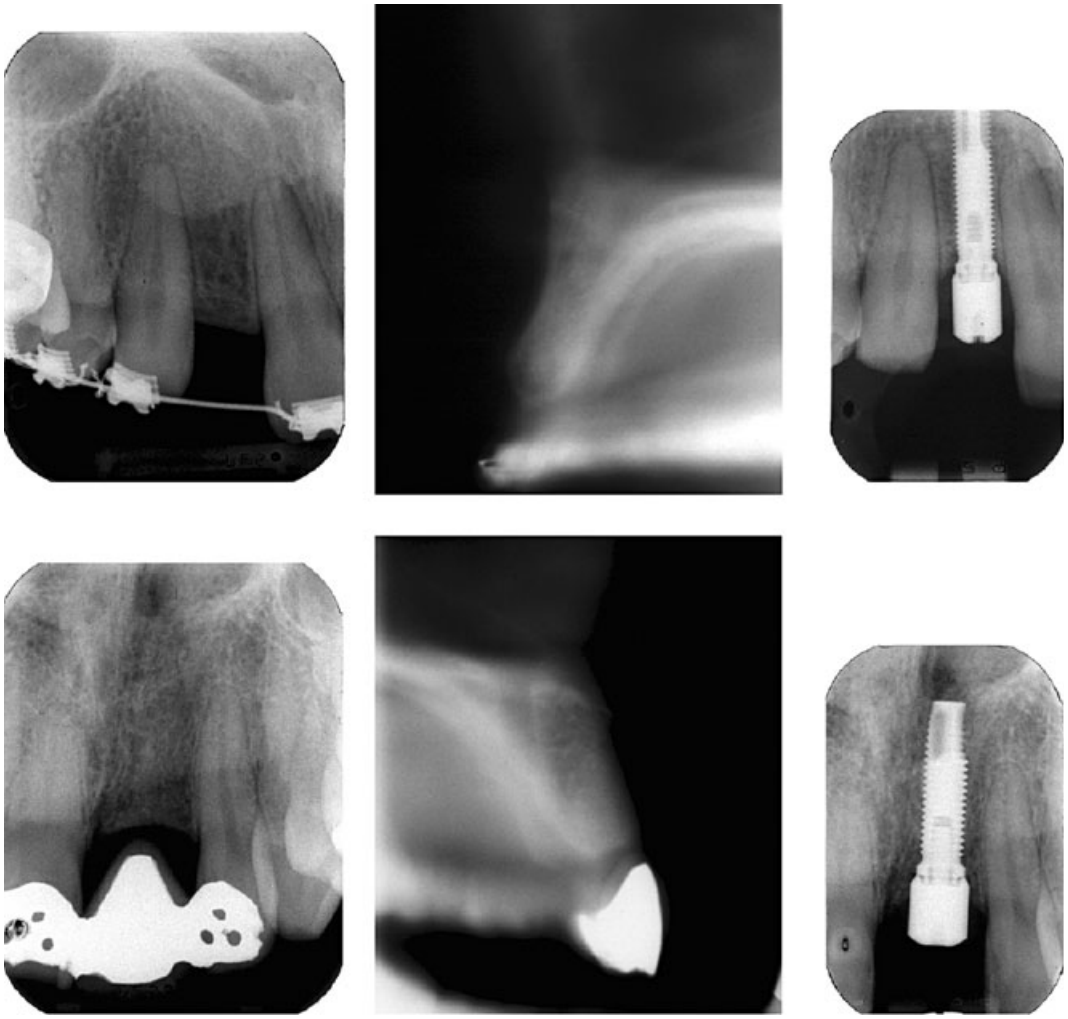

Fig. 28-16 Two cases of missing upper incisors in which the pre-operative radiographic examination was made by intraoral radiographs and conventional spiral tomography. In the lower row case an implant could be placed buccal to the nasopalatine canal.

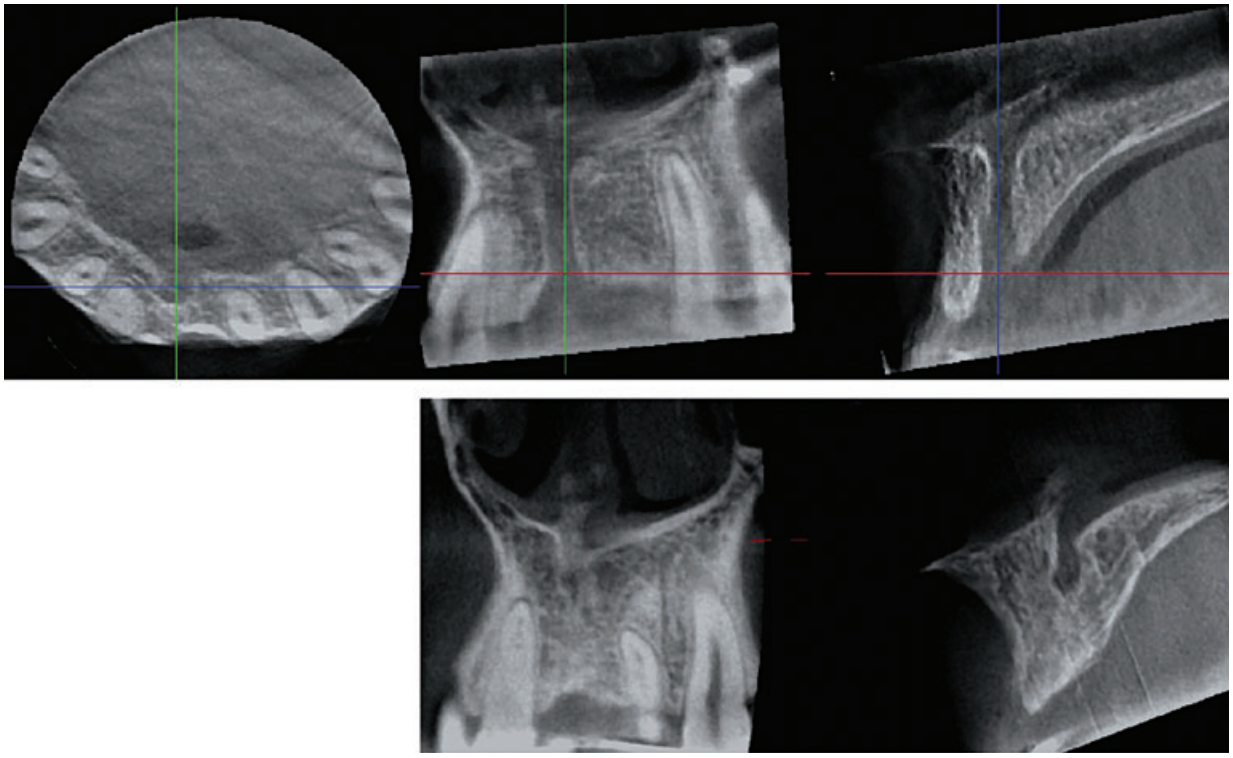

Fig. 28-17 Pre-operative (upper row) and post-operative images of a patient in whom a bone substitute was placed both buccally and in the nasopalatine canal to enable insertion of an implant in an optimal position.

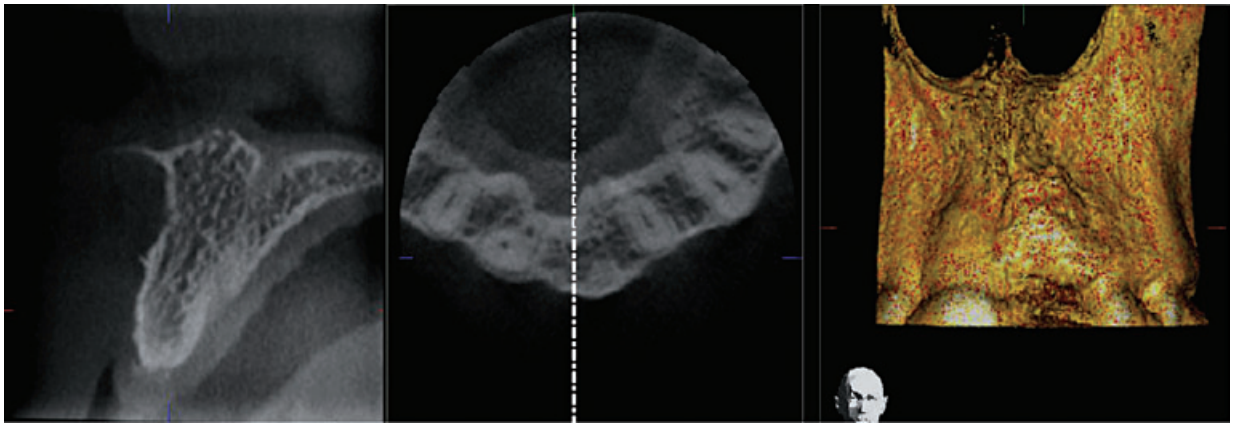

Fig. 28-18 A sagittal (left) and an axial tomographic image (middle) after a bone substitute has been placed on the buccal surface. The dotted line indicates the position of the sagittal slice. To the right is a three-dimensional image reconstructed from the volume data.

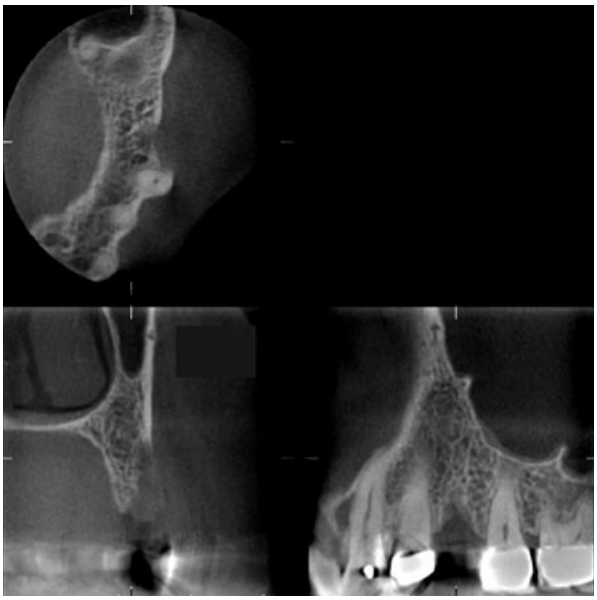

Fig. 28-19 Digital volume tomography in the upper first premolar area. Notice the lack of complete bone filling of the extraction socket and the relation of the alveolar bone to the nasal and maxillary sinus cavity.

filled with new bone, digital volume tomography is a helpful tool. This is illustrated in Fig. 28-19, where it is also apparent how well this technique is able to demonstrate the conditions anterior and inferior to the frontal border of the maxillary sinus.

In some patients in whom the available bone height below the maxillary sinus is too small one can occasionally find bone suitable for implant placement on the palatal side of the sinus. Tomography must be performed so that this can be determined (Fig. 28-20).

In the posterior parts of the upper jaw the maxillary sinus may extend so far down into the alveolar bone that there is not enough bone available in which to insert an implant. By entering the sinus through a buccal window, bone substitutes can be placed under the mucosal lining. Digital volume tomography is an ideal method to evaluate how the bone substitute is positioned and its relation to the adjacent bone (Fig. 28-21).

When implants are intended to be placed in more than one region, the use of computed tomography may be justified (Buser *et al*. 2002) provided that low-dose protocols are applied (Rustemeyer *et al*. 2004). A panoramic radiograph and, when remaining teeth are not well displayed in it, complementary intraoral radiographs are nevertheless important. Figure 28-22 describes how the results of such an examination can look. From the stack of axial images a representative image is chosen in which the curvature of the jaw is drawn. A dedicated computer program then makes new tomographic images at chosen distances. These images describe layers that are perpendicular to the curve and in which measurements of bone height and width can be made.

Computed tomography is mostly performed in medical radiology departments and images considered relevant for the purpose are sent to the clinician. Sometimes these are limited to the axial image describing the curvature of the jaw and the reconstructed cross-sectional images. We recommend that the referring dentist should also receive the scout image and the stack of axial images. In the scout image it is possible to see what reference plane that was used and, if needed, make the appropriate adjustment of the measurements taken in the cross-sectional views. In the axial images one may be able to pick up information about the remaining teeth not displayed in the panoramic or intraoral radiographs (Huumonen *et al*. 2006).

Radiographic examination for implant planning purposes – lower jaw examination

In the lower jaw there is a distinction between implant placement in the region anterior to the mental foramina and in regions posterior to the foramina. The height of the anterior region is usually well preserved

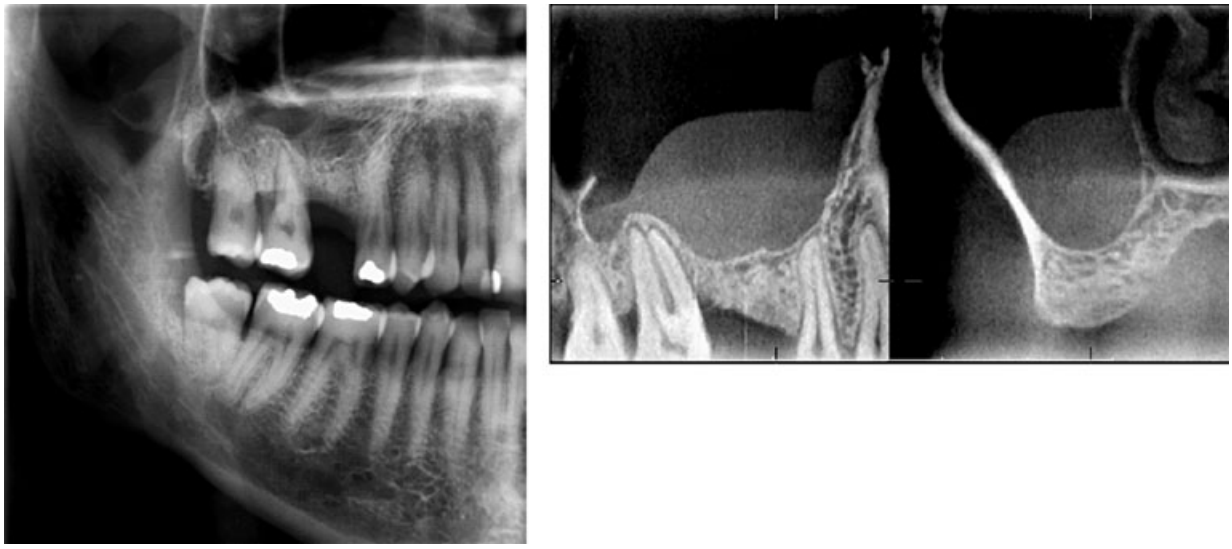

Fig. 28-20 From the panoramic image (left) it is not possible to determine that bone for implant placement is available on the palatal side of the maxillary sinus, as is clearly seen in the tomographic image (right). Notice the soft tissue swelling in the sinus.

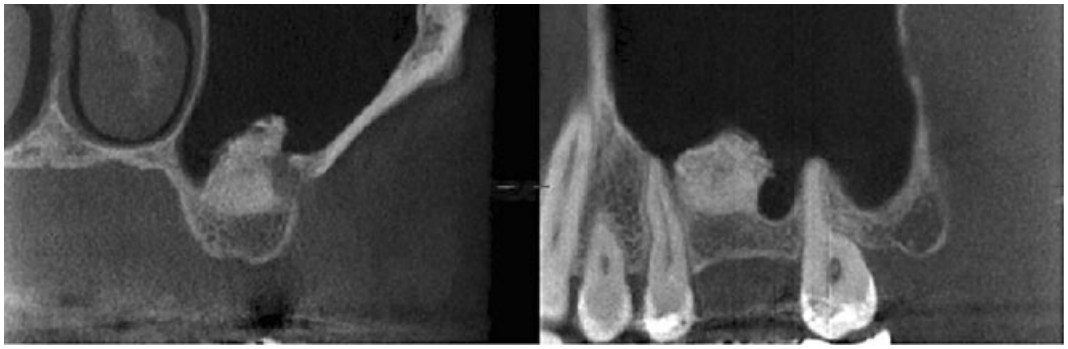

Fig. 28-21 A coronal and a sagittal tomographic layer of the lower part of the maxillary sinus in which a bone substitute has been placed.

if teeth have not been missing for a long time. This is rarely the case in the partially dentate patient. Its width, however, may be a limiting factor. One can get an indication that the alveolar bone is thinner than normal from periapical radiographs or from panoramic images, provided that the anterior region is well reproduced. This is often the case when one can see vertically running radiolucent structures corresponding to the blood vessel canals in the inner walls of the cortex. They become visible when the bone is thin or has fewer and thinner bone trabeculae than normal. In such cases a tomographic examination may be advisable so that one can determine beforehand whether a thin upper ridge will be removed or a bone augmentation procedure applied.

When implants are to be placed posterior to the mental foramina one must not only take into account the factors one had to consider in the frontal regions. One must also be able to identify the path of the mandibular canal and accurately assess the distance between the upper level of the alveolar bone, where it is sufficiently wide, to the upper border of the canal. To do this before surgery requires that tomography is performed, so that the jawbone anatomy can be evaluated in image layers that correspond to cross sections of the mandible. Estimating this distance in panoramic radiographs, as many seem to do (Worthington 2004), requires so many assumptions of unknown variables that mistakes can easily be made (Fig. 28-23). These can result in temporary or permanent damage to the inferior alveolar nerve. These problems "are more frequent than expected" (Worthington 2004). We are convinced that careful presurgical planning, including the use of tomography, will keep the incidence of nerve damage to an absolute minimum.

The entire distance from where sufficient width of the mandible is found to the upper border of the mandibular canal cannot be used for implant surgery. One reason is that the drill used for preparing the implant site will go deeper than the implant itself. Another is that one cannot always measure distances in radiographs with absolute accuracy and precision. Therefore, prudent clinicians make use of at least a 2 mm safety zone between the upper border of the

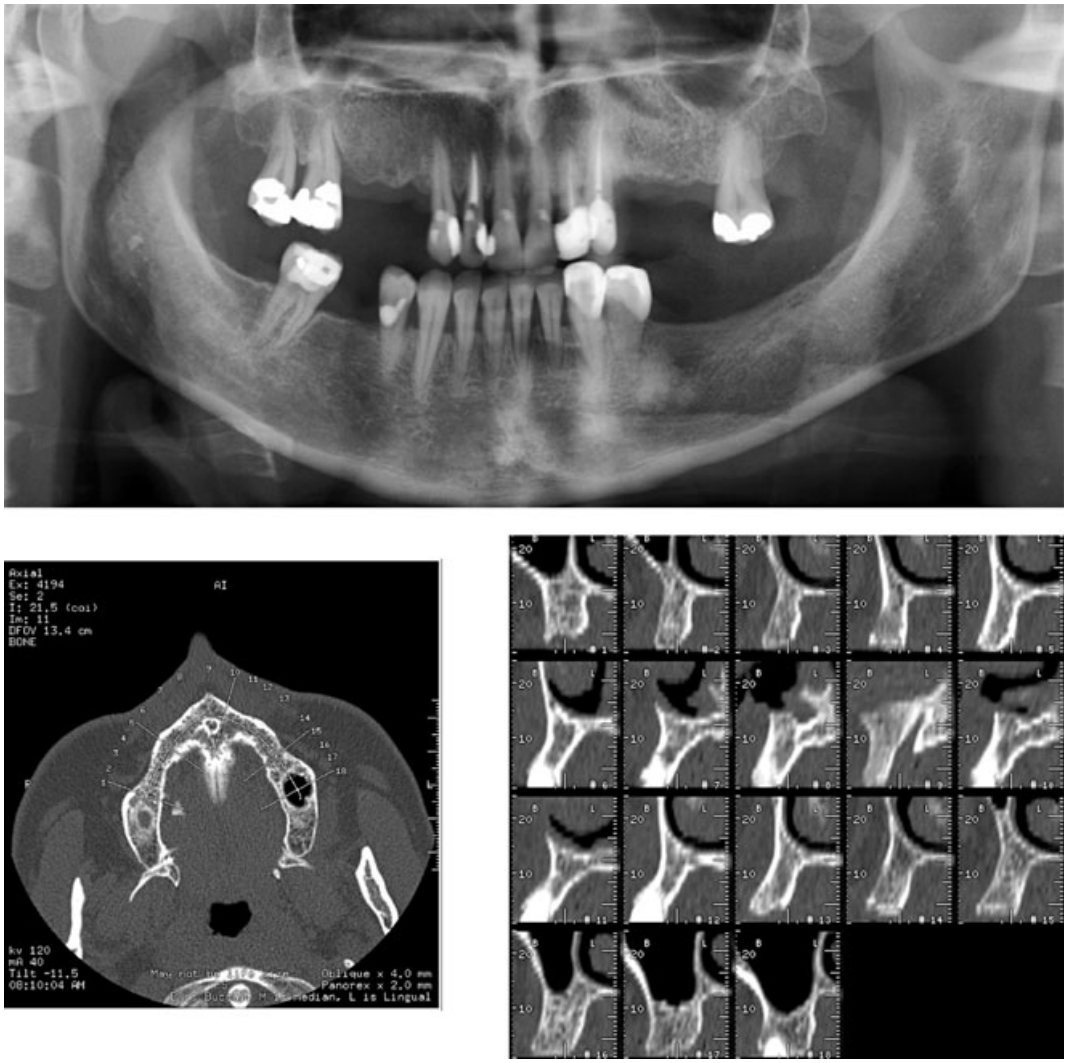

Fig. 28-22 Computed tomography of the upper jaw where implants are planned to be installed on both sides. To the lower right are cross-sectional views from one side to the other, perpendicular to the curve seen in the axial view to the left.

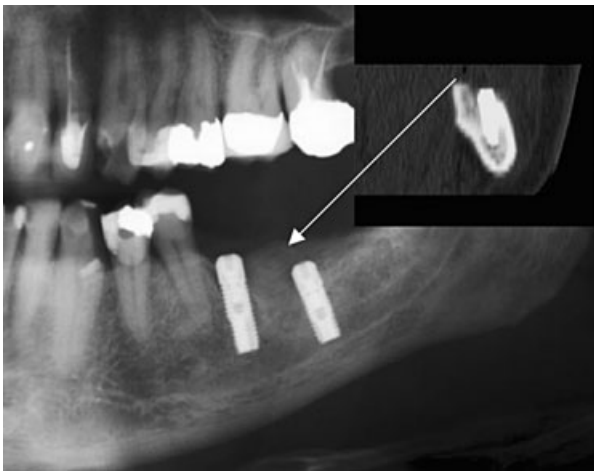

Fig. 28-23 In this case implant treatment planning was based on a panoramic radiograph only. One of the implants was placed with its tip into the mandibular canal as seen in a subsequent CT image. The positioning of the implant into the canal may have been caused by a misinterpretation of the panoramic radiograph. It is the lingual part of the upper alveolar bone that gives rise to the upper contour in the panoramic image.

mandibular canal, as seen in the radiograph, and the planned level of the tip of the implant (Fig. 28-24).

Among other factors that must be considered in the planning process is the outer shape of the mandible. Both concavities and the lingual tilt differ in extension between patients and between different parts of the jaw (Figs. 28-25 and 28-26). Accidental penetration of the lingual wall of the mandible can more easily occur under those conditions than when they are not present. Severing of arteries in the underlying soft tissues can cause severe, even fatal, bleeding (Darriba & Mendonca-Caridad 1977; Niamtu 2001).

Sometimes the mandibular canal, before it ends at the mental foramen, continues a little bit in an anterior direction before going upwards and distally toward the foramen making a so-called anterior loop (Arzouman *et al*. 1993). Therefore it is recommended not to place an implant immediately anterior to the foramen. In other cases there can be a relatively wide anterior continuation of the canal, as indicated by Fig. 28-27. It is then recommended that a radiographic

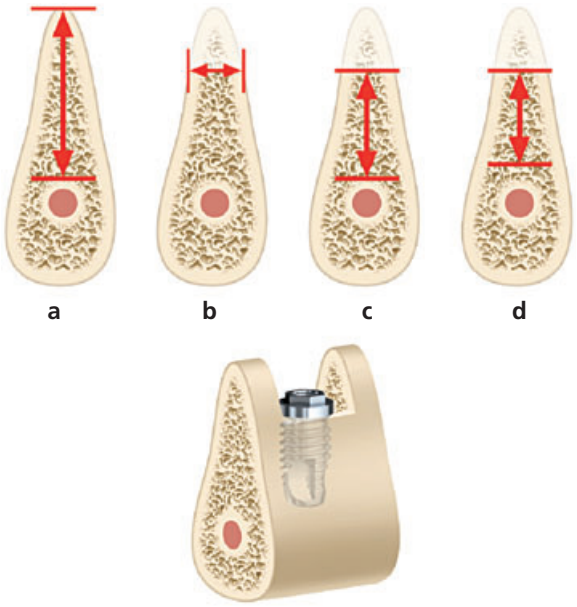

Fig. 28-24 How measurements can be made in tomographic images to ensure that the tip of the implant will not enter the mandibular canal. (a) Measure the entire height from the upper border of the canal to the marginal bone crest. (This value can be used as a reference during surgery.) (b) Assess where the bone is wide enough for the implant. (c) Measure from this level to the canal. (d) Subtract 2 mm from the latter value. From Gröndahl *et al*. (2003).

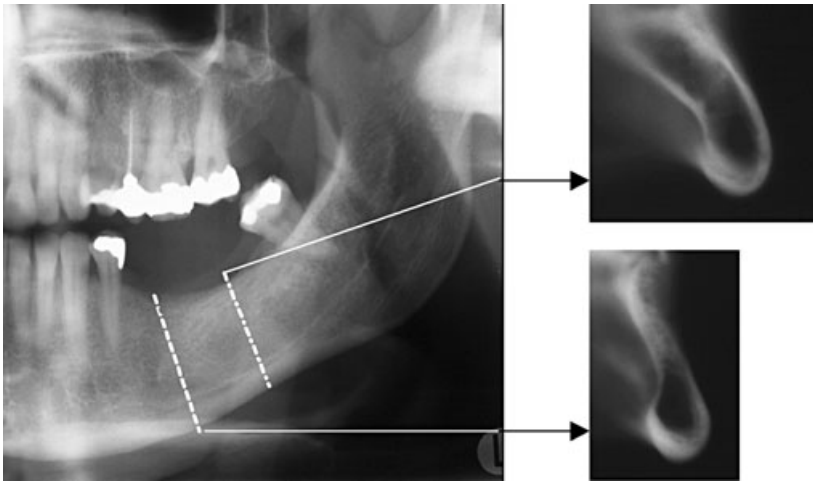

Fig. 28-25 Lingual concavity and a small bucco-lingual width just distal to the mental foramen and a different shape and width in a more distal position.

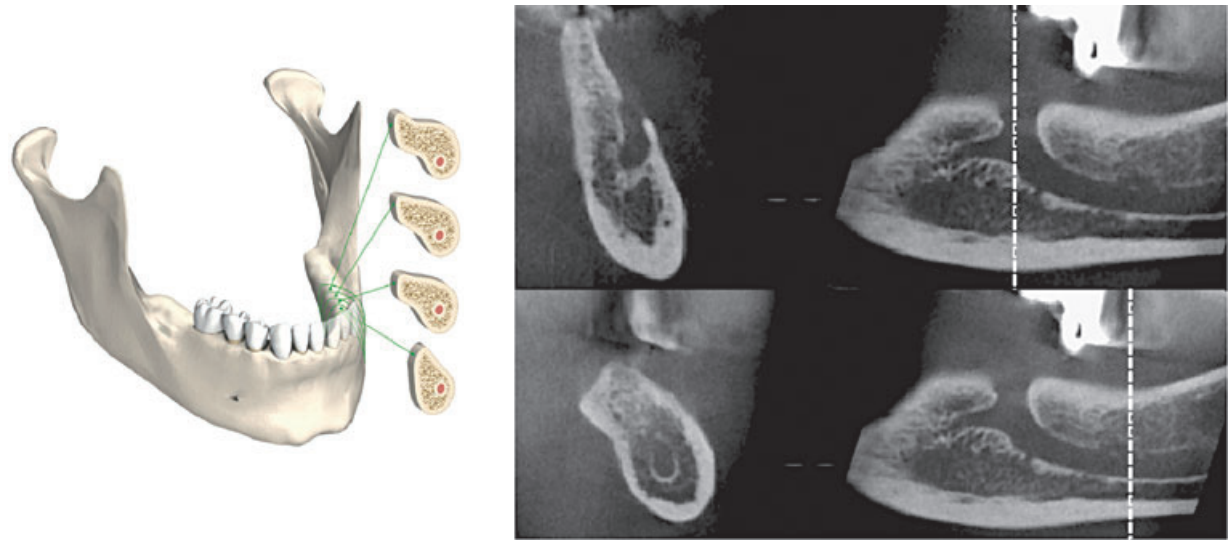

Fig. 28-26 The shape and angulation of the mandibular jawbone can be very different just a short distance apart. The dotted lines in the sagittal tomograms indicate the positions of the cross-sectional tomographic layers. This information can only be obtained pre-operatively by means of tomography.

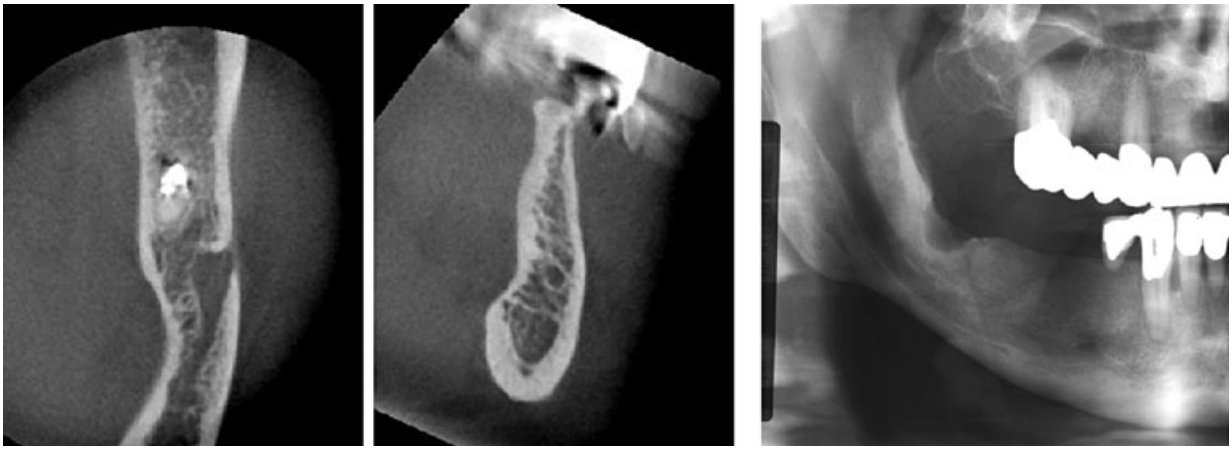

Fig. 28-27 An anterior continuation of the mandibular canal from the mental foramen as seen in tomographic images (same patient as in Fig. 28-26) and as it may appear in a panoramic view (different patient).

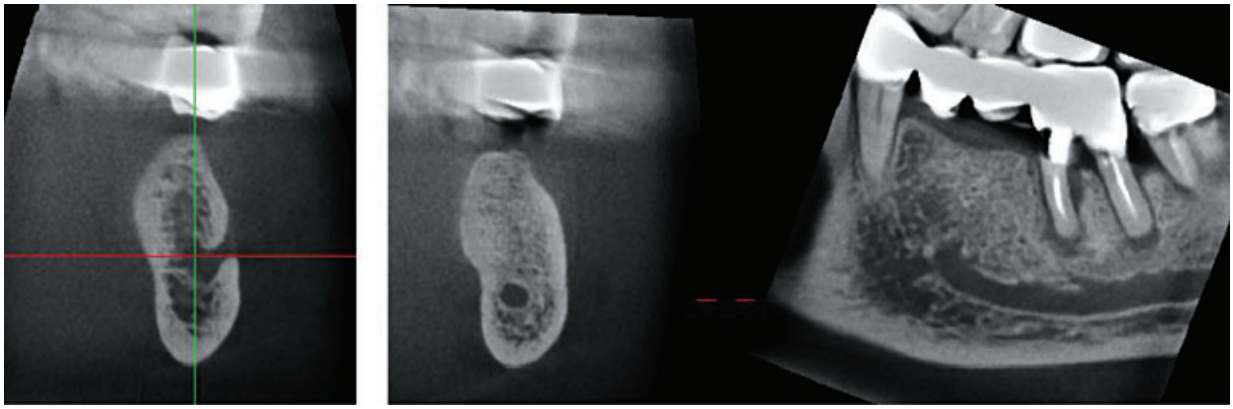

Fig. 28-28 Large local differences in bone density and architecture. The much denser bone in the most distal tomographic layer most probably is due to the inflammatory conditions at the adjacent molar.

evaluation is performed to determine its position relative to potential implant positions.

This is not the place to discuss factors related to general health that may have an influence on bone structure and architecture. In can be noted however, that in tomographic images, given that their resolution is sufficiently high, the cancellous bone pattern in intended implant sites can be studied and the thickness of the cortical bone evaluated. Local factors can contribute to local variations in bone density. In Fig. 28-28 large differences in bone density can be seen in tomographic images less than 1 cm apart. The higher density in the more distal region is most likely a reaction to the inflammatory conditions seen at an adjacent tooth.

Radiographic monitoring of implant treatment

Meticulous planning of the implant treatment together with gentle surgical technique for the insertion of the implants make immediate post-operative radiographic examination superfluous unless something unexpected occurs during surgery. Under normal conditions, however, there is simply nothing, apart from the expected, to be found. Should the patient experience symptoms before the first post-operative radiographic examination is scheduled, one should of course not hesitate in taking radiographs if information from them is considered essential for a proper diagnosis.

The radiographs in Fig. 28-29 are from a patient who presented with severe pain very soon after implants were inserted. The images show unevenly demarcated radiolucent areas around the implants, especially the most distally and the most mesially placed. This is a strong indication of bone infection. In addition, the most mesially placed implant appears to have its tip in close proximity to the anterior loop of the mandibular canal. This is confirmed by a tomographic examination. The affected implants were removed and the symptoms soon subsided.

When implants are inserted in dense bone heat necrosis can occur around the "apical" part of the implants, particularly when the implants are long and effective cooling during their insertion has not been applied. Usually this is accompanied by pain. In the radiograph one can see a radiolucent area surrounding the apical part of the implant. A radiolucent area just beneath the apical part and caused by

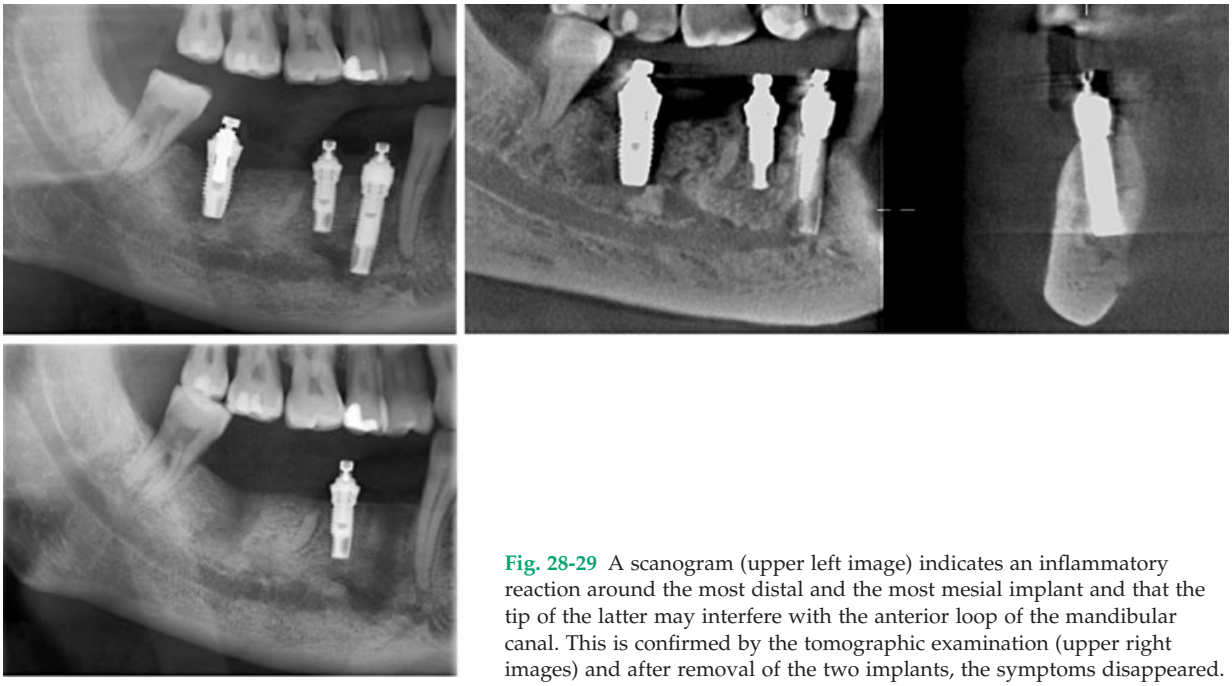

Fig. 28-29 A scanogram (upper left image) indicates an inflammatory reaction around the most distal and the most mesial implant and that the tip of the latter may interfere with the anterior loop of the mandibular canal. This is confirmed by the tomographic examination (upper right images) and after removal of the two implants, the symptoms disappeared.

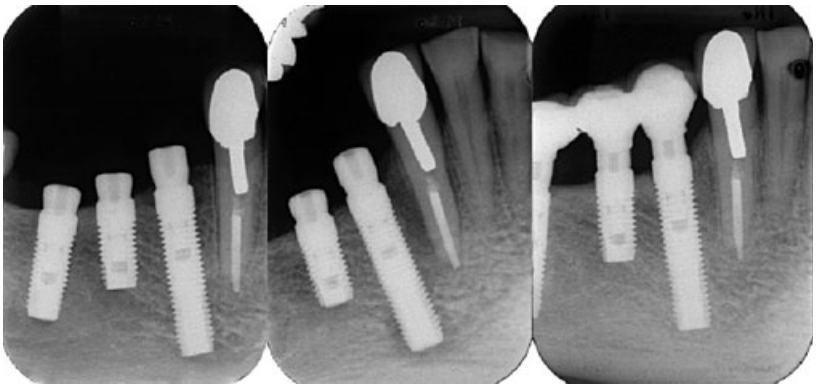

Fig. 28-30 Soon after implant insertion the patient presented with slight pain. A radiograph (left image) was interpreted as showing normal conditions. Two weeks later the pain had increased in intensity and a radiolucency could now be seen around the tip of the most mesial implant (middle image). The right image, taken some months later shows completely normal conditions.

the drill should not be confused with the radiolucency that is a result of heat necrosis. Heat necrosis is most commonly seen in the lower jaw (Fig. 28-30).

Often it is not possible to take radiographs of implants using standard intraoral techniques. One either has to take radiographs more from below or use panoramic radiography or, better yet, so-called scanograms (Fig. 28-31).

Implants that have not been correctly placed in the bone may cause symptoms as well. Should an intraoral examination fail to show the cause of the problem a tomographic examination may be needed (Fig. 28-32). It should preferably be performed with digital volume tomography, as it is less prone to cause artifacts from the implants than computed tomography.

Depending upon the implant system used there may or may not be a need for a radiographic examination when abutments are placed. To examine

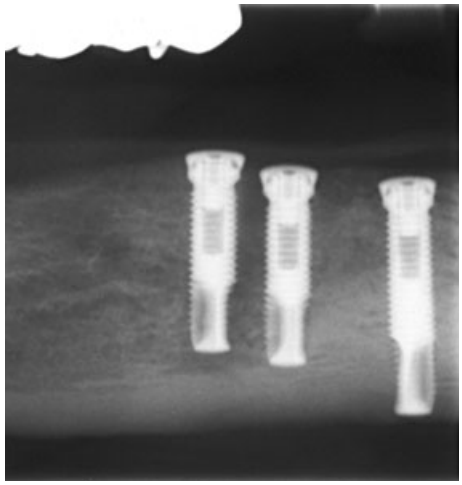

Fig. 28-31 A so-called scanogram by which even deeply seated implants can be displayed in their entirety.

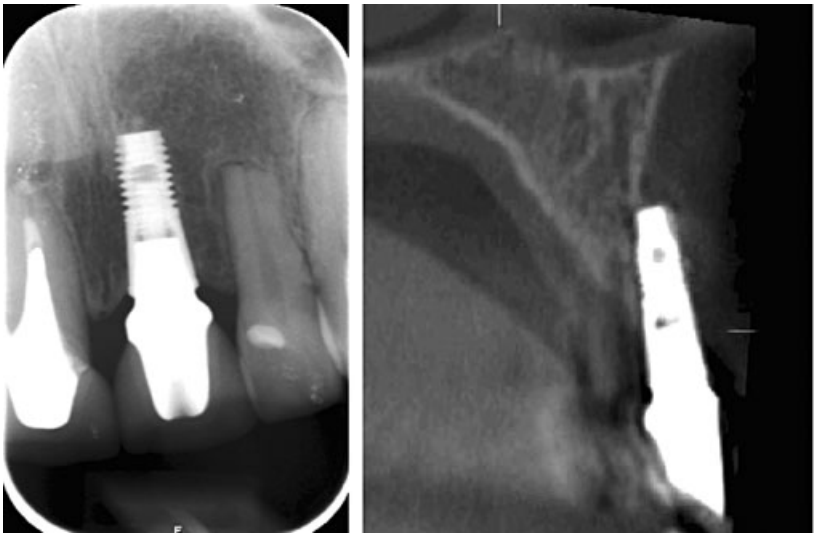

Fig. 28-32 An intraoral radiograph (left) failed to reveal the cause of the problem in a patient with pain in the region of a newly placed implant A DVT image demonstrated that most of the implant was not placed in the bone.

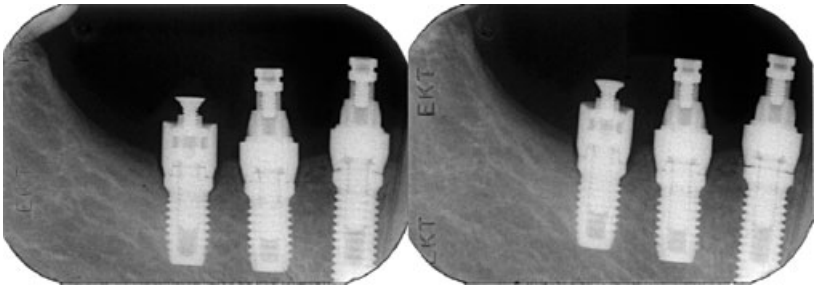

Fig. 28-33 Small gaps between abutment and implant pillar (most mesial implant) may go unnoticed in radiographs taken with less than perfect geometry (left image).

whether abutments are correctly positioned on top of the implant pillar the X-rays need to pass at right angles to the implant. If not, gaps between the abutment and implant pillar may go unnoticed and uncorrected for (Fig. 28-33). The occlusal load will then not be optimally distributed which can later cause component fractures. Marginal bone loss has also been attributed to gaps between the abutment and the implant pillar (Hermann *et al*. 2001; King *et al*. 2002).

Reference radiographs, with which later radiographs can be compared to monitor the interaction between implant and bone, are preferably taken when crowns or bridges are placed. Little can come out of such comparisons if the quality of the radiographs is not high. It must be possible to notice small marginal bone level differences over time as well as the condition of the bone–implant interface. This requires radiographs to be taken with the X-rays being directed perpendicular to the longitudinal axis of the implant and the surface of the detector. When threaded implants are used the radiographic appearance of the threads provides useful information about the irradiation geometry used and how to change it should it not be correct to start with. One must be able to get a clear picture of the inner parts of the threads on either side of the implant (Fig. 28-34).

Intraoral radiography is the method of choice for monitoring of implant treatment. Irradiation geometry and exposure can be individualized for different implants or group of implants. Panoramic radiography cannot provide the same detailed information and should be reserved for the few cases when intraoral radiography cannot be tolerated. A better alternative can be used by those who have access to multimodality units able to provide multiple exposures of selected small areas using slightly different irradiation geometry.

With high-quality intraoral radiography it is possible to follow the course of events in the marginal and peri-implant bone over time. A fairly typical course of events for lower jaw implants, from abutment placement via bridge installation to a 5-year follow-up examination, can be seen in Fig. 28-35. With well trained and motivated personnel it is possible to get high-quality and comparable radiographs over long periods of time even without going to the effort of using particular film-holding devices. The images in Fig. 28-36 are taken over a 5-year period by different radiographers.

High-quality radiographs make it possible to detect, observe, and quantify bone level changes over time. In the majority of patients the bone level remains at the position it had after the post-surgical remodeling over as long periods that it has been hitherto possible to cover in longitudinal studies (Adell *et al*. 1990; Snauwert *et al*. 2000; Ekelund *et al*. 2003). In other patients one can find loss of bone at the marginal bone crest that affects all implants or, more often, one or a few. It is important to detect those so that the cause of the bone loss can be identified (Figs. 28-37 and 28-38).

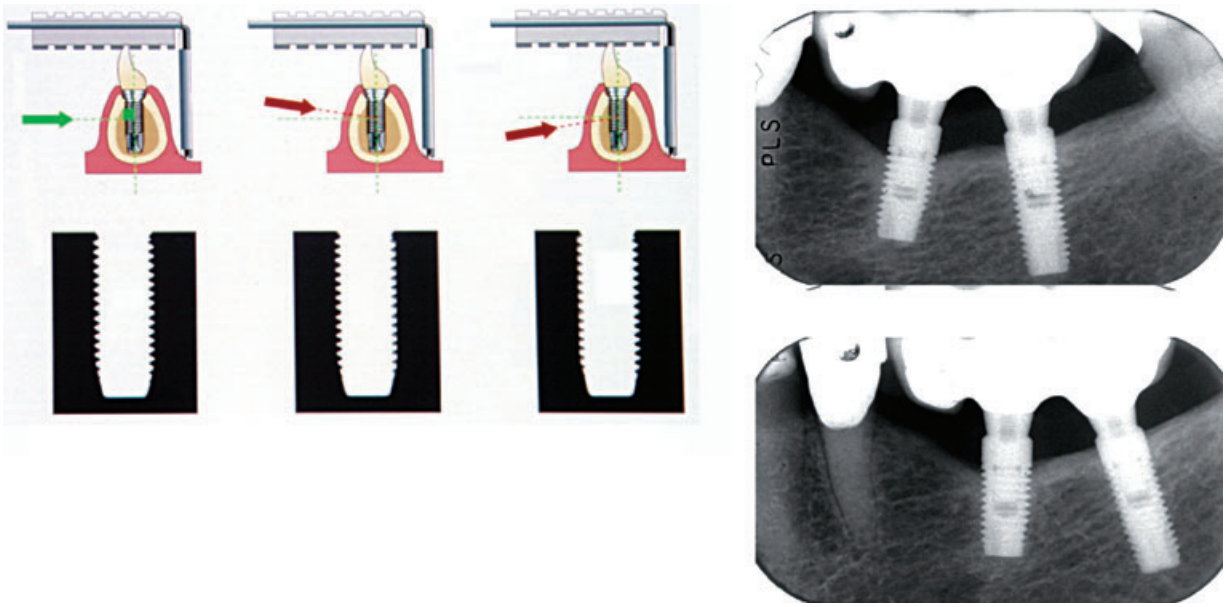

Fig. 28-34 The appearance of the threads of an implant provides useful information about how to change the direction of the X-ray beam so that it can become directed perpendicular to the implant. From Gröndahl *et al*. (1996).

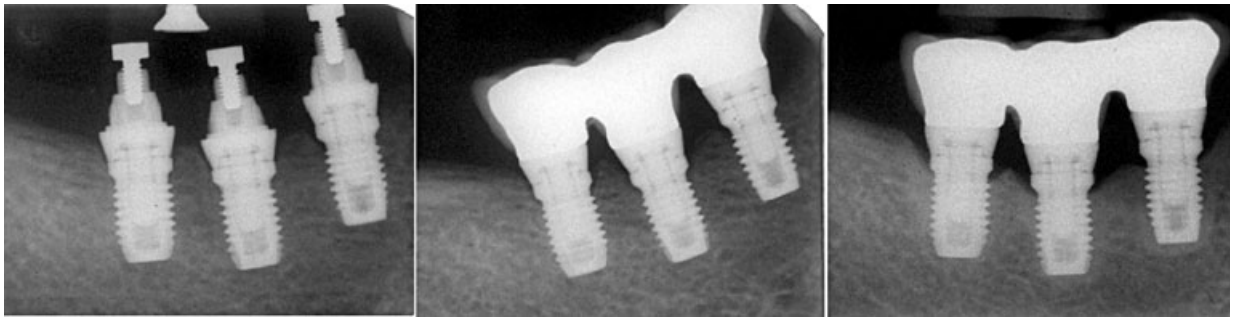

Fig. 28-35 From abutment connection via bridge installation to a 5-year follow-up examination.

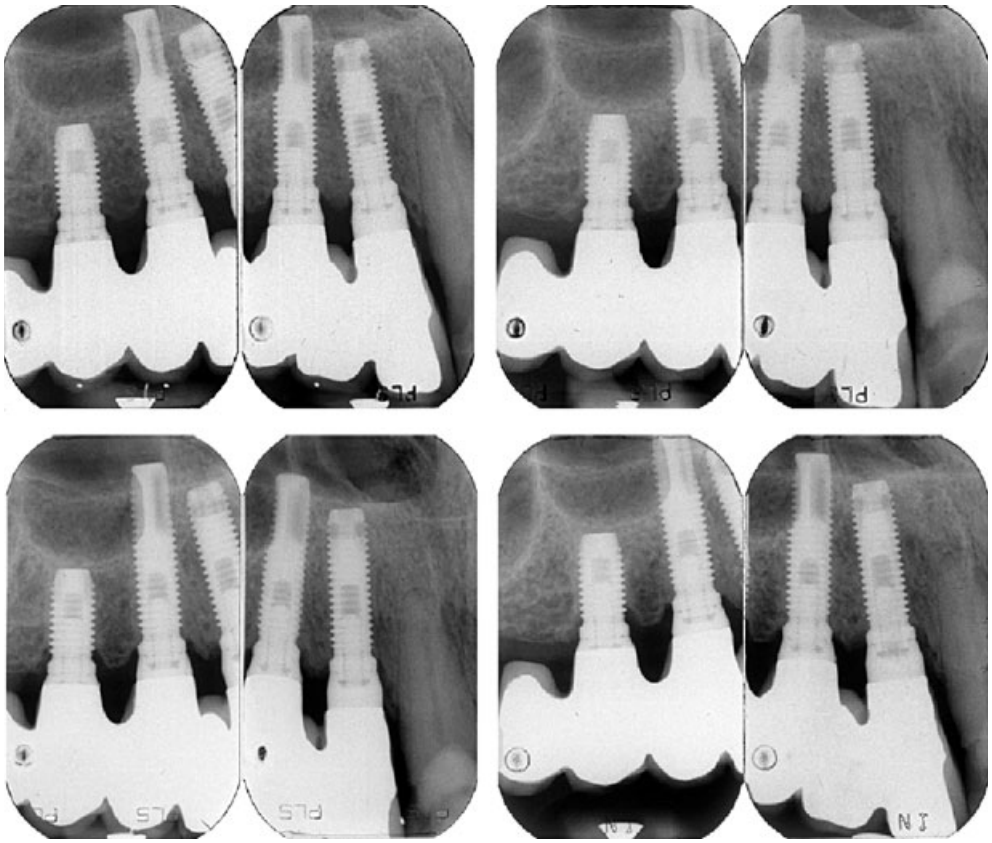

Fig. 28-36 Intraoral radiographs taken with a free-hand technique and by different radiographers at bridge installation (upper left corner) and at follow-up examinations (1, 3, and 5 years later) demonstrate excellent possibilities of monitoring the post-operative course of events.

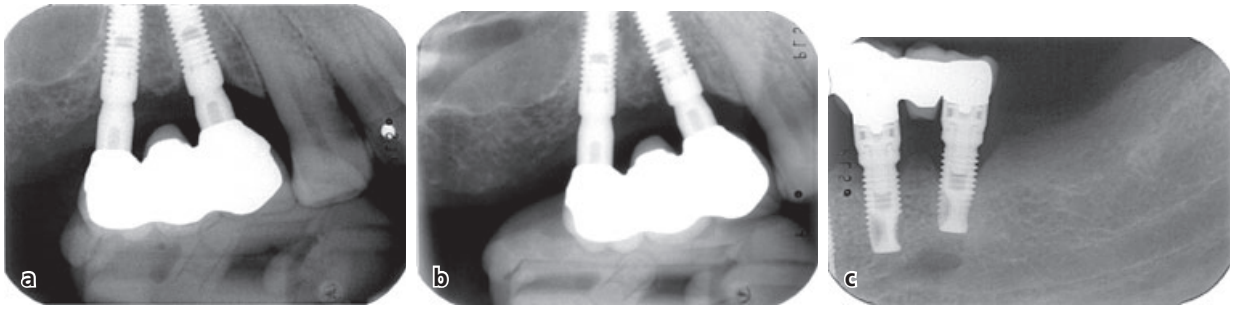

Fig. 28-37 In radiograph (b), the mesial implant has marginal bone loss that was not evident a year before. In radiograph (c), the most distal implant has marginal bone loss involving about a third of the implant length.

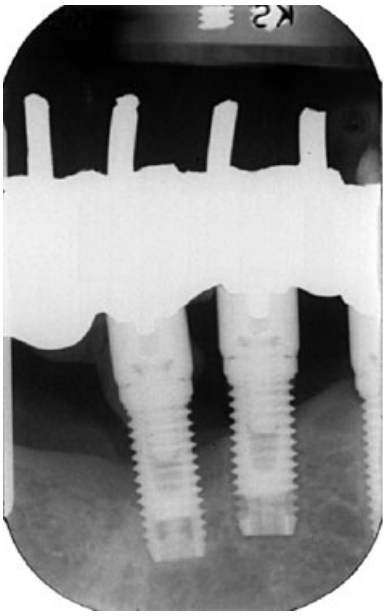

Fig. 28-38 Both implants show marginal bone loss exceeding one third of the implant length. The implant to the right is also surrounded by a thin radiolucent zone. This indicates that the implant is not osseointegrated. At a clinical examination it was found to be mobile and consequently removed.

In high-quality radiographs it is possible to identify implants that are not osseointegrated with an accuracy that is on a par with what one can find when radiography is used for other dental diagnostic purposes (Sundén *et al*. 1995; Gröndahl & Lekholm 1997). Since the first radiographic signs are very subtle, as seen in the radiographs in Fig. 28-39, it is very helpful if one is able to compare radiographs with ones taken previously. Most implants that have not become integrated are found during the first year after bridge installation, or even before that. This stresses the importance that radiographs taken at abutment connection and at bridge installation are of the highest possible quality. Radiographs should be of a quality so that it is possible to evaluate not only the conditions in the surrounding bone and the marginal bone level but also the conditions of all the technical implant components. Such conditions are, for example, fractures of the centre screw or of the implant pillar itself and gaps between abutment and implant pillar, or between bridgework and abutment (Figs. 28-40, 28-41 and 28-42).

Radiation detectors for intraoral radiography

Although a correctly exposed and optimally processed film, in our opinion, provides the best quality images for implant monitoring we have to accept that digital imaging techniques are gaining wider and wider acceptance among dentists. There are some advantages of digital images over film-based ones, in that they can be subjected to image processing algorithms that can enhance their diagnostic quality and adapt them to various diagnostic tasks (Analoui 2001a,b). This can of course be of value when the diagnostic tasks are so varied as they are in implant monitoring when one must be able to evaluate both thin marginal bone and the metal components of the implant construction.

As we have pointed out several times in this chapter the irradiation geometry is essential when implants are to be monitored. The X-rays should come perpendicular to the longitudinal axis of the implant and to the detector plane. Therefore one must have a digital detector that can be placed in the mouth, and relative to the implants, as easily as can film. When the X-ray beam has passed through a jaw in which implants have been inserted, the transmitted radiation consists of a wide spectrum of X-rays of different intensity. Thus, the detector has to be able to respond to a wide range of exposure differences; its exposure latitude must be wide. Image plate systems possess a wider exposure latitude than most solid-state systems (Farman & Farman 2005). With solid-state systems it is therefore easier that thin bone structures become over-exposed and not visible in the radiograph (Fig. 28-43). For this reason, and because image plates are as easy to use as films, we have chosen image plate systems for implant monitoring purposes. Image plates are, however, not without problems. They can easily get scratched if not handled with extreme care.

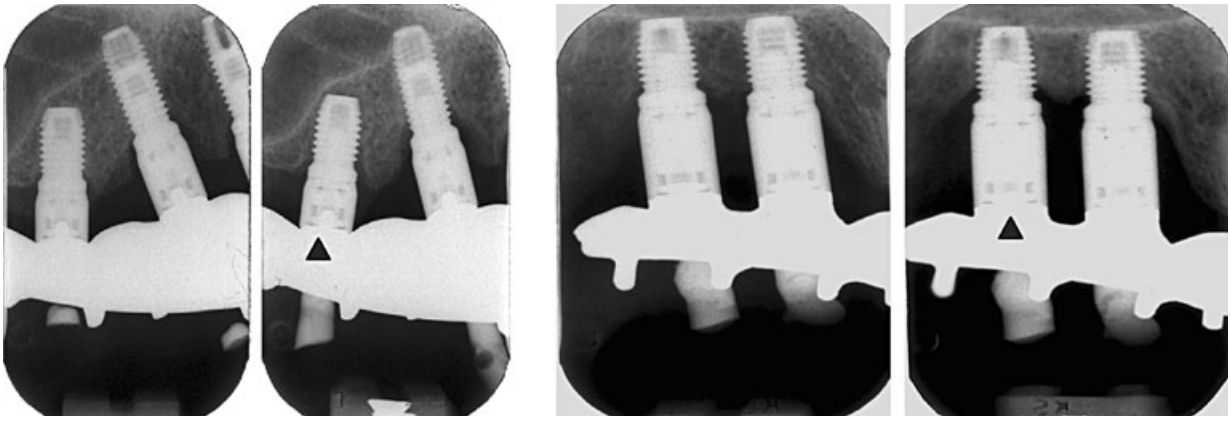

Fig. 28-39 Notice the very subtle sign, a thin radiolucent zone around the implants, indicating that the implants marked by arrows are not osseointegrated. Comparison of the radiographs with those taken earlier, the ones to the left in each image pair, makes the detection of subtle signs much easier.

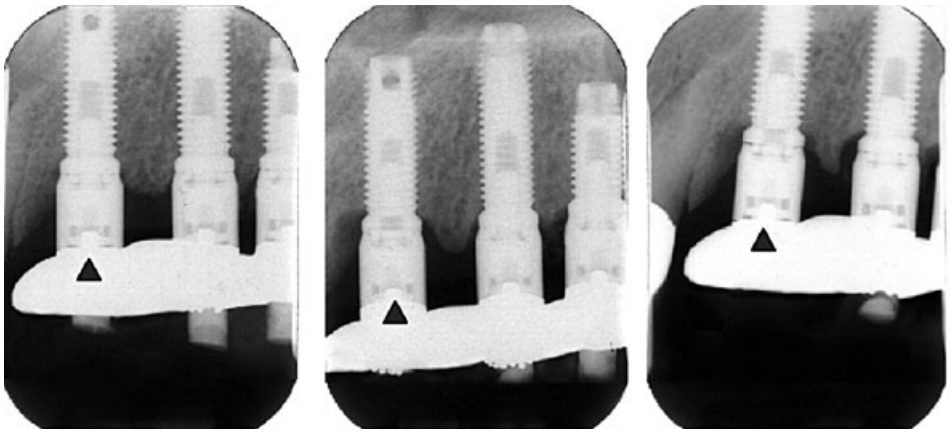

Fig. 28-40 In the implant marked by an arrow normal conditions were found at bridge installation (left image). One year later, a fracture of the centre screw went unnoticed (middle image) resulting in a gap between abutment and implant pillar seen in an image taken another year later. Notice that the irradiation geometry was not optimal at the second occasion.

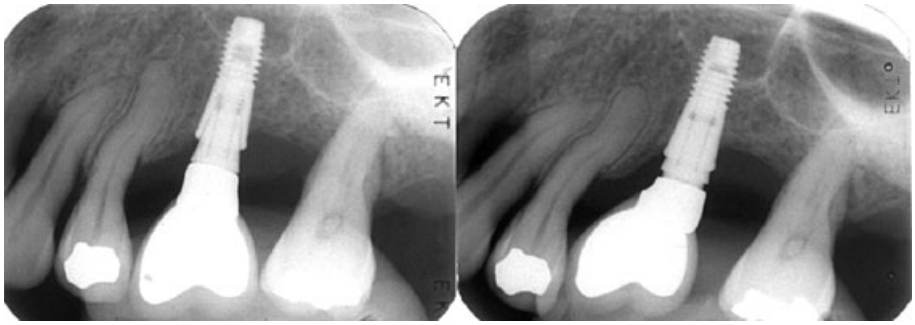

Fig. 28-41 In this case the conical abutment was not correctly placed (left image). After correction for this, the crown was remade but a later control then found a gap between crown and abutment. Notice the difference in marginal bone height on the distal side.

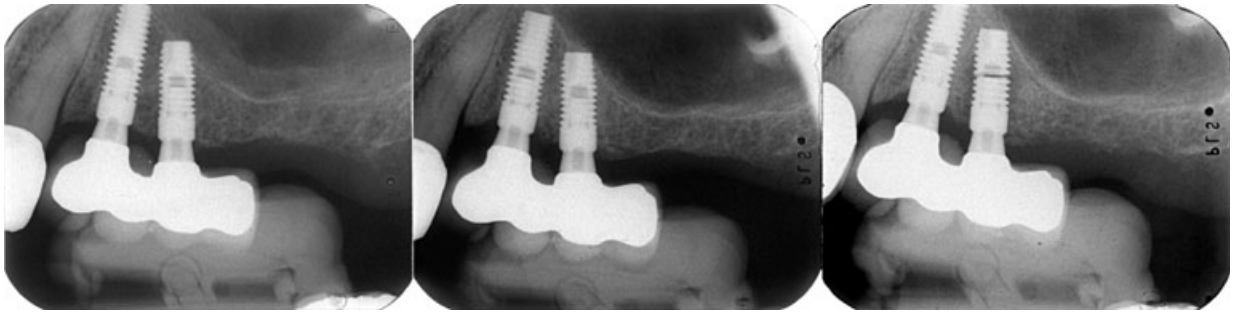

Fig. 28-42 Fracture of the implant pillar seen in radiographs taken 2 years after bridge installation. Neither the image from the latter occasion, nor the one taken at a 1-year control examination show any sign of fracture. Notice the inflammatory reaction along both sides of the implant.

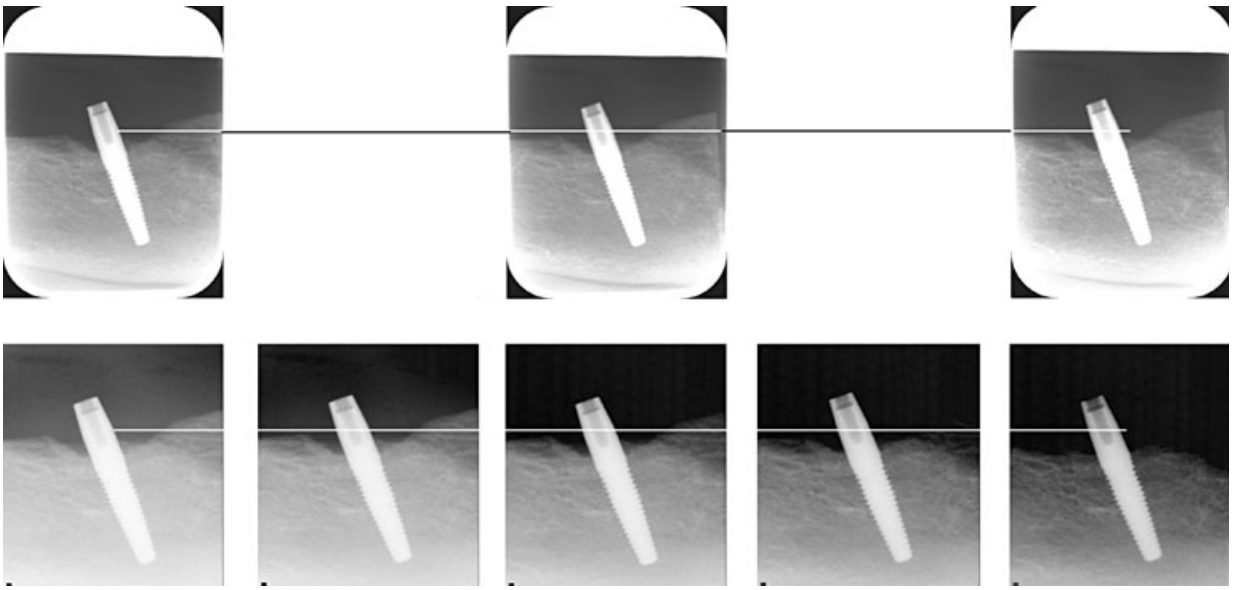

Fig. 28-43 Images taken with an image plate system, exposure times: 0.25 sec, 0.40 sec and 0.63 sec (upper row) and a CMOS system, exposure times: 0.25 sec, 0.32 sec, 0.40 sec, 0.50 sec and 0.63 sec (lower row). In the upper images the marginal bone is seen at the same level. In the lower ones it seems lower with increasing exposure. Compare with the horizontal reference line.

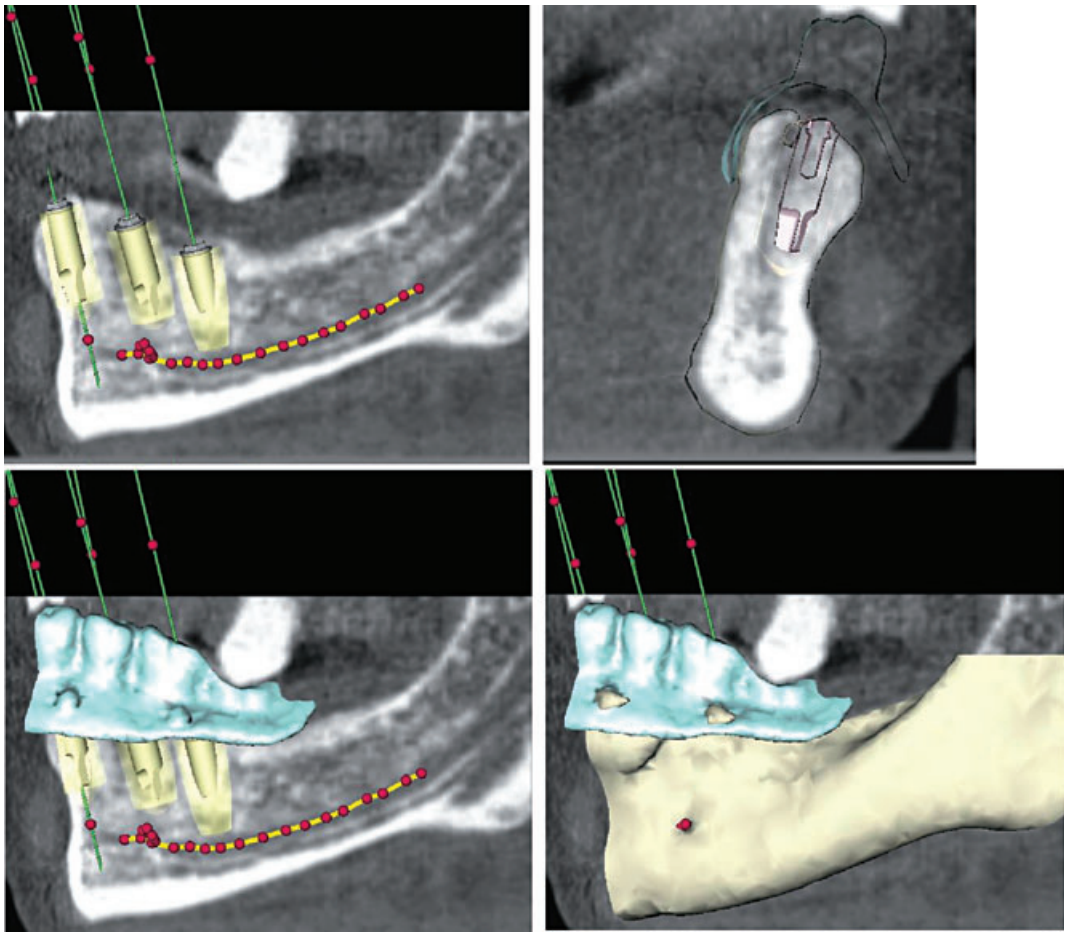

Fig. 28-44 Images describing the use of a system for surgical planning and image-guided surgery. Courtesy of Matts Andersson and Andreas Pettersson, Nobel Biocare, Göteborg, Sweden.

Image-guided surgery

Due to the three-dimensional information offered by computed tomography and digital volume tomography it is possible to use those techniques to play a more direct role in the surgical placement of the implants (BouSerhal 2001; Guerrero 2005). The exact placement and angulation of implants are determined by means of the radiographs. Guiding templates are then constructed and applied during surgery so that the implants will be positioned as intended, so-called image-guided surgery. It is also possible to build up images in which the result of the treatment, with specific implants and the final prosthesis "in place". Development in this area is rapid with implant companies, manufacturers of radiographic equipment, and software companies all working to develop and refine these techniques. For that reason we will do no more than mention the possibility and show just a few images that can shed some light on how these techniques can be used (Fig. 28-44). We strongly recommend that radiographic techniques that limit the radiation dose to the patient as much as possible are used. We also recommend that a careful scrutiny for diagnostic purposes is made of all radiographs before they are used for surgical implant planning and guiding.

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Chapter 29

Examination of Patients with Implant-Supported Restorations

Urs Brägger

Identification of the presence of implants and implant systems

Screening

With the growing use of dental implants, the number of patients with implant-supported restorations seeking dental care will soon affect most dentists on a regular basis (Österberg *et al*. 2000; Berge 2000; Zitzmann & Hagmann 2007). Cohorts with fixed or removable implant-supported restorations demonstrated considerable amounts of technical and biological failures and complications over 5- and 10-year observation periods (Berglund *et al*. 2002; Pjetursson *et al*. 2004; Brägger *et al*. 2005; Widbom *et al*. 2005; Fransson *et al*. 2005; Roos-Jansaker *et al*. 2006). In the coming decades, the profession will be challenged to prevent, diagnose, and treat technical and biological problems of implant-supported restorations. Screening of all new patients, identification of the implants, and assessment of the condition of the implants, the restoration, and the surrounding structures are therefore mandatory. Aspects related to general health, smoking, etc, which may affect the quality of implant integration and function, are discussed in Chapters 27 and 30.

Implant pass

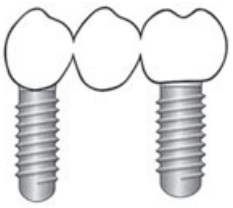
Information gathered by means of questionnaires can often be incorrect or incomplete. After a few years, patients may not be aware of how many implants were placed or even where exactly they are located. In addition, patients cannot be expected to remember and list brand names, names of biomaterials or complex interventions.

Several professional associations and manufacturers of implant systems have therefore developed an implant pass for patients (Fig. 29-1). All implant-related information can be filled out on the pass, avoiding the loss of important data. Furthermore, tracking of components back to their origin is possible applying the corresponding lot numbers in the patient chart as well as in an implant pass. Patients with implant-supported restorations would benefit from this document whenever a dental service needs to be provided, including emergency situations, maintenance, repairs or even a new restoration. Just a simple tightening of a screw-retained implant-supported prosthesis might be tedious if the dental team is unable to identify the components and if no corresponding screwdriver is available.

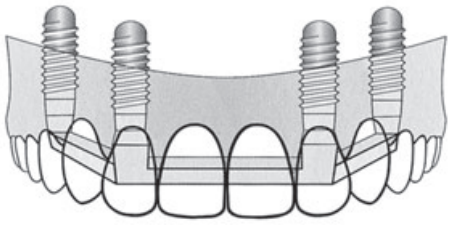
CERTIFICATE FOR DENTAL IMPLANTS

This certificate is issued to patients who have received dental implants.
This certificate gives information about the implant type, implant localisation and suprastructure components.
The patient is advised to show this document at any dental examination or treatment.
This certificate must be updated at any surgical or prosthodontic treatment.

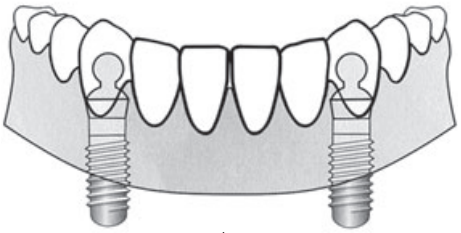
Single Crowns



Bridge



Bar Device



Overdenture

Name _____

First name _____

Date of birth _____

Street _____

Postal code/city _____

date	implant localisation	implant type, length, diameter	abutment type	supraconstruction			dentist/city	visum
				type*	screwed: occlusal access temporary or definitive	cemented: temporary or definitive		

*bridges: please indicate if segmented or not

Fig. 29-1 Proposal for an implant pass developed by the Swiss Society of Implantology. Copyright © Schweizerische Gesellschaft für orale Implantologie.

Questionnaire for new patients

The most straightforward way to obtain information on the presence of implants and implant-supported restorations in new patients is to ask questions related to any past implant experiences. The following comprehensive list of questions can be added to currently used questionnaires in educational programs, clinics, and private practices:

- Do you carry an implant pass?
- Did your dentist ever place implants into your jaw bones (name, address of the dentist, surgeon)?
- How many implants were placed?
- When were these implants placed (if remembered)? (How old were you when implants were placed?)
- Where are they located?
- Why were these implants placed or what were the reasons for the loss of teeth?
- Do you wear a prosthesis/crown supported by an implant (name of the dentist, prosthodontist, technician)?
- Did you have enough bone to have the implant placed?
- Were there additional treatments performed before implants could be placed?
- Did the surgeon perform a bone augmentation, sinus lift procedure?
- What was the brand name of the implants (if remembered)?
- Were bone graft particles used (if remembered)?
- What was the brand name of the biomaterials used (if remembered)?
- Have you ever experienced failures/complications with the implants?
- Have you ever experienced failures/complications with the prostheses/crowns?
- How often has this occurred?
- Are you satisfied with the way you can function with the implant-supported prosthesis/crown?
- Are you satisfied with the esthetic situation?
- Did you have to pay for the implants and prosthesis or was there insurance involved?
- How do you clean the neck portion of the implant/abutment?
- How do you clean the prosthesis/crowns?
- Do you use any special aids/disinfectants to carry out the cleaning?
- Does the mucosa/do the gums around your implant bleed?
- Do you notice a bad taste coming from underneath the prosthesis/crown?
- Is your implant mobile?
- Have you recently noticed a change with the implant-supported restorations?

Anamnestic information from patients on maintenance

Before starting to examine the oral conditions at maintenance visits, questions related to implant-supported restorations should include:

- Have you noticed a change with your implant-supported restorations?
- Are your implants stable?
- Do the gums around your implant(s) bleed?
- Are you able to clean the area around the neck portion of the implant(s) easily?
- Do you still have enough cleaning aids/disinfectants to perform daily plaque control?

In addition, general questions related to patient's satisfaction with the implant-supported reconstruction should be part of a quality management concept (Vermylen *et al*. 2003; Pjetursson *et al*. 2005).

The development of implant recognition software

Sahiwal *et al*. (2002a,b,c) collected implants from more than 50 manufacturers and divided them into threaded and non-threaded, as well as tapered and non-tapered categories. Radiographs were then taken at different angulations. Using tables and flow charts, test implants could be correctly identified in radiographs taken within ±10 degrees, according to their identifying features.

A very recent method to assist in identifying unknown implant systems applies an implant recognition software (IRS) (Michelinakis *et al*. 2006). The internet was searched for implant manufacturing companies worldwide in all languages. Relevant information on the implant designs was collected. A program was devised using key design factors for the identification of specific implants. The search revealed 87 implant manufacturers with 231 different designs. A valuable adjunct to the identification of implant systems was thus introduced for both general dental practice use and forensic identification.

Clinical inspection and examination

Characteristics of implant-supported restorations

Following the conventional extraoral and intraoral examination, the distribution of implants in the dental arch is marked in a dental record. A detailed description of the implant-borne restoration, the prosthetic components, and the components of the respective implant system may include material and design aspects.

- Restorations:
  - Crown
  - FDP, number of units
  - Extension prosthesis
  - Telescopic restoration
  - Removable partial denture
  - Bar device
  - Overdenture

- Defect prosthesis
- Other

- Material of:
  - Veneer
  - Framework
  - Denture teeth
- Fixation:
  - Cemented
  - Removable by the patient/dentist
  - Screw retained: transocclusal, transversal, access closed, access free, type of screw head, component of what system
  - Friction
  - Via attachments
  - Connection to teeth: one piece, detachable, attachments
  - Material.

Characteristics of prosthetic components and components of implant systems

- Prosthetic components:
  - Telescopic or conus crowns
  - Bar device
  - Riders
  - Matrices, patrices
  - Mesostructures
  - Individualized components
  - Material
- Components of implant systems:
  - Abutments for cementation
  - Abutments for transocclusal screw retention
  - Abutments for transversal screw retention
  - Angulated abutment
  - Anchors: ball anchor, magnets, locator system
  - Mesostructures
  - Material
  - CAD/CAM components
- Connection of abutments to the implants:
  - Localization of microgaps
  - How many gaps
  - Platform
  - Internal, external
  - Morse taper, butt joint
  - Geometry
  - Abutment screw: access free, closed, type of screwhead, components of what system.

Technical failures/complications

Until the first European Workshop on evidence-based reconstructive dentistry, held in Hünigen, Switzerland, 4–7 November 2006, there was no generally accepted definition for success and survival for reconstructions. Zöllner and Belser (2007) therefore suggested the following definitions:

- Success of abutment-reconstruction complex ("reconstruction"): survival without any biologic and/or technical complication
- Survival of abutment-reconstruction complex ("reconstruction"):
  - On abutment level: abutment is still *in situ*
  - On reconstruction level: reconstruction remaining *in situ* with or without modification
  - Alternatively: reconstruction remaining *in situ* in its original extension with or without modification.

In addition, factors regarded as biological or technical failures were listed but not further defined:

- Biological complications of abutment-reconstruction complex ("reconstruction"):
  - Natural abutment tooth: caries, loss of sensitivity, apical periodontitis, periodontitis
  - Implant: peri-implant diseases, implant mobility, loss of sensitivity of adjacent tooth
- Technical complications of abutment-reconstruction complex ("reconstruction"):
  - Tooth supported reconstruction: loss of retention, fracture of abutment, fracture of framework, fracture of veneering material
  - Implant supported reconstruction: loss of retention/screw loosening/abutment loosening, loss of access hole restoration, fracture of implant, fracture of abutment, screws, fracture of framework, fracture of veneering material.

While describing the above-mentioned detailed characteristics of the implant-supported restorations, any defects and irregular observations are marked.

The suprastructures are inspected for signs of loosening, loss of retention, loss of friction, wear, attrition, fractures of frame work, of denture teeth, of porcelain, of veneers, discolorations, bacterial deposits, precision or misfit at margins, cement rests (Figs. 29-2 and 29-3).

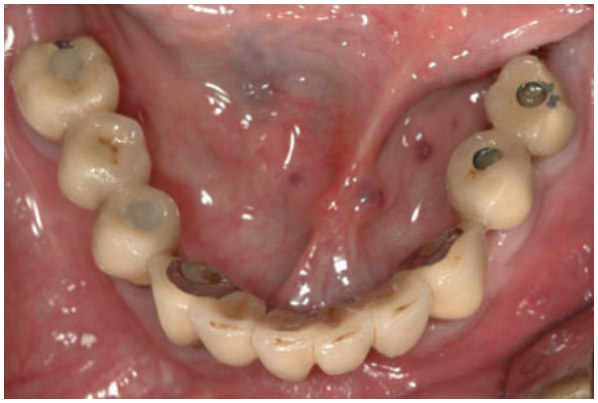


Fig. 29-2 Fractures of porcelain veneer at the distal aspects 35 and 46 as well as a porcelain chip off at 33. The patient was restored with three screw-retained porcelain fused to metal FDPs (I46 × I44/I43xxxxI33/I35I35). Three repairs within 3 years were needed. In the opposing jaw, the patient still had all his natural teeth. At night the patient wears an occlusal protective splint on an irregular basis.

The torque of occlusal screws can be checked where corresponding equipment is available. Obviously, loose screw-retained suprastructures are removed for further inspection, cleaning and retightening. Stable fixed restorations do not need to be disassembled if there were no complications reported by the patient and if the clinical examination did not reveal any technical problems.

Defective screw heads might complicate the removal of the suprastructure since screw drivers might not catch anymore. Occlusal screws that were tightened together with cementation might as well be very difficult to be removed with the regular instruments. In such cases, repair sets are needed to remove defective screws in a controllable standardized manner (Fig. 29-4). Repair sets might also be very helpful in cases with fractured abutment screws that are completely blocked in the implant (Luterbacher *et al*. 2000a) (Fig. 29-5). Abutments are also checked for their torque, the presence of bacterial deposits, corrosion products, cement rests, fractures, and deformations.

If replacement of a component is needed, the corresponding brand name and ordering number should be identified; a task that can be very tedious in the light of numerous implant producers and, in addition, a long list of copycat products (Jokstad *et al*. 2003).

Some manufacturers of implant components offer a complaint system to protect their customers from

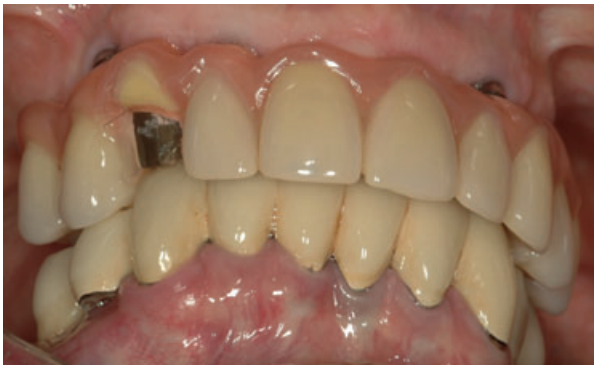


Fig. 29-3 Fracture of the denture tooth 13 as well as part of the veneer from a screw-retained extension prosthesis on five implants. In the lower jaw, the patient was restored with a fixed partial denture with bilateral distal extensions. The prosthesis could be removed and repaired.

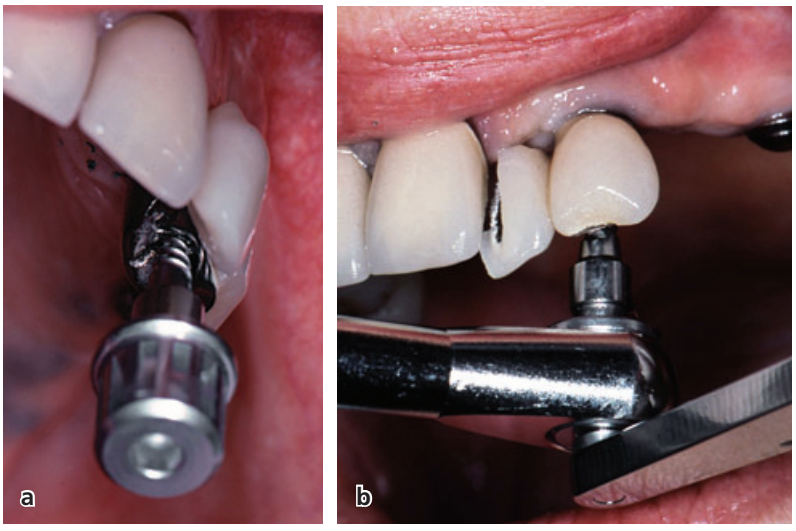


Fig. 29-4 (a) Removal of a screw-retained FDP using a screwdriver was impossible since the head of the occlusal screw was completely worn down due to attrition. The components of the repair set developed for the Straumann Dental Implant System® include an extraction bolt which can be tightened into a hole prepared with drills into the head of the occlusal screw. (b) Applying sufficient torque, the segmented part of the FDP is being removed together with the occlusal screw, the abutment, and the abutment screw. The implant was then used again for the support and fixation of a new extension prosthesis shown in Fig. 29-3.

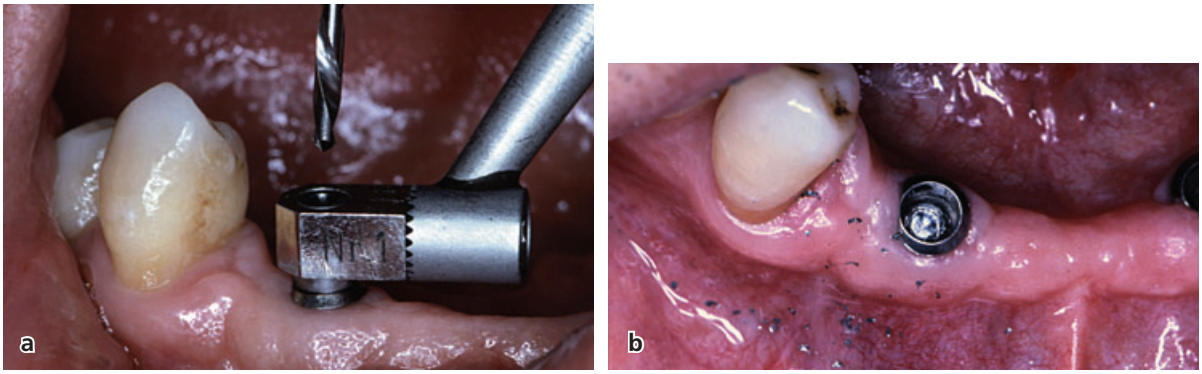


Fig. 29-5 (a) Application of the assembled components of the repair system developed for the Straumann Dental Implant System® for the removal of fractured abutment screws. The conical insert at the end of the handle secures the centered guidance of the drill. (b) After counter-clockwise drilling with ample cooling, the fractured portion of the abutment screw is removed. The threads are then recut by hand instruments with conical and cylindrical configurations.

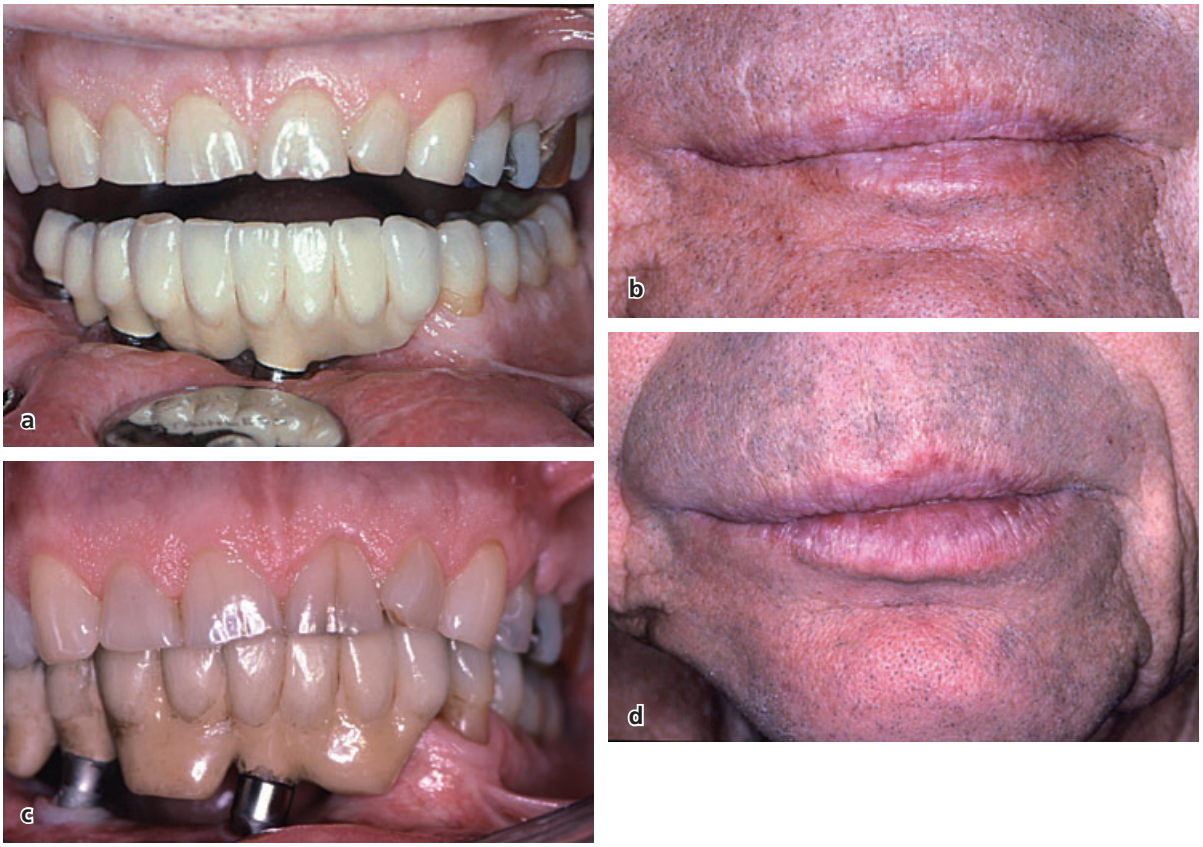


Fig. 29-6 (a,b) Screw-retained defect prosthesis on three implants in a fibula graft after excision of a malignant tumor. Function and phonetics are acceptable considering the severity of the defect. (c,d) After 5 years, some of the grafted bone has been resorbed. The soft tissues receded, leaving a large space underneath the pontics. Articulation and phonetics became more and more difficult. In addition, loss of saliva during speaking became intolerable. The FDP was removed and reshaped to fill out the missing soft tissues.

undue costs arising because of a potential error in production. Forms are completed with all the relevant information related to the loss of implants or a damaged component of the respective implant system. The defective components are sent in and exposed to a metallurgic evaluation and other tests. If the components were applied for the correct indications and a possible production error has been confirmed, the manufacturer will replace components and may even help to finance part of a new restoration as decided case by case.

If the abutment was individualized, it may also be impossible to just replace the component and use the existing suprastructure. In such cases, a new impression at the implant level will be needed to replace the abutment; a remake of the entire restoration may be necessary.

Function

Functional analysis

A functional analysis of the dentition with fixed and/or removable dental prostheses on implants needs to be carried out according to standard protocols in prosthodontics and includes parameters assessing articulation, occlusion, phonetics, denture stability, etc.

Articulation, phonetics

Disturbed articulation after placement of implant supported restorations may be very difficult to assess without the use of objective parameters (Fig 29-6). Heydecke *et al*. (2004) recorded test words articulated by 30 patients having adjusted to different implant-supported maxillary restorations for 2 months. Lay judges were asked to rate the quality of the articulation. This within-subjects crossover trial demonstrated that overdentures with or without palate enabled patients to produce better speech quality than with fixed prostheses on the implants.

Implant

Cases with removable implant-borne restorations allow direct access for clinical inspection and examination of the implant components and the peri-implant soft tissue conditions. Cemented or screw-retained crowns or fixed dental prostheses may complicate the access for visual inspection and probing.

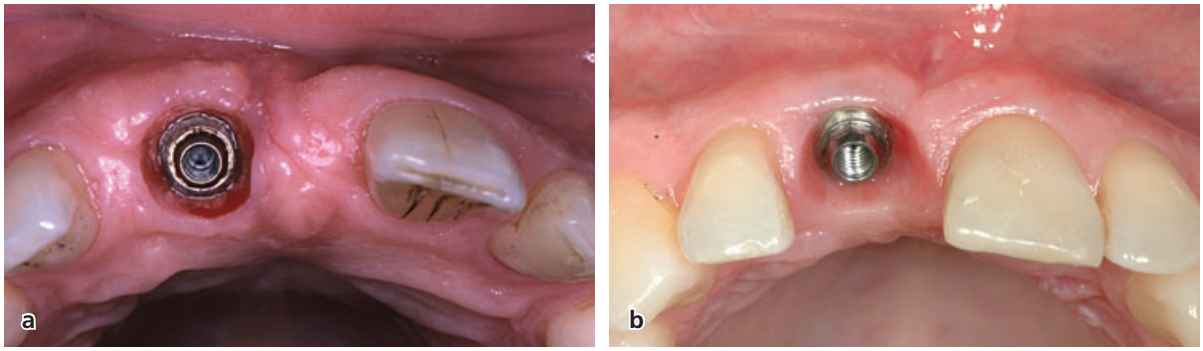


Fig. 29-7 (a) After removal of a screw-retained crown on an octa abutment, the amount of submucosal biofilm was impressive (3 years after placement of the crown). The epithetical lining of the emergence profile was ulcerated which led to bleeding after removal of the crown. (b) In a similar case, there were no obvious bacterial deposits detectable. The peri-implant soft tissues appeared epithelialized with few signs of inflammation.

Clinical test of mobility

Presence or absence of mobility is checked manually/digitally or with the help of instruments trying to move the implants. A perceived mobility of the restoration *per se* does not necessarily mean that the implant is loose. The connection suprastructure/abutment and/or abutment/implant might be loose leading to the mobility. Implant mobility can only be confirmed after disassembling all the components.

In the case of a multi-unit fixed restoration, the absence of mobility does not necessarily mean that the implants are all well integrated. Actual mobility might be obscured by the splinting effect.

Electronic tools to assess the quality of osseointegration

Resonance frequency analyses and Periotest® readings were part of numerous study protocols to quantitate the stability of implants. Changes in the readings were interpreted to reflect biological processes such as bone apposition, bone remodeling, bone maturation or, in a negative sense, deterioriation of the firmness of the bone to implant connection. Recent evidence from the literature was condensed to the following consensus statements (Hobkirk & Wiskott 2006): stability may be confirmed by performing repeated Periotest® measurements of the same implant over time. Increases of these measurements, however, became evident, when the implants are clinically obviously loose. Implants with high implant stability quotient (ISQ) values during maintenance appear to stay firmly integrated, while decreasing ISQ values may be indicative of developing instability. For both biomechanical testing methods, however, the lack of normative values and the wide range of reported values for stable implants and potentially failing implants would not justify their routine clinical use.

Bacterial deposits

The amount and distribution of visual bacterial deposits are evaluated at the emerging portion of the implant-borne restorations (implant neck, abutment, mesostructures, patrices) (Fig. 29-7). A *yes* or *no* for presence of bacterial deposits may be noted or marked in a scheme. In clinical studies, a gradual index such as the mPl (by Mombelli *et al*. 1987) has often been used.

Soft tissues

Mucosa

The inspection of the soft tissues will include the detection and description of visual signs of infection and/or other pathologic conditions, such as swelling, edema, redness, irregular keratinization, tattoos, pigmentation, hyperplasia, ulceration, soft tissue dehiscencies, or fistula. All soft tissues of the oral cavity, not only the peri-implant tissues, need to be examined (Fig. 29-8).

Palpation/sensitivity

Palpation at the buccal aspects of the implants may assist in the detection of loose implants (osseo-disintegration). Palpation furthermore reveals pus, swelling and pain, and the exudation of grafting particles. During palpation and sensitivity testing any morbidity due to, for example, grafting procedures (Clavero & Lundgren 2003) or side effects of implant placement, e.g. close to the mandibular nerve, may be detected.

Recession, pocket probing depth, probing attachment level, bleeding on probing

Measuring the localization of the margin of the mucosa in relation to a fixed reference point such as the connection suprastructure/abutment, abutment/

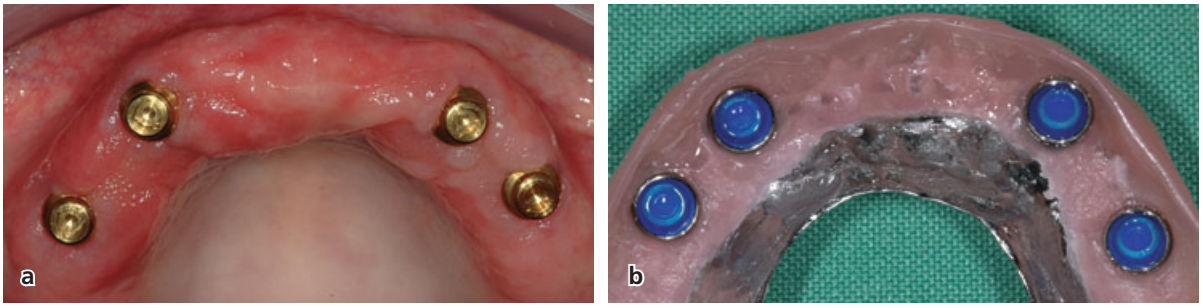


Fig. 29-8 (a) This 55-year-old female patient is wearing a palate free overdenture. Signs of denture stomatitis are an alarming signal to reinforce plaque control using chlorhexidine gel and rinses. (b) The base of the overdenture as well as the locator® matrices appear to be kept clean.

implant, suprastructure/implant, suprastructure/mesostructure as well as the pocket probing depth (PPD) reflects the anatomic situation after implant placement and reconstructive rehabilitation. Clinical parameters assessed by means of probing were first described around the neck of a one-piece transmucosal implant and included the distance between the implant shoulder and the mucosal margin (DIM), and the pocket probing depth (PPD). By adding PPD and DIM, the probing attachment level was calculated (PAL) (Buser *et al*. 1990).

Applying similar force, the insertion depth of a periodontal probe is usually deeper at implants compared to contralateral natural teeth. In addition, it seems to be easier to provoke bleeding after probing at implants compared to teeth (Brägger *et al*. 1997; Karoussis *et al*. 2004). Repeated probing using similar direction, localization, force, and the same references reveals stable conditions or increasing probing depths and/or increasing recession as signs of continuous loss of tissue or osseointegration.

With increasing PPD, the accuracy of repeated probing will decrease (Christensen *et al*. 1997). Precise readings of tissue destruction in deeper lesions are hindered by blocked access for probing and the lack of a continuous smooth surface to guide the probe tip apically. This occurs mostly at screw threads no longer covered by bone or horizontal steps between implants and abutments (Mombelli *et al*. 1997).

Similarly to periodontal disease, the absence of bleeding on probing (BoP) may reflect a stable condition, while repeated BoP may be indicative of a higher chance to develop tissue disintegration. Clinical and microbiological tests for monitoring tissue conditions during supportive periodontal therapy were performed in 19 patients, and the results indicated statistically significant better diagnostic characteristics of both tests at implants compared to teeth. The inclusion of an additional microbiologic test significantly enhanced the diagnostic characteristics of BoP alone at teeth as well as at implants (Luterbacher *et al*. 2000b).

Increased PPD combined with BoP and/or pus secretion may indicate various stages of mucositis or peri-implantitis.

According to one of the proposed concepts for the prevention and treatment of mucositis and peri-implantitis (cumulative interceptive supportive therapy), a cascade of anti-infective and corrective treatment modalities is applied depending on the severity of the findings (Lang *et al*. 2000). The treatment decisions are based on the clinical findings described above. In case of a suspected peri-implantitis, radiographic evaluation may be required to visualize bone levels or changes in bone levels in relation to reference points. If antibiotics are considered, information on the microbiologic composition of plaque samples as well as resistance testing will assist in decision making.

Esthetics

Papillae, interdental space and type of mucosa

A comprehensive assessment and documentation of the soft tissue condition may be of importance, especially for fixed restorations in esthetically critical areas (Fig. 29-9). The appearance of papillae and interdental spaces can be evaluated objectively using various indices, possibly including metric measurement (Jemt 1997). When linear measurements and stable reference points were used, valuable parameters for the long-term observation of changes in the papilla characteristics could be obtained (Jemt & Lekholm 2005). This also required that no changes to the crown contour were made (Klinge & Meyle 2006).

Some factors, such as the thickness of the peri-implant soft tissues, the amount of the available keratinized mucosa, the space between implants or between teeth and implants, and the underlying bone levels, may influence the esthetic appearance of the papilla/interdental space complex (Tarnow *et al*. 2000; Choquet *et al*. 2001; Gastaldo *et al*. 2004; Lee *et al*. 2005). In some cohorts reformation of papillae was also described (Jemt 1997; Chang *et al*. 1999). Metallic markers can be used to indicate the tip of the papilla in a radiograph in order to assess the distance between the underlying bone level and a papilla (Tarnow *et al*.

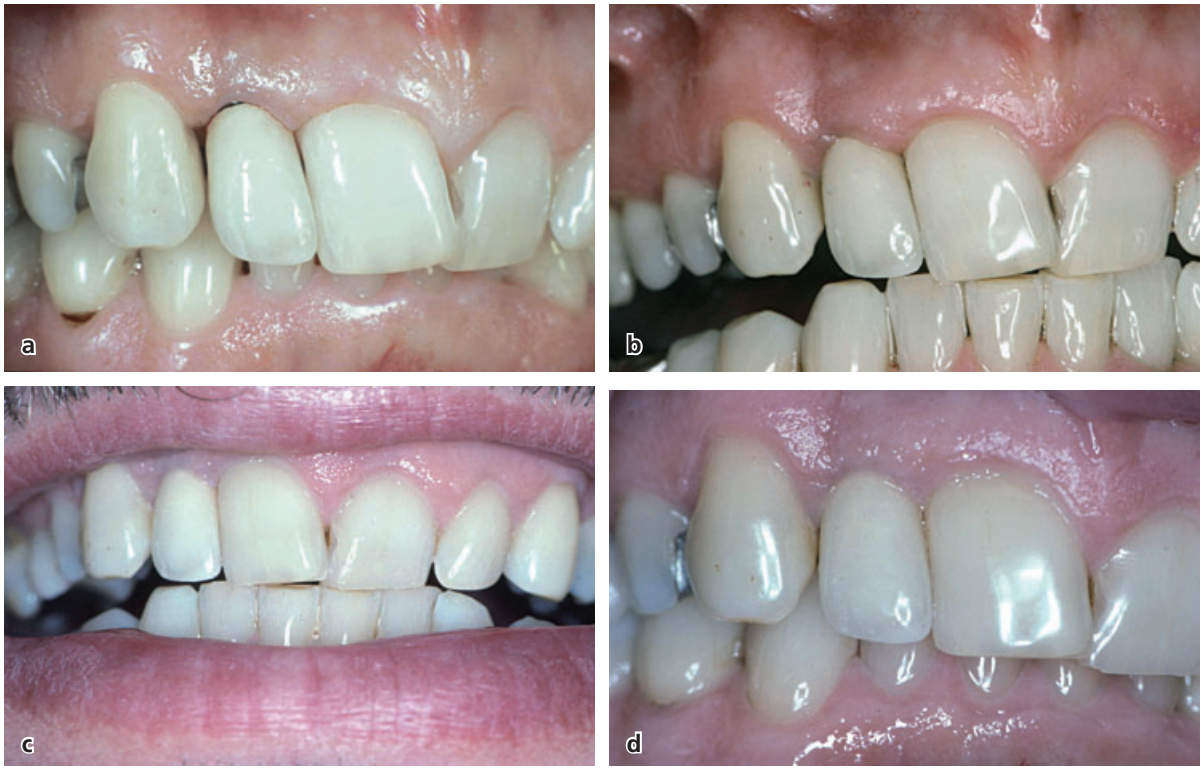


Fig. 29-9 A porcelain fused to metal crown was cemented on an implant of the Straumann Dental Implant System®. The clinical slides document the situation after cementation and after 1, 5, and 10 years. After 1 year, soft tissue seems to cover the implant shoulder and fill the interdental space: a result that was completely maintained over 5 and 10 years.

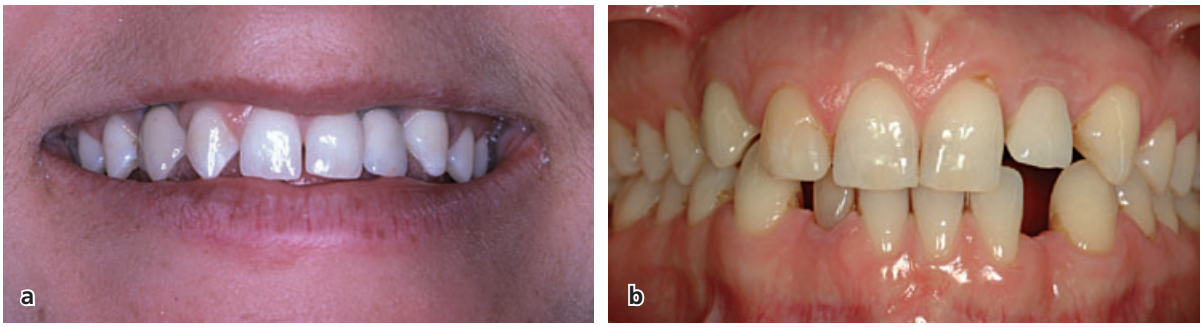


Fig. 29-10 Fifteen years ago, implants were sometimes not correctly placed to fulfill today's esthetic expectations. As a disappointing result, implant margins as well as the implant body were shining through the thin mucosa of this 20-year-old female patient. Due to the continuous eruption of the neighboring teeth, soft tissues now cover the dark implants. The crowns on I13 and I22, however, are no longer in occlusion.

1992). Assessment of the width of the keratinized mucosa can be facilitated by staining the lining non-keratinized mucosa with Schiller's (IKI) solution (Fasske & Morgenroth 1958; Brägger *et al*. 1997).

Condition of adjacent teeth

Implants placed too closely to adjacent teeth might lead to unfavorable periodontal conditions. In some studies, alveolar bone loss was observed if distances were chosen below a minimum distance (Krennmair *et al*. 2003). Adjacent teeth might have been damaged while preparing the implant bed. Delayed loss of sensitivity (vitality) may lead to endodontic interventions.

Long-term vertical changes of anterior maxillary teeth adjacent to implants in 14 young and 14 mature adults were measured in radiographs. In both groups, the tooth eruption process resulted in considerable changes ranging between 0.1 mm and 1.65 mm and 0.12 mm to 1.86 mm (Bernard *et al*. 2004) after an average observation period of about 4 years.

The lack of an implant eruption may result in the formation of steps related to adjacent teeth, incisal edges, etc. Occlusal contacts may still be present, however, due to the different eruption in the opposing jaw; step formation can also be observed (Zachrisson 2006) (Fig. 29-10).

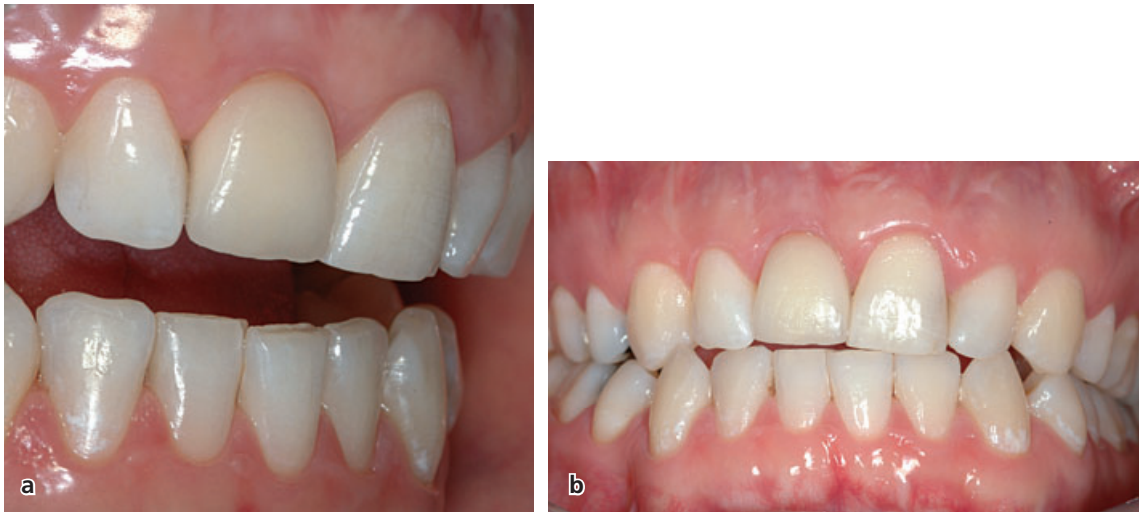


Fig. 29-11 In this 25-year-old female patient, a full ceramic crown and mesostructure were placed on an implant of the Straumann Dental Implant System®. After only 3 years, a step appeared in relation to the adjacent incisal edges. In addition, the color shade of the full ceramic crown appears to be too dark due to the fact that the patient had been bleaching her teeth.

Color shades

For a complete documentation of implant-supported restoration, a set of intraoral images of the area of interest may be desirable. In addition, an assessment of color shades based on visual or digital/electronic measurements are helpful. Of special concern are changes in color shade due to aging or bleaching of the adjacent natural teeth leading to noticeable unpleasant shade differences (Fig. 29-11).

Receding margins of the peri-implant mucosa result in visible implant components, potentially interfering with esthetics in visible zones. Even white ceramic components may result in an esthetically unfavorable situation if color matching over a wider range is not possible (Zachrisson 2006). Coverage of recessions or enlargement of the thickness of the mucosa can technically be achieved by means of free mucosa transplants. The predictability and the long-term success of such interventions remains to be assessed.

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Chapter 30

Risk Assessment of the Implant Patient

Gary C. Armitage and Tord Lundgren

In the past few decades the widespread availability and successful use of dental implants have greatly expanded the treatment options for replacement of missing teeth. Data from numerous follow-up studies of the retention rates of implants indicate that well over 90% of the fixtures are functional for 5–10 years after insertion (Lindh *et al*. 1998; Berglundh *et al*. 2002; Weng *et al*. 2003; Fugazzotto *et al*. 2004; Pjetursson *et al*. 2004; Romeo *et al*. 2004). It is clear, however, that some implants fail. In addition, the risk for implant failures and complications is not evenly distributed among all people in a given population since implant problems tend to cluster in certain subsets of patients (Weyant & Burt 1993). There are many possible reasons for failure but it is generally acknowledged that biological, mechanical, or behavioral causes can be important. In general, any factor that increases the risk of developing periodontitis also increases the risk of implant failure. Therefore, in clinical practice it is essential that practitioners understand the possible reasons for implant failures so these threats to implant survival can be minimized. Risk assessment for endosseous implants is an evolving field and it is essential that clinicians have a working knowledge of the current literature dealing with risk factors for the development of implant complications and failure. Without this knowledge an intelligent assessment of risk cannot be conducted.

Principles of risk assessment

Risk assessment is the deliberate and thoughtful evaluation of all circumstances that can affect the outcome of a therapeutic intervention. In the case of dental implants the assessment is intended to identify variables that increase the risk of complications leading to implant loss. In many cases, early identification of these variables makes it possible to avoid or eliminate them. At the very least, knowledge of the risk-altering variables allows the clinician to discuss with the patient circumstances that might affect implant survival. Risk assessment should be performed: (1) before placement of implants (designed to avoid high failure rates by identifying suitable candidates for implant treatment), (2) during the phase of implant placement and osseointegration (designed to identify and avoid technical issues that can affect implant survival), (3) during the phase of implant maintenance (designed to minimize failure by heading off problems), and (4) after an implant has failed and been removed. This "post-mortem" analysis tries to identify the causes of failure and incorporates the experience into future risk-assessment analyses of other patients.

In the literature the therapeutic outcomes of implant placement are usually described in terms of the fixture's survival, success, or its failure. A detailed

Table 30-1 Criteria for implant success, as suggested by Albrektsson *et al*. (1986)

1. That an individual, unattached implant is immobile when tested clinically
2. That a radiograph does not demonstrate any evidence of peri-implant radiolucency
3. That vertical bone loss be less than 0.2 mm annually following the implant's first year of service
4. That individual implant performance be characterized by an absence of persistent and/or irreversible signs and symptoms such as pain, infections, neuropathies, paresthesia, or violation of the mandibular canal
5. That, in the context of the above, a successful rate of 85% at the end of a 5-year observation period and 80% at the end of a 10-year period be a minimum criterion for success

discussion of these terms has been reviewed by others and will not be repeated here (Mombelli 1994; Esposito *et al*. 1998a). Criteria for these outcomes have not been consistently used in the literature. Success is often difficult to define since it implies that a large number of criteria have been met, such as stability, functionality, little or no change in bone support, radiographic evidence of osseointegration, absence of infection, lack of paresthesia, comfort, acceptable esthetics, and overall patient satisfaction. However, the criteria for "success" as presented by Albrektsson *et al*. (1986) over 20 years ago are still useful (Table 30-1).

Many authors simply use the outcome of implant "survival" which implies that at least some criteria for overall success have been met. An implant can, of course, survive and meet all of the criteria for success except those dealing with patient satisfaction. If the patient regards the implant as a failure, it is a failure since a major criterion for success has not been met (i.e. patient satisfaction). Since implant failure is often the end result of a gradual accumulation of unwanted events, most studies use surrogates for failure such as the development of implant mobility, abscess formation, and loss of function. Therefore in many papers, failure is defined as the appearance of failure-associated complications such as the development of peri-implantitis.

There are very few *absolute* or unequivocal contraindications to the placement of dental implants. Depending on a number of patient-centered circumstances, dental implants can be considered even in individuals who are at an elevated risk for implant failure. Like most situations in clinical practice, the potential benefits of an intervention need to be weighed against the morbidity of potential adverse outcomes.

A *risk factor* is an environmental, behavioral, or biological factor that, if present directly increases the probability of a disease (or adverse event) occurring and, if absent or removed, reduces that probability. Risk factors are part of the causal chain, or expose the host to the causal chain (Genco *et al*. 1996). In the case of risk assessment for implant failure, risk factors can be broadly categorized as local, systemic, or behavioral factors (Table 30-2). In general, risk factors for implant failure make outcomes of implant treatment less predictable. A *risk indicator* is a probable risk

Table 30-2 Potential risk factors for peri-implantitis and implant failure that should be considered in the risk-assessment process

Local risk factors

Presence of ongoing (or incompletely treated) oral infections
- Periodontal infections
- Oral hygiene
- Probing depths around remaining teeth (deep pockets are habitats or reservoirs of microorganisms that can lead to implant failure)
- Endodontic infections

Parafunctional habits (e.g. bruxism, clenching, grinding)

Dentoalveolar conditions
- Ridge anatomy (e.g. width, height)
- Bone quality
- Existing prosthetic restorations in region

Maxillary sinus location

Systemic risk factors

Age

Smoking

Medication history
- Bisphosphonate therapy
- Phenytoin, calcium-channel antagonists
- Cancer chemotherapy
- Anticoagulants
- Immunosuppressive agents (e.g. corticosteroids)

Immunosuppression
- HIV infection/AIDS

History of radiation therapy to the jaws

Diabetes mellitus

Bone disorders
- Osteoporosis

Connective tissue and autoimmune disorders
- Scleroderma
- Lupus erythematosus

Xerostomia
- Sjögren syndrome

Hematological and lymphoreticular disorders
- Neutrophil defects or insufficiency
- Aplastic anemia

Genetic traits and disorders
- Polymorphisms (e.g. proinflammatory genotype)
- Down syndrome
- Papillon-Lefèvre syndrome
- Crohn's disease
- Ectodermal dysplasia
- Vitamin D-resistant rickets

Behavioral risk factors

History of poor compliance

Substance use/abuse

Psychiatric/psychological issues

Lack of understanding or communication

factor that has not been confirmed by carefully conducted longitudinal studies. A *risk predictor* is a characteristic that is associated with an elevated risk for a disease (or adverse event), but may not be part of the causal chain (Genco *et al*. 1996). In the case of dental implants, a good risk predictor might be a documented history of the failure of previously inserted implants. In the risk assessment process for multifactorial conditions, such as implant failure, it is important to remember that the presence of several risk factors is required to result in implant loss. One or two risk factors are rarely sufficient to cause implant failure.

Clinical information required for risk assessment

The process of risk assessment begins with taking thorough medical/dental histories and conducting a complete examination of the prospective candidate for dental implants. Details of these procedures are discussed in Chapters 27–29 and will not be repeated here. However, items that are required for risk assessment include anything that helps identify individuals who might be at an increased risk of implant complications and failure.

A comprehensive evaluation of the patient should contain a review of past dental history including earlier periodontal treatment, reasons for tooth loss, how extraction sockets were treated at the time of extraction, history of increased susceptibility to infection, and awareness of parafunctional habits such as clenching and grinding. It should also include an evaluation of the patient's socioeconomic status and willingness to adjust to an often long treatment process. Dissatisfaction with earlier dental treatment may indicate an increased risk for complications during implant therapy.

The comprehensive medical history should include past and present medications and any substance use or abuse. A standard medical history form filled out and signed by the patient is an efficient way to collect basic information. This should always be followed by a verbal interview to explore in more depth any potential medical risks of implant therapy. If any uncertainties remain regarding the patient's health after the interview, a written medical consultation should be obtained from the patient's physician.

Components of a complete examination

A complete intraoral examination should be performed to determine the feasibility of placing implants in desired locations. This examination includes oral hygiene status, periodontal status, jaw relationships, occlusion, signs of bruxism, temporomandibular joint conditions, endodontic lesions, status of existing restorations, presence of non-restored caries, crown–root ratio, interocclusal space, available space for implants, ridge morphology, soft and hard tissue conditions, phonetics, and prosthetic restorability.

An appropriate radiographic evaluation of the quality and quantity of available bone is required in order to determine the optimal site(s) for implant placement. Assessments from periapical radiographs, panoramic projections, and tomographic cross-sectional imaging can individually or in combination be helpful diagnostic tools. It is important to understand that accurate estimations of bone height and width cannot be made without a comprehensive clinical examination followed by cross-sectional tomographic images. A comprehensive radiographic evaluation minimizes the risk of injuring vital anatomic structures during the surgical procedure and is also helpful in determining which cases require bone augmentation surgery before implants can be placed. A custom-made stent with radiopaque markers worn by the patient during the radiographic imaging can help locate the proper position for implant placement and also help in evaluation of the relationship between the planned implant location and available bone.

An evaluation of the quality and quantity of peri-implant soft tissues at the proposed implant site will help determine how closely this tissue will mimic the appearance of gingival tissue once the implant has been inserted. The presence of keratinized mucosa around a dental implant is an important part of an esthetically successful dental implant. It is important to evaluate the patient's perception of esthetics prior to implant placement. This is especially true in situations with compromised hard and soft tissues where esthetics can be a real challenge. Diagnostic casts and intraoral photographs can be helpful in evaluating potential esthetic outcomes as well as in the overall treatment-planning process. In general, to minimize the risk of implant complications and failure, any diseases of the soft or hard oral tissues should be treated before implant therapy.

Technical procedures to help minimize risk

Minimizing post-surgical infection

Post-operative infections increase the risk of early implant failure. It is important to perform implant surgeries with a strict hygiene protocol to minimize bacterial contamination of the surgical site. Although the incidence of post-operative infection associated with implant placement is only about 1% (Powell *et al*. 2005), some clinicians attempt to reduce this risk by prescribing pre-operative systemic antibiotics (Dent *et al*. 1997; Laskin *et al*. 2000). However, the value of pre-operative antimicrobial treatment has not been established in randomized placebo-controlled clinical trials (Lawler *et al*. 2005). In addition, the results of several case–control studies indicate that there is no advantage in using antibiotics in conjunction with implant placement (Gynther *et al*. 1998; Morris *et al*. 2004; Powell *et al*. 2005).

Minimizing tissue damage

Surgical techniques that are designed to avoid unnecessary tissue damage should be used whenever possible. Thermal damage to bone can be caused during the drilling sequence if dull drills are used or if osteotomy is performed without using enough liquid coolant. It is important to follow the manufacturer's guidelines and change the drills in the surgical kit accordingly.

Achieving early stability of implant

An important goal of the osteotomy is to prepare a site for the implant that will allow good stability of the implant during the healing process (Sennerby *et al*. 1992). Post-insertion stability lowers the risk of implant complications or failure. The presence of good-quality bone with a sufficient amount of cortical bone at the implant site is desirable to achieve this objective. In situations where there are less than optimal bone conditions (i.e. thin cortex, low trabecular density), increased initial stability can still be established by using implants with rough surfaces, parallel walls, and optimal height and width. In a study of implants placed in rabbit tibias it was found that good initial stability could be achieved by bicortical placement of an implant that engages two cortical layers of bone (Ivanoff *et al*. 1996). However, the same authors found that in a 15-year retrospective study in humans, bicortically anchored implants failed nearly four times more often than the monocortical ones (Ivanoff *et al*. 2000). They speculated that the overambitious fixation of the bicortical anchorage increased the likelihood of implant fractures that accounted for 80% of the failures in the study.

Avoiding anatomic structures

Anatomic structures that are at risk of serious collateral or accidental damage during the placement of implants include: nerves, blood vessels, floor of the mouth, nasal cavity, maxillary sinuses, and adjacent teeth. The risks to these structures can be minimized by careful assessment of radiographs and meticulous treatment planning. It is important to remember that the drills used for osteotomies penetrate further than the depth indicators on the drills. In certain situations radiographic indicator methods should be performed during surgery to help determine direction of the implant and its proximity to vital structures.

For implants that are to be placed in the mandible, the distance from the edentulous alveolar crest to the upper border of the inferior alveolar canal should be assessed from cross-sectional tomographic radiographs. The safety zone between the tip of the implant and the border of the canal should be at least 1–2 mm. Patients with compromised vertical bone dimension can sometimes be treated by placing multiple shorter implants of optimal width followed by splinting the prosthetic crowns together during the restorative phase of therapy.

The position of the mental foramen should be identified and located when implant surgeries in the premolar and molar areas of the mandible are performed. In some situations a loop of the nerve can be found to extend mesially. In one report the anterior loop of the mental neurovascular bundle extended mesially from 1.1–3.3 mm and a safety zone of 4 mm was recommended to avoid damaging the nerve during implant placement (Kuzmanovic *et al*. 2003). When placing an implant in the anterior part of the maxilla the size and location of the incisive papilla need to be determined. In addition, it must be established if there is enough bone in the area to place an implant or if the area needs to be grafted.

Anatomic concavities are frequently found on the lingual side of the mandible. It is important to avoid perforating the lingual plate during preparation of the implant site since perforations in this location can result in extensive and even life-threatening bleeding (Bruggenkate *et al*. 1993). A safe way of performing surgery in this area is to reflect a lingual flap at least to a level corresponding to the length of the implant to be placed. If this precaution is taken, any perforation that might occur is detected before any extensive damage and serious bleeding occur.

Some of the challenges of treating the partially edentulous patient are related to biological and functional differences between teeth and implants. If these differences are ignored there is an increased risk for complications. For example, in cases where there are compromised hard and soft tissues a few implants may not be able to withstand heavy occlusal forces associated with extensive posterior reconstructions (Albrektsson *et al*. 1988). Differences in morphology between implants and teeth can present another challenge. In the anterior part of the mouth an implant should blend in with the neighboring natural teeth. To accomplish this, an implant with the correct diameter must be selected and then placed in the optimal position in order to mimic a tooth esthetically and functionally.

After tooth extractions in the maxillary anterior region the alveolar ridge resorbs in a palatal direction. This will affect the position in which the anterior implants need to be placed since the relation of the implants to the lip and opposing dentition is critically important for a successful outcome (Jansen & Weisgold 1995). Where to place anterior implants in patients with a high smile line and thin periodontal tissues should be carefully evaluated to achieve acceptable esthetic and functional results.

Local risk factors and conditions

Presence of ongoing oral infections

There are abundant data showing that poor oral hygiene and microbial biofilms are important

etiologic factors leading to the development of peri-implant infections and implant loss (Mombelli *et al*. 1987; Jepsen *et al*. 1996; Salcetti *et al*. 1997; Esposito *et al*. 1998a,b; Lindquist *et al*. 1988; Listgarten & Lai 1999; van Winkelhoff *et al*. 2000; Heydenrijk *et al*. 2002; Quirynen & Teughels 2003; Fugazzotto *et al*. 2004). Therefore any risk assessment for implant survival should include an evaluation of the patient's ability to perform oral hygiene procedures (Salvi & Lang 2004).

Periodontitis

There are several reasons to believe that untreated or incompletely treated periodontitis increases the risk for implant failure. First, there are case reports that suggest an association (Malmstrom *et al*. 1990; Fardal *et al*. 1999). Second, a similar subgingival microbiota has been found in pockets around teeth and implants with similar probing depths (Papaioannou *et al*. 1996; Sbordone *et al*. 1999; Hultin *et al*. 2000; Agerbaek *et al*. 2006). Third, evidence exists that periodontal pockets might serve as reservoirs of pathogens (Apse *et al*. 1989; Quirynen & Listgarten 1990; Papaioannou *et al*. 1996) that hypothetically can be transmitted from teeth to implants (Quirynen *et al*. 1996; Sumida *et al*. 2002).

Studies dealing with the microbiota of failing or failed implants clearly indicate the presence of multiple periodontal pathogens (Table 30-3). However, one of the striking features of the microbiota associated with implant failures is its extensive diversity. It would be naïve to assume that infections around implants are due to a narrow range of microorganisms. A more realistic view is that peri-implant infections are caused by a consortium of multiple

Table 30-3 Components of the subgingival microbiota frequently (≥10%) detected around failed or failing implants

Elevated microbial component	Reference	Elevated microbial component	Reference
Spirochetes	Hultin *et al*. 2000	*Aggregatibacter actinomycetemcomitans*†	Alcoforado *et al*. 1991
	Listgarten & Lai 1999		Hultin *et al*. 2000
	Mombelli *et al*. 1987		Leonhardt *et al*. 1999
	Quirynen & Listgarten 1990		Rutar *et al*. 2001
	Rosenberg *et al*. 1991		Van Winkelhoff & Wolf 2000
Fusobacterium spp.	Alcoforado *et al*. 1991		
	Laine *et al*. 2005	*Tannerella forsythia*§	Hultin *et al*. 2000
	Listgarten & Lai 1999		Listgarten & Lai 1999
	Malmstrom *et al*. 1990	*Campylobacter rectus*	Alcoforado *et al*. 1991
	Mombelli *et al*. 1987		Listgarten & Lai 1999
	Rams *et al*. 1991		Malmstrom *et al*. 1990
	Rosenberg *et al*. 1991	*Eikenella corrodens*	Listgarten & Lai 1999
	Salcetti *et al*. 1997		Malmstrom *et al*. 1990
*Micromonas micros**	Alcoforado *et al*. 1991	*Actinomyces* spp.	Laine *et al*. 2005
	Laine *et al*. 2005	*Streptococcus anginosus* (milleri) group	Laine *et al*. 2005
	Listgarten & Lai 1999	*Streptococcus sanguinis*	Fardal *et al*. 1999
	Rosenberg *et al*. 1991	*Streptococcus oralis*	Fardal *et al*. 1999
	Salcetti *et al*. 1997	*Capnocytophaga* spp.	Fardal *et al*. 1999
Peptostreptococcus prevotii	Rams *et al*. 1991	Enteric rods	Alcoforado *et al*. 1991
Porphyromonas gingivalis	Hultin *et al*. 2000		Leonhardt *et al*. 1999
	Leonhardt *et al*. 1999		Listgarten & Lai 1999
	Listgarten & Lai 1999		Rams *et al*. 1991
	Rutar *et al*. 2001		Rosenberg *et al*. 1991
	Van Winkelhoff *et al*. 2000	*Escherichia coli*	Leonhardt *et al*. 1999
Prevotella intermedia	Alcoforado *et al*. 1991	Enterococci	Rams *et al*. 1991
	Hultin *et al*. 2000	Yeasts (*Candida* spp.)	Alcoforado *et al*. 1991
	Laine *et al*. 2005		Laine *et al*. 2005
	Leonhardt *et al*. 1999		Leonhardt *et al*. 1999
	Listgarten & Lai 1999		Rosenberg *et al*. 1991
	Mombelli *et al*. 1987	*Klebsiella* spp.	Leonhardt *et al*. 1999
Prevotella nigrescens	Laine *et al*. 2005	Pseudomonads	Alcoforado *et al*. 1991
	Leonhardt *et al*. 1999		Rams *et al*. 1991
	Listgarten & Lai 1999	*Staphylococcus* spp.	Alcoforado *et al*. 1991
	Salcetti *et al*. 1997		Leonhardt *et al*. 1999
			Rams *et al*. 1990, 1991
			Rosenberg *et al*. 1991

* Formerly *Peptostreptococcus micros*.
† Formerly *Actinobacillus actinomycetemcomitans*.
§ Formerly *Bacteroides forsythus and Tannerella forsythensis*.

microorganisms living on the implant surface in a biofilm. Contrary to the view of some (Heydenrijk *et al*. 2002), peri-implant infections are not simply caused by Gram-negative anaerobic bacteria. Certainly this group of bacteria is important, but yeasts and Gram-positive bacteria such as *Micromonas micros* and *Staphylococcus* species are often implicated in peri-implant infections (Table 30-3). Furthermore, in the implant literature the methods used to examine subgingival biofilms have primarily relied on microscopic (morphologic), cultural, and DNA probe analyses to characterize the microbiota. Culture-independent molecular analyses (e.g. studies of 16S ribosomal RNA gene sequences) have not been used to characterize the microbiota associated with implant failures. Application of such techniques to the subgingival microbiota associated with periodontitis has revealed the existence of a more diverse and complex microbial community than can be detected by conventional methods (Paster *et al*. 2001; Brinig *et al*. 2003; Lepp *et al*. 2004). In the case of periodontitis it is estimated that only about 50% of the subgingival flora can be characterized using conventional methods (Wilson *et al*. 1997) and therefore culture-independent analyses are required to get a more complete picture. This will probably also be true of the peri-implant subgingival microbiota once culture-independent molecular methods of analyses are applied to this ecosystem. Based on the documented diversity of the microbiota associated with failing implants, it is unlikely that testing for the presence of a small number of suspect bacteria for risk assessment purposes would have any clinical value.

Subgingival sites are micro-ecosystems that are preferentially colonized by oral bacteria well adapted to thriving in such environments. Indeed, subgingival sites are the natural or preferred habitat of a diverse group of oral microorganisms. In an interesting study of 15 patients, Devides and Franco (2006) sampled mucosa-associated biofilms of edentulous sites with paper points and analyzed the specimens using polymerase chain reaction (PCR) methods to detect certain periodontal pathogens. At the edentulous sites *Aggregatibacter actinomycetemcomitans* was detected in 13.3% of subjects, *Prevotella intermedia* was detected in 46.7% of subjects, and *Porphyromonas gingivalis* was not detected. Six months after placement of endosteal implants at the same sites, subgingival plaque samples taken from around the implants were positive for *A. actinomycetemcomitans* in 73.3% of subjects, *Pr. intermedia* in 53.3% of subjects, and *P. gingivalis* in 53.3% of subjects. None of the implants showed any clinical signs of either failure or peri-implantitis. These results indicate that healthy subgingival sites around implants are readily colonized by periodontal pathogens without any concomitant development of clinically detectable disease. The mere presence of PCR-detected pathogens is not a valid surrogate for peri-implant disease.

It is important to remember that the microbiota adjacent to failing implants will differ depending on the cause of the failure. For example, Rosenberg *et al*. (1991) demonstrated that the microbiota associated with implants failing because of traumatic loads was different to that found around implants failing because of infection.

There are several reports that the survival rate of implants is decreased when the patient has a history of periodontitis (Hardt *et al*. 2001; Evian *et al*. 2004; Karoussis *et al*. 2004; Wagenberg & Froum 2006). One implication of these observations is that patients who have had periodontitis might also be more susceptible to peri-implant infections. However, this is clearly not always the case since it has also been demonstrated that periodontally compromised patients who have lost a considerable amount of alveolar bone can be successfully treated with dental implants (Nevins & Langer 1995; Ellegaard *et al*. 1997; Sbordone *et al*. 1999). Since there is no clear-cut consensus in the literature on this topic, in risk-assessment discussions with patients it is a good idea to emphasize that based on their history of periodontitis they might be at an increased risk of developing peri-implantitis and therefore should be extra diligent in adhering to a rigorous post-insertion implant maintenance program.

Endodontic infections

The presence of untreated or insufficiently treated endodontic infections adjacent to the site of implant placement can adversely affect the outcome (Sussman & Moss 1993; Shaffer *et al*. 1998). There are numerous reports of retrograde peri-implantitis in which it is hypothesized that a periapical infection on a tooth spreads to an adjacent implant (Ayangco & Sheridan 2001; Chaffee *et al*. 2001; Jalbout & Tarnow 2001; Quirynen *et al*. 2005b). However, successful retention of implants has been reported when implants were inserted immediately after extraction of endodontically infected teeth (Villa & Rangert 2005).

Based on the strength of existing data discussed above, it is highly recommended that any existing periodontal or endodontic infections should be controlled before dental implants are placed. Although the presence of ongoing oral infections does not guarantee that implants will fail, such infections appear to increase the risk of failure. Finally, since it has been documented that some peri-implant infections may be associated with *Candida* spp. (Table 30-3) it is probably wise to control and treat any existing candidiasis before implants are inserted.

Systemic risk factors

Age

In adult patients, age is usually not considered an important risk factor for implant loss. Indeed, most

longitudinal studies of survival rates of implants include some subjects who are well over 75 years of age (Dao *et al*. 1993; Hutton *et al*. 1995; Nevins & Langer 1995; Davarpanah *et al*. 2002; Becktor *et al*. 2004; Fugazzotto *et al*. 2004; Karoussis *et al*. 2004; Fransson *et al*. 2005; Herrmann *et al*. 2005; Quirynen *et al*. 2005a; Mundt *et al*. 2006; Wagenberg & Froum 2006). An upper age limit is usually not listed as an exclusion criterion in such studies. It is clear that implants can be quite successful when placed in patients who are in their eighth and ninth decades of life. Several reports indicate that there is not a statistically significant relationship between age of the patient and implant failure (Dao *et al*. 1993; Hutton *et al*. 1995; Bryant & Zarb 1999; Fransson *et al*. 2005; Herrmann *et al*. 2005; Mundt *et al*. 2006; Wagenberg & Froum 2006). However, a thorough risk-assessment process involves evaluation of multiple possible risk factors. It is possible that there may have been some selection bias in the above studies since some older patients might have been excluded for medical reasons. Older individuals included in the above studies may be atypical in that they were healthy enough to be good candidates for implant placement.

In one retrospective study of the success of 4680 dental implants placed by a single surgeon over a 21-year period in 1140 patients, it was reported that increasing age was strongly associated with implant failure (Moy *et al*. 2005). A univariate analysis of the data indicated that compared to patients younger than 40 years (n = 181), patients in the 60–79-years age group (n = 499) had a significantly higher risk of implant failure (relative risk = 2.24; $P < 0.05$). However, in a multivariate analysis of the data from the entire study population, age was not a significant predictor of implant failure (Moy *et al*. 2005).

At the other end of the spectrum, a potential problem associated with the placement of dental implants in still-growing children and adolescents is the possibility of interfering with growth patterns of the jaws (Op Heij *et al*. 2003). Osseointegrated implants in growing jaws behave like ankylosed teeth in that they do not erupt and the surrounding alveolar housing remains underdeveloped. Dental implants can be a superb service to young people who have lost teeth due to trauma or have congenitally missing permanent teeth. However, because of the potential deleterious effects of implants on growing jaws it is highly recommended that implants not be placed until craniofacial growth has ceased or is almost complete (Thilander *et al*. 2001).

Smoking

Based on data generated by several follow-up studies of implant survival, cigarette smoking is often identified as a statistically significant risk factor for implant failure (Bain & Moy 1993; Lindquist *et al*. 1997; Wilson & Nunn 1999; Feloutzis *et al*. 2003; Gruica *et al*. 2004; Karoussis *et al*. 2004; Levin *et al*. 2004; Galindo-Moreno *et al*. 2005; Moy *et al*. 2005; Nitzan *et al*. 2005; Mundt *et al*. 2006). In addition, smoking has been associated with increased post-operative complications after sinus-lift operations and placement of onlay bone grafts (Levin *et al*. 2004).

Smoking is now generally accepted as an important modifiable risk factor for the development and progression of periodontitis (Johnson & Hill 2004). The reasons that smokers are more susceptible to both periodontitis and peri-implantitis are complex, but usually involve impairment of innate and adaptive immune responses (Kinane & Chestnutt 2000; Johnson & Hill 2004) and interference with wound healing (Johnson & Hill 2004; Labriola *et al*. 2005). Smoking is such a strong risk factor for implant failure that some clinicians highly recommend smoking-cessation protocols as part of the treatment plan for implant patients (Bain 1996; Johnson & Hill 2004).

Nevertheless, it should be emphasized that smoking is not an absolute contraindication for the placement of dental implants. Indeed, there are reports indicating that smoking did not adversely affect the rate of implant survival (Peleg *et al*. 2006; Wagenberg & Froum 2006). For multifactorial problems such as peri-implantitis and implant failure, the presence of one risk factor alone is usually insufficient to cause the adverse outcome.

Medication history

Bisphosphonates

Bisphosphonates are a widely prescribed class of drugs used for the treatment of osteoporosis and to reduce the bone-lytic effects of certain malignancies such as multiple myeloma and metastatic breast cancer (Woo *et al*. 2006). These pyrophosphate drugs are potent inhibitors of osteoclast activity that also have anti-angiogenic effects. The drugs have a high affinity for hydroxyapatite and are rapidly incorporated into all parts of the skeleton and have a very long half-life (i.e. decades). Relative potencies of the agents depend on their formulation (Table 30-4). An uncommon complication associated with the use of bisphosphonates is the increased risk of developing osteochemonecrosis or osteonecrosis of the jaws (ONJ) (Ruggiero *et al*. 2004; Marx *et al*. 2005; Braun & Iacono 2006). The vast majority of cases of ONJ occur in cancer patients who have received high-potency aminobisphosphonates (e.g. zoledronate, pamidronate) given intravenously to decrease the osteolytic effects of multiple myeloma or malignancies that have metastasized to bone (e.g. breast or prostate cancer).

Of major concern to the prospective implant patient who has been taking an oral bisphosphonate for osteoporosis is the possible risk of developing ONJ after implant placement. Oral bisphosphonates

Table 30-4 Relative potency for inhibition of osteoclast activity of various bisphosphonates, adapted from Braun & Iacono (2006)

Drug	Manufacturer	Potency factor
Etidronate (Didronel®)	Procter & Gamble	1
Tiludronate (Skelid®)	Sanofi	10
Clodronate (Bonefos®)	Schering	10
Clodronate (Loron®)	Roche	10
Neridronate (Nerixia®)	Abiogen	100
Pamidronate (Aredia®)	Novartis	100
Alendronate (Fosamax®)	Merck	500
Ibandronate (Bondronat®)	Roche	1 000
Risedronate (Actonel®)	Procter & Gamble	2 000
Zoledronate (Zometa®)	Novartis	10 000

have been reported to be associated with implant failure (Starck & Epker 1995) and ONJ (Ruggiero *et al*. 2004; Marx *et al*. 2005). Although rare, the risk is real. Since bisphosphonates tightly bind to hydroxyapatite and have a very long half-life, it is likely that the length of time a patient has been taking oral bisphosphonates is important in determining the level of risk. Since oral bisphosphonates slowly accumulate in bone with time, an osteoporosis patient who has been taking the drug for 1 year is at a lower risk of developing ONJ or implant failure than someone who has been on the drug for many years. In general, it is not recommended that implants be placed in patients who have been on the drug for more than 3 years. It has been suggested by some that prolonged use of bisphosphonates is a contraindication to implant placement (Scully *et al*. 2006).

It is important to remember that bone-remodeling processes are severely inhibited in patients who have been chronically taking oral bisphosphonates for osteoporosis. Because of this such patients are poor candidates for bone-grafting procedures and sinus-lift operations. Therefore, many ridge-augmentation procedures that often make implant placement possible are ill advised in these individuals.

Drug-influenced gingival enlargement

It is well known that one of the side effects of phenytoin, calcium-channel antagonists, and cyclosporin is gingival enlargement in about 25–50% of the individuals who take one or more of these drugs (Peñarrocha-Diago *et al*. 1990; Hassell & Hefti 1991). Gingival enlargement has also been reported around dental implants in individuals taking either phenytoin (Chee & Jansen 1994) or a calcium-channel antagonist (Silverstein *et al*. 1995). When there is significant gingival enlargement around teeth or implants, oral hygiene and maintenance procedures can become quite difficult. Therefore, medications associated with gingival enlargement should be considered in the overall risk assessment prior to implant placement.

Cancer chemotherapy

Oral cancer patients are frequently candidates for the placement of endosteal dental implants since prostheses designed to replace missing portions of the jaws need to be anchored to implants. Since antimitotic drugs used as chemotherapy for cancer might affect wound healing and suppress certain components of the immune system, it is important to know if these drugs interfere with osseointegration and success of dental implants. In a retrospective study, implant success was compared in 16 oral cancer patients who had no chemotherapy with the success in 20 patients who received postsurgical adjuvant chemotherapy with either cis- or carboplatin and 5-fluorouracil (Kovács 2001). It was found that these drugs did not have any detrimental effects on the survival and success of implants placed in the mandible.

It has also been reported that some cancer patients who received cytotoxic antineoplastic drugs experienced infections around existing transmucosal or endosteal dental implants (Karr *et al*. 1992). Therefore, it is important to recognize that many anticancer drugs suppress or kill cells necessary for optimal innate and adaptive immunity. Patients who are receiving cancer chemotherapy should have thorough periodontal and implant maintenance care to minimize the development of adverse events.

Anticoagulants

Patients who have blood-coagulation disorders or are taking high doses of anticoagulants are at an elevated risk of experiencing post-operative bleeding problems after implant surgery. Some patients with coagulation disorders may be at an elevated risk of implant failure (van Steenberghe *et al*. 2003) whereas other patients who chronically take oral anticoagulants can safely receive dental implants (Weischer *et al*. 2005). Patients who are on continuous oral anticoagulant therapy (e.g. coumarin derivatives) to reduce the risk of thromboembolic events and require dental implants for optimal restorative care should be evaluated on a case-by-case basis. Most of these patients can safely continue their warfarin or other anticoagulant therapy when they have their dental implant surgery (Wahl 1998, 2000). In such patients, local bleeding after the placement of dental implants can usually be well controlled by conventional hemostatic methods. The risk of developing life-threatening bleeding or bleeding that cannot be controlled using local measures following placement of dental implants is so low that there is no need to stop oral anticoagulant therapy (Beirne 2005).

Therapeutic levels of an anticoagulant drug such as warfarin are measured by the international normalized ratio (INR) which is the patient's prothrombin time (PT) divided by the mean normal PT for the laboratory (i.e. PTR). The PTR is then adjusted for the reagents used to arrive at a standardized INR value that will be comparable anywhere in the world. A higher INR reflects a higher level of anticoagulation with an attendant increased risk of hemorrhage (Herman *et al*. 1997). Although there are insufficient data to draw any evidence-based conclusions, placement of single implants is regarded as safe when the INR target values are 2.0–2.4 (Herman *et al*. 1997).

Immunosuppressive agents

Any medication that interferes with wound healing or suppresses components of innate and adaptive immunity can theoretically increase the risk of implant failure. Corticosteroids are a good example. They are potent anti-inflammatory agents that are widely used for the management of a wide variety of ailments. These drugs can interfere with wound healing by blocking key inflammatory events needed for satisfactory repair. In addition, through their immunosuppressive effects on lymphocytes, they can increase the rate of post-operative infections. In general, these undesirable effects are greatest in patients who take high doses of the drugs for long periods of time.

Immunosuppression

In the early years of the AIDS epidemic placement of dental implants was ill advised since affected patients developed major life-threatening oral infections. With the advent of effective HAART (highly active anti-retroviral therapy) regimens, most HIV-positive patients who take their medications live for many years without developing severe opportunistic infections. There have been no controlled studies dealing with the risk of dental implant failures in HIV-positive individuals. However, several case reports suggest that placement of dental implants in HIV-positive patients is not associated with elevated failure rates (Rajnay & Hochstetter 1998; Baron *et al*. 2004; Shetty & Achong 2005; Achong *et al*. 2006). Low T-helper (CD4) cell counts (i.e. <200/μL) do not appear to predict increased susceptibility to intraoral wound infections or elevated failure rates of dental implants (Achong *et al*. 2006). Although more studies are needed, it appears that it is safe to place dental implants if the patient's HIV disease is under medical control.

History of radiation therapy to the jaws

Patients who have received radiation (i.e. absorbed dose of ≥60 Gy) to the head and neck as part of the treatment for malignancies are at an increased risk of developing osteoradionecrosis (ORN). Most cases of this complication of cancer treatment are triggered by the extraction of teeth or other oral surgery procedures such as insertion of implants. Implant failure rates of up to 40% have been reported in patients who have had a history of radiation therapy (Granström *et al*. 1993, 1999; Beumer *et al*. 1995; Esposito *et al*. 1998a,b; Lindquist *et al*. 1988). At one time it was believed that ORN was due to vascular derangement and hypoxia of bone cells caused by the tissue-damaging effects of radiation (Teng & Futran 2005). Based on this hypothesis, it has been recommended that oral surgical procedures in patients at risk of ORN be performed in conjunction with hyperbaric oxygen (HBO) therapy. Indeed, Granström *et al*. (1999) reported that use of HBO therapy improved implant survival rates. However, the value of HBO therapy for the management of ORN has been called into question partly based on a placebo-controlled, randomized clinical trial (Annane *et al*. 2004) and other reports showing no advantage to HBO interventions (Maier *et al*. 2000; Gal *et al*. 2003). In addition, a systematic review by Coulthard *et al*. (2003) indicated that there is no high-quality evidence that HBO therapy improves implant survival in irradiated patients.

It is now believed that the pathogenesis of ONR is much more complex than a simple hypoxia-related phenomenon related to poor vascularity of irradiated tissues. Current evidence supports the view that ONR is a fibroatrophic process (Teng & Futran 2005). From the perspective of risk-assessment procedures for implant placement, patients who have a history of irradiation to the jaws should be considered at high risk for implant failure and HBO interventions will probably not lower that risk.

Diabetes mellitus

Although there is a slight tendency for more failures of implants in a diabetic compared to a non-diabetic population, the increased risk is not substantial in patients who are under good metabolic control (Shernoff *et al*. 1994; Kapur *et al*. 1998; Balshi & Wolfinger 1999; Fiorellini *et al*. 2000; Morris *et al*. 2000; Olson *et al*. 2000). In the general population the 5-year overall success rate for implants is approximately 95% (Buser *et al*. 1997; Weber *et al*. 2000; Davarpanah *et al*. 2002; Fugazzotto 2005), whereas in a diabetic population the rate is approximately 86% (Fiorellini *et al*. 2000).

Diabetics under suboptimal metabolic control often experience wound-healing difficulties and have an increased susceptibility to infections due to a variety of problems associated with immune dysfunctions (Geerlings & Hoepelman 1999). In the risk evaluation of diabetics it is important to establish the level of metabolic control of the disease. A useful test to determine the level of control over the last 90 days is a blood test for glycosylated hemoglobin (HbA_{1c}). This is a test for the percentage of hemoglobin to

which glucose is bound. Normal values for a non-diabetic or a diabetic under good metabolic control are HbA_{1c} <6–6.5% and fasting blood glucose <6.1 mmol/L (110 mg/dL). Diabetics with HbA_{1c} values of ≥8% are under poor control and have an elevated risk of encountering wound healing problems and infection if dental implants are placed.

Metabolic bone disease

Osteoporosis

Osteoporosis is a complex group of systemic skeletal conditions characterized by low bone mass and microarchitectural deterioration of bone tissue. Osteoporotic bone is fragile and has an increased susceptibility to fracture. Primary osteoporosis is a common condition and is diagnosed when other disorders known to cause osteoporosis are not present. Secondary osteoporosis is diagnosed when the condition is related to, or occurs as a consequence of, osteoporosis-inducing circumstances. These might include diet (e.g. starvation, calcium deficiency), congenital conditions (e.g. hypophosphatasia, osteogenesis imperfecta), drugs (e.g. alcohol abuse, glucocorticoids), endocrine disorders (e.g. Cushing's syndrome), and certain systemic diseases (e.g. diabetes mellitus, rheumatoid arthritis). Osteoporosis is assessed using bone densitometry in which a patient's bone mass or bone mineral density (BMD) is determined. BMD refers to grams of bone mineral per square centimeter of bone cross-section and is expressed in units of g/cm^2.

There are multiple case reports that conclude that osteoporosis alone is not a significant risk factor for implant failure (Dao *et al*. 1993; Friberg 1994; Fujimoto *et al*. 1996; Friberg *et al*. 2001). Implants placed in individuals with osteoporosis appear to successfully osseointegrate and can be retained for years. However, in cases of secondary osteoporosis there are often accompanying illnesses or conditions that increase the risk of implant failure (e.g. poorly controlled diabetes mellitus, corticosteroid medications). Therefore, in the risk-evaluation process the presence of osteoporosis should alert the clinician to the possible presence of osteoporosis-associated circumstances that are known to increase the risk of implant failure.

In the implant literature the concept of "poor bone quality" was introduced by Lekholm and Zarb (1985). This is something quite different to osteoporosis. Poor bone quality refers to the subjective appraisal of the presence and amount of compact and trabecular bone as visualized in radiographs. The radiographic appraisal of bone quality is reassessed during explorative drilling at the fixture-preparation site. The assessment system uses the following four groups:

- Type 1 = almost the entire jaw is comprised of homogenous compact bone
- Type 2 = a thick layer of compact bone surrounds a core of dense trabecular bone
- Type 3 = a thin layer of cortical bone surrounds a core of dense trabecular bone of favorable strength
- Type 4 = a thin layer of cortical bone surrounds a core of low density trabecular bone.

The system has serious reproducibility problems that limit its usefulness in the risk-assessment process. Nevertheless, there are reports indicating that jaw bone quality is significantly related to implant failure especially when there is type 4 bone (Jaffin & Berman 1991; Hutton *et al*. 1995; Herrmann *et al*. 2005).

Connective tissue and autoimmune disorders

Scleroderma

Systemic sclerososis or scleroderma is a chronic autoimmune disease that targets the skin, lungs, heart, gastrointestinal tract, kidneys, and musculoskeletal system. The disease is characterized by widespread tissue fibrosis, endothelial dysfunction of small blood vessels, and formation of auto-antibodies against a number of tissue components. The skin loses much of its flexibility and becomes leatherlike. Patients often experience stiffening of the finger joints making it almost impossible to grasp items such as a toothbrush and other oral hygiene devices. The lips become so stiff and taut that opening the mouth is restricted to only a few centimeters. As a result of these access problems, all types of dental care (i.e. self-administered and professionally delivered) become extraordinarily difficult. The overall effect is long-standing poor oral hygiene leading to the inevitable loss of multiple teeth due to caries and periodontal disease.

There are no well controlled studies on the success rates of dental implants in patients with scleroderma. However, there are some case reports showing that patients with this disease can have implants successfully placed and maintained for several years (Jensen & Sindet-Pedersen 1990; Patel *et al*. 1998; Hodgson *et al*. 2006). If the decision is made to place dental implants in patients with scleroderma, it is critical that a rigorous maintenance program be incorporated into the treatment plan.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects many organ systems, with the joints, kidneys, heart, and lungs being the most commonly affected. It is well established that SLE patients have increased susceptibility to many opportunistic infections (Zandman-Goddard & Shoenfeld 2003; Bosch *et al*. 2006). The reasons for this increased susceptibility are not well understood but SLE-

associated abnormalities of both humoral and cellular immunological responses and use of immunosuppressive therapy (e.g. corticosteroids) are undoubtedly important. If implants are absolutely required for a patient with SLE, it should be emphasized that bacteremias from oral surgery procedures increase the risk of developing infections of SLE-affected joints. In such cases it is recommended that antibiotic coverage be considered to minimize this potential problem (Fitzgerald *et al*. 2003). There are no well controlled studies, or even a well documented case series, of the success rates of implants placed in patients with SLE.

Xerostomia

Xerostomia or dry mouth can be caused by a wide range of factors, including certain medications, aging, and damage to salivary glands (Beikler & Flemmig 2003). Sjögren syndrome (SS) is a group of autoimmune diseases that may be limited to lacrimal and salivary glands leading to xerostomia and keratoconjunctivitis (primary SS). In secondary SS the xerostomia and keratoconjunctivitis occur along with a number of connective tissue disorders such as rheumatoid arthritis and scleroderma. One of the main oral problems associated with SS is severe xerostomia that often leads to severe dental caries, burning sensations of the oral mucosa, oral candidiasis, and difficulty in swallowing. In many cases all of the teeth are lost because of rampant root and coronal caries. Patients with severe xerostomia find wearing artificial dentures to be a difficult and very unpleasant experience because of the lack of lubrication ordinarily supplied by saliva. Based on a few case reports it appears that dental implants can be successfully used in patients with SS (Payne *et al*. 1997; Isidor *et al*. 1999; Binon 2005). However, since SS often accompanies other conditions that increase the risk of implant failure (e.g. scleroderma, lupus erythematosus), it is important that implant candidates with SS be carefully evaluated for numerous other risk factors that might be present.

Hematologic and lymphoreticular disorders

A number of hematologic and lymphoreticular disorders carry with them an increased susceptibility to periodontitis and other infections (Kinane 1999). Among these disorders are: agranulocytosis, acquired neutropenias, cyclic neutropenias, leukocyte adherence deficiency, and aplastic anemia (e.g. Fanconi's syndrome). Since patients with these diseases frequently lose teeth early in life they often have extensive prosthetic needs that can be met by the placement of dental implants. In the risk-assessment process prior to implant placement the major concern to be considered is the increased susceptibility to infections that could occur around any implants that might be placed. There are no well controlled studies of the success rates of implants placed in patients with these disorders. However, implants can be placed if the patient's disease is under control or in remission and a rigorous post-insertion implant maintenance program is an integral part of the overall treatment plan.

Genetic traits and disorders

Polymorphisms (IL-1 and MMP)

Polymorphisms are small variations in base-pair components of DNA that occur with a frequency of approximately 1–2% in the general population (Kornman & Newman 2000). These small variations in genes are biologically normal and do not cause disease. However, gene polymorphisms can affect in subtle ways how different people respond to environmental challenges. Within the context of risk assessment for implant failure, they affect how people respond to a microbial challenge and how efficiently their wounds heal.

Polymorphisms in the interleukin-1 (IL-1) gene cluster on chromosome 2q 13 have been associated with a hyper-responsive inflammatory reaction to a microbial challenge. A specific composite genotype of *IL-1A* and *IL-1B* polymorphisms, consisting of allele 2 of both IL-1A –889 (or the concordant +4845) and *IL-1B* +3954 has been associated with an increased risk of severe chronic periodontitis in non-smokers (Kornman *et al*. 1997). Several investigators have attempted to determine if this composite IL-1 genotype can serve as a risk factor for complications associated with implants such as bone loss or their eventual failure (Wilson & Nunn 1999; Rogers *et al*. 2002; Feloutzis *et al*. 2003; Gruica *et al*. 2004; Jansson *et al*. 2005). All of these reports found that being positive for the composite IL-1 genotype was not associated with an increased risk of bone loss or other implant-related problems. However, in some populations there appears to be a synergistic effect between a positive IL-1 genotype and smoking that puts dental implants at a higher risk of developing peri-implant bone loss (Feloutzis *et al*. 2003; Gruica *et al*. 2004).

Matrix metalloproteinases (MMPs) are a family of at least 15 zinc-dependent endopeptidases that function extracellularly. They are important in both normal and pathologic remodeling of tissues and differ in some of their substrate specificities. For example, MMP-1 is an interstitial collagenase capable of cleaving collagen types I, II, III, VII, and X. While another enzyme called MMP-9 or gelatinase B cleaves collagen types IV, V, VII, and XIV. In a pilot study of 46 patients it was found that a polymorphism in the promoter region of the *MMP-1* gene was associated with early implant failure, whereas a polymorphism

in the promoter region of the *MMP-9* gene had no relationship with implant loss (Santos *et al*. 2004). Further studies in this general area are warranted since a validated genetic risk factor for implant failure would have immense clinical utility.

Genetic disorders

A number of genetic disorders such as those associated with chromosomal defects (e.g. Down syndrome) or those transmitted as Mendelian traits (e.g. Papillon-Lefèvre syndrome) often lead to tooth loss due to increased susceptibility to infections. An important question in the restorative care of these individuals is, will the increased susceptibility to periodontal infections also increase the risk of implant failure? In the risk-evaluation process it is probably best to assume that the answer to this question is "yes". However, with good post-operative and effective long-term maintenance care, implants can be successfully placed and retained in high-risk patients. For example, Papillon-Lefèvre syndrome is due to loss-of-function mutations in the cathepsin C gene that impairs innate immune responses (Toomes *et al*. 1999). Even in patients with this genetic disorder dental implants can be successful (Ullbro *et al*. 2000).

Importance of behavioral considerations in risk assessment

In the examination and evaluation of a candidate for dental implants, one of the most difficult tasks is to analyze the behavioral aspects of risk assessment. This area has not been well studied and falls within the realm of the art, rather than the science, of clinical practice. Important behavioral issues that need to be assessed include compliance history, substance use/abuse habits, psychiatric/psychological issues, practitioner–patient communications, and expectations of the patient.

Dental history of compliance behaviors

Long-term success of dental implants requires that the patient is able and willing to comply with the recommended post-insertion maintenance procedures required for long-term survival and success of implants. Since poor oral hygiene is a documented risk factor associated with failure of implants, it is critically important that patients understand this and are taught the skills necessary to perform plaque removal on a daily basis (Mombelli *et al*. 1987; Lindquist *et al*. 1988; Jepsen *et al*. 1996; Salcetti *et al*. 1997; Esposito *et al*. 1998a,b; Listgarten & Lai 1999; van Winkelhoff *et al*. 2000; Heydenrijk *et al*. 2002; Fugazzotto *et al*. 2004; Quirynen & Teughels 2003). The teaching of oral hygiene is not a trivial task and often requires a considerable investment of time over multiple visits. In addition, since patient-performed oral hygiene does not adequately remove or disrupt dental plaque biofilms at subgingival locations, periodic maintenance visits are needed so the oral healthcare provider can deliver this care. It is recommended that these visits be at 3-month intervals until it can be established that a less intense schedule is sufficient. The patient's compliance with the recommended maintenance schedule is a major key to long-term success.

Substance use/abuse

Cigarette smoking as a risk factor for peri-implantitis and implant loss has been discussed earlier in this chapter. Smoking is a well documented risk factor that has both local and systemic effects on implant success. In addition, smoking is a powerful addiction with many complex behavioral components. In the consultation visit with the patient it is important that the clinician explain that smoking can contribute to complications after implant insertion. Referral to experts who conduct smoking-cessation programs is often helpful.

Patients who have addictions to alcohol and drugs are usually poor candidates for dental implants. Since the success of implant therapy requires a considerable amount of patient cooperation at all stages of care, individuals with substance-abuse problems should receive prosthetic care that does not depend on implants.

Psychiatric/psychological issues

In general, patients who have severe mental health problems or exhibit psychotic behavior are not good candidates for dental implants. As in the case of individuals with substance-abuse problems, the cooperation needed for successful implant therapy is missing. However, people with medically controlled mental health problems, such as depression, can be successfully treated with implants. In cases where there is uncertainty regarding how well the problem is under medical control, a consultation with the patient's physician is advisable.

Lack of understanding or communication

Most practitioners explain to their patients what the proposed dental care involves. However, in many cases patients do not understand what has been explained to them. It is important that the practitioner determine if the information they tried to convey was understood. One of the best ways to do this is to convey the information in easily understood (non-technical) language and in small increments. A common mistake is to rapidly present too much

information. It is highly recommended that the patient be encouraged to give some feedback showing that they actually understand what they have been told. Patients who understand what is being done are usually quite cooperative and this cooperation leads to the increased probability of successful therapeutic outcomes.

Patient's expectations

It is important to remember that the practitioner's and patient's perspectives may be somewhat different regarding the primary criteria used to measure implant success. From the patient's point of view the successful implant should be esthetically acceptable, comfortable, low-cost, and functional. Practitioners usually discuss implant success in terms of extent of osseointegration, level of alveolar bone, probing depths, and stability. Although the two sets of criteria are not in conflict, they emphasize different things. During the consultation visit, before any care is delivered, the practitioner should discuss, using patient-centered outcomes, what can be expected from placement of the implant.

A final comprehensive treatment plan should be presented to the patient that includes all recommended dental therapy and alternative treatment options. The patient should also be informed about the sequencing of the clinical procedures, risks and costs involved, and the anticipated total treatment time. This discussion between practitioner and patient is critically important in lowering the overall risk of treatment problems. Patients who understand what will be done, and why, are more likely to cooperate with the recommended treatment.

Interest and commitment to post-treatment care and maintenance program

As discussed above, daily self-care (oral hygiene) and adherence to a maintenance-recall schedule is absolutely required for long-term success. This is best discussed and conveyed to the patient at the consultation visit. Long-term success of both periodontal and implant therapy depends on an effective partnership between the patient and practitioner. Many patients play a passive role when it comes to oral care. They place themselves in the hands of the therapist and expect most of the care to be done for them. An effective way to reduce the risk of implant complications and failure is to stress the importance of the patient's role as an active participant in the overall therapeutic program.

Summary and conclusions

A key part of implant therapy is the risk-assessment process in which an attempt is made to identify variables that increase the risk of complications leading to implant failure. In many cases, early identification of these variables makes it possible to avoid or eliminate them, thereby increasing the chances of long-term implant survival. Risk factors for implant failure are environmental, biologic, or behavioral factors that are part of the causal chain leading to implant complications. For multifactorial problems, such as peri-implantitis and implant failure, the presence of one risk factor alone is usually insufficient to cause the adverse outcome. It is the combination of multiple risk factors that has clinical importance.

To minimize the risk of implant complications clinicians can use a number of technical procedures, such as adhering to a strict hygienic surgical protocol, performing the osteotomies with sharp drills, achieving early implant stability, and avoiding damage to vital anatomic structures during surgery. Since ongoing oral infections can lead to implant complications it is highly recommended that any endodontic, periodontal, and other oral infections be treated prior to implant placement. Conventional microbiologic methods have revealed that a large number of microorganisms are associated with peri-implant infections. Because of this microbial diversity, it is unlikely that testing for the presence of a small number of suspect bacteria for risk-assessment purposes will have any clinical value. Existing evidence does not support the routine use of pre-operative systemic antibiotics in implant therapy.

Most of the systemic risk factors for implant complications are those that increase the patient's susceptibility to infections or those that interfere with wound healing. Particularly important risk factors that suppress or alter neutrophil function are cigarette smoking, poor metabolic control of diabetes mellitus, and certain hematologic disorders. Factors that can significantly suppress adaptive immune functions are chronic use of corticosteroid medications and the presence of systemic lupus erythematosus. Important risk factors that can interfere with healing around implants are long-term use of bisphosphonates, history of radiation therapy to the jaws, and poor metabolic control of diabetes mellitus.

An effective risk-assessment process includes thorough medical and dental histories, a complete clinical examination, and an appropriate radiographic survey. Important behavioral issues that need to be assessed include compliance history, substance use/abuse habits, psychiatric/psychologic issues, effectiveness of practitioner–patient communication, and expectations of the patient. Depending on a number of circumstances, dental implants can be considered even in individuals who are at an elevated risk for implant complications. Risk assessment of the implant patient is a critically important preamble to treatment planning and if properly done can minimize the complications associated with endosseous implants.

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Part 10: Treatment Planning Protocols

Chapter 31

Treatment Planning of Patients with Periodontal Diseases

Giovanni E. Salvi, Jan Lindhe, and Niklaus P. Lang

Caries and periodontal diseases represent opportunistic infections associated with biofilm formation on the surfaces of teeth. Factors such as bacterial specificity and pathogenicity as well as the disposition of the individual for disease, e.g. local and general resistance, may influence the onset, the rate of progression, and clinical characteristics of plaque-associated dental disorders. Findings from animal experiments and longitudinal studies in humans, however, have demonstrated that treatment, including the elimination or the control of the biofilm infection and the introduction of careful plaque control measures, in most, if not all, cases results in dental and periodontal health. Even if health cannot always be achieved and maintained, the arrest of disease progression following treatment must be the goal of modern dental care.

The treatment of patients affected by caries and periodontal disease, including symptoms of associated pathologic conditions such as pulpitis, periapical periodontitis, marginal abscesses, tooth migration, etc., may from a didactic point of view be divided into four different phases:

1. Systemic phase of therapy including smoking counseling
2. Initial (or hygiene) phase of periodontal therapy, i.e. cause-related therapy
3. Corrective phase of therapy, i.e. additional measures such as periodontal surgery, and/or endodontic therapy, implant surgery, restorative, orthodontic and/or prosthetic treatment
4. Maintenance phase (care), i.e. supportive periodontal therapy (SPT).

Treatment goals

In every patient diagnosed with periodontitis, a treatment strategy, including the elimination of the opportunistic infection, must be defined and followed. This treatment strategy must also define the clinical outcome parameters to be reached through therapy. Such clinical parameters include:

- Reduction or resolution of gingivitis (bleeding on probing; BoP). A patient full mouth mean BoP ≤25% should be reached.
- Reduction in probing pocket depth (PPD). No residual pockets with PPD >5 mm should be present.
- Elimination of (through-and-through) open furcations in multi-rooted teeth. Initial furcation involvement should not exceed 3 mm.
- Absence of pain.
- Individually satisfactory esthetics and function.

In this context it must be emphasized that risk factors for periodontitis that can be controlled must be addressed as well. The three main risk factors for chronic periodontitis are (1) improper plaque control, (2) cigarette smoking, and (3) uncontrolled diabetes mellitus (Kinane *et al.* 2006).

Systemic phase

The goal of this phase is to eliminate or decrease the influence of systemic conditions on the outcomes of therapy and to protect the patient and the dental care

providers against infectious hazards. Contact with a physician or specialist should enable appropriate preventive measures to be taken, if necessary. Efforts must be undertaken to stimulate a smoker to enroll in a smoking cessation program. Additional aspects are discussed in Chapter 33.

Initial (hygiene) phase

This phase represents the cause-related therapy. The objective of this phase is the achievement of clean and infection-free conditions in the oral cavity through complete removal of all soft and hard deposits and their retentive factors. Furthermore, this phase should aim at motivating the patient to perform optimal plaque control. The initial phase of periodontal therapy is concluded by re-evaluation and planning of both additional and supportive therapies.

Corrective phase (additional therapeutic measures)

This phase addresses the sequelae of the oportunistic infections and includes therapeutic measures, such as periodontal and implant surgery, endodontic therapy, restorative and/or prosthetic treatment. The amount of corrective therapy required and the selection of the type of restorative and prosthetic therapy can be determined only when the degree of success of the cause-related therapy can be properly evaluated. The patient's willingness and ability to cooperate in the overall therapy must determine the type of corrective treatment. If this cooperation is inadequate, it may not be worth initiating treatment procedures: permanent improvement of oral health, function and esthetics may therefore not be achieved. The validity of this statement can be exemplified by the results of studies aimed at assessing the relative value of different types of surgical methods in the treatment of periodontal disease. A number of clinical trials (Lindhe & Nyman 1975; Nyman *et al.* 1975, 1977; Rosling *et al.* 1976a,b; Nyman & Lindhe 1979) have demonstrated that gingivectomy and flap procedures performed in patients with proper plaque control levels often result in gain of alveolar bone and clinical attachment, while surgery in plaque-contaminated dentitions may cause additional destruction of the periodontium.

Maintenance phase (supportive periodontal therapy)

The aim of this treatment is the prevention of reinfection and disease recurrence. For each individual patient a recall system must be designed that includes (1) assessment of deepened sites with bleeding on probing, (2) instrumentation of such sites, and (3) fluoride application for the prevention of dental caries. In addition, this treatment involves the regular control of prosthetic restorations incorporated during the corrective phase of therapy. Tooth sensitivity testing should be applied to abutment teeth as loss of vitality is a frequently encountered complication (Bergenholtz & Nyman 1984; Lang *et al.* 2004; Lulic *et al.* 2007). Based upon the individual caries activity, bitewing radiographs should be incorporated into SPT at regular intervals.

Screening for periodontal disease

A patient seeking dental care is usually screened for the presence of carious lesions by means of clinical and radiographic tools. Likewise, it is imperative that such a patient is screened for the presence of periodontitis as well, using a procedure termed the basic periodontal examination (BPE) (or periodontal screening record; PSR).

Basic periodontal examination

The goal of the BPE is to screen the periodontal conditions of a new patient and to facilitate treatment planning. BPE scoring will allow the therapist to identify:

- A patient with reasonably healthy periodontal conditions, but in need of long-term preventive measures
- A patient with periodontitis and in need of periodontal therapy.

In the BPE the screening of each tooth or implant is evaluated. For this purpose, the use of a thin graduated periodontal probe is recommended. At least two sites per tooth/implant (i.e. mesio-buccal and disto-buccal) should be probed using a light force (i.e. 0.2 N). Each dentate sextant within the dentition is given a BPE code or score, whereby the *highest* individual site score is used.

BPE system code

- Code 0 = probing pocket depth (PPD) ≤3 mm, BoP negative, no calculus or overhanging fillings (Fig. 31-1a)
- Code 1 = PPD ≤3 mm, BoP positive, no calculus or overhanging fillings (Fig. 31-1b)
- Code 2 = PPD ≤3 mm, BoP positive, presence of supra- and/or subgingival calculus and/or overhanging fillings (Fig. 31-1c)
- Code 3 = PPD >3 mm but ≤5 mm, BoP positive (Fig. 31-1d)
- Code 4 = PPD >5 mm (Fig. 31-1e).

If an examiner identifies a single site with a PPD >5 mm within a sextant, the sextant will receive a code of 4, and no further assessments are needed in this particular sextant. Patients with sextants given codes of 0, 1 or 2 belong to the relatively periodontally healthy category. A patient exhibiting a sextant with codes of 3 or 4 must undergo a more comprehensive periodontal examination (for details see Chapter 26).

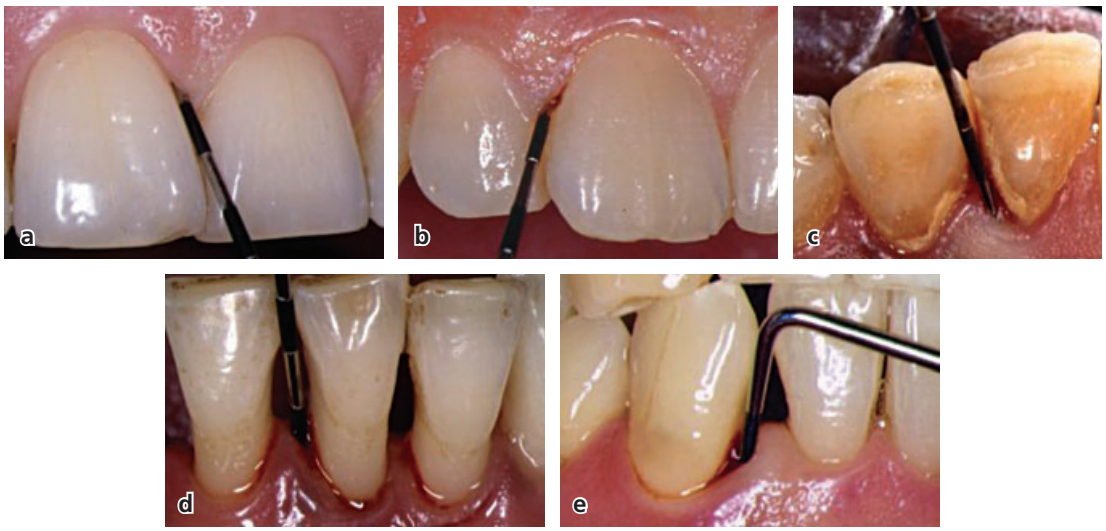

Fig. 31-1 Clinical illustration of the basic periodontal examination scores. (a) BPE code 0. (b) BPE code 1. (c) BPE code 2. (d) BPE code 3. (e) BPE code 4.

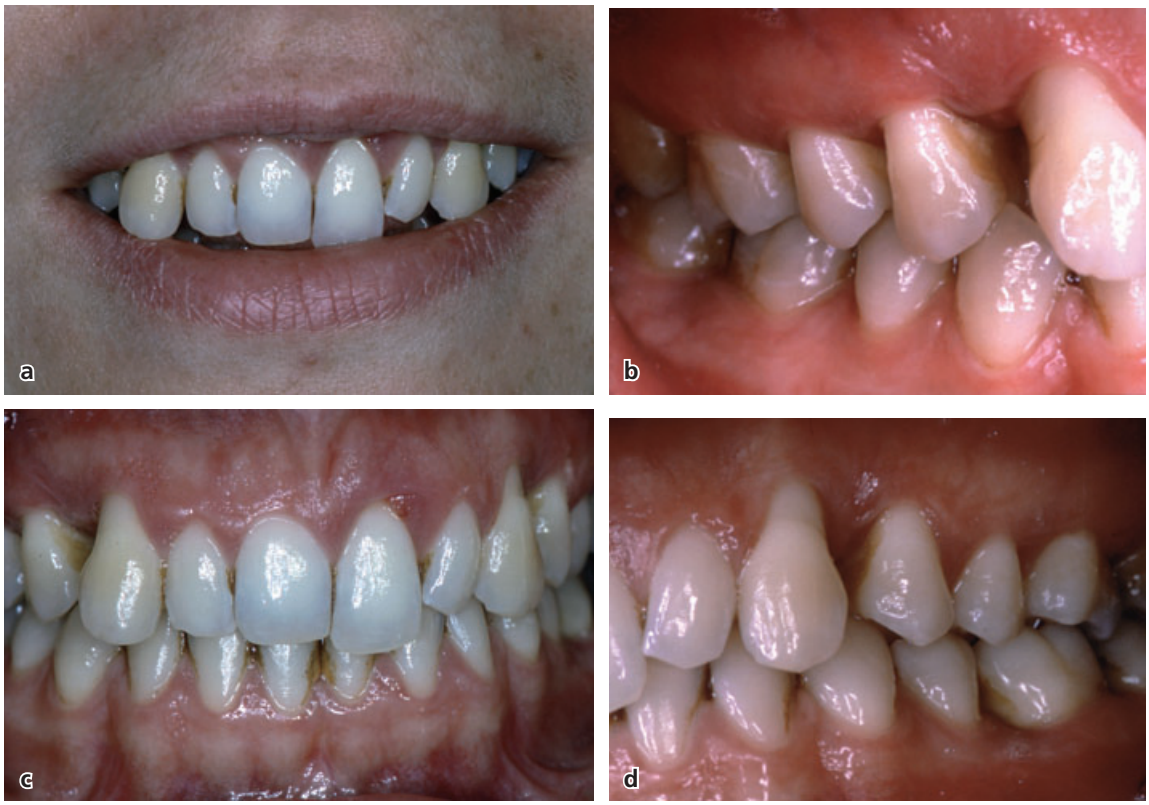

Fig. 31-2 (a–d) Clinical status of a 27-year-old female patient (S.B.) diagnosed with generalized aggressive periodontitis with furcation involvement.

The aim of the following text is to explain the overall objectives of the treatment planning of patients with BPE codes of 3 and 4 undergoing a comprehensive diagnostic process.

Diagnosis

The basis for the treatment planning described in this chapter is established by the clinical data collected from the patient's examination (see Chapter 26). This patient (Ms. S.B., 27 years of age) was systemically healthy and a non-smoker. She was examined with respect to her periodontal conditions, i.e. gingival sites displaying signs of *bleeding on probing* were identified, *probing pocket depths* were measured, the *periodontal attachment level* was calculated, *furcation involvements* were graded, *tooth mobility* was assessed, and the radiographs were analyzed to determine the *height* and *outline* of the *alveolar bone crest*.

The clinical characteristics of the dentition of this patient are shown in Fig. 31-2. The periodontal chart

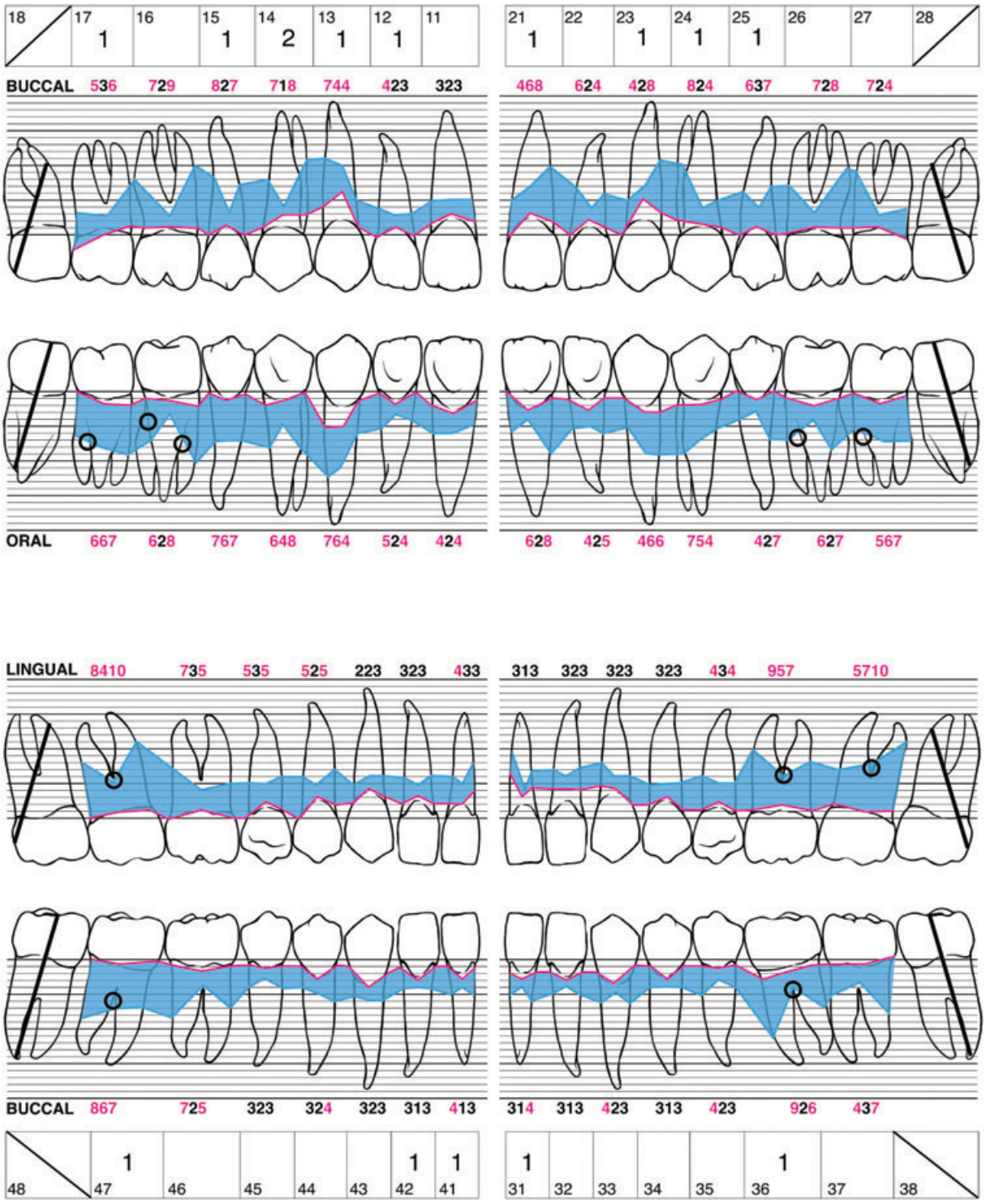

Fig. 31-3 Periodontal chart of the patient presented in Fig. 31-2.

and the radiographs are presented in Figs. 31-3 and 31-4, respectively. Based on these findings, each tooth in the dentition was given a diagnosis (Fig. 31-5) and a pre-therapeutic prognosis (Fig. 31-6). In addition to the examination of the periodontal condition, detailed assessments of primary and recurrent caries were made for all tooth surfaces in the dentition. Furthermore, the patient was examined with respect to endodontic and occlusal problems as well as temporomandibular joint dysfunction.

Treatment planning

Initial treatment plan

Provided that the patient's examination has been completed (see Chapter 26) and a diagnosis of all pathologic conditions has been made, an initial treatment plan can been established. At this early stage in the management of a patient, it is, in most instances,

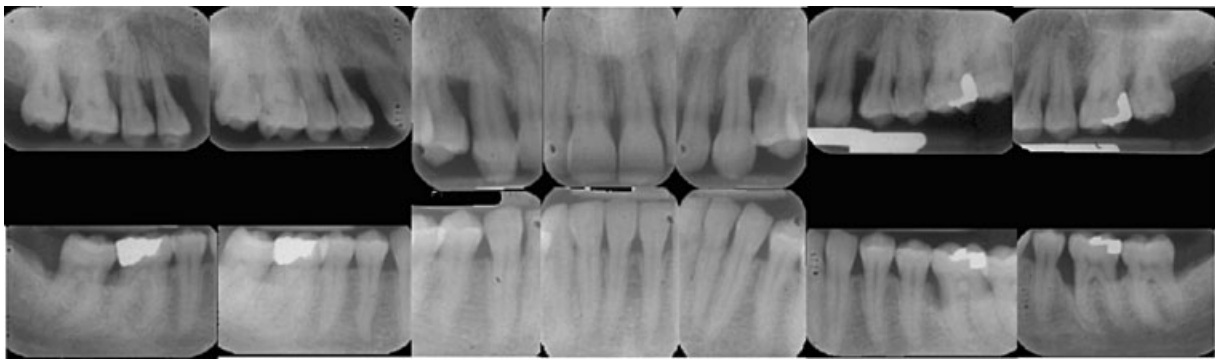

Fig. 31-4 Radiographs of the patient presented in Fig. 31-2.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Gingivitis																
Parodontitis superficialis							X	X								
Parodontitis profunda		X	X	X	X	X			X	X	X	X	X	X	X	
Parodontitis interradicularis		X	X											X	X	
Parodontitis interradicularis		X	X											X	X	
Parodontitis profunda		X	X											X	X	
Parodontitis superficialis				X	X			X	X		X		X			
Gingivitis						X	X			X		X				
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Fig. 31-5 Single tooth diagnosis of the patient presented in Fig. 31-2.

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Irrational to treat																
Doubtful (unsecure)			X	X	X	X					X	X		X	X	
Good (secure)							X	X	X	X			X			
Good (secure)				X	X	X	X	X	X	X	X	X	X			
Doubtful (unsecure)		X	X											X	X	
Irrational to treat																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Fig. 31-6 Pre-therapeutic single tooth prognosis of the patient presented in Fig. 31-2.

impossible to make definite decisions regarding all aspects of the treatment sequence, because:

1. *The degree of success of initial therapy is unknown*. The re-evaluation after initial, cause-related therapy forms the basis for the selection of means for additional therapy. The degree of disease elimination that can be reached depends on the outcome of subgingival instrumentation, but also on the patient's ability and willingness to exercise proper plaque control and to adopt adequate dietary habits.
2. *The patient's "subjective" need for additional (periodontal and/or restorative) therapy is unknown*. When the dentist has completed the examination of the patient and an inventory has been made regarding periodontal disease, caries, pulpal disease, and temporomandibular joint disorders, the observations are presented to the patient (i.e. "the case presentation"). During the case presentation

session it is important to find out if the patient's subjective need for dental therapy coincides with the dentist's professional appreciation of the type and amount of therapy that is required. It is important that the dentist understands that the main objective of dental therapy, besides *elimination of pain*, is *to satisfy the patient's demands regarding chewing function (comfort) and esthetics*, demands that certainly vary considerably from one individual to another.

3. *The result of some treatment steps cannot be predicted.* In patients exhibiting advanced forms of caries and periodontal disease it is often impossible to anticipate whether or not all teeth that are present at the initial examination can be successfully treated, or to predict the result of certain parts of the intended therapy. In other words, critical and difficult parts of the treatment must be performed first, and the outcome of this treatment must be evaluated before all aspects of the definitive corrective treatment can be properly anticipated and described.

Pre-therapeutic single tooth prognosis

Based on the results of the comprehensive examination, including assessments of periodontitis, caries, tooth sensitivity, and the resulting diagnosis, as well as considering the patient's needs regarding esthetics and function, a pre-therapeutic prognosis for each individual tooth (root) is made. Three major questions are addressed:

1. Which tooth/root has a "*good*" (secure) prognosis?
2. Which tooth/root is "*irrational-to-treat*"?
3. Which tooth/root has a "*doubtful*" (unsecure) prognosis?

Teeth with a *good* prognosis will require relatively simple therapy and may be regarded as secure abutments for function.

Teeth that are considered "irrational-to-treat" should be extracted during initial, cause-related therapy. Such teeth may be identified on the basis of the following criteria:

- Periodontal:
  - Recurrent periodontal abscesses
  - Combined periodontal–endodontic lesions
  - Attachment loss to the apex
- Endodontal:
  - Root perforation in the apical half of the root
- Dental:
  - Vertical fracture of the root
  - Oblique fracture in the middle third of the root
  - Caries lesions that extend into the root canal
- Functional:
  - Third molars without antagonists and with periodontitis/caries.

Teeth with a *doubtful* prognosis are usually in need of comprehensive therapy and must be brought into the category of teeth with a *good* prognosis by means of additional therapy. Such teeth may be identified on the basis of the following criteria:

- Periodontal:
  - Furcation involvement
  - Angular (i.e. vertical) bony defects
  - "Horizontal" bone loss involving more than two thirds of the root
- Endodontal:
  - Incomplete root canal therapy
  - Periapical pathology
  - Presence of voluminous posts/screws
- Dental:
  - Extensive root caries.

Case presentation

The "case presentation" is an essential component of the initial treatment plan and must include a description for the patient of different therapeutic goals and the modalities by which these may be reached. At the case presentation for Ms. S.B. the following treatment plan was described:

- The teeth in the dentition from 12 to 22 and from 45 to 35 will probably not confront the dentist with any major therapeutic challenges. For the remaining teeth in the dentition, however, the treatment plan may involve several additional measures.

Expected benefits inherent to a certain treatment plan versus obvious disadvantages should always be explained to and discussed with the patient. His/her attitude to the alternatives presented must guide the dentist in the design of the overall treatment plan.

Based on the pre-therapeutic single tooth prognosis (Fig. 31-6), the following detailed treatment plan was presented to the patient.

Systemic phase

Owing to the fact that the patient was systemically healthy and a non-smoker, no medical examination and smoking cessation counseling were required.

Initial phase (cause-related therapy)

The treatment was initiated and included the following measures to eliminate or control the bacterial infection:

1. *Motivation* of the patient and *instruction* in oral hygiene measures with subsequent check-ups and re-instruction
2. *Scaling and root planing* under local anesthesia in combination with removal of plaque-retentive factors

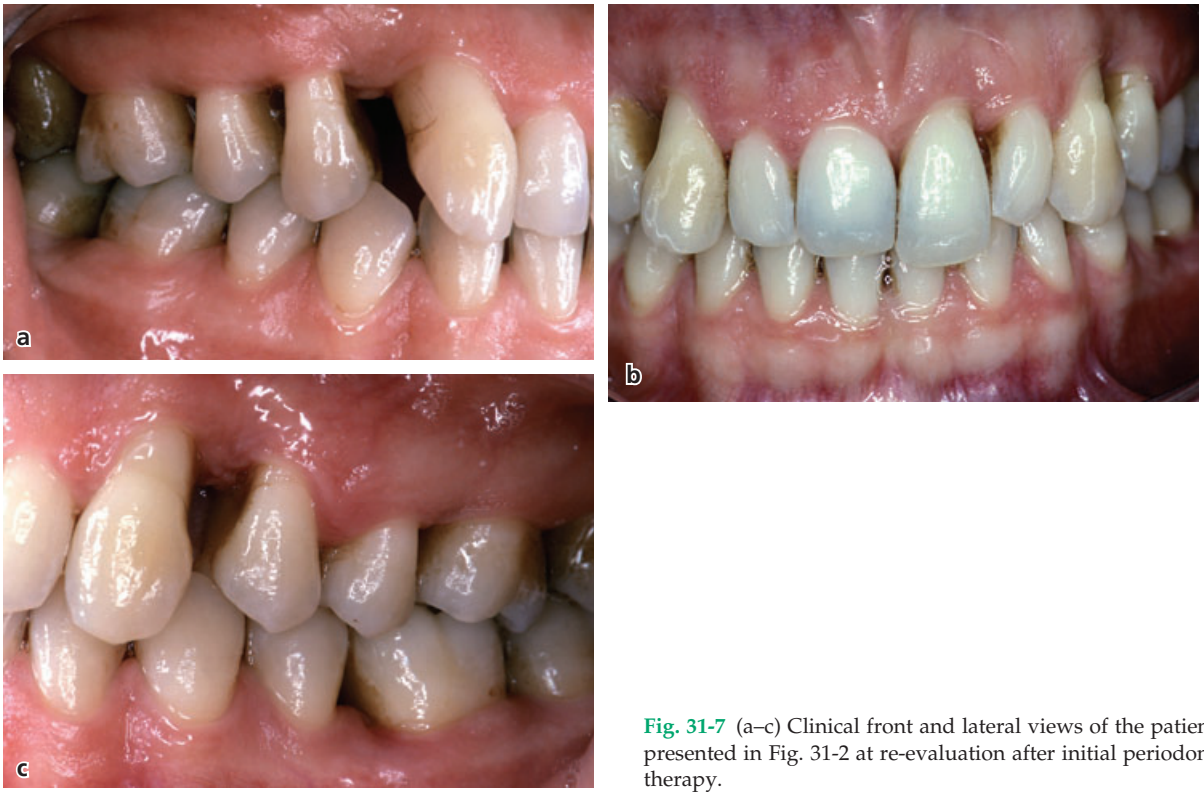

Fig. 31-7 (a–c) Clinical front and lateral views of the patient presented in Fig. 31-2 at re-evaluation after initial periodontal therapy.

3. *Excavation and restoration* of carious lesions (16 and 26)
4. *Endodontic treatment* of tooth 46.

Re-evaluation after initial phase

The initial phase of therapy is completed with a thorough analysis of the results obtained with respect to the elimination or degree of control of the dental infections. This implies that a re-evaluation of the patient's periodontal conditions and caries activity must be performed. The results of this re-evaluation (Figs. 31-7 and 31-8) form the basis for the selection, if necessary, of additional corrective measures to be performed in the phase of definitive treatment (i.e. corrective phase). In order to provide time for the tissues to heal, the re-evaluation should be performed no earlier than 6–8 weeks following the last session of instrumentation.

Planning of the corrective phase (i.e. additional definitive therapy)

If the results from the re-evaluation, made 6–8 weeks after the termination of the initial treatment phase, show that periodontal disease and caries have been brought under control, the additional treatment may be carried out. The main goal of this phase is to correct the sequelae caused by oral infections (i.e. periodontal disease and caries). The following procedures may be performed:

- *Additional endodontic treatment with/without post-and-core build-ups*
- *Periodontal surgery*. The type (i.e. open-flap debridement, regenerative or resective surgery) and extent of surgical treatment should be based on probing depth measurements, degree of furcation involvement and BoP score assessed at re-evaluation. Periodontal surgery is often confined to those areas of the dentition where the inflammatory lesions were not resolved by root instrumentation and in areas with angular bony defects or in furcation-involved molars.
- *Installation of oral implants*. In regions of the dentition where tooth abutments are missing, implant therapy for esthetic and functional reasons may be considered. It is essential to realize that implant therapy must be initiated once all dental infections are under control, i.e. after successful periodontal therapy.
- *Definitive restorative and prosthetic treatment* including fixed or removable dental prostheses.

Corrective phase (additional therapy)

After initial therapy the patient (Ms. S.B.) exhibited low plaque and gingivitis scores (i.e. 5–10%) and no active carious lesions. The corrective phase therefore included the following components:

1. *Periodontal surgery* (i.e. open-flap debridement) in the maxillary left and right quadrants as well as in the mandibular molar regions (Fig. 31-9)
2. *Guided tissue regeneration* (GTR) for tooth 36
3. *Re-evaluation* after periodontal surgery (Figs. 31-10 and 31-11)

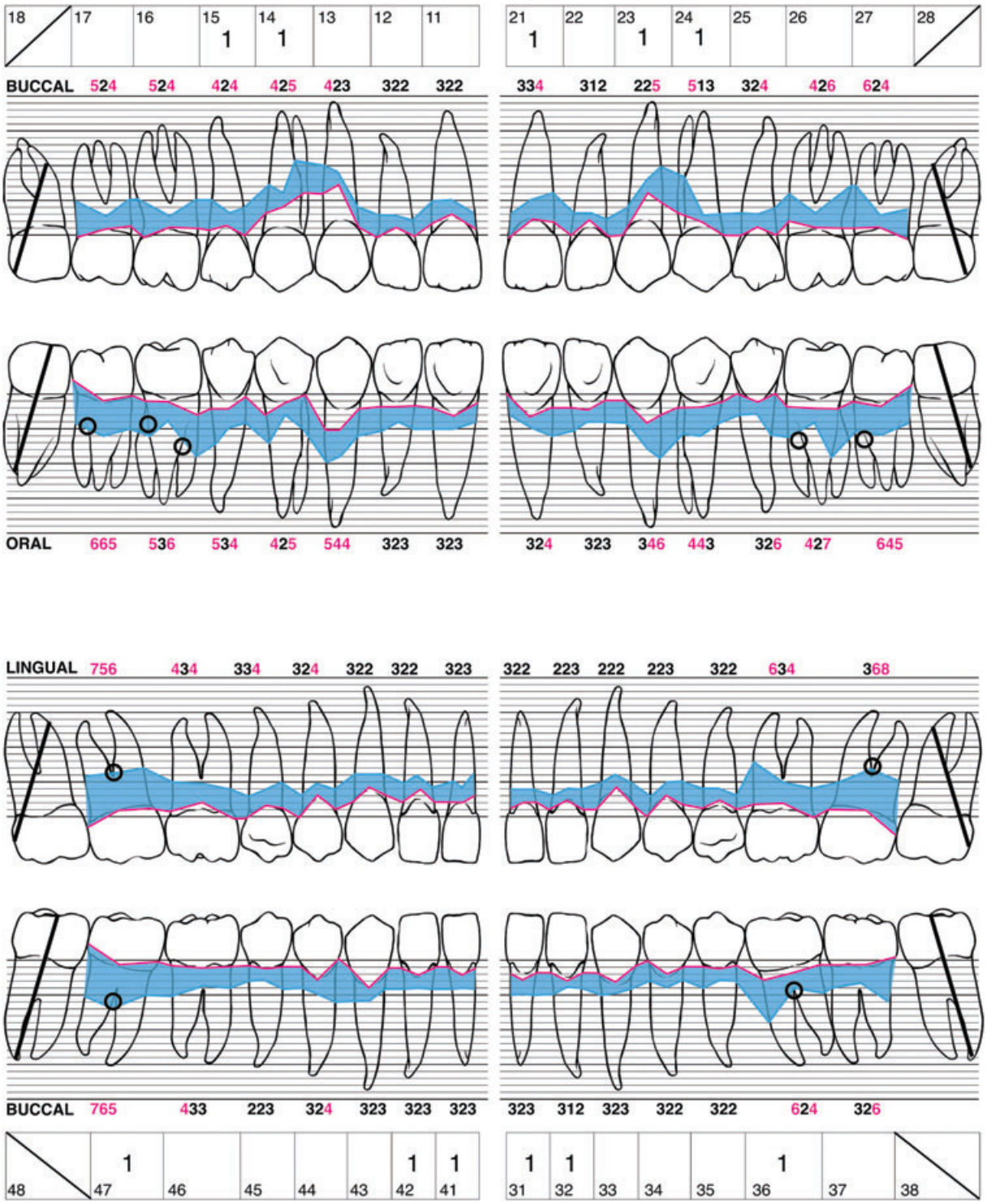

Fig. 31-8 Periodontal chart of the patient presented in Fig. 31-2 at re-evaluation after initial periodontal therapy.

4. *Orthodontic therapy* in the maxillary front area (Fig. 31-12)
5. *Restorative therapy* in the maxillary front area for esthetic reasons (Fig. 31-13).

Re-evaluation after corrective phase

The corrective phase of therapy is completed with a thorough analysis of the results obtained with respect to the elimination of the sequelae of periodontal tissue destruction (Figs. 31-14, 31-15 and 31-16). This implies that a re-evaluation of the patient's periodontal and peri-implant conditions must be performed. The results of this re-evaluation form the basis for the assessment of the residual periodontal risk. The outcomes of the periodontal risk assessment (PRA), in turn, will determine the recall frequency of the patient during maintenance phase.

Maintenance phase (care)

Following completion of cause-related therapy, the patient must be enrolled in a recall system aiming at

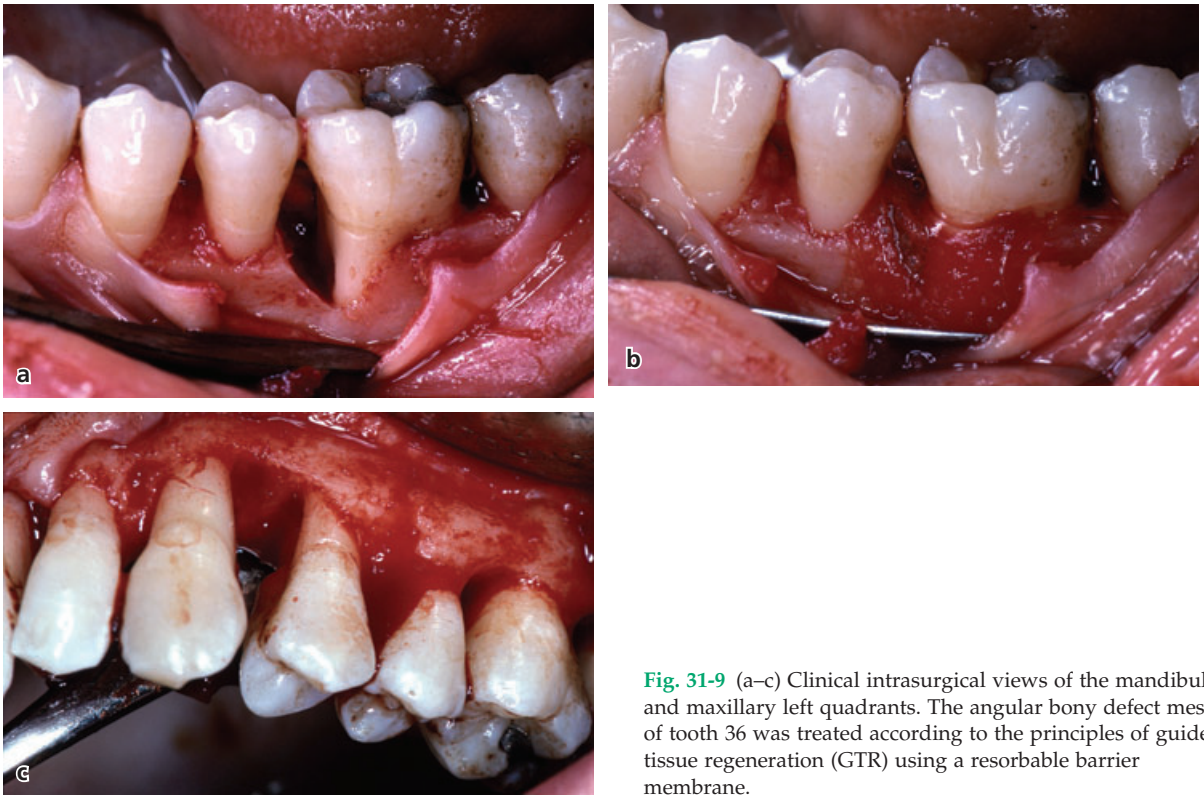

Fig. 31-9 (a–c) Clinical intrasurgical views of the mandibular and maxillary left quadrants. The angular bony defect mesial of tooth 36 was treated according to the principles of guided tissue regeneration (GTR) using a resorbable barrier membrane.

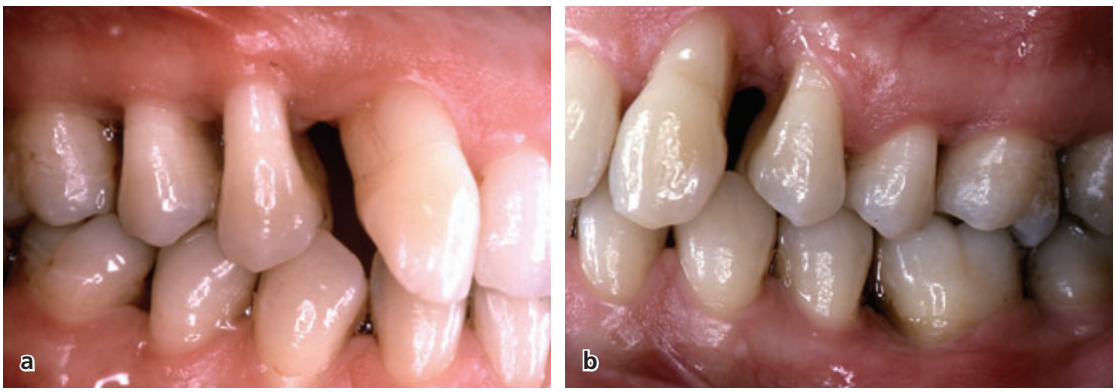

Fig. 31-10 (a,b) Clinical lateral views of the patient presented in Fig. 31-2 at re-evaluation after periodontal surgery.

preventing the recurrence of oral infections (i.e. periodontitis, caries, and peri-implantitis). Supportive periodontal therapy (SPT) should be scheduled at the re-evaluation after initial therapy and independently of the need for additional therapy. The time interval between the recall appointments should be based on a periodontal risk assessment established at the re-evaluation after the corrective phase. It is well established that self-performed plaque control combined with regular maintenance care visits following active periodontal treatment represents an effective means of controlling gingivitis and periodontitis and limiting tooth mortality over a 30-year period (Axelsson *et al.* 2004). It is important to emphasize, however, that the recall program must be designed to meet the individual needs of the patient. According to a PRA performed after completion of active therapy, some patients should be recalled every 3 months, while others may have to be checked only once a year (Lang & Tonetti 2003).

At the various recall visits the following procedures should be carried out:

1. Update of the medical and smoking history
2. Soft tissue examination as cancer screening
3. Recording of the full-mouth PPD ≥5 mm with concomitant BoP
4. Re-instrumentation of bleeding sites with PPD ≥5 mm
5. Polishing and fluoridation for the prevention of dental caries.

The patient (Ms. S.B.), presented to describe the guiding principles of treatment planning, was recalled twice during the first 6 months after active treatment (i.e. every 3 months) and subsequently only once every 6 months based on the individual PRA.

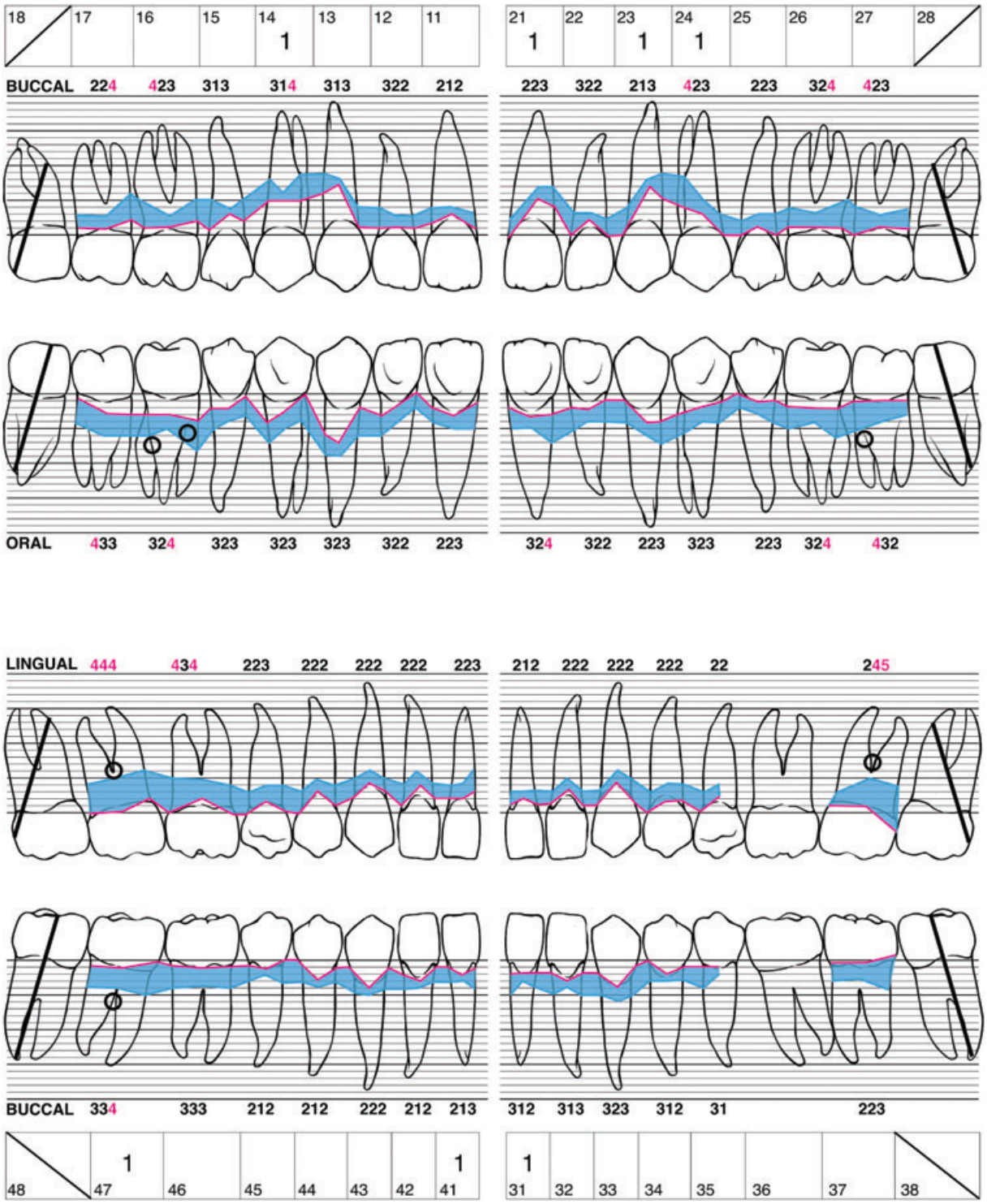

Fig. 31-11 Periodontal chart of the patient presented in Fig. 31-2 at re-evaluation after periodontal surgery.

Concluding remarks

The overall treatment plan and the sequence of the different treatment procedures used in this case were selected for presentation in order to illustrate the following principle: *in patients exhibiting a generalized advanced breakdown of the periodontal tissues, but with an intact number of teeth, considerable efforts should be made to maintain all teeth*. Extraction of a single tooth in such a dentition will frequently also call for the extraction of several others for "prosthetic reasons". The end result of such an approach thus includes a prosthetic rehabilitation that, if the treatment planning had been properly done, would have been unnecessary.

The large variety of treatment problems that different patients present may obviously require deviations from the sequence of treatment phases (i.e. systemic phase, initial cause-related therapy, corrective therapy, and maintenance care) discussed above.

Fig. 31-12 (a–c) Clinical front and lateral views of the patient presented in Fig. 31-2 during orthodontic therapy of the maxillary front teeth.

Fig. 31-13 (a–c) Clinical front and lateral views of the patient presented in Fig. 31-2 at the final re-evaluation. To improve the esthetic outcome, the maxillary front teeth were restored with composite fillings.

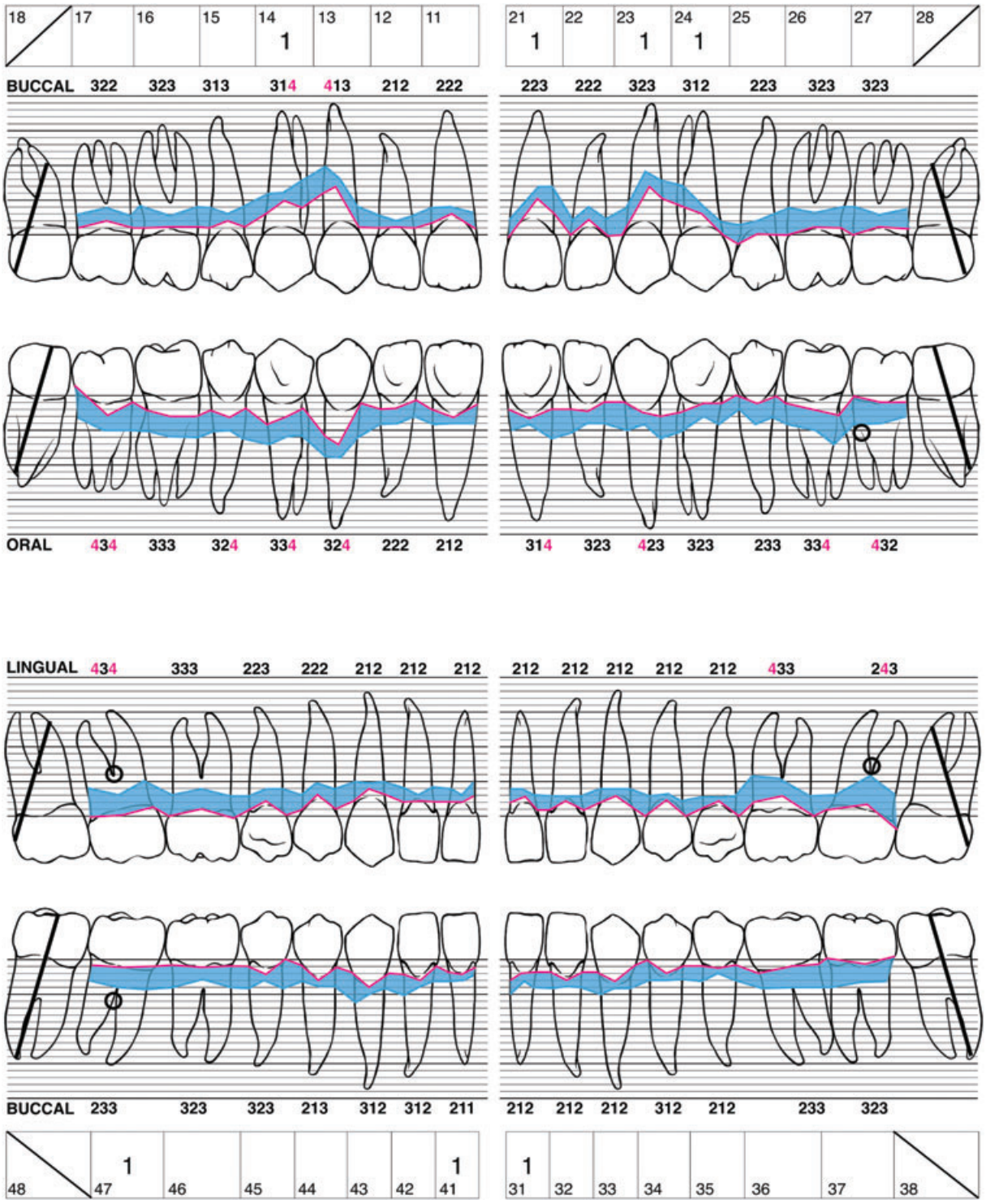

Fig. 31-14 Periodontal chart of the patient presented in Fig. 31-2 at the final re-evaluation.

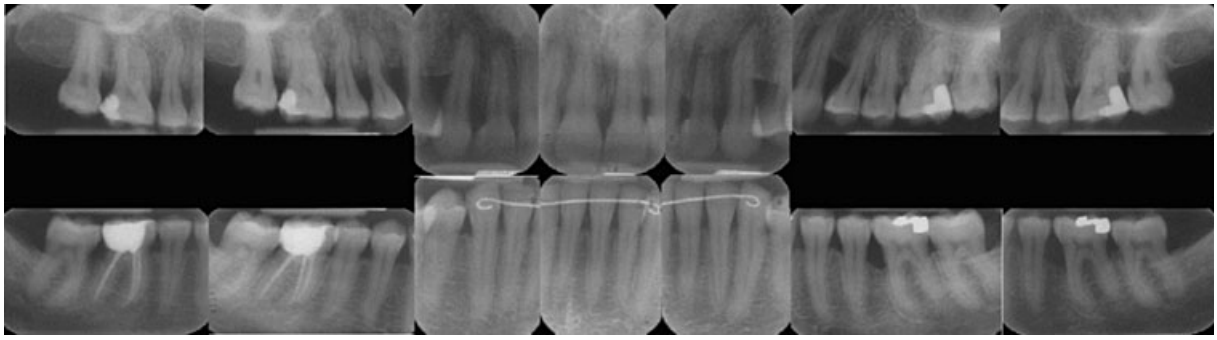

Fig. 31-15 Radiographs of the patient presented in Fig. 31-2 at the final re-evaluation.

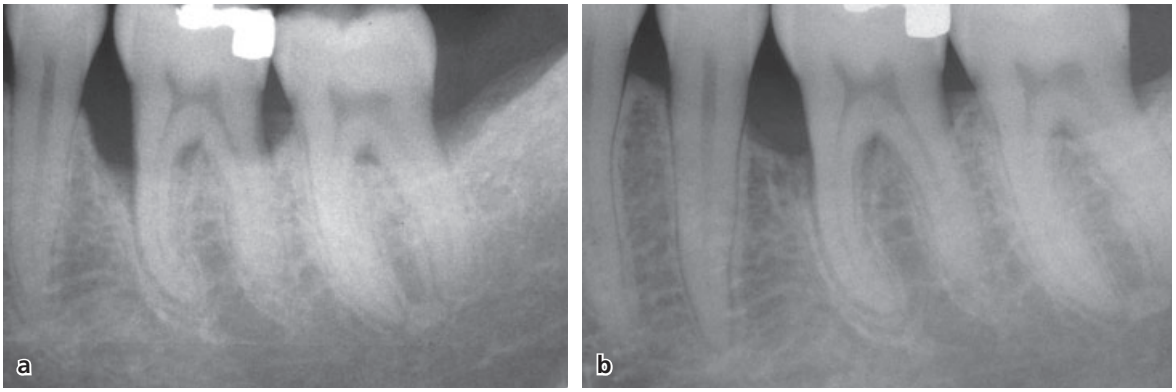

Fig. 31-16 (a,b) Radiographs of tooth 36 of the patient presented in Fig. 31-2 before and after regenerative periodontal therapy according to the principles of GTR.

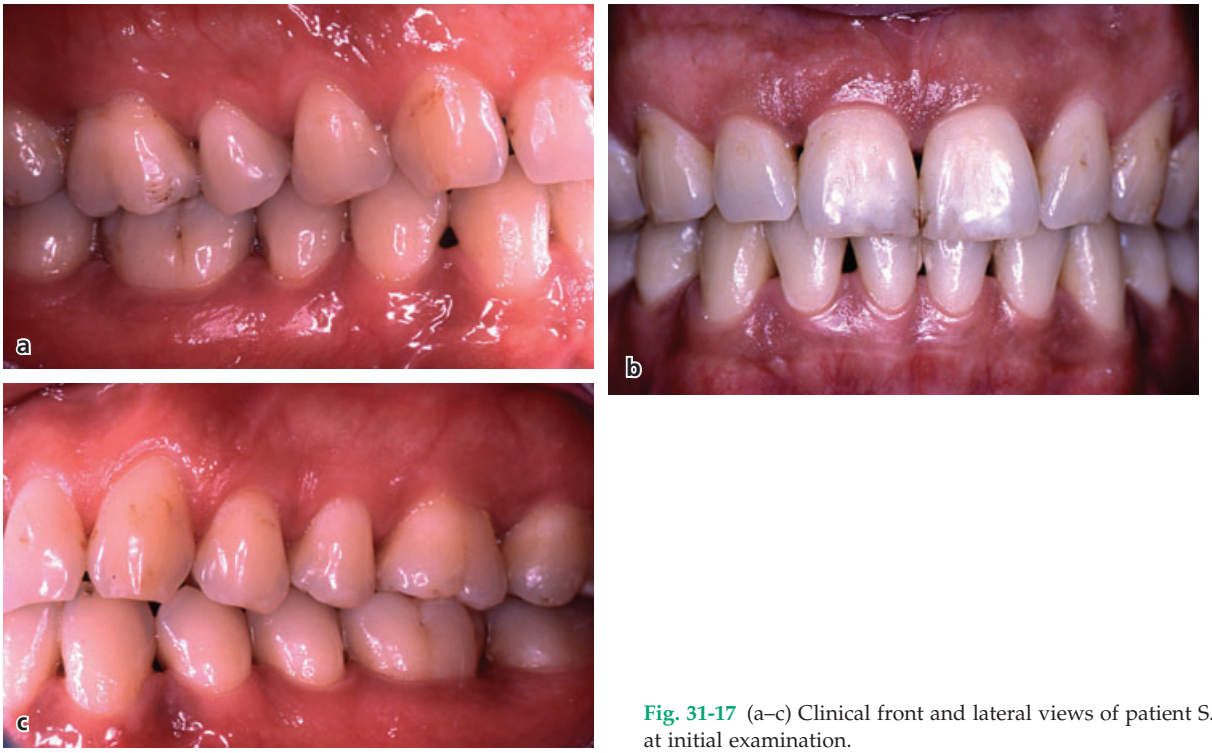

Fig. 31-17 (a–c) Clinical front and lateral views of patient S.K. at initial examination.

Such deviations may be accepted as long as the fundamental principles characterizing the treatment phases are understood.

Case report

A patient will be presented below together with a brief description of his specific dental problems and the treatment delivered in order to demonstrate the rationale behind such treatment phases.

Patient S.K. (male, 35 years old)

Initial examination

The chief complaint of the patient was the slightly increased mobility of tooth 21. The periodontal conditions (i.e. probing pocket depths, furcation involvements, tooth mobility, and periapical radiographs) from the initial examination are shown in Figs. 31-17, 31-18, and 31-19.

The data obtained from the initial examination disclosed the presence of an advanced destruction of the supporting tissues in most parts of the dentition (Fig. 31-18) and the presence of several angular bony defects (Fig. 31-19). The full-mouth plaque score (FMPS) and full-mouth bleeding score (FMBS) were 32% and 86%, respectively. The patient was systemically healthy and a former smoker.

Diagnosis

The patient was diagnosed with generalized chronic periodontitis with furcation involvement.

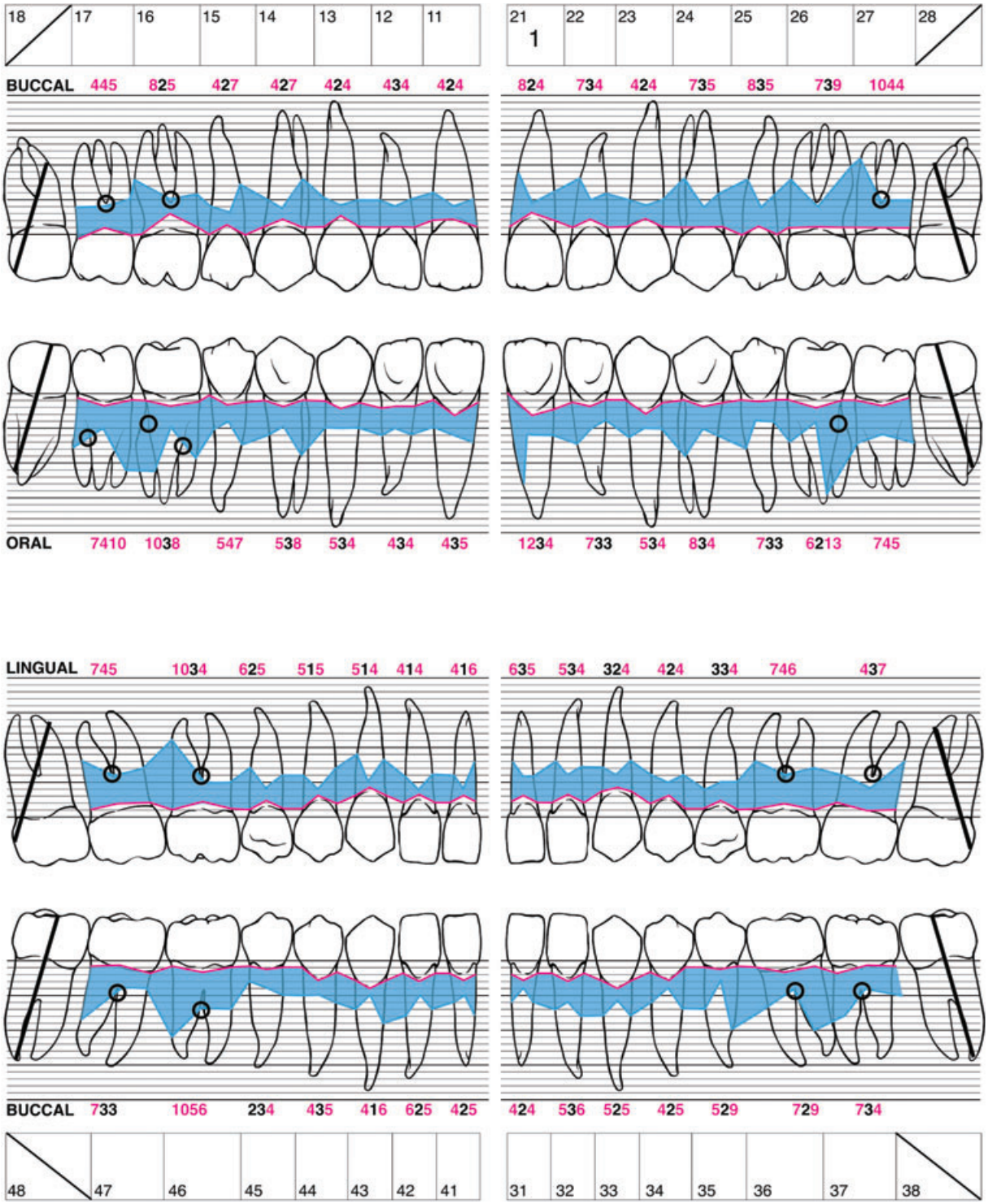

Fig. 31-18 Periodontal chart of the patient presented in Fig. 31-17.

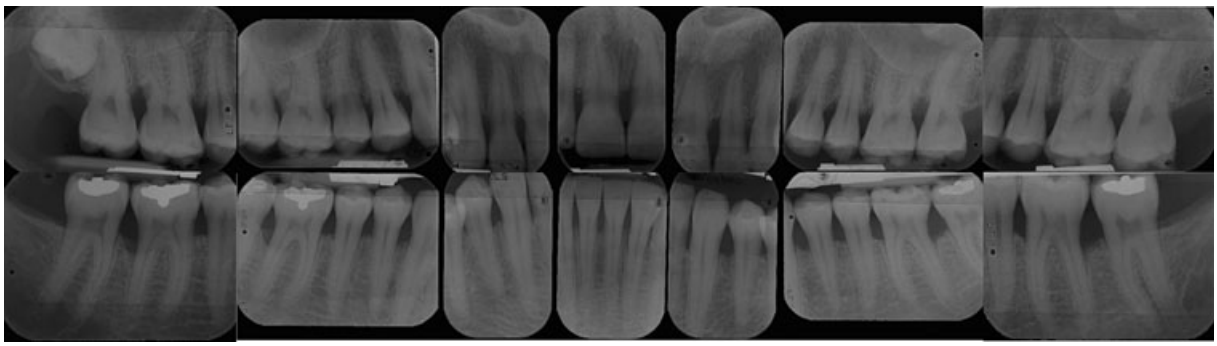

Fig. 31-19 Radiographs of the patient presented in Fig. 31-17.

Etiology

The supra- and subgingival bacterial deposits were identified as the main etiologic factors. Past cigarette smoking was considered a modifying factor.

Pre-therapeutic single tooth prognosis

Teeth 28, 38, and 48 were missing. Tooth 18 was impacted and considered irrational-to-treat. Teeth 13, 12, 11, and 23 in the maxilla and from 45 to 35 in the mandible were classified as secure. A doubtful prognosis was assigned to 17, 16, 15, 14, 21, 22, 24, 25, 26, and 27 in the maxilla and to 36, 37, 46, and 47 in the mandible (Fig. 31-20).

Treatment planning

In the treatment planning of this young patient, it seemed reasonable to anticipate the retention of all teeth of his periodontally compromised dentition. The prerequisites for a good long-term prognosis after therapy included (1) optimal self-performed plaque control, (2) proper healing of the periodontal tissues following non-surgical and surgical therapy, and (3) a carefully monitored maintenance care program. As stated above, tooth 21 displayed increased mobility. This mobility, however, did not disturb the chewing comfort of the patient.

In such a young patient, extensive efforts were made to treat inflammatory periodontal disease pro-

	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Irrational to treat	X															
Doubtful (unsecure)		X	X	X	X				X	X		X	X	X	X	
Good (secure)						X	X	X			X					
Good (secure)				X	X	X	X	X	X	X	X	X	X			
Doubtful (unsecure)		X	X											X	X	
Irrational to treat																
	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Fig. 31-20 Pre-therapeutic single tooth prognosis of the patient presented in Fig. 31-17.

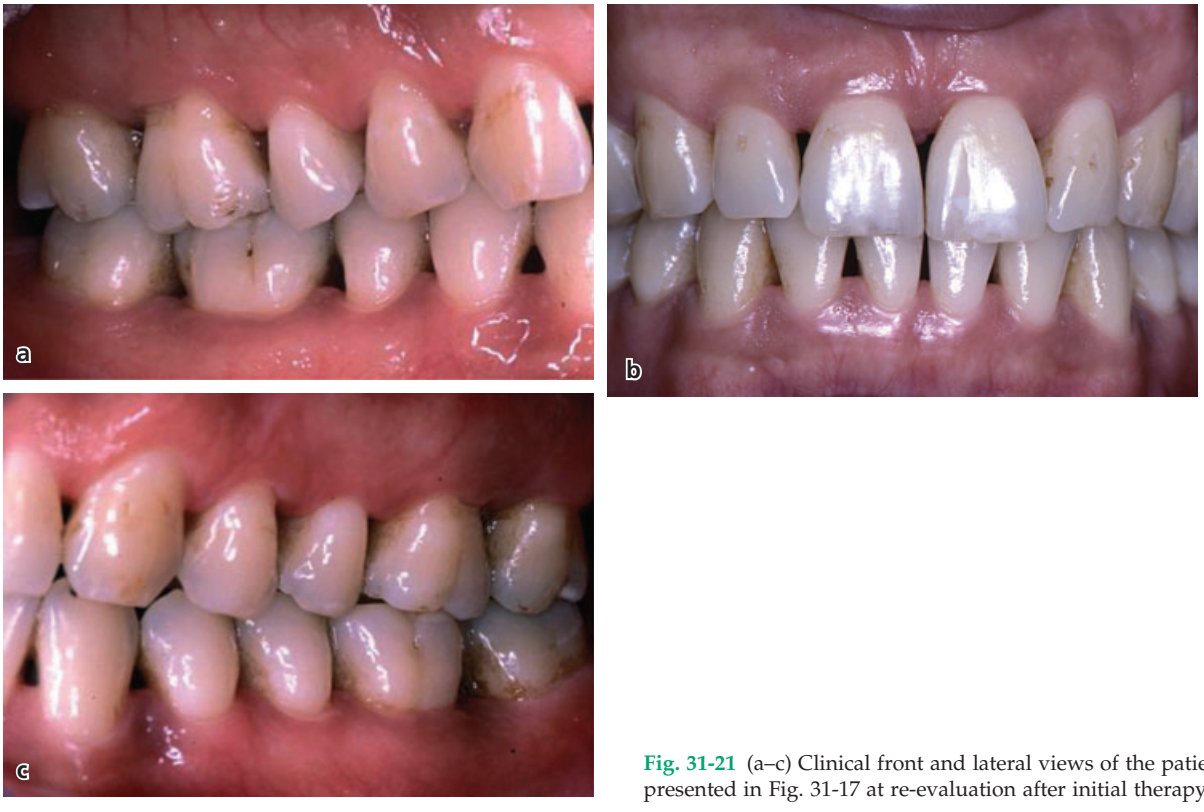

Fig. 31-21 (a–c) Clinical front and lateral views of the patient presented in Fig. 31-17 at re-evaluation after initial therapy.

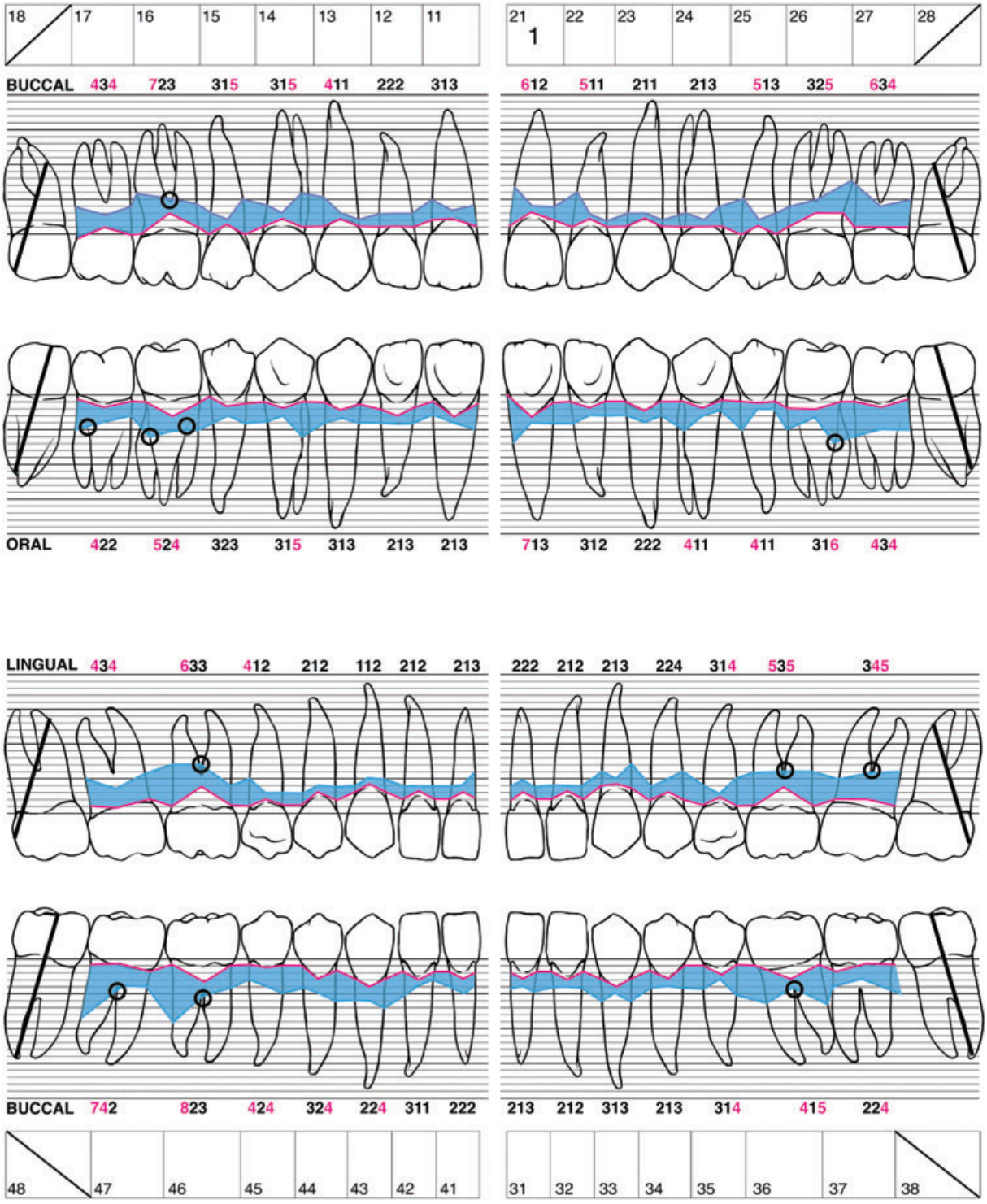

Fig. 31-22 Periodontal chart of the patient presented in Fig. 31-17 at re-evaluation after initial therapy.

perly in the entire dentition, in order to avoid tooth extraction and subsequent prosthetic rehabilitation.

Treatment

Subsequent to initial examination, the patient was given a detailed "case presentation" and information regarding alternative goals of and prerequisites for the overall treatment. This information included a description of the role of dental biofilms in the etiology of periodontal disease and the significance of optimal plaque control for a successful outcome of therapy. A treatment program was subsequently planned which aimed at maintaining all teeth. The overall treatment was performed in the sequence described below.

Initial cause-related therapy

The patient was counseled not to start smoking again. After thorough motivation, the patient was instructed

Fig. 31-23 (a-c) Intra- and postsurgical views of the upper front area of the patient presented in Fig. 31-17.

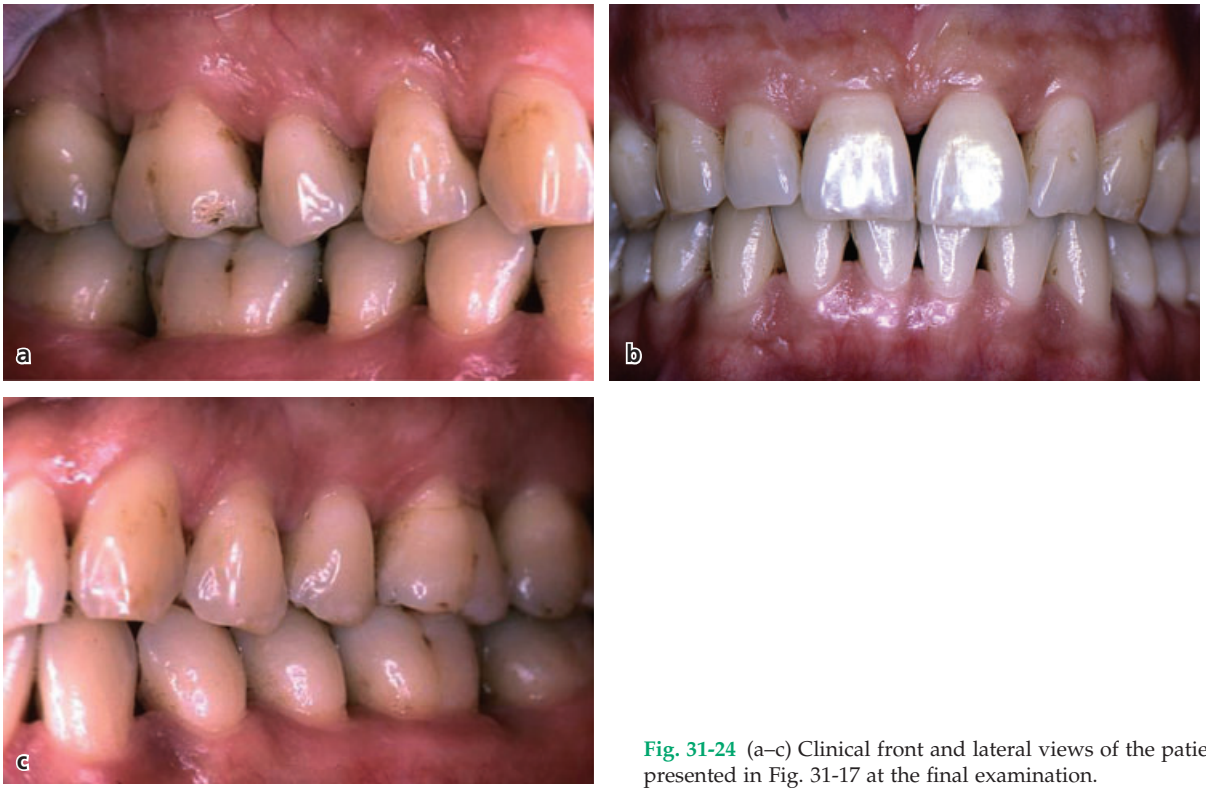

Fig. 31-24 (a–c) Clinical front and lateral views of the patient presented in Fig. 31-17 at the final examination.

in the toothbrushing technique according to Bass and in the use of interdental brushes. Scaling and root planing of all teeth were performed under local anesthesia. The front and lateral views as well as the periodontal chart at re-evaluation after initial therapy are presented in Figs. 31-21 and 31-22, respectively.

Additional therapy

The need for additional therapy was based on the re-evaluation after initial therapy (Fig. 31-22). Periodontal surgery in conjunction with regenerative procedures was deemed necessary in all quadrants. During access flap surgery in the first quadrant extending from 13 to 17, tooth 18 was extracted.

Between the upper front teeth 11 and 21, the modified papilla preservation technique (Cortellini *et al.* 1995) was incorporated in the surgical procedure to gain access to the angular bony defect of tooth 21 (Fig. 31-23). In this area, the application of enamel matrix derivatives (i.e. Emdogain®) aimed at regenerating the lost periodontal tissues on the mesial aspect of 21.

In the third quadrant, the surgical access flap extended from 35 to 37. In the fourth quadrant, flap surgery in conjunction with the simplified papilla preservation technique (Cortellini *et al.* 1999) was used to gain access to the angular bony defect on the distal aspect of 46. In this area, the application of enamel matrix derivatives (i.e. Emdogain®) aimed at regenerating the lost periodontal tissues. Six months after completion of the corrective phase (Fig. 31-24), a re-evaluation of the periodontal conditions (Fig. 31-25), including radiographs (Figs. 31-26 and 31-27) followed by a PRA, were performed.

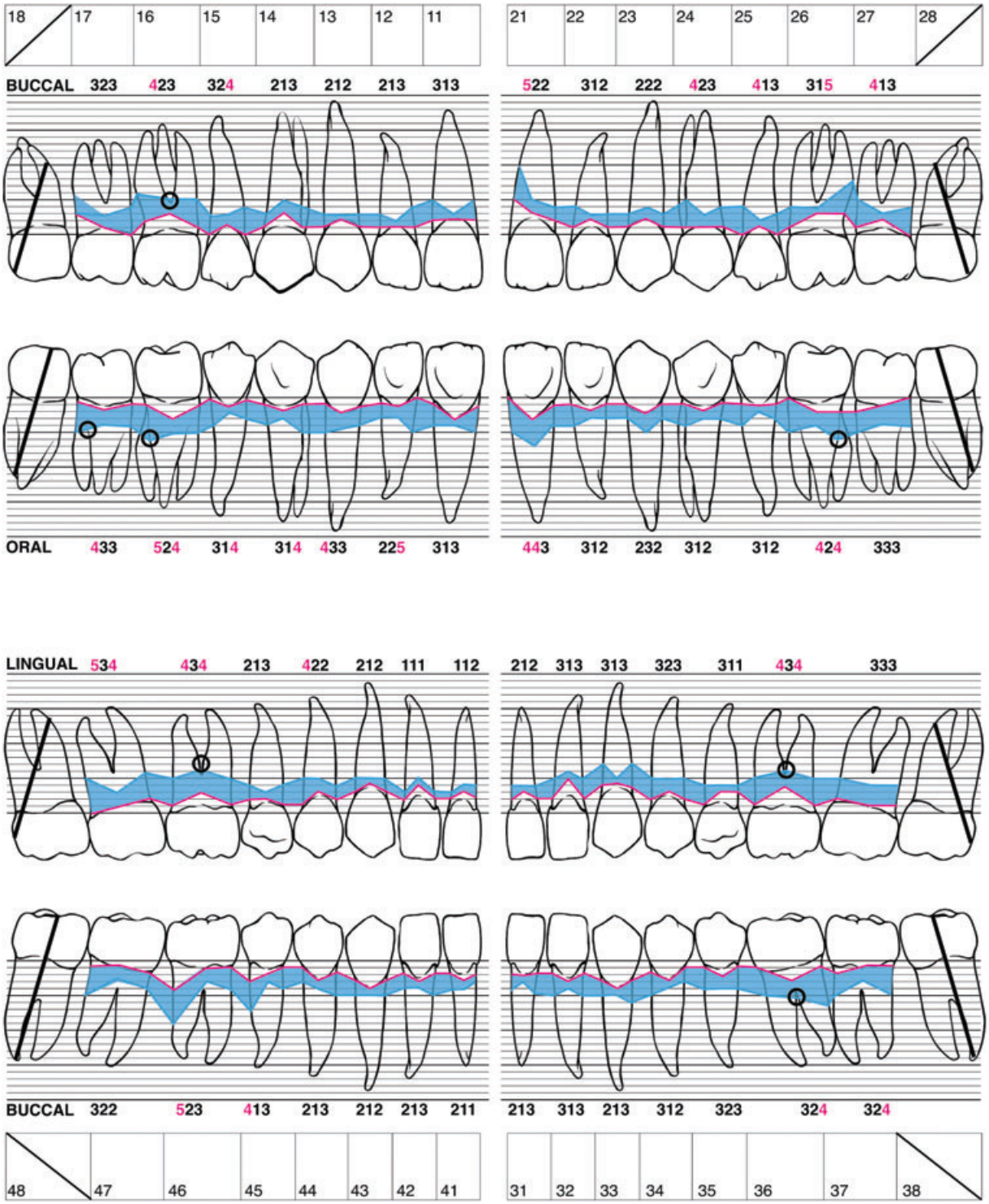

Fig. 31-25 Periodontal chart of the patient presented in Fig. 31-17 at the final examination.

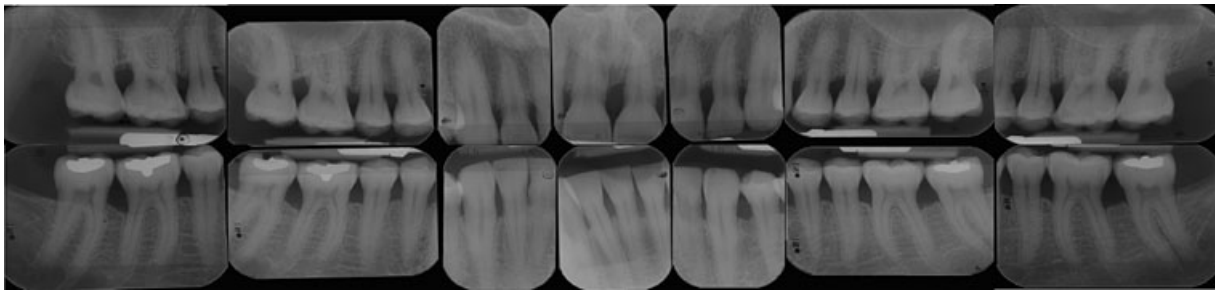

Fig. 31-26 Radiographs of the patient presented in Fig. 31-17 at the final examination.

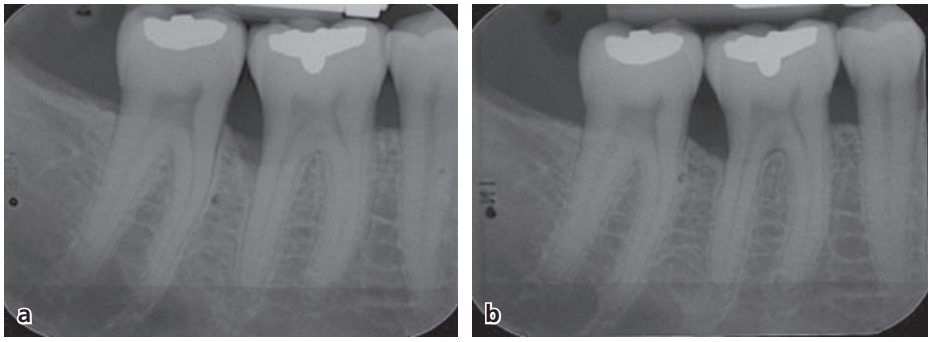

Fig. 31-27 Radiographs before (a) and after (b) periodontal regeneration of the angular bony defect on the distal aspect of tooth 46.

Supportive periodontal therapy

After completion of initial and corrective therapy, the patient was recalled for maintenance care every 3 months. During recall appointments, sites bleeding on probing and with a PPD ≥5 mm were re-instrumented. If necessary, the patient was remotivated and re-instructed in oral hygiene procedures. Fluoride was regularly applied in order to prevent the onset of dental caries.

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Chapter 32

Treatment Planning for Implant Therapy in the Periodontally Compromised Patient

Jan L. Wennström and Niklaus P. Lang

The use of dental implants for replacement of missing teeth is a viable option in the rehabilitation of the periodontally compromised patient, and certainly the availability of this treatment option may also influence our decisions regarding the preservation of teeth with varying degrees of periodontal tissue destruction.

Prognosis of implant therapy in the periodontally compromised patient

Global data on survival rates of dental implants indicate a rather low incidence of implant loss. The question is, however, whether the long-term prognosis for implants is better than that for teeth. In a systematic review by Berglundh *et al.* (2002), including 16 studies reporting data on implant-supporting fixed partial dentures (FPDs), the overall 5-year failure rate was calculated as about 5%. In the few studies that included a follow-up of 10 years the figure for implant loss was about 10%. It should be noted, however, that these studies did not specifically address the prognosis of implant therapy in periodontally compromised patients. Hardt *et al.* (2002) reported from a 5-year study that 8% of the implants were lost in patients who at time of implant placement presented advanced loss of periodontal support at their natural teeth. The corresponding figure in patients without periodontal tissue destruction was only 3% (Table 32-1). In the periodontally compromised patients most of the implants that were lost were so-called late failures. Furthermore, after 5 years 64% of the periodontally compromised patients showed a mean bone loss at the implants of >2 mm compared to only 24% among the non-compromised patients. Karoussis *et al.* (2003) found a failure rate of 10% after 10 years in patients that had been treated for periodontitis before implant placement, compared to 4% in patients who had received implant therapy because of tooth loss for reasons other than periodontal disease. The data reported above indicate that there is an increased risk for implant failure in individuals susceptible to periodontitis.

A question of concern in relation to treatment decisions in a periodontally compromised patient is whether the failure rate of implants is different from that of teeth. In order to give an answer to this

Table 32-1 Proportion (%) of implants lost in relation to experience of destructive periodontal disease

Authors	Follow-up (years)	No history of destructive periodontal disease (%)	History of destructive periodontal disease (%)
Hardt *et al.* (2002)	5	3.3	8.0
Karoussis *et al.* (2003)	10	3.5	9.5

Table 32-2 Proportion (%) of teeth lost in patients treated for advanced destructive periodontal disease and maintained in supportive care programs

Authors	Mean follow-up (years)	Percentage of teeth lost	Percentage of teeth lost per 10 years
Lindhe & Nyman (1984)	14	2.3	1.6
Yi *et al.* (1995)	15	8	5
Rosling *et al.* (2001)	12	1.9	1.6
König *et al.* (2002)	12	3.1	2.6
Karoussis *et al.* (2004)	10	5	5

question we have to know the incidence of tooth loss in periodontally treated patients. Based on data from studies involving patients that have been treated for advanced periodontal disease and thereafter been provided with regular supportive periodontal therapy (SPT), the average incidence of tooth loss during a 10-year period can be estimated to be between 2 and 5% (Table 32-2). These figures, in comparison with the data for implant loss presented above, indicate that the prognosis for long-term survival of implants is not better than that of properly treated periodontitis-affected teeth. Furthermore, evidence is accumulating that suggests that longitudinal bone loss at implants is positively correlated with periodontal disease susceptibility and that implant therapy in the periodontally compromised patient may not be as successful as the global data for implant therapy in general has indicated.

Strategies in treatment planning

A comprehensive clinical and radiographic examination forms the basis for the treatment planning of the periodontally compromised patient. In relation to implant therapy, careful risk assessments should also be made (see Chapter 30) and additional radiographic examinations may be required (see Chapter 28). The goal of the treatment is to satisfy the patient's demands regarding chewing comfort and esthetics, with a favorable long-term prognosis of the restoration. The use of implants as a means to restore chewing function and esthetics in the periodontitis-susceptible patient has to be carefully evaluated in relation to the patient's standard of infection control. In partially dentate patients with remaining periodontal lesions, implants are rapidly colonized by periodontal pathogens, which indicates that periodontal pockets may act as reservoirs for microbial colonization of implants (see Chapter 10). Since there is no evidence that the host response to the microbial challenge is altered when a tooth is substituted with an implant, it should be anticipated that a periodontitis-susceptible individual with improper infection control will face similar risk for disease-induced bone loss at implants and teeth.

Elimination of periodontitis lesions before implant placement and the establishment of a high standard of infection control are consequently decisive factors for the success of implant therapy. Regular recalls for supportive care should be scheduled after the completion of the therapy (see Chapter 59). Provided such a treatment program is adhered to, the long-term success of implant therapy in the periodontally compromised patient may not deviate from that in a non-susceptible patient (Baelum & Ellegaard 2004; Wennström *et al.* 2004).

Treatment decisions – case reports

Posterior segments

In the periodontally compromised patient the posterior segments of the dentition are usually those that are most severely affected by the disease and tooth loss. Figure 32-1 shows the clinical and radiographic status of a 53-year-old male following the completion of basic periodontal therapy for the establishment of infection control. Following periodontal treatment, the patient, originally diagnosed with severe chronic periodontitis, demonstrated a high standard of self-performed infection control and all lesions in the periodontal tissues have now been resolved. Because of the severity of the periodontal destruction, remaining teeth posterior to the canines in the maxilla as well as one remaining mandibular molar had to be removed. Hence, the dentition is markedly reduced, not only with regard to the number of teeth but also in terms of the amount of remaining periodontal support. From a chewing comfort point of view the patient is in need of prosthetic rehabilitation, particularly in the posterior segments of the maxilla. The treatment options available include (1) a removable prosthesis or (2) implant-supported FPDs. Considering that the remaining teeth show slightly increased mobility, the treatment alternative involving implant-supported FPDs seems most appropriate. In addition, the patient would if possible prefer to have fixed prosthetic reconstructions.

Clinical and radiographic evaluation of the posterior jaw segments of the maxilla revealed that two implants might be placed in quadrant 1 between the canine and the anterior border of the maxillary sinus, while the dimension of the bone inferior of the sinus was judged inadequate for placement of implants (Fig. 32-1b,c). If the implant in position 15 was placed along the anterior wall of the sinus cavity and was angulated slightly distally, space might be available to insert a pontic between the two implants and to provide the patient with a three-unit FPD. In the quadrant 2, the bone dimensions were more

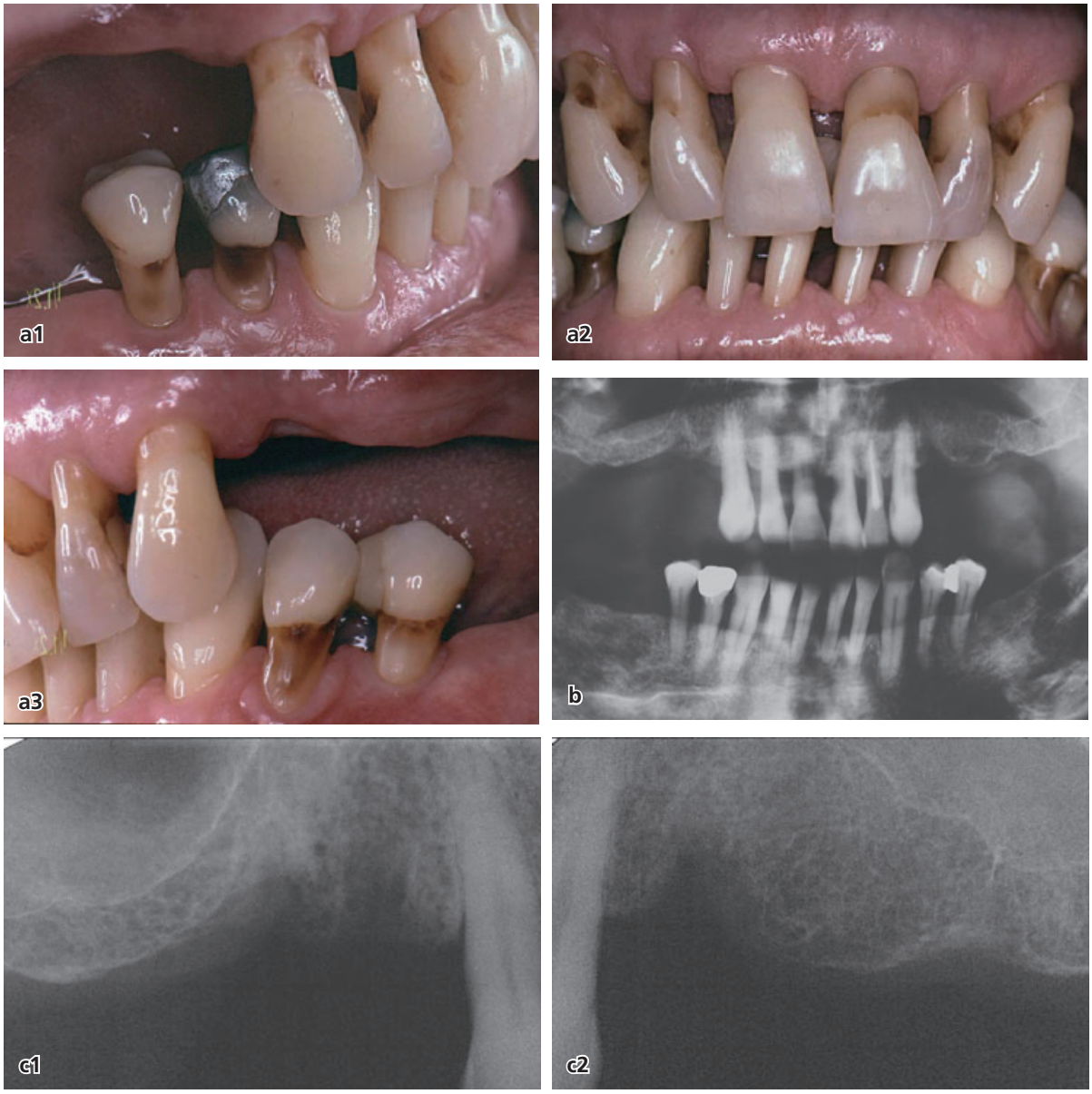


Fig. 32-1 (a–c) A 53-year-old male patient (H.L.) with periodontally compromised dentition. Clinical and radiographic status after periodontal treatment and establishment of infection control.

favorable and it was judged feasible to install three implants. Hence, by providing the patient with two three-unit implant-supported FPDs in the posterior segments of the maxilla a premolar occlusion could be established. The patient considered this treatment solution to be satisfactory with regard to his demands for improved chewing function. He had no requests for improved esthetics in the anterior segments, most likely because of a low lip line and because he only exposed the incisial half of the crown when smiling.

Figure 32-1d–f shows the outcome of the restorative treatment. In order to further improve the patient's chewing comfort a single implant was inserted in the left side of the mandible, after the second premolar had been tilted mesially. After completion of the restorative treatment the patient was enrolled in a maintenance care program, including recalls once every 6 months to secure a high standard of infection control and to provide preventive means to reduce the risk for development of root caries. The 10-year follow-up status (Fig. 32-1g–h) reveals healthy marginal tissues and no loss of supporting structures, neither at the implants nor at the teeth. The standard of self-performed infection control has been excellent throughout the follow-up period.

In conclusion: The treatment outcome in this case clearly illustrates that the periodontitis-susceptible patient can be successfully treated with the use of implants and without signs of peri-implant bone loss over time, provided proper infection control is established and maintained. The recall visits for supportive therapy must include careful evaluation of both the periodontal and the peri-implant tissues for detection of signs of pathology, and proper decisions regarding indicated treatment (see Chapter 59).

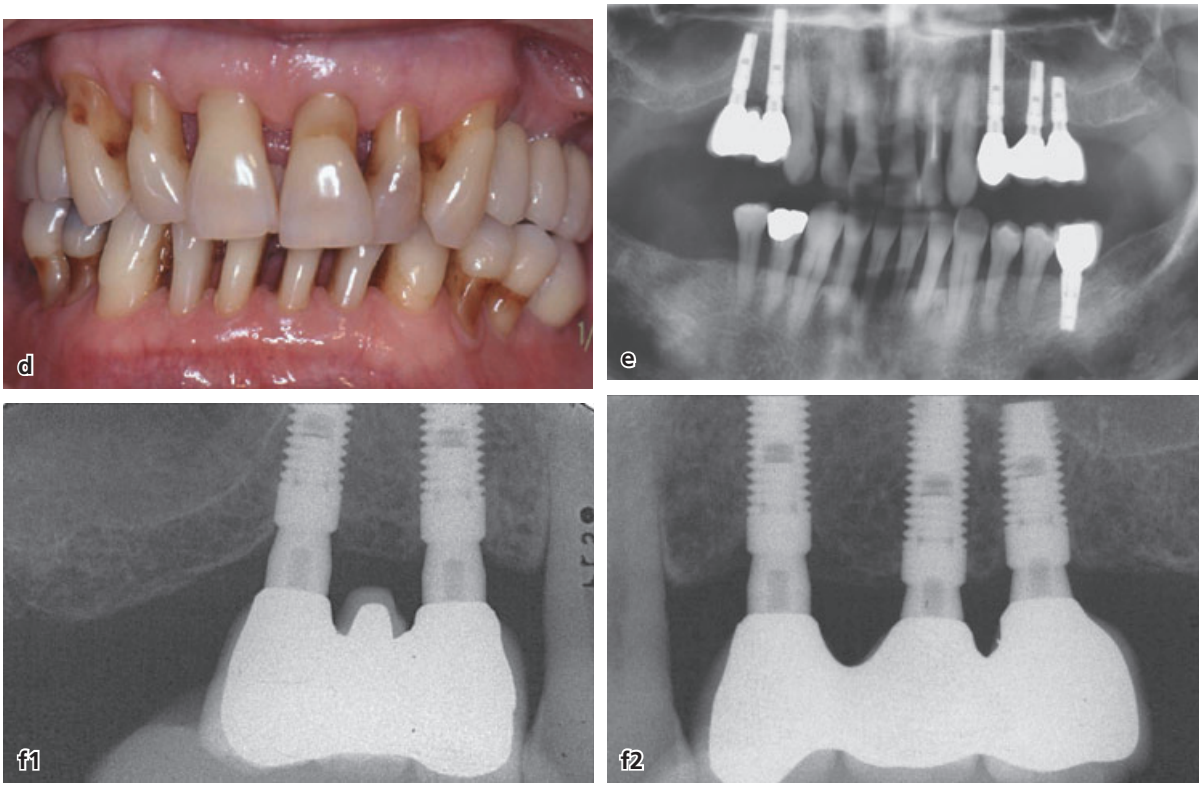


Fig. 32-1 (d–f) Clinical and radiographic status of patient H.L. after completion of the implant treatment.

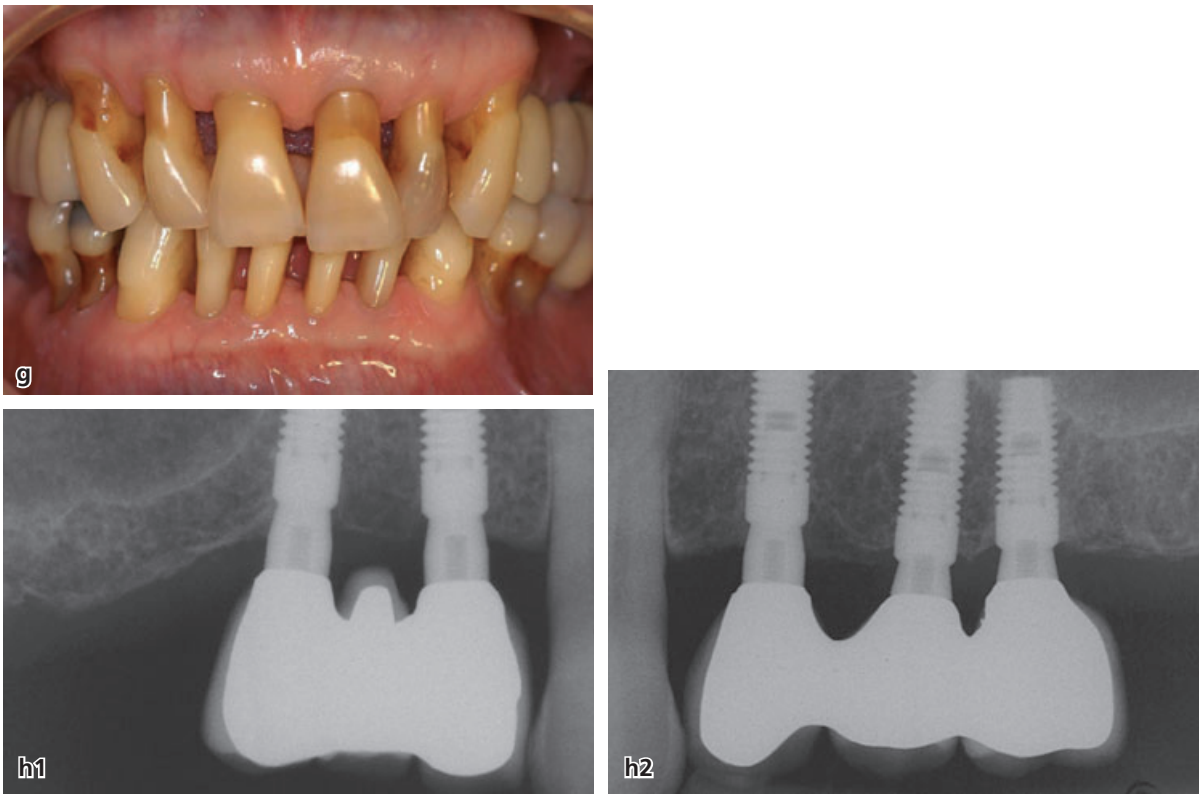
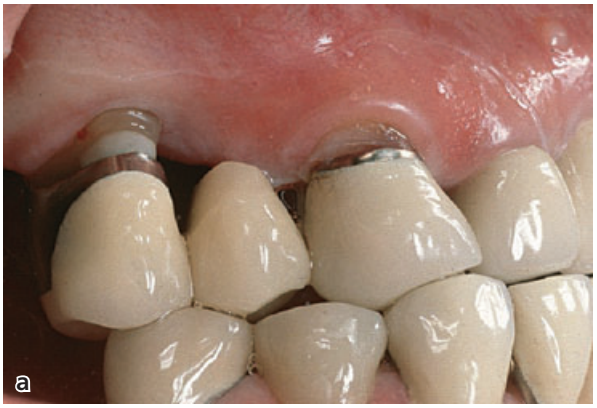


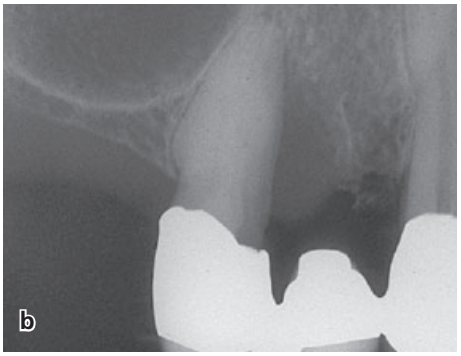
Fig. 32-1 (g,h) Clinical and radiographic status of patient H.L. 10 years after completion of the implant treatment. Note that there is no loss of bone support at the implants.

Tooth versus implant

Our treatment decisions regarding implant therapy or advanced periodontal therapy often relate to a single tooth. Figure 32-2(a,b) illustrates such a case. A 67-year-old woman presents with a localized advanced periodontal lesion at an abutment tooth in a three-unit FPD. The FPD is about 15 years old and the patient has no esthetic or functional complaints with regard to the FPD. Tooth 15 has a 10 mm deep pocket at the mesial aspect. The pocket is associated with a wide angular bone defect, and the tooth is positioned with its root in close proximity to the anterior wall of the maxillary sinus. If the tooth is extracted one may anticipate a marked remodeling of the ridge in the area, and the amount of bone available in the region might become insufficient for implant placement to support a new FPD, unless sinus elevation and bone grafting procedures are performed.

The question in the treatment planning with regard to tooth 15 is whether there is a reasonable chance to save 15 and maintain the FPD with periodontal therapy, or should the tooth be extracted and implants placed to support a new FPD? Considering the great functional value of the tooth, it was decided to perform flap elevation and to evaluate the potential for tissue regeneration. Following debridement (Fig. 32-2c), it was observed that the defect was wide and had the morphology of a combined one-/two-/three-wall defect. A regenerative approach (application of enamel matrix proteins; see Chapter 43) was selected. The healing resulted in 6 mm gain in clinical attachment level and radiographic bone fill. The amount of

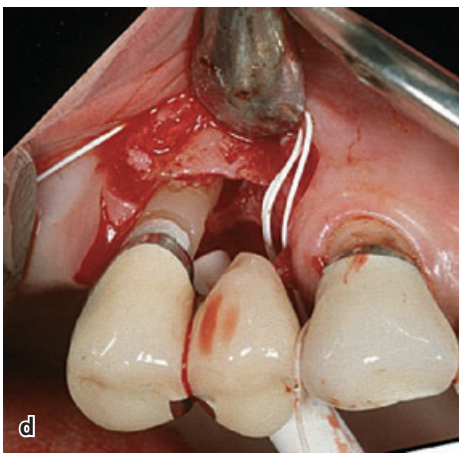


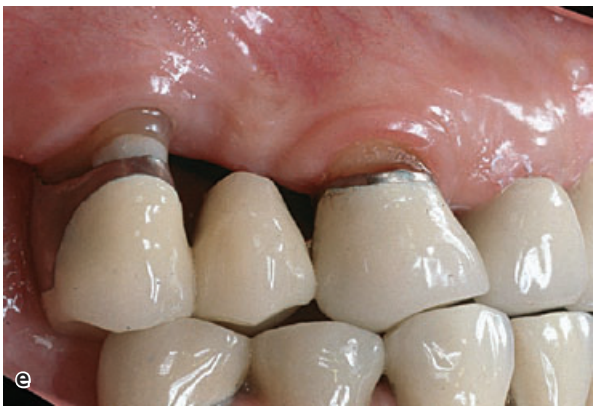


Clinical charting

Tooth	Probing Depth				Mob
	m	b	d	l	
-					
15	10	4		6	
-					
13			4		
12					

c





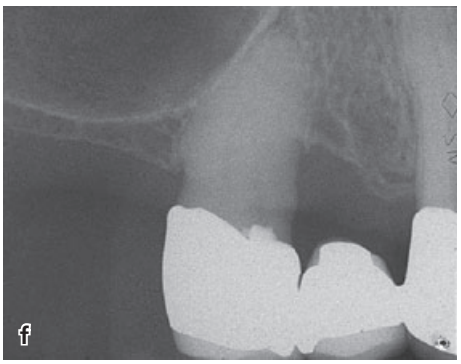


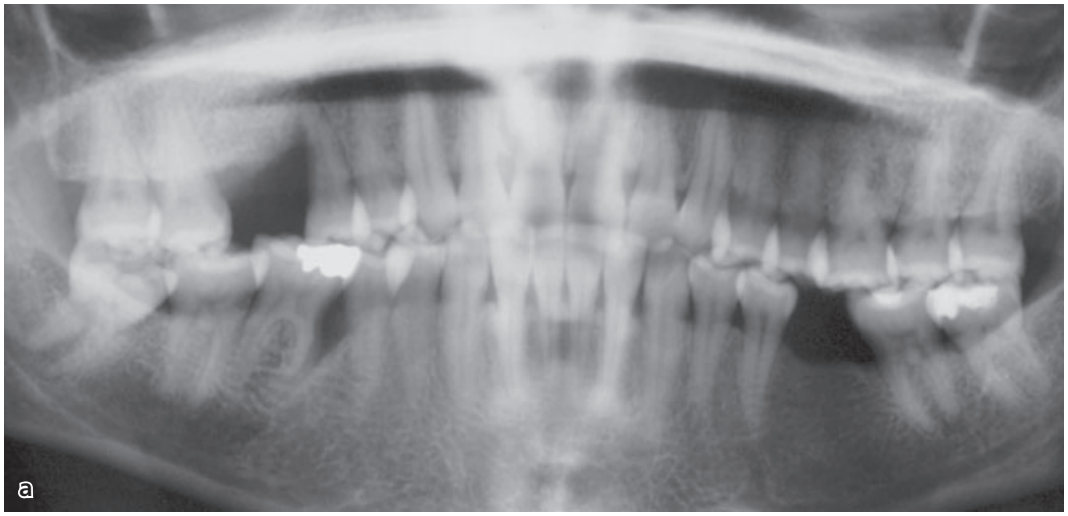
Fig. 32-2 A 67-year-old female patient with a localized advanced periodontal defect at tooth 15. (a–c) Clinical and radiographic status at the initial examination. (d) Flap elevated and the morphology of the defect can be determined as a wide combined one-/two-/three-wall defect. (e,f) Clinical and radiographic status 6 years after active treatment. Courtesy of Dr. G. Heden, Sweden.

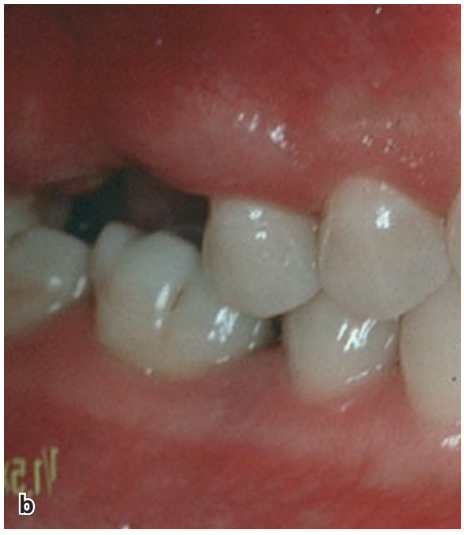
soft tissue recession was minimal as seen from the 6-year follow-up documentation (Fig. 32-2d, e).

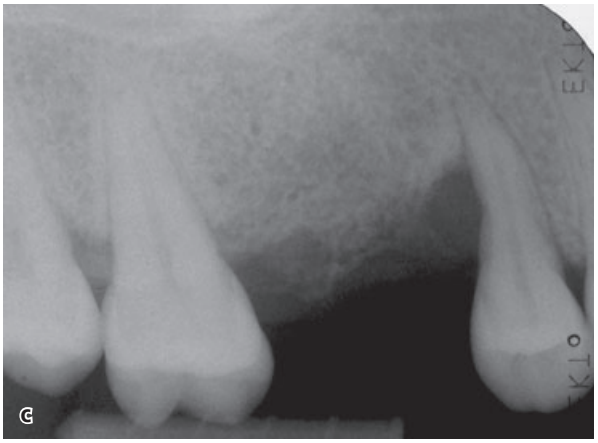
In conclusion, considering that implant therapy in this case most likely would have required sinus elevation and bone grafting to satisfy the patient's demands for esthetics and chewing function, the maintenance of 15 through proper periodontal therapy was of great benefit for the patient.

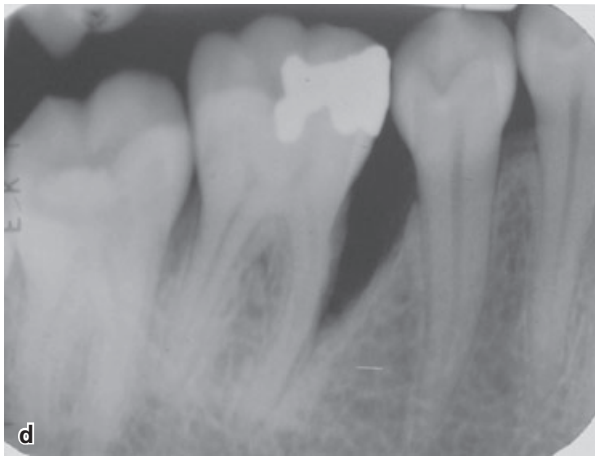
Aggressive periodontitis

Figure 32-3 shows a 22-year-old female patient diagnosed as a case of aggressive periodontitis. The first molar in the maxillary right quadrant and in the mandibular left quadrant have already been lost due to advanced periodontal destruction. The patient is asking for prosthetic replacement of the missing









Clinical charting

Tooth	Probing Depth m	b	d	l	Mob
17	4		4		
-					
15			9	5	
14					
47			4		
46	10		4	5	
45					
44					

e

Fig. 32-3 A 22-year-old female patient (A.A.) diagnosed as a case of aggressive periodontitis. (a–e) Clinical and radiographic status at the initial examination. Localized advanced periodontal lesions are diagnosed at teeth 15 and 46. (f) Radiographic view after periodontal and implant treatment. (g–j) Clinical and radiographic status 12 years after active treatment.

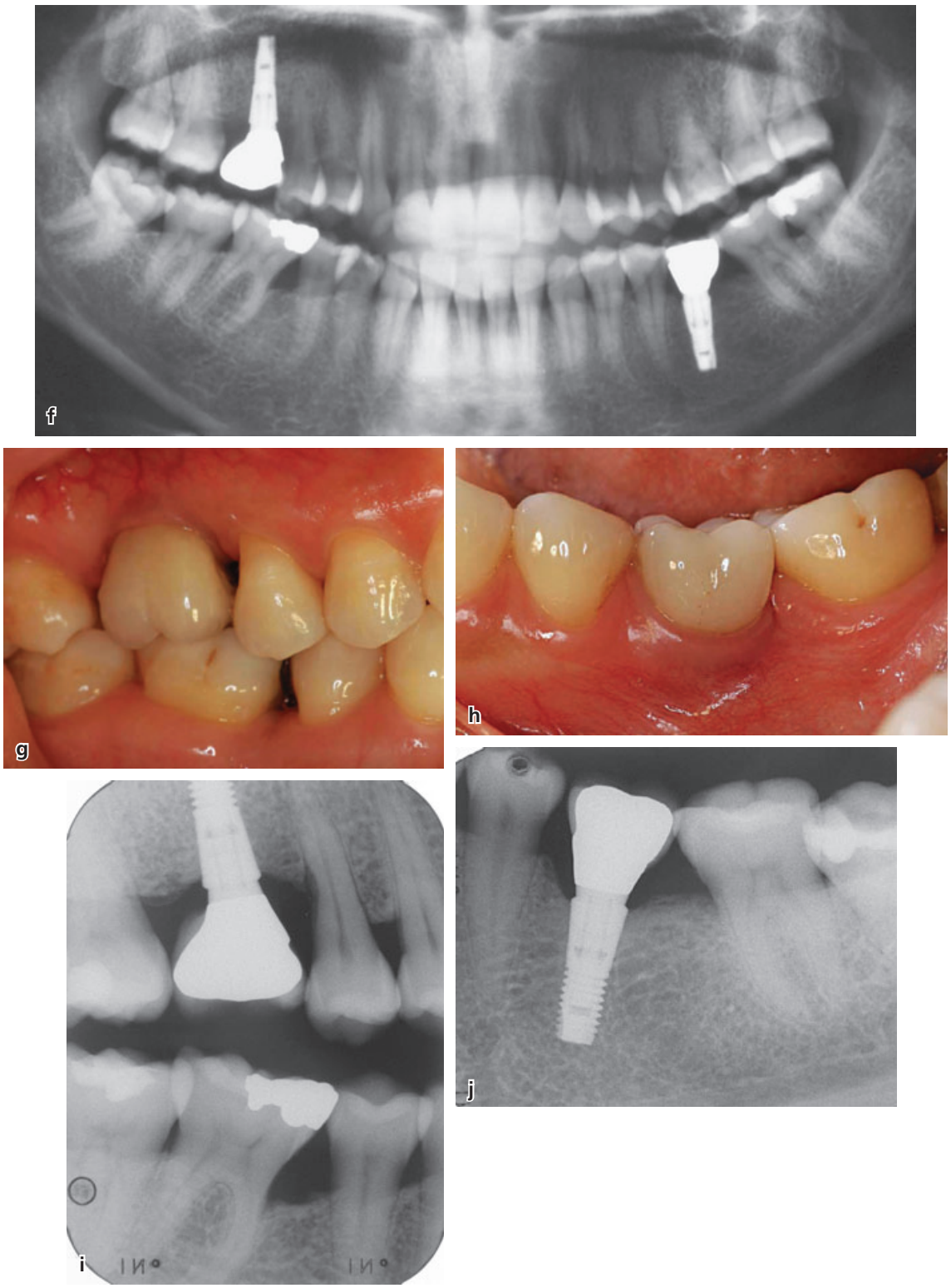


Fig. 32-3 *Continued*

teeth. The clinical examination also disclosed the presence of deep angular defects at the first molar in the mandibular right quadrant and at the second premolar in the maxillary right quadrant. It seems reasonable to plan for implant-supported restorations to replace the missing 16 and 36. The more difficult question, however, is related to the treatment of the periodontally compromised 15 and 46 (Fig. 32-3c,d). Is it possible to successfully eliminate the periodontal lesions at 15 and 46 with a good long-term prognosis for the teeth? Or should the teeth be removed and replaced with implant-supported restorations? For tooth 15 extraction may be seen as a rational decision since implant therapy is planned in the region of 16. However, from an esthetic perspective it would be preferable to maintain 15 because the crown is intact

and there is no loss of attachment or soft tissue height at the mesial aspect of the tooth (Fig. 32-3b).

Patients with aggressive periodontitis can be successfully treated, and this is well documented in the literature. Further, by applying a regenerative method in the surgical treatment of deep angular defects like those at 15 and 46, the chance of attachment gain of a magnitude of >4 mm is markedly increased (Giannobile *et al.* 2003; Murphy & Gunsolley 2003). Hence, the treatment decisions made in this case were to first establish proper infection control and then to apply a regenerative surgical approach (guided tissue regeneration) in the periodontal treatment of the lesions at 15 and 46.

Evaluation of the periodontal healing revealed closure of the pockets and *de novo* bone tissue formation. Single implant-supported restorations were subsequently performed to restore for the loss of teeth 16 and 36 (Fig. 32-3e). After completion of the active treatment the patient was assigned to a supportive care program with recall appointments once every 6 months. Fig. 32-3f–i illustrates the outcome at 12 years post treatment. The regained height of the periodontal tissue support at 15 and 46 following the active treatment was maintained over the years, and optimal bone height is seen around the single implants. The good long-term prognosis in this case is attributed to a high quality of infection control and careful monitoring during the maintenance period.

Furcation problems

Even if the goal of the treatment of patients with periodontitis should be to preserve the teeth, there may be situations when this goal seems less meaningful in relation to the patient's need for prosthetic rehabilitation. Such a situation is illustrated in Fig. 32-4(a–d). The patient is missing the two premolars in the first quadrant and the molars present with advanced periodontal destruction and through-and-through furcation involvement (grade III). The patient requests a fixed restoration to substitute for the missing premolars. A possible treatment solution following periodontal therapy could include root sepa-

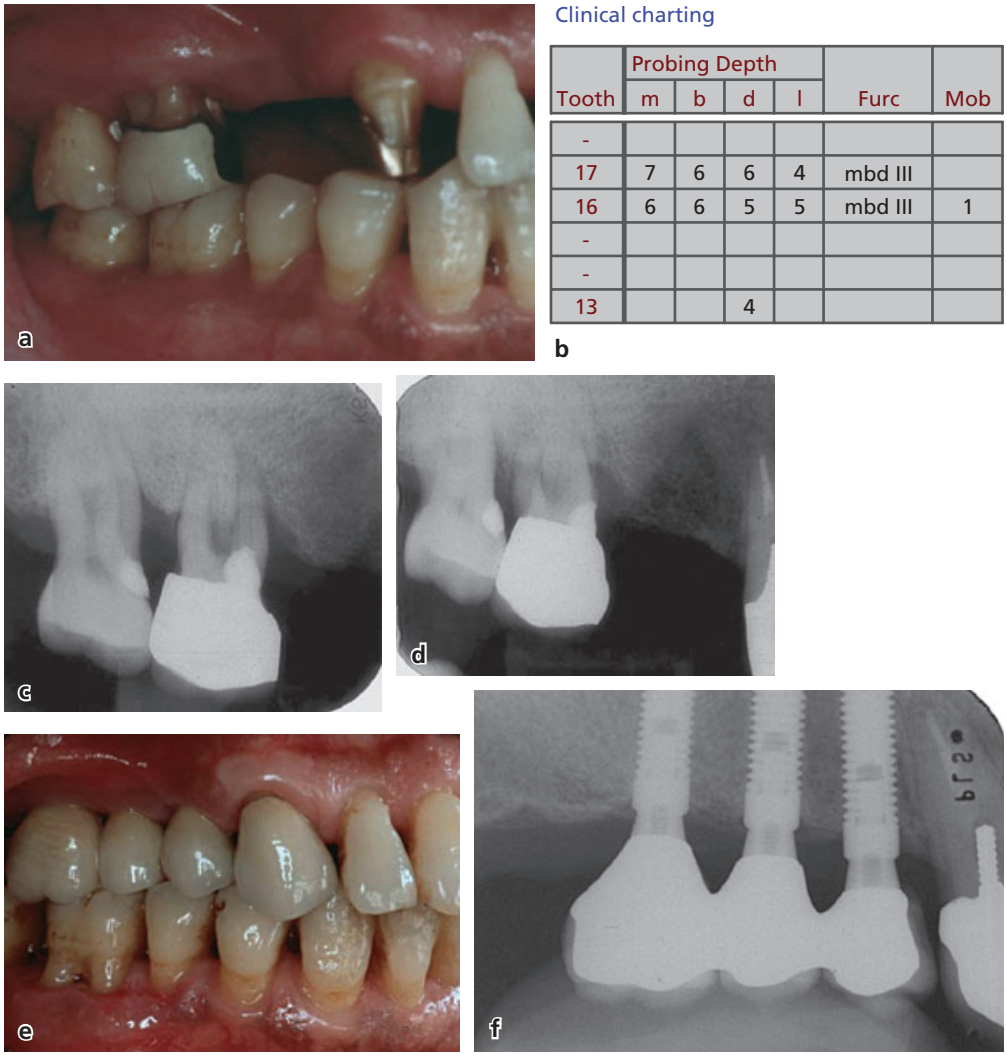


Fig. 32-4 A 52-year-old male patient with advanced periodontal destruction at remaining molars in the maxillary right quadrant. (a–d) Clinical and radiographic status at the initial examination. (e,f) Clinical and radiographic status 2 years after active treatment.

ration of the molars, after proper endodontic therapy, and the maintenance of, for example, the palatal roots of the molars to be used as posterior abutments in a fixed tooth-supported prosthesis 17 . . . 13. However, advanced inter-radicular periodontal destruction was identified by furcation probing, indicating that the palatal roots might not have enough remaining periodontal support in order to provide functional stability of a straight FPD (17 . . . 13). The clinical and radiographic examination reveals that the alveolar process in the premolar–molar region has proper dimensions for implant placement. An alternative treatment solution to satisfy the patient's demands for improved function and esthetics could therefore include implant placement to support a FPD.

The decision made in this case was to extract the two molars and, following proper periodontal treatment of the remaining dentition and establishment of adequate infection control, provide the patient with a three-unit implant-supported FPD and a single-crown restoration on tooth 13 (Fig. 32-4e,f). After completion of active treatment this patient was enrolled in a maintenance care program including recall appointments once every 4 months.

Single-tooth problem in the esthetic zone

Figure 32-5(a–e) illustrates the maxillary front tooth region of a 45-year-old female patient diagnosed with generalized chronic periodontitis. The right central incisor has severe periodontal destruction with probing pocket depths of 10–11 mm and obvious signs of inflammation at its distal and palatal surfaces. The tooth responded positively to sensibility testing. Interdental black triangles can be seen in the entire anterior tooth region because of approximal loss of periodontal attachment and soft tissue recession. Based on the results of the comprehensive examination, tooth 11 was judged to have a questionable prognosis, whereas it would be possible to resolve the periodontal lesions at the other anterior teeth by non-surgical means and improved self-performed infection control. Since the patient had a high lip line, potential recession of the soft tissue margins as a consequence of the treatment was a factor that had to be considered, particularly in relation to the treatment decision for the severely affected right central incisor. By regenerative therapy it might be possible to maintain the tooth, but will the treatment result in acceptable esthetics? The fact that the defect had a wide extension (buccally–lingually) and that the adjacent teeth presented with approximal attachment loss indicated that there was an obvious risk for loss of tissue height during healing following a surgical intervention. An alternative treatment approach could include the extraction of tooth 11 and to perform installation of a single implant. This alternative solution would also offer the possibility of correcting the position of the crown of 11. In discussing the different treatment alternatives and their consequences with the patient, it was apparent that she preferred to have the position of the tooth corrected as part of the treatment. Hence, based on the careful analysis of the esthetic problems associated with the treatment of the tooth, the decision made was to extract the tooth and make an implant-supported restoration. By the use of the crown together with a portion of the root as a pontic, support to the surrounding soft tissues during initial healing of the extraction socket was provided (Fig. 32-5f).

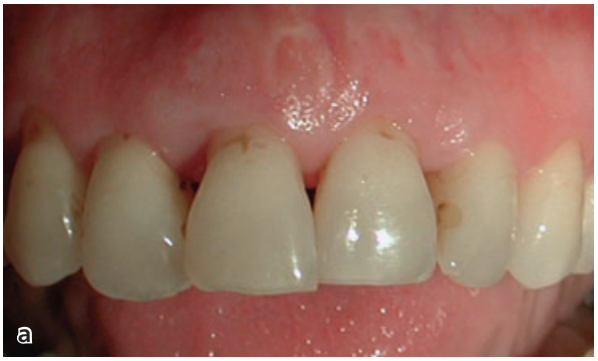
Evaluation of the outcome of the cause-related phase of therapy, which included oral hygiene instructions, plaque control evaluations, and full-mouth pocket/root debridement, disclosed no remaining pathologically deepened pockets in the front tooth region (Fig. 32-5g). The radiographic evaluation of the extraction site 2 months after the removal of 11 (Fig. 32-5h) showed a preserved bone height at the neighboring approximal tooth sites and gain of bone in the extraction socket. Clinically only minor changes had taken place in the position of the soft tissue margin at the extraction site. A single implant was installed and after 3 months the prosthetic therapy was completed.

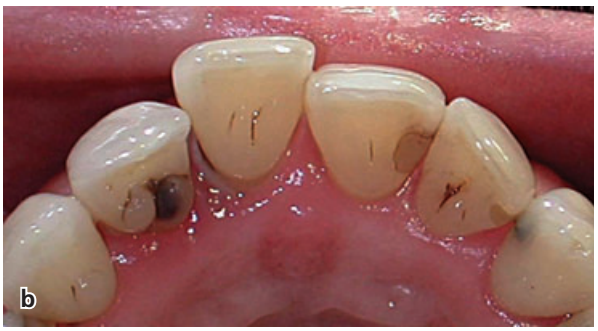
Following the completion of the active treatment, the patient was scheduled for supportive care every 6 months. Figure 32-5(i–k) shows the clinical and radiographic status at the 1-year follow-up examination. The position of the soft tissue margin is located at a similar level at the implant-supported crown and the contralateral incisor. Compared to the pre-treatment conditions (Fig. 32-5a), only minimal changes in the position of the soft tissue margins at the implant-borne restoration are evident. Overall some recession of the soft tissue margin has occurred as a consequence of the establishment of healthy marginal tissues.

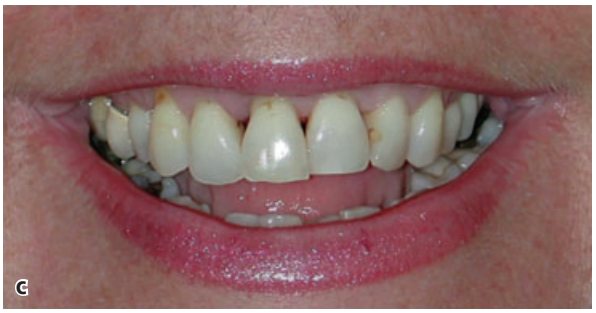
In conclusion: Although it may be possible to maintain a tooth with severe local periodontal destruction by regenerative periodontal surgery, soft tissue recession as a consequence of the treatment may render the treatment outcome unsatisfactory from an esthetic perspective. Selection of a treatment approach involving tooth extraction and implant therapy instead of periodontal therapy should be based on a careful evaluation of the potential of the various treatment approaches to satisfy the patient's demands for esthetics.

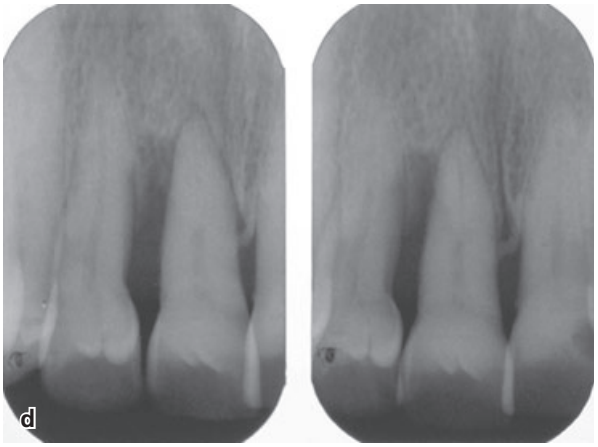
Conclusions

- The prognosis for the properly treated periodontitis-affected tooth is at least as good as that for the implant.
- An increased risk of failure of implant therapy has been reported for periodontitis-susceptible patients.
- Proper infection control is a critical factor for the long-term success of implant therapy in the periodontally compromised patient.





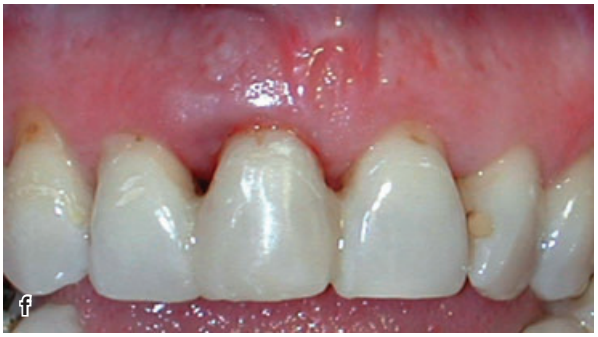




Clinical charting

Tooth	Probing Depth				Mob
	m	b	d	l	
13	4				
12	5		4	4	
11	4	5	11	10	1
21	5				
22	4				
23			4		

e



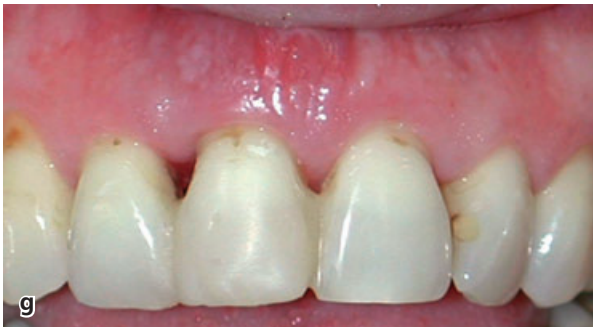
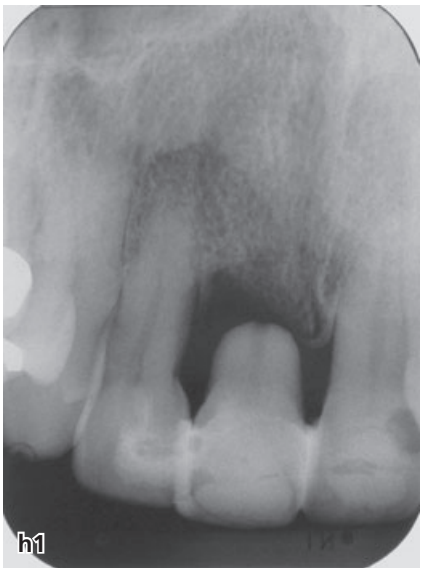
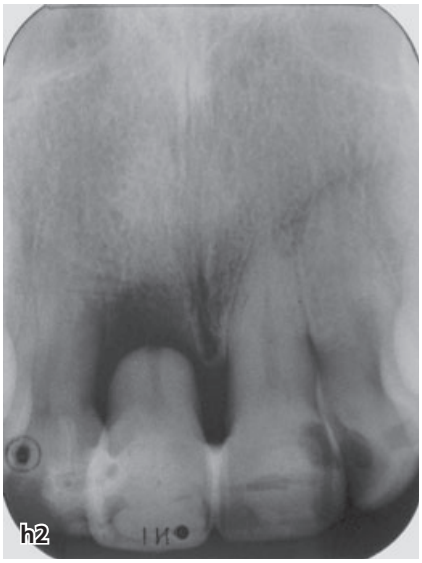
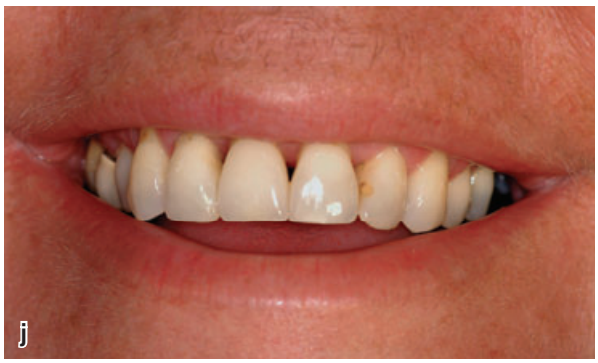


Fig. 32-5 A 45-year-old female patient with generalized chronic periodontitis. (a–e) Clinical and radiographic status of the maxillary anterior teeth at the initial examination. The right central incisor has severe periodontal destruction with probing pocket depths of 10–11 mm. (f) Tooth 11 was extracted and the tooth was reshaped and fixed to the neighboring teeth to support the soft tissues during the initial healing of the extraction socket. (g,h) Clinical and radiographic status 2 months post extraction when the implant placement surgery was performed. (i–k) Clinical and radiographic status 1 year after completion of the periodontal and implant treatment.







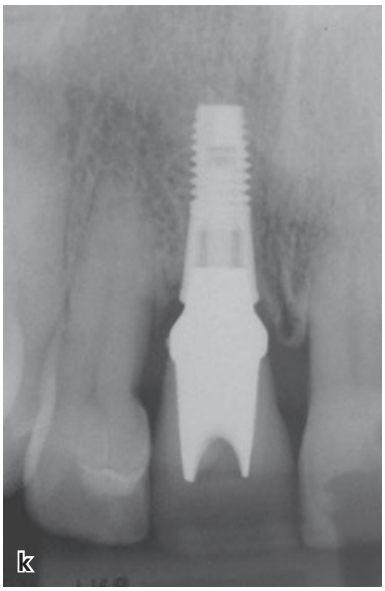


Fig. 32-5 *Continued*

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Chapter 33

Systemic Phase of Therapy

Niklaus P. Lang and Hans-Rudolf Baur

Introduction

The systemic phase of periodontal therapy should be concerned with general health implications of periodontal diseases and periodontal treatment. While the former aspects are described in Chapters 12, 13, 16, and 21, the latter aspects are presented in this chapter.

The systemic phase of periodontal therapy is designed to protect the patient against unforeseen systemic reactions, to prevent complications affecting the general health of the patient and to protect the health care providers from (predominantly infectious) hazards in conjunction with the treatment of risk patients.

In order to adequately plan the systemic phase, results from a health questionnaire (Chapter 26) filled in by the patient in the waiting area, the family and social history, the general medical and, in particular, the smoking history have to be evaluated. Also, any extra- and intraoral findings pertinent to the patient's systemic health have to be considered.

The systemic phase of periodontal therapy encompasses:

- Precautions for protecting the general health of the dental team and other patients against infectious and contagious diseases
- Protection against potentially harmful systemic effects of routine therapy
- Making allowances for systemic diseases or disorders that may influence the etiology of the patient's periodontal conditions, the healing potential, and the systemic response to therapy
- Controlling anxiety and low pain threshold
- Risk assessment and considerations of systemic supportive therapy
- Smoking counseling and instituting tobacco use cessation programs.

Protection of the dental team and other patients against infectious diseases

As a rule, routine periodontal therapy should be postponed in a patient with an active contagious state of a disease until the patient has received adequate medical treatment. Given the fact that patients may not always be aware of such a state or that all manifestations of disease may have abated, but the patient may still be carrier of infectious agents, routine dental treatment should be carried out under special precautions against transmission of the most serious diseases being transmitted orally. These include infectious hepatitis (Levin *et al*. 1974), HIV infection, and venereal diseases (Chue 1975). Hygiene in the dental office, therefore, has to address the most contagious level of infective agents, the hepatitis virus, and cope with the prevention of the transmission of these infections. As a minimal precaution, the wearing of rubber gloves and mouth masks is strongly recommended for all dental therapy in all patients. Also protective glasses for both the therapist and the patient should be worn during procedures generating aerosols.

Herpes simplex virus (Nahmias & Roizman 1973) and tuberculosis are other infectious diseases with a high transmission potential. Special precautions should be observed in patients with a recent history (2–3 years) of infectious hepatitis, although the dental team may be vaccinated against hepatitis. If the medical history and the oral examination reveal that the patient may have overt or hidden systemic

disease, she/he should be referred for medical examination prior to enrolling the patient into comprehensive periodontal therapy.

Protection of the patient's health

A number of systemic conditions may affect treatment planning, although there may be no direct relevance in the pathogenesis and healing potential of periodontal lesions. Since over 50% of all patients over 40 years of age may have systemic conditions or take medications affecting periodontal therapy, these aspects have to be carefully appraised prior to instituting therapy.

For patients with life-threatening systemic conditions, such as coronary insufficiency or hypertensive heart disease, the patient's physician should be consulted about appropriate patient management and whether treatment should be performed in a hospital or clinic rather than a private practice setting. If the dental office is considered to be the adequate environment for treating these patients, short appointments should be planned and treatment performed with complete pain control using local anesthesia without any or with minimal vasoconstrictive drugs.

Prevention of complications

The complications most commonly encountered in the dental office are:

- Infection
- Bleeding
- Cardiovascular incidents
- Allergic reactions.

These may be prevented if appropriate precautions are taken. Hence, gaining awareness of possible complications from a medical history is an important step for treatment planning and total patient care.

Infection, specifically bacterial endocarditis

Patients with cardiac disease or disorders involving the endocardium are susceptible to endocarditis as a result of blood-borne infection. Such conditions include rheumatic heart disease, congenital valvular heart defects, aortic valvular diseases, and collagen diseases involving the endocardium. In addition, patients wearing prosthetic heart appliances belong to this risk group.

The major procedures thought to be the cause of bacterial endocarditis are extractions and scaling and/or root planing leading to significant bleeding and possible bacteremia (Durack 1995). Hence, it is not surprising that national societies have issued guidelines for antibiotic prophylaxis against bacterial endocarditis (USA: Dajani *et al*. 1997; UK: Gould *et al*. 2006; FDI, 1987). The common belief is that a bacteremia occurs only when dental procedures cause bleeding and does not occur when there is no bleeding. Hence, procedures such as extractions, root instrumentation, and periodontal and implant surgical procedures would require antibiotic prophylaxis, while for example the placement of fillings does not. This hypothesis was addressed in a study in children in which 14 various dentogingival manipulative procedures were evaluated (Roberts *et al*. 1997). It was clearly demonstrated that no relationship existed between the existence of bleeding and bacteremia. However, the number of oral organisms isolated from the blood where bleeding was present was statistically significantly higher than when there was no bleeding. It was concluded that the cumulative exposure to bacteremia is significantly greater from "everyday" procedures, when compared to dental procedures and hence, the cause of bacterial endocarditis may be attributable to such cumulative everyday exposures that are often thousands to millions of times greater than that occurring following surgical procedures, such as extractions of teeth (Roberts 1999).

Antibiotic prophylaxis to prevent bacterial endocarditis is predominantly based on anecdotal and circumstantial evidence suggesting a causal association between various procedures and bacteremia (Baltch *et al*. 1982). A case study, however, did not identify a link between endocarditis and dental treatment (Guntheroth 1984; Strom *et al*. 1998). Moreover, accumulating evidence suggests that bacteremia may easily be produced, e.g. by toothbrushing or chewing, rather than by single procedures causing bleeding. Hence, endocarditis causation has shifted from procedure-related bacteremia to cumulative or "everyday" bacteremia (Gould *et al*. 2006).

Indeed, a recent systematic review of the Cochrane Collaboration (Oliver *et al*. 2004) concluded that there was no conclusive evidence to support the use of prophylactic penicillin to prevent bacterial endocarditis in invasive dental procedures. This review did not find any randomized controlled clinical trials, any controlled clinical trials or any cohort studies. From a total of three case–control studies (Imperiale & Horowitz 1990; Van der Meer *et al*. 1992; Lacassin *et al*. 1995), only one study (Van der Meer *et al*. 1992) complied with the inclusion criteria. Details of 349 individuals who developed definite native-valve endocarditis in the Netherlands within a 2-year period were collected. Controls had not been diagnosed with endocarditis, but had one of the cardiac conditions and were outpatients of one of five hospitals. Controls were matched for age and had undergone dental procedure within 180 days of their interview. No significant protective effect of antibiotic prophylaxis was seen against endocarditis.

It has to be realized, however, that clinicians feel bound by guidelines and medico-legal considerations to provide antibiotic prophylaxis rather than by the best scientific evidence available. Ethically, practitio-

Table 33-1 Recommendations of the British Society for Antimicrobial Chemotherapy (BSAC) for prophylaxis of bacterial endocarditis

Population	Age			Timing of dose before procedure
	>10 years	≥5 to <10 years	<5 years	
General	Amoxicillin 3 g *per os*	Amoxicillin 1.5 g *per os*	Amoxicillin 750 mg *per os*	1 hour
Allergic to penicillin	Clindamycin 600 mg *per os*	Clindamycin 300 mg *per os*	Clindamycin 150 mg *per os*	1 hour
Allergic to penicillin and unable to swallow capsules	Azithromycin 500 mg *per os*	Azithromycin 300 mg *per os*	Azithromycin 200 mg *per os*	1 hour

From Gould *et al*. (2006).
Where a course of treatment involves several visits, the antibiotic regimen should alternate between amoxicillin and clindamycin.
Pre-operative mouth rinse with chlorhexidine gluconate 0.2% (10 ml for 1 minute).

Table 33-2 British Society for Antimicrobial Chemotherapy (BSAC) Prevention of Infective Endocarditis Guidelines Information for Patients and Parents February 2006

A BSAC group of experts has spent a lot of time carefully looking at whether dental treatment procedures are a possible cause of infective endocarditis (IE) (sometimes called bacterial endocarditis (BE)), which is infection of the heart valve.

After a very detailed analysis of all the available evidence they have concluded that there is no evidence that dental treatment procedures increase the risk of these infections.

Therefore, it is recommended that the current practice of giving patients antibiotics before dental treatment be stopped for all patients with cardiac abnormalities, except for those who have a history of healed IE, prosthetic heart valves and surgically constructed conduits.

The main reasons for this are the lack of any supporting evidence that dental treatment leads to IE and the increasing worry that administration of antibiotics may lead to other serious complications such as anaphylaxis (severe allergy) or antibiotic resistance.

The advice from the BSAC is that patients should concentrate on achieving and keeping a high standard of oral and dental health, as this does reduce the risk of endocarditis. Help for this will be provided by your Dental Professional.

British Society for Antimicrobial Chemotherapy (BSAC), 2 February 2006

ners need to discuss the potential benefits and harms of antibiotic prophylaxis with the patients and their cardiologists before the decision is made about administration (Oliver *et al*. 2004). Considering the change in paradigms regarding bacterial endocarditis, a task force of the British Society for Antimicrobial Chemotherapy has recently published new guidelines (Gould *et al*. 2006) (Table 33-1). According to these, the practice of giving patients antibiotics is reserved for those patients with a history of healed bacterial endocarditis, prosthetic heart valves, and surgically constructed conduits, while patients with cardiac abnormalities should no longer receive antibiotic prophylaxis before dental procedures. A patient information form has also been published (Table 33-2).

Bleeding

Due consideration must be given to patient on anticoagulant medication or patients on preventive anticoagulant drugs such as salicylates. For the first group of patients, a consultation with the patient's physician is indispensable. Especially prior to periodontal or implant surgical procedures, temporary adjustment of the intake of anticoagulant medication may have to be initiated in cooperation with the physician. Careful planning and timing of these procedures is mandatory.

Preventive anticoagulant therapy does not generally create problems for routine dental therapy, including surgical procedures, although consultation with the patient's physician still is advisable.

Individuals with known cirrhosis of the liver, or even patients with high alcohol consumption over many years without diagnosed cirrhosis, are at a potential risk for bleeding complications during periodontal and/or implant surgery, as their clotting mechanisms may be affected (Nichols *et al*. 1974). Again, medical consultation is recommended prior to periodontal treatment of such patients.

Extra precautions against bleeding should be taken when treating patients with any kind of blood dyscrasia or hemophilia. Following mandatory consultation with the patient's physician, it is recommended to render treatment in small segments (only a few teeth being instrumented at each visit) and to apply periodontal dressings over the treated area, even if the treatment only consisted of root instrumentation. With systematic periodontal treatment and institution of efficacious oral hygiene measures, the annoying symptom of oral bleeding can often be controlled irrespective of the patient's bleeding disorder.

Cardiovascular incidents

Cardiac patients are often treated with anticoagulants and, hence, may develop bleeding problems (as indicated above), especially if given drugs (e.g. aspirin, indomethacin, sulfonamide, tetracycline) that interact with coagulation. Other cardiovascular drugs (antihypertensive, anti-arrhythmic, diuretic) are often used in these patients which may increase the danger of hypotensive episodes during dental treatment.

Stress associated with dental procedures may precipitate anginal pain or congestive heart failure in patients with cardiovascular disease. Therefore, every effort should be made to keep procedures short and control anxiety and pain in this patient population.

Allergic reactions and drug interactions

Full knowledge of the patient's known allergies and the medications administered is essential before any drug is prescribed, administered or used during treatment. The most common allergic reactions encountered in the dental office are allergies to some local anesthetics (Novocain®), penicillins, sulfa derivatives, and disinfectants, such as iodine. In case of known allergies, such drugs have to be avoided. A consultation with the patient's physician is advisable to discuss the possible administration of replacement drugs.

Many patients – over 90% over the age of 60 years – regularly take medications for various systemic conditions, special attention has to be devoted to possible drug interactions, especially in the elderly. Drugs prescribed as part of periodontal therapy or used during treatment may interfere with the effectiveness of drugs the patient is already taking or create hazardous or synergistic action with such drugs. Hence, no new drugs should be prescribed without fully understanding their possible interaction with drugs already in use. Dentists should never change an existing drug therapy without prior discussion and preferably written consent of the physician.

Many patients regularly take tranquilizers and antidepressant drugs that have the potential for summation and synergistic effects with drugs that may be used during periodontal therapy. Moreover, the interaction with and potentiation of these drugs with alcohol should be discussed with the patient.

Systemic diseases, disorders or conditions influencing pathogenesis and healing potential

All possible attempts should be made to alleviate the effects of systemic diseases, such as blood disorders and diabetes mellitus, as much as possible before definitive periodontal treatment is initiated. However, cause-related therapy may easily be carried out and generally results in remarkable success even during active stages of these systemic conditions. How far the treatment plan should progress with respect to pocket reduction and/or regenerative procedures depends on the seriousness of the patient's systemic involvement and likewise, to a great extent, on the potential threat to the patient's health from incomplete periodontal therapy.

Diabetes control, as an example, may be facilitated by successful control of the periodontal infection (Grossi *et al*. 1997; Genco *et al*. 2005). Thus, periodontal treatment may have a beneficial effect on the systemic health of the patient (see Chapter 21). Palliative treatment of advanced periodontitis with furcation involvement and residual deep pockets that cannot be reduced should not be undertaken for such patients. Rather the involved teeth with repeated abscesses and pus formation should be extracted if needed to accomplish infection control.

Clinical experience indicates that the healing response of the periodontal tissues is as good in diabetic as in non-diabetic patients provided that the diabetes is fairly well controlled. However, juvenile diabetics may have angiopathic changes associated with a lowered resistance to infection that may require the use of antibiotics following periodontal or implant surgery. With controlled diabetes, premedication with antibiotics is not indicated. Hypoglycemia may become aggravated by the stress of periodontal surgery and, hence, precautions have to be taken to avoid hypoglycemic reactions in such patients.

Patients taking therapeutic doses of cortisone over a long period of time may yield considerable metabolic effects with systemic manifestations of a reduced rate of fibroblastic activity and hence, a lowered resistance to infection during wound healing. Nevertheless, such patients can be treated successfully by regular cause-related therapy with no significant delay in healing. The use of antibiotics is not recommended for these patients, unless there is a serious infectious condition in the mouth associated with the development of fever.

Control of anxiety and pain

Many patients interested in maintaining a healthy dentition do not regularly seek dental care because of anxiety and apprehension related to such treatment. Since modern dentistry offers a variety of effective means for controlling pain and apprehension, patients should no longer suffer from dental treatment. During history taking and the oral examination, the patient's profile regarding anxiety and pain thresholds should be explored.

Prior to therapy, it may be advisable to premedicate an apprehensive patient using diazepams (Benzodiazepine, Valium®, 2–5 mg) to be taken the night before, in the morning and half an hour before an

extensive and/or surgical procedure. Painless dental care can be achieved by carefully applying local anesthetics.

Post-operative analgesic medication, such as non-steroidal anti-inflammatory drugs (NSAIDs) with analgesic and antipyretic properties are recommended. Diclofenac potassium, the active ingredient of Voltaren® Rapide, inhibits prostaglandin synthesis by interfering with the action of prostaglandin synthetase. Following any kind of periodontal and implant surgery, 50 mg twice daily of Voltaren® Rapide is administered for 3 days. In addition, further adjunctive pain killers (Mefenaminic acid, e.g. Ponstan®, 500 mg not more than every 6–8 hours) may be prescribed depending on the individual patient's need and pain threshold.

Favorable personality interactions between the patient, the therapist, and the entire office staff may contribute to the control of anxiety, but may require more time and consideration than that allocated to the routine patient.

Smoking counseling

Cigarette smoking constitutes the second most important risk factor in the etiology and pathogenesis of periodontal diseases after poor oral hygiene standards. A careful assessment of the patient's smoking history is therefore indispensable. Depending on the duration of the exposure to tobacco smoking, daily consumption, and the patient's periodontal status, smoking counseling has to be undertaken as one of the primary measures. In all patients that smoke, the contributory role of tobacco consumption to the pathogenesis of periodontitis has to be addressed. Depending on the patient's response, smoking cessation programs may be instituted. Short-term interventions lasting 3–5 minutes using motivational interviewing techniques (Chapter 34) may be included during the initial phase of periodontal therapy. If a heavy smoker is ready to quit the habit, professional cessation programs may be the appropriate measures to take. Smoking counseling is further discussed in Chapter 34.

Conclusions

The goals of the systemic phase of periodontal therapy are to appraise the aspects that may require protection of both the dental team and the systemic health of the patient. Infection control in the dental office plays a central role. Protecting the patient against presumptive complications, such as infection, especially bacterial endocarditis, bleeding, cardiovascular incidences, and allergies, requires in-depth knowledge of the patient's medical history and oral examination.

Bacterial endocarditis prophylaxis is nowadays reserved for those patients with a history of a healed bacterial endocarditis, prosthetic heart valves or surgically constructed conduits, while the use of antibiotics before dental treatment is not necessary for patients with cardiac abnormalities. Patients with systemic diseases such as diabetes mellitus or cardiovascular diseases usually are treated with a number of medications that may interact with drugs prescribed during periodontal therapy. Precautions should be taken, and consultation with the patient's physician prior to systematic periodontal therapy is recommended.

It has to be realized that periodontal treatment may have a beneficial effect on the systemic health of the patient as well. Glycemic control may be facilitated in diabetics if proper periodontal therapy is rendered.

Finally, smoking counseling is part of modern periodontal treatment owing to the fact that, after inadequate oral hygiene standards, cigarette smoking constitutes the second most important risk factor for periodontitis.

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Part 11: Initial Periodontal Therapy (Infection Control)

Chapter 34

Motivational Interviewing

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The importance of behavioral change counseling in periodontal care

Periodontal health is supported by appropriate behaviors such as regularly self-performed plaque control, avoidance of tobacco, and consumption of a healthy diet. Inadequate oral hygiene, tobacco use, and uncontrolled diet in type 2 diabetes mellitus, on the other hand, are shown to have a destructive impact on periodontal tissues. The prevention and control of periodontal disease needs to be addressed on both the population and the individual level. Efficient public health approaches consider the entire population and focus on health issues that present the largest burden within a community. The dental community involved with oral health care should gain an understanding of the health effects of inappropriate behaviors in order to successfully target prevention and disease control. As a consequence, services for primary and secondary prevention on an individual level oriented towards the change of inappropriate behavior become a professional responsibility for all oral health care providers.

Data from epidemiologic studies consistently reveal the prevalence of periodontal disease in more than 50% of the adult population (Albandar *et al*. 1999; Albandar 2002). In addition to the causal relationship with dental biofilms, a positive association with tobacco use has been documented (Bergstrom 1989; Haber *et al*. 1993; Tomar & Asma 2000). Tobacco use contributes to the global burden of public health with almost one third of the adult population using various forms of tobacco and an increasing number of annual deaths from tobacco-related diseases. Moreover, dietary excess has been shown to significantly impact chronic diseases including obesity, cardiovascular diseases, type 2 diabetes, cancer, osteoporosis, and oral diseases (Petersen 2003).

There is growing evidence that the patient's individual behavior is seen to be influential or even critical for the success of periodontal therapy; since the results of periodontal therapy appear to be limited in patients who especially lack appropriate behavior. In a recent literature review by Ramseier (2005) it was shown that second to plaque control, smoking cessation was the most important measure for the management of chronic periodontitis. Therefore, it appears to be reasonable in clinical concepts for periodontal care to (1) include assessments of patient behavior, and (2) if necessary apply effective behavior change counseling methods.

Traditional periodontal care includes the instruction of proper oral hygiene methods. In practice, as an example, a demonstration of a suitable toothbrushing method is given to the patient, followed by recommendations of both the frequency and the time spent per brushing. Past and recent studies on the effectiveness of oral hygiene instructions consistently revealed that the patient adherence to a proper daily oral hygiene regime generally remains poor (Johansson *et al*. 1984; Schuz *et al*. 2006). The reinforcement of oral hygiene habits through additional appointments can compensate somewhat for the ineffectiveness of one-time or repeated oral hygiene instructions. However, due to weak patient adherence, visits for supportive periodontal care are often cancelled,

resulting in a lack of professional maintenance care and the potential recurrence of periodontal disease (Wilson *et al*. 1984; Demetriou *et al*. 1995; Schuz *et al*. 2006).

Unfortunately, many health education approaches seem to be inefficient in accomplishing long-term change, potentially leading to frustration of both the patient and the clinician. The following hypothetical dialogue between a clinician (Dr) and a patient (P) illustrates how using a directive advice-oriented method for behavior change counseling can lead to an unproductive conversation and little likelihood of change by the patient:

Dr Are you flossing regularly?
P Yes, but not as often as I should.
Dr I strongly recommend that you floss every day. There are serious consequences if you don't floss frequently enough.
P I know I should do it more often, but . . .
Dr It is really important!
P I know . . . . . but I don't have the time!

Since the clinician doesn't offer the patient a chance to discuss the reasons to floss as well as the patient's perceived barriers to flossing, the conversation reaches an impasse and behavior change will be unlikely. In certain cases, the patient may even be blamed for poor compliance and further oral health education may be seen to be pointless.

There is a shortage of evidence in both the dental and behavioral literature on effective methods for behavior counseling in periodontal care, in particular regarding:

- Individual oral hygiene instructions for optimal oral hygiene
- Effective tobacco use prevention and cessation counseling to help abstain from tobacco
- Appropriate dietary counseling for a healthy diet.

In order to get reliably effective outcomes in periodontal care, it may be necessary to apply different behavior change counseling methods for each individual behavior. According to the best available evidence for oral hygiene instructions, the repeated demonstration of a cleaning device may be applied, while for tobacco use cessation, in addition to pharmacotherapy, the method of the five As (ask, advise, assess, assist, arrange) may be used (Fiore 2000). Additionally, type 2 diabetic patients or patients with a high carbohydrate diet may be referred to nutritionists for dietary counseling. From a practical point of view, however, it may be complicated and even discouraging to approach the periodontal patient with a variety of different methods targeting the same purpose: establishing appropriate behavior to improve the outcomes of both periodontal therapy and long-term supportive periodontal care.

Hence, aiming for simplicity, it may be preferable to apply one single method for behavior change counseling in periodontal care that is shown to be effective in both primary and secondary prevention of oral diseases. This method should be:

- Based on the best available evidence
- Applicable to oral hygiene behavior, tobacco use prevention and cessation, and dietary counseling
- Suitable for implementation by the dental practice team in a cost-effective way.

Development of motivational interviewing

As discussed, health *education* efforts provided by practitioners are frequently ineffective in changing patient behavior. Considerable behavioral research suggests that the root of this common problem can be traced back to a false assumption inherent in the health education approach. Specifically, that behavior change is simply a function of a patient having the requisite knowledge or understanding, and that it is up to the practitioner to provide the relevant information. Motivational interviewing (MI), in contrast, is based on a different assumption of human behavior change. It assumes that the knowledge is insufficient to bring about behavior change and that, instead, sustained behavior change is much more likely when change is connected to something the individual values. In other words, motivation is elicited "from within the patient" rather than externally imposed upon the patient by a practitioner. In MI, the assumption is that individuals have "within them" their own reasons for changing and that the role of the practitioner is to elicit and reinforce these reasons.

MI originated in the field of addictive behavior but has increasingly been applied to a wide variety of other behavior change problems, including health behaviors such as tobacco use and diet and exercise (Burke *et al*. 2004; Hettema *et al*. 2005). MI principles and methods have also been specifically adapted for brief interventions in medical settings (Butler *et al*. 1999; Rollnick *et al*. 1999) and have recently been tested in a dental setting (Weinstein *et al*. 2006).

History of motivational interviewing

William Richard Miller, the originator of MI, developed the method in response to his observations regarding the treatment of patients with alcohol problems in the 1970s. The standard approach to the treatment of alcoholic patients was confrontational, and failure of treatment was attributed either to "denial", seen as a personality deficit on the part of the client, or the failure of the client to engage with the program (Miller 1983). In contrast, he observed that the research literature suggested that positive outcomes were mostly related to a strong bond or "therapeutic alliance" between the counselor and the patient. Miller began to test his empathy-centered treatments on problem drinkers and found that change was occurring more quickly than with traditional methods (Moyers 2004). This brief treatment which used the *therapeutic alliance* and *empathy* to engender the client's inherent motivation to change was first described in an article by Miller in Behavioural Psychotherapy (1983). Subsequently Miller met Stephen Rollnick, the co-founder of the MI method, who had been concentrating on ambivalence, or the extent to which the client envisioned the pros and cons of changing. Miller and Rollnick began to explore the use of language during MI, concentrating on the elicitation of client "change talk" to promote behavior change. In 1991, Miller and Rollnick published the first edition of "*Motivational Interviewing: Preparing People to Change Addictive Behaviors*" in which they provided a detailed description of the approach. Since then there has been an explosion in the research and application of MI with many researchers addressing the applicability of the method to addressing health behavior change (Resnicow *et al*. 2002).

What is motivational interviewing?

MI has been defined as "a client-centered, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (Miller & Rollnick 2002). The client-centered element refers to the emphasis that is placed on understanding and working from the perspective of the patient and their view of what it means to make a behavior change. For example, rather than a clinician simply telling a patient about the benefits of quitting smoking (from the practitioner perspective), the practitioner invites the patient to describe *his or her own view* of the advantages and disadvantages of quitting continuing to smoke. Although the patient's perspective is central, because MI is also directive, the practitioner takes deliberate steps to facilitate a particular behavioral outcome. For example, without ignoring patient concerns about changing, the practitioner selectively reinforces and encourages elaboration of any patient statements that are oriented toward the possibility or benefits of making a change. By eliciting and elaborating upon the patient's own reasons for change the motivation for change that is fostered is intrinsic or internal, rather than externally imposed. This approach rests on the assumption that individuals are almost always ambivalent about changing their behavior (i.e., it is almost always the case that individuals can identify both pros and cons of changing). MI practitioners therefore attempt to enhance intrinsic reasons for change by facilitating an exploration and resolution of the patient's underlying ambivalence.

Evidence for motivational interviewing

Because MI was initially developed for the treatment of addictive behavior, particularly alcohol addiction, the bulk of empirical studies has been conducted in this area. Nevertheless, the explosion in the application (Hettema *et al*. 2005) of MI to other areas of behavior change has been sufficient that there are now four published meta-analyses (Burke *et al*. 2003, 2004; Hettema *et al*. 2005; Rubak *et al*. 2005), the more recent of which include more than 70 clinical trials. Generally, the meta-analyses indicate that MI-based interventions are at least equivalent to other active treatments and superior to no-treatment or placebo controls for problems involving addictive behavior (drugs, alcohol, and gambling), adoption of water purification/safety technology, diet and exercise, and treatment engagement, retention, and adherence. Effect sizes are on average in the small to medium range but are highly variable (Hettema *et al*. 2005). Of particular relevance to dental settings where only brief counseling is feasible, is that MI-based interventions are just as efficacious as alternative active interventions despite involving significantly less contact time, suggesting that MI may be a particularly efficient method of counseling (Burke *et al*. 2004). Rubak *et al*. (2005) report that in brief encounters of 15 minutes, 64% of studies showed an effect. In addition, when the intervention was delivered by physicians an effect was observed in approximately 80% of studies suggesting that it is feasible for professionals who are not counseling experts to deliver effectively MI in brief encounters.

Studies of MI for tobacco use cessation are also of particular relevance. Although fewer studies were available, the meta-analyses cited above did not find

MI to be efficacious for smoking cessation. Nevertheless, most of the smoking cessation studies can be criticized for various reasons, including not having procedures to ensure and document fidelity to MI principles by the interventionists (Colby *et al*. 1998; Butler *et al*. 1999; Stotts *et al*. 2002; Wakefield *et al*. 2004), testing the intervention with smokers who are already motivated to quit which may be counterproductive (Smith *et al*. 2001; Ahluwalia *et al*. 2006), and not providing sufficient guidance on *how* to quit once participants were motivated by MI (Butler *et al*. 1999; Okuyemi *et al*. 2007). On the positive side, these studies also show that MI leads to significantly more quit attempts (Wakefield *et al*. 2004; Borrelli *et al*. 2005); greater reductions in smoking level (Borrelli *et al*. 2005); greater advances in readiness to quit (Butler *et al*. 1999); greater self-reported abstinence in the previous 24 hours (Butler *et al*. 1999); and a lower rate of increased smoking among pregnant women who were smoking early in pregnancy (Tappin *et al*. 2005). Importantly, a recent study (published subsequent to the meta-analyses) of primary care patients has shown that three 20-minute sessions of MI delivered by family physicians can increase smoking cessation more than five-fold compared to brief advice (Soria *et al*. 2006). This study addressed many of the limitations of prior studies by recruiting a large proportion of smokers not necessarily ready to quit, and incorporating procedures to ensure fidelity to MI principles.

Another particularly relevant target behavior for oral health is dietary habits. As indicated, meta-analyses have found significant effects of MI for changing diet. Specifically, these studies have documented changes due to MI in overall dietary intake (Mhurchu *et al*. 1998), fat intake (Mhurchu *et al*. 1998; Bowen *et al*. 2002), carbohydrate consumption (Mhurchu *et al*. 1998), cholesterol intake (Mhurchu *et al*. 1998), body mass index (BMI) (Mhurchu *et al*. 1998), weight (Woollard *et al*. 1995), salt intake (Woollard *et al*. 1995), alcohol consumption (Woollard *et al*. 1995), and consumption of fruits and vegetables (Resnicow *et al*. 2001; Richards *et al*. 2006).

At the time of writing, there was only one published study focused on oral health. This study examined the effect of using MI compared to traditional health education for motivating 240 mothers of young children with high risk for developing dental caries to use dietary and non-dietary behaviors for caries prevention (Weinstein *et al*. 2004, 2006). An MI session and six follow-up phone calls over a year in addition to an educational pamphlet and video was more effective than the pamphlet and video alone in preventing new dental caries among the children after 2 years. This result is consistent with the results of the meta-analyses that have found MI to be efficacious for dietary change (Burke *et al*. 2003; Hettema *et al*. 2005).

In summary, there is generally a wealth of support for MI as an effective method of counseling for behavior change. MI has also been shown to be relatively efficient and has been successfully delivered by medical practitioners. In areas of specific relevance to oral health practitioners, MI has either already been shown to be efficacious or offers significant promise. Given the extraordinary explosion in the application of MI we anticipate that it will not be long before there will be many more studies specific to dental settings.

Implementation of motivational interviewing into the periodontal treatment plan

Key principles of motivational interviewing

Although MI methods and techniques provide a wealth of guidance of what to do and what not to do when counseling patients, Miller and Rollnick have emphasized that to be an effective MI practitioner it is more important to embody the underlying philosophy than to be able to apply the collection of techniques. They have identified four general principles that capture the underlying philosophy of the method. First, a practitioner should *express empathy* for the patient's behavior change dilemma. In other words, the practitioner should communicate acceptance of the patient's perspective, providing and *expressing* full acknowledgement of the patient's feelings and concerns. The second principle is to *develop discrepancy* between the patient's current behavior and how they would ideally like to behave to be consistent with their broader goals and values. For example, the goal of being strong or responsible, or a good spouse or parent, can often be linked to being healthy and suggest the need for improved health behaviors. The third principle is to *roll with resistance*. When patients argue against change there is a strong tendency to fall into the trap of providing counter arguments. As a result the patient expends all of their energy arguing against change which is precisely the opposite of what is desired, perhaps making them even less likely to change. MI practitioners therefore avoid arguing and instead use MI methods to "roll with resistance". The fourth principle is to *support self-efficacy* or the patient's confidence in their ability to make a change. Patients are unlikely to succeed in making a change even if they are motivated, when they don't know how or don't believe they can. MI practitioners therefore make efforts to enhance their patients' confidence through such means as expressing their belief in the patient's ability to change or pointing out past successes or steps in the right direction.

Basic communication skills

Implementing MI in a dental setting requires consideration of how to ensure the collaborative and

Fig. 34-1 Appropriate position for a conversation: the clinician is facing the patient on the same seating level.

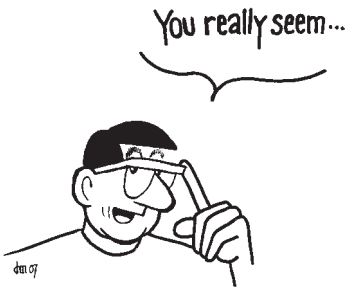
Fig. 34-2 Inappropriate position for a conversation: the clinician is wearing a face mask and is at a higher level than the supine patient.

empathic spirit of the method. Even such basic matters as how the patient and practitioner are seated can contribute to the patient feeling like they are truly being invited to engage in a dialogue as a partner (Fig. 34-1), rather than feeling they are simply to be the recipient of expert advice (Fig. 34-2).

There are four primary activities for the beginning stages of a brief MI session. These can be summarized with the acronym OARS, for **o**pen-ended questions, **a**ffirm the patient, **r**eflect, and **s**ummarize.

- *Ask open-ended questions*. Approaching the patient with multiple closed-ended questions (question that will be answered with "yes" or "no") sets the patient's role to be a rather passive one. In contrast, open-ended questions invite thought, collaboration, and effort on the part of the patient. Example: "How do you feel about your smoking?"

- *Affirm the patient*. It is human nature to presume a negative attitude, particularly when one's own behavior is coming under scrutiny. Acknowledging the patient's strengths and appreciation of his or her honesty will decrease defensiveness, increase openness, and the likelihood of change. Example: "You're telling me clearly why you're not very concerned about your toothbrushing and I appreciate that honesty."



- *Reflect what the patient is communicating*. Reflection is the primary way to demonstrate empathy (ability to understand another person's perspective). Appropriate reflection includes the genuine effort to understand the patient's perspective. It (1) captures the underlying meaning of the patient's words, (2) is concise, (3) is spoken as an observation or a comment, and (4) conveys understanding rather than judgment. Example: "You really seem to have lost hope that you can ever really quit smoking."

- *Summarize*. Summarizing the patient demonstrates interest, organizes the interview, and gets things back on track if necessary. It involves the compilation of the patient's thoughts on change mentioned during the counseling. Example: "So there's a big part of you that doesn't feel ready to change right now. You really enjoy smoking, but you have been a little worried by the way some people react when they find out that you smoke. Is that about right?"

Giving advice

Although we have highlighted the distinction between advice-oriented health education and MI in this chapter, it is important to recognize that at times it is appropriate to provide information to address patient's questions, misapprehensions, or lack of knowledge. The Motivational Interviewing Skill Code (Moyers *et al*. 2003), which is used to assess practitioner's adherence to principles of MI distinguishes between giving advice *without* permission, which is proscribed, and giving advice *with* permission, which is consistent with MI principles. In essence, it is consistent with MI to provide information when the patient is willing and interested in receiving it. Practitioners commonly err by providing advice too soon in an encounter with a patient, resulting in patients perceiving the practitioner as having an agenda that they are trying to "push". In contrast, it is common in MI practice to find that the process of eliciting the patient's perspective reveals gaps in knowledge, questions and concerns, and misapprehensions that the patient would appreciate receiving more information about. The practitioner can then provide particularly relevant information that is much more likely to be well received. Rollnick *et al*. (1999) have outlined a three-step process that serves as a useful framework for providing advice in an MI consistent style:

- Step 1: *elicit* the patient's readiness and interest in hearing the information. For example a practitioner might say to a patient "I have some information related to (that topic) that you may be interested in. Would you be interested in hearing more about that?"
- Step 2: *provide* the information in as neutral a fashion as possible. For example, a practitioner might say "Research indicates that. . . ." or "Many of my patients tell me that . . ." This allows factual information to be presented in a manner that supports the patient's autonomy.
- Step 3: *elicit* the patient's reaction to the information presented. Following up will often facilitate the patient to integrate the new information in a way that brings about a new perspective and increases motivation to change. Alternatively, following up may reveal further gaps in knowledge or misunderstandings that can be addressed. If a patient "rejects" the information it is important not to get into a debate. It is generally better to simply acknowledge the patient's perspective with statements such as "This information doesn't fit with your experience" or "This information doesn't seem relevant to your situation" and then move on to a more productive area of conversation.

Case examples for oral hygiene motivation

Oral hygiene motivation 1

Using the following case example, MI is demonstrated in a dialogue for oral hygiene motivation between a periodontist (Dr) and a patient (P) diagnosed with chronic periodontitis at the beginning of periodontal therapy.

Dr Would you mind if we talk about methods to improve your oral hygiene during and after your gum treatment?
P No, I don't mind.
Dr Good. Let me know a little bit about how you usually clean your teeth.
P I usually brush once or twice a day.
Dr So you brush your teeth regularly. What are you using when you clean your teeth?
P I use a toothbrush and toothpaste.
Dr Very good. Could you let me know how you use your toothbrush?
P I brush all upper and lower teeth on the outside and the inside as I was shown a long time ago.
Dr And how do you feel about brushing your teeth that way?
P I generally feel quite good about it. But since I have been told I have gum disease, I'm wondering if I haven't been brushing enough?
Dr So you have been making efforts to keeping your teeth clean but you're worried that maybe you haven't been brushing enough.
It can be difficult to get to all the areas of your teeth and gums to remove the plaque that causes gum disease. I have some information related to prevention of gum disease that you might be interested in. Would you like to hear about it?
P Yes.
Dr The chronic gum or periodontal disease you are diagnosed with was caused by bacterial plaque attached to your teeth over time.
Plaque has to be entirely removed from all the tooth surfaces on a daily basis in order to prevent and control this disease.
How confident are you that you were cleaning all the surfaces on a regular basis?
P Not very, although I thought that I was doing enough.

Dr Well actually, research indicates that using a toothbrush alone is not sufficient to clean between the teeth. In order to clean these areas, an interdental device is needed such as a dental floss, a toothpick, or an interdental brush. Are you using any one of these devices?
P Yes, I've tried using dental floss.
Dr How did you find the use of dental floss?
P I had some trouble getting to some of the spaces between my teeth. In other areas, the floss used to rip up too, so I quit using it.
Dr I am sorry to hear that you had trouble using the dental floss. The floss can rip up at the edges of dental fillings or crowns. In spaces with extensive tartar built-up, the gap between your teeth may even be blocked out with tartar. Are you using anything else for cleaning?
P Yes, I use a toothpick whenever I have something stuck between my teeth.
Dr So in addition to your regular brushing with toothpaste you are also using a toothpick from time to time to clean your teeth?
P That's right.
Dr Good. During gum treatment, fillings and crowns with rough edges will be smoothed over and tartar can be removed which should make it easier to use things like dental floss or a toothpick between your teeth. Thinking of a 10-point scale where 0 is not at all important and 10 is extremely important, how important is it to you to floss or use a toothpick every day to clean the gaps between your teeth?
P Probably a 7.
Dr That sounds quite important. What makes this so important to you?
P I want to do everything needed to keep my teeth. However, I am not quite sure if I will be able to keep doing it over time.
Dr So you are quite motivated now because you want to look after your teeth, but you are worried about the long term. If you were to use the same 10-point scale to rate how confident you are that you can do it over the long-term, where would rate yourself?
P I would be at a 6.
Dr That sounds fairly confident. What gives you that level of confidence?
P Well, taking care of my teeth and gums is part of my routine already so this would just need to be added to it. But it does take extra effort, so it's a matter of realizing that it's really that important for my gums.
Dr So the fact that it can be part of your existing routine will help. But perhaps I can help you remain motivated in the long run by showing you at your follow-up visits the benefits you are achieving with your treatment by doing it regularly. How do you think that might help you to stick with it over time?
P Well, yes I think that would probably help a lot to see or learn from you that it really is making a difference to the success of my treatment.
Dr Great! So let me summarize what we have discussed. You plan to keep brushing on a regular basis with toothbrush and toothpaste and you will start to use a device for cleaning the gaps between your teeth after the issues with the rough filling and crown margins have been resolved. Then, each time you visit we'll see how you are progressing with your cleaning at home and see if we need to find any other ways to help. Does that sound like it would work for you?
P Yes, that sounds like it would work.

Oral hygiene motivation 2

In this second case example dialogue, MI is used in a conversation about oral hygiene at a visit for supportive periodontal therapy (SPT).

Dr From looking at your plaque index, I noticed today that compared to your visit 3 months ago there is more plaque around the areas between your teeth. I was wondering if you could tell me a little bit about how you find the cleaning between your teeth.
P Oh . . . I guess that I don't do it as often as I should. I barely have time now to do it every day, you know.
Dr I understand. It takes time to clean all the areas between your teeth, you are right. May I ask you a few questions about your current oral hygiene habits so I could understand your situation better?
P Sure you can.
Dr Good. So what do you use to clean your teeth currently?
P I am using an electric toothbrush and the interdental brushes you showed me.
Dr OK. How often do you use these?
P I use the electric toothbrush every day and I use the interdental brushes from time to time.
Dr So you are using the toothbrush on a regular basis, but only occasionally using the interdental brushes. What is prompting you when you do decide to use the interdental brushes?
P Well, sometimes I just feel guilty that I haven't been using them and sometimes I can see the tartar on my teeth and am reminded to use them again.
Dr So you sometimes worry that you are not using them enough and sometimes you can see on your teeth that you are not using them enough.
P Right, I suppose I should be doing better.

Dr Well let me ask you this. If you had to rate how important it is for you to use the interdental brushes every day on a scale from 0 to 10, 0 being not important at all and 10 being very important, where would you place yourself?
P I guess the use of these brushes is pretty important. I'd say an 8.
Dr Well that sounds very motivated. What makes it that important for you?
P Well I don't want to have a lot of problems with my teeth – I hate having fillings and of course I don't want to lose any teeth in the long run.
Dr So avoiding pain and discomfort and keeping your teeth is important to you. So how confident are you that you can use the brushes on a daily basis? Where would you rate yourself on that 0 to 10 scale?
P As I said, I know that I should use them more often, but finding the time is hard and I even just forget sometimes. I'd give it a 3.
Dr Using them daily seems quite hard for you. Out of curiosity, though, it seems you do have a little bit of confidence in doing this – may I ask you why a 3 instead of a 0 or a 1?
P Well, I just think that I would use them more often if they would become a part of my routine tooth cleaning, you know? I used to have toothpicks on my dinner table too and so I used them whenever I saw them sitting there. I could think about putting my interdental brushes on my sink next to my toothbrush. So I would be reminded to use them after brushing my teeth with the electric toothbrush.
Dr That sounds like a really good plan. Can you see any problems with doing that?
P No, not really. Once I have that reminder in place it's just a matter of staying committed to doing it.
Dr Very good. So if I can summarize, it sounds like you feel quite motivated to use the interdental brushes everyday, and that you think that if you put your interdental brushes on your sink next to your electric toothbrush that would help you remember to actually do it.
P Yes, that's right.
Dr Well does that sound like something you want to do?
P Yes, I'll do that tonight.

Case example for tobacco use cessation

A brief intervention for tobacco use cessation using MI is presented in a clinical case example dialogue between a periodontist (Dr) and a patient (P) at the beginning of periodontal therapy.

Dr According to your tobacco use history, you are currently smoking cigarettes. May I ask you a few questions about your smoking?
P Yes.
Dr Tell me how you feel about your smoking.
P Well I know I should quit. I know it's not good for my health. But I don't want to quit right now.
Dr So you don't feel that you want to quit right now, but you do have some concern about the health effects.
P Yes.
Dr Well, tell me more about what concerns you?
P Well, mainly that I would get lung cancer or something.
Dr So you worry a bit about getting cancer because of smoking. Is there anything else that you don't like about smoking?
P Well if I quit my clothes would stop smelling.
Dr So the smell of tobacco smoke is something you would like to be rid of?
P Yes, but I've smoked for many years, you know and I tried to quit once before.
Dr So even though you would like to be a non-smoker for health and other reasons you haven't had much success quitting.
P Yes, and right now I'm enjoying smoking so there's not much motivation to try.
Dr Well it sounds like even though you have some important reasons to quit, you're not very confident you could succeed and you don't feel ready to take on this challenge right now. I wonder if it would be OK for us to talk about this again next time to see where you are with it and whether I could help?
P Yes that sounds fine.

Conclusion

Chronic damaging behaviors not only affect general and oral health that individuals face but also impact the burden of disease on a community level. Hence, the services for primary and secondary prevention on an individual level oriented towards the change of inappropriate behavior become a professional responsibility for all oral health care providers. Motivational interviewing, encouraging the modification of all common risk factors for periodontal diseases such as insufficient oral hygiene, tobacco use, unhealthy dietary habits, and alcohol abuse, appears to be suitable for implementation into the periodontal treatment plan.

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Chapter 35

Mechanical Supragingival Plaque Control

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Importance of supragingival plaque removal

Dental plaque is a bacterial biofilm that is not easily removed from the surface of teeth. Biofilms consist of complex communities of bacterial species that reside on tooth surfaces or soft tissues. It has been estimated that between 400 and 1000 species may, at some time, colonize oral biofilms. In these microbial communities, there are observable associations between specific bacteria due in part to synergistic or antagonistic relationships and in part to the nature of the available surfaces for colonization or nutrient availability (Chapter 9). The products of biofilm bacteria are known to initiate a chain of reactions leading to host protection but also to tissue destruction (Chapter 11).

The dental biofilm is a complex configuration leading many to speculate that traditional plaque indices are inadequate because they fail to evaluate qualitative features. Furthermore, the term *plaque* is not precise. Plaque may be supragingival or subgingival and may be adherent or non-adherent to tooth or tissue. In addition the microbial composition of plaque varies from person to person and from site to site within the same mouth (Thomas 2004).

Supragingival plaque is exposed to saliva and to the natural self-cleansing mechanisms existing in the oral cavity. Friction through mastication may have a limiting effect on occlusal and incisal extensions of plaque. However, in most populations natural cleaning of the human dentition appears unimportant (Löe 2000). Therefore, in order to maintain oral health, regular personal plaque removal measures must be undertaken. The most widespread means of actively removing plaque at home is toothbrushing. There is substantial evidence which shows that plaque and gingivitis/periodontitis can be controlled most reliably through toothbrushing supported by other mechanical cleansing procedures. Thus, evidence stemming from large cohort studies demonstrated that high standards of oral hygiene will ensure the stability of periodontal tissue support (Hujoel *et al*. 1998; Axelsson *et al*. 2004).

As meaningful as oral hygiene measures are for disease prevention, they are relatively ineffective when used *alone* for treatment of moderate and severe forms of periodontitis (Loos *et al*. 1988; Lindhe *et al*. 1989). On the other hand, without an adequate level of oral hygiene in periodontitis-susceptible subjects, periodontal health tends to deteriorate once periodontitis is established and further loss of attachment may occur (Lindhe & Nyman 1984).

Meticulous, self-performed plaque removal measures can modify both the quantity and composition of subgingival plaque (Dahlén *et al*. 1992). The Socransky group (Haffajee 2001) confirmed this finding and reported that a permanent optimal supragingival plaque control regimen can alter the composition of the pocket microbiota and lower the percentage of periodontopathic bacteria.

At present both primary prevention of gingivitis and primary and secondary prevention of periodontitis are based on the achievement of sufficient plaque removal. Almost 50 years of experimental research, clinical trials in different geographical and social settings, have confirmed that effective removal of dental plaque is essential to dental and periodontal health (Löe 2000). The concept of the primary prevention of gingivitis derives from the assumption that gingivitis is the precursor of periodontitis and that maintenance of a healthy gingiva will prevent periodontitis.

Consequently, preventing gingivitis could have a major impact on expenditure for periodontal care (Baehni & Takeuchi 2003). Primary prevention of periodontal diseases includes educational interventions on periodontal diseases and related risk factors as well as regular self-performed plaque removal and professional mechanical removal of plaque and calculus. Optimal oral hygiene requires appropriate motivation of the patient, adequate tools, and professional oral hygiene instruction.

Self-performed plaque control

Personal oral hygiene refers to the effort of the patient to remove supragingival plaque. Procedures used to remove supragingival plaque are as old as recorded history. The earliest record of the chewstick which has been considered the primitive toothbrush dates back in the Chinese literature to about 1600 BC (Carranza & Shklar 2003). In his writings, Hippocrates (460–377 BC) included commentaries on the importance of removing deposits from the tooth surfaces. The observation that self-performed plaque removal is one of the foundations of periodontal health was clearly described by Antonie van Leeuwenhoek in 1683, who wrote (Carranza & Shklar 2003):

"Tis my wont of a morning to rub my teeth with salt and then swill my mouth out with water; and often, after eating, to clean my back teeth with a toothpick, as well as rubbing them hard with a cloth; wherefore my teeth, back and front, remain as clean and white as falleth to the lot of few men of my years, **and my gums never start bleeding**."

The Chinese are given credit for developing the first bristle toothbrush which was introduced in the Western world in the sixteenth century. Currently, toothbrushes of various kinds are important aids for mechanical plaque removal. Furthermore, a fluoridated dentifrice is an integral component of daily home care. The use of toothbrush and dentifrices is almost universal. The use of interdental cleaning devices, mouthrinses, and other oral hygiene aids is less well documented, but available evidence tends to suggest that only a small percentage of the population use such additional measures on a regular basis (Bakdash 1995).

There is an increasing public awareness of the value of good oral health practices. This fact is proven by a recorded increase in both public spending on oral hygiene products (over $3.2 billion a year in the US) and industry spending on consumer-related advertising (over $272 million a year in the US) (Bakdash 1995).

Brushing

Different cleaning devices have been used in different cultures (toothbrushes, chewing sticks, chewing sponges, etc.). Toothbrushing is currently the most commonly used measure in oral hygiene practice. Toothbrushing alone, however, does not provide adequate interdental cleaning since a toothbrush may only reach the facial, oral, and occlusal tooth surfaces. It was suggested (Frandsen 1986) that the outcome of toothbrushing is dependent on: (1) the design of the brush, (2) the skill of the individual using the brush, and (3) the frequency and (4) duration of brushing.

Dental professionals must become familiar with the variety in shapes, sizes, textures, and other characteristics of available toothbrushes in order to provide their patients with proper advice. From the numerous products present on the market only a few should be selected for the individual patient. It is important that the dental care provider understands the advantages and disadvantages of the various toothbrushes (and other aids) to provide the patient with proper information during the oral hygiene instruction session.

For the most part, studies that have compared the effectiveness of different manual brushes have found relatively little difference among designs (see below). It is quite possible that a given patient may obtain better results with one particular toothbrush than with another. Providing oral hygiene information should therefore be tailored to the individual.

Motivation

Oral hygiene education is essential in primary prevention of gingivitis. Improvement in a patient's oral hygiene is often accomplished through cooperative interaction between the patient and the dental professional. The role of the patient is to seek education regarding efficient self-performed plaque removal and accept regular check-ups to ensure a high level of oral hygiene. The patient must be interested in maintaining the health of the tissues, interested in a proposed treatment plan, and motivated to participate. Without compliance, which has been described as the degree to which a patient follows a regimen prescribed by a dental professional, a good treatment outcome will not be achieved. In this context it should be realized that compliance with treatment recommendations is generally poor, particularly in patients with chronic diseases in which the risk of complications is not immediate or life threatening. Also compliance with oral hygiene recommendations is generally poor (Thomas 2004).

So, however effective any toothbrushing method is, it will only be of any real value if the patient is prepared to use the technique on a regular basis (Warren & Chater 1996a). Merely the patient's positive attitude to treatment may have a positive long-term effect on her/his tooth cleaning efforts. Thus, well motivated patients who are compliant with professional advice and instruction are likely to achieve and sustain ideal levels of plaque control.

There is an increasing public awareness of the value of personal oral hygiene. Good oral hygiene should form an integral part of overall health practices, such as regular exercise, stress management, diet and weight control, smoking cessation, and moderation in alcohol consumption. If the clinician can establish the link between oral health and general health for the patient, this individual may be more willing to establish proper oral hygiene measures as part of her/his lifestyle.

The issue of changing a patient's lifestyle is the more difficult part of motivational sessions (Chapter 34). The principles of brushing and flossing are easy to learn. Integrating them into one's daily routine is far more difficult. This can form a source of frustration for the clinician who has provided a patient with information about the necessity of personal oral hygiene measures.

Toothbrush (see Procedure 1)

It is believed that the first toothbrush made of hog's bristles was mentioned in the early Chinese literature. In 1698 Cornelis van Solingen, a doctor from The Hague, published a book in which he presented the first illustration of a toothbrush in Europe (Fig. 35-1). Nylon filaments were introduced in 1938 since complications of World War II prevented the Chinese export of wild boar bristles. Nearly all current toothbrushes are made exclusively of synthetic materials (Wilkins, 1999). Such nylon filaments and plastic handle are easy to manufacture, and therefore more affordable. This has made toothbrushing a common practice in most societies.

During toothbrushing the removal of dental plaque is achieved primarily through direct contact between the filaments of the toothbrush and the surfaces of teeth and soft tissues. At the European Workshop on Mechanical Plaque Control, it was agreed that the features of an ideal manual toothbrush should include (Egelberg & Claffey 1998):

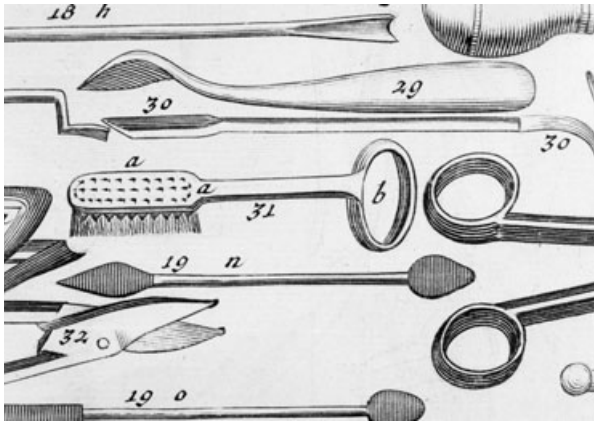


Fig. 35-1 Illustration of a toothbrush and tongue scraper from the book of Cornelis van Solingen with special thanks to the University Museum of Dentistry in Utrecht, The Netherlands.

1. Handle size appropriate to user age and dexterity so that the brush can easily and efficiently be manipulated
2. Head size appropriate to the size of the individual patient's requirements
3. Use of end-rounded nylon or polyester filaments not larger than 0.23 mm (0.009 inches) in diameter
4. Use of soft filament configurations as defined by the acceptable international industry standards (ISO)
5. Filament patterns which enhance plaque removal in the approximal spaces and along the gum line.

Additional characteristics could be: inexpensive, durable, impervious to moisture, and easily cleaned.

Modern toothbrushes have filament patterns designed to enhance plaque removal from hard-to-reach areas of the dentition, in particular from proximal areas. Cross-placed filaments, crimped, and tapered filaments are the most recent improvements. Such designs are based on the premise that the majority of subjects in any population use a simple horizontal brushing action. In order to improve patient comfort brush head shape, filament shape, and placement of filaments into the handles also have been subject to change over time. Multiple tufts of filaments, sometimes angled in different directions, are currently used (Jepsen 1998). Thus, when the head of the toothbrush is located horizontal to the tooth surface, there are filaments angled in the direction of the approximal tooth surfaces. Toothbrushes with this design facilitate more plaque removal in such difficult-to-reach areas when compared with flat-headed brushes (Cugini & Warren 2006).

Double- and triple-headed toothbrushes have been proposed in order to reach lingual surfaces more easily, especially in molar areas, which are normally the tooth surfaces hardest to reach with a regular toothbrush. Although some studies have indicated that the use of such multi-headed toothbrushes may improve plaque control in lingual areas (Agerholm 1991; Yankell *et al*. 1996), their use is not widespread.

Where handles used to be straight and flat, nowadays round and curved handles are more common. Today, a modern toothbrush has a handle size that is appropriate to the hand size of the prospective user, and much emphasis has been placed on new ergonomic designs (Löe 2002). Several studies have investigated differences in plaque removal between brushes with different handle design. In such studies brushes with long and contoured handles appeared to remove more plaque than brushes with traditional handles (Saxer & Yankell 1997).

When brushes with hard, soft, multi-tufted, and space-tufted filaments were compared, no significant clinical differences were found with respect to plaque removal. It is worth considering that most of such

toothbrush studies involved highly motivated participants such as dental students, who do not represent the general population. Most studies on manual brushes are 'single-use' tests. Although such short-term trials may be useful as pilot experiments, they need to be supplemented with studies of longer duration. Numerous manual toothbrushes are available on the market. There is still, however, insufficient evidence that one specific toothbrush design is superior to another. In 1994, two well performed clinical trials which assessed the efficacy of two toothbrushes came to entirely different conclusions (Grossman *et al*. 1994; Sharma *et al*. 1994). In the one trial toothbrush A was more effective than brush B while in the other trial brush B was superior to brush A. The trial which proved that brush A was most effective was sponsored by the manufacturer of brush A. The finances of the other trial which proved that brush B was more effective came from the manufacturer of brush B. As with many other aspects of oral hygiene aids, there is insufficient information to make evidence-based recommendations. Thus, in absence of this evidence, the best toothbrush continues to be the one that is (properly) used by the patient (Cancro & Fischman 1995; Jepsen 1998).

Efficacy of toothbrushing

The enthusiastic use of the toothbrush is not synonymous with a high standard of oral hygiene. Adults, despite their apparent efforts, appear not to be as effective in their plaque removal as might be expected. Most individuals only remove about 50% of plaque by toothbrushing (Jepsen 1998). De la Rosa and coworkers (1979) studied the pattern of plaque accumulation and removal with daily toothbrushing during a 28-day period following a dental prophylaxis. On average about 60% of the plaque was left after the self-performed brushing. Morris *et al*. (2001) reported on the 1998 UK Adult Dental Health survey and observed that the mean proportion of teeth with plaque deposits was 30% in the 25–34-year age group and 44% in those aged 65 years and above. At the Academic Centre for Dentistry Amsterdam (ACTA) a study was conducted which assessed the efficacy of a single 1-minute brushing exercise in subjects adhering to their customary brushing method (Van der Weijden *et al*. 1998a). It was observed that after 1 minute of brushing, approximately 39% of the plaque had been removed. The results of the studies described above indicate that most subjects are not effective brushers and that they probably live with large amounts of plaque on their teeth, even though they brush once every day.

Methods of toothbrushing

There is no single oral hygiene method that is correct for all patients. The morphology of the dentition (crowding, spacing, gingival phenotype etc.), the type and severity of the periodontal tissue destruction, as well as the patient's own manual dexterity determine what kind of hygiene aids and cleaning techniques are to be recommended. It should also be realized that during the course of periodontitis therapy, the techniques may have to be changed or adapted to the morphologic situation (longer teeth, open interdental spaces, exposed dentin).

The ideal brushing technique is the one that allows complete plaque removal in the least possible time, without causing any damage to the tissues (Hansen & Gjermo 1971). Different toothbrushing methods have been recommended over time, but also been abandoned. Such methods can be classified based on the position and motion of the brush.

Horizontal brushing is probably the most commonly used toothbrushing method. It is most frequently used by individuals who never had instruction in oral hygiene techniques. Despite the efforts of the dental profession to instruct patients to adopt other more efficient brushing techniques, most individuals use horizontal brushing since it is simple. The head of the brush is positioned perpendicular to the tooth surface and then a horizontal back and forth movement is applied. The occlusal, lingual, and palatal surfaces of the teeth are brushed with open mouth. In order to reduce pressure of the cheek on the brush head the vestibular surfaces are cleaned with the mouth closed.

Vertical brushing (Leonard (1939) technique) is similar to the horizontal brushing technique, but the movement is applied in vertical direction using up and down strokes.

Circular brushing (Fones (1934) method): with the teeth closed the brush is placed inside the cheek and a fast circular motion is applied that extends from the maxillary gingiva to the mandibular gingiva using light pressure. Back and forth strokes are used on the lingual and palatal tooth surfaces. The *scrubbing method* includes a combination of horizontal, vertical, and circular strokes.

Sulcular brushing (Bass (1948) technique): this method emphasizes cleaning of the area directly beneath the gingival margin. The head of the brush is positioned in an oblique direction towards the apex. Filament tips are directed into the sulcus at approximately 45° to the long axis of the tooth. The brush is moved in a back and forth direction using short strokes without disengaging the tips of the filaments from the sulci. On the lingual surfaces in the anterior tooth regions the brush head is kept in the vertical direction. The Bass technique is widely accepted as an effective method for removing plaque not only at the gingival margin, but also subgingivally. A few studies have been carried out on teeth affected with periodontal disease and scheduled for extraction, where the gingival margin was marked with a groove and the depth of subgingival cleaning was measured. These studies showed that with the use of this brushing method the plaque removal could reach a depth of approximately 1 mm subgingivally (Waerhaug 1981a).

Vibratory technique (Stillman (1932) method): as originally described by Stillman the method was designed for massage and stimulation of the gingiva as well as for cleaning the cervical areas of the teeth. The head of the brush is positioned in an oblique direction toward the apex, with the filaments placed partly in the gingival margin and partly on the tooth surface. Light pressure together with a vibratory (slight rotary) movement is then applied to the handle, while the filament tips are maintained in position on the tooth surface.

Vibratory technique (Charters (1948) method): this method was originally developed to increase cleansing effectiveness and gingival stimulation in the interproximal areas. It uses a reverse position of the brushhead as compared to the Stillman technique. The head of the brush is positioned in an oblique direction with the filament tips directed towards the occlusal or incisal surfaces. Light pressure is used to flex the filaments and gently force the tips into the interproximal embrassures. A vibratory (slight rotary) movement is then applied to the handle while the filament tips are maintained in position on the tooth surface. This method is particularly effective in cases with receded interdental papillae because the filament tips can easily penetrate the interdental space (Fig. 35-2).

Roll technique: the head of the brush is positioned in an oblique direction toward the apex of the teeth, with the filaments placed partly in the gingival margin and partly on the tooth surface. The sides of the filaments are pressed lightly against the gingiva. Next the head of the brush is rolled over the gingiva and tooth in occlusal direction.

Modified Bass/Stillman technique: the Bass and Stillman methods were designed to concentrate on the cervical portion of the teeth and adjacent gingival tissues. Each of these methods can be modified to add a roll stroke. The brush is positioned similarly to the Bass/Stillman technique. After activation of the brushhead in a back and forth direction, the head of the brush is rolled over the gingiva and tooth in occlusal direction making it possible for some of the filaments to reach interdentally.

In the 1970s several investigators compared various methods of brushing. Because of varying experimental conditions the outcomes of such studies are difficult to compare. To date no methods of toothbrushing have been shown to be clearly superior to others. As early as 1986, Frandsen commented on this issue by stating: "Researchers have realized that improvement in oral hygiene is not as dependent upon the development of better brushing methods as upon improved performance by the persons using any one of the accepted methods." Therefore, since no particular toothbrushing method has been found to be clearly superior to another, there is no reason to introduce a specific toothbrushing technique in each new periodontal patient. In most cases, small changes in the patient's own method of toothbrushing will suffice, always bearing in mind that more important than the selection of a certain method of

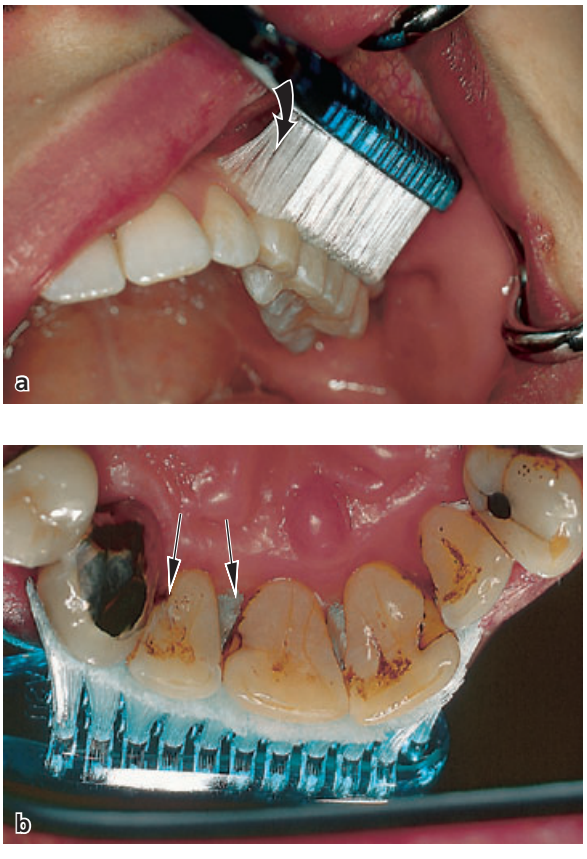


Fig. 35-2 (a) The Charters method of toothbrushing. The head of the toothbrush is placed in the left maxilla. Note the angulation of the bristles against the buccal tooth surfaces. The bristles are forced into the interproximal areas. (b) The palatal aspect of the incisor region in the maxilla illustrating the penetration of the bristles through the interproximal spaces (arrows).

toothbrushing is the willingness and thoroughness on the part of the patients to effectively clean their teeth. Implementation of the toothbrushing methods described above must be made according to patient´s needs. For example, since the Bass method has been associated with gingival recession (O'Leary 1980), it would be hardly indicated in individuals with energetic toothbrushing habits who have a thin gingival biotype.

Frequency of toothbrushing

There is no consensus as to the optimum frequency of toothbrushing. How often and how much plaque has to be removed in order to prevent dental disease from developing is not known. The majority of individuals, including periodontal patients, are usually not able to remove dental plaque completely as a result of daily brushing. However complete plaque removal does not seem to be necessary. A proper level of oral hygiene theoretically is the extent of plaque removal that prevents gingivitis/periodontal disease and tooth decay in the individual patient. Prevention of gingival inflammation is important because the inflammatory condition of soft tissues also favors plaque accumulation (Ramberg *et al*. 1994; Rowshani *et al*. 2004).

Results in cross-sectional studies have been equivocal when the self-reported frequency of tooth cleaning has been related to caries and periodontal disease. Disease appears to be more related to quality of cleaning than to its frequency (Bjertness 1991). Kressin and co-workers (2003) evaluated the effect of oral hygiene practices on tooth retention in a longitudinal study with a 26-year follow-up. They observed that consistent brushing (at least once a day) resulted in a 49% reduction of the risk of tooth loss compared to a lack of consistent oral hygiene habits.

If plaque is allowed to accumulate freely in the dentogingival region, subclinical signs of gingival inflammation (gingival fluid) appear within 4 days (Egelberg 1964). The minimum frequency of tooth cleaning to reverse experimentally induced gingivitis is once every day or every second day. Bosman and Powell (1977) induced experimental gingivitis in a group of students. The signs of gingival inflammation persisted in those students who removed plaque only every third or fifth day. In groups who properly cleaned their teeth once a day or every second day, the gingivae healed within 7–10 days.

Based on the observation that the onset of gingivitis appears to be more related to the maturation and age of the plaque than to its amount, the minimum frequency needed to prevent the development of gingivitis has been investigated in a prospective study. Dental students and young dental faculty members with healthy periodontal conditions were assigned to study groups with different cleaning frequencies over periods of 4–6 weeks. The results showed that that students who thoroughly removed plaque once daily or even every second day, did not develop clinical signs of gingival inflammation over a 6-week period. This tooth cleaning included the use of interproximal aids (dental floss and woodsticks) as well as the toothbrush (Lang *et al*. 1973). Caution should be excercised in extrapolating the results obtained from studies including dentally aware subjects to the average patient.

From a practical standpoint, it is generally recommended that patients brush their teeth at least twice daily, not only to remove plaque but also to apply fluoride through the use of dentifrice in order to prevent caries. This advice is also conceivable based on reasons of practibility and feeling of oral freshness. For most patients, it may be desirable to perform all necessary procedures (e.g. brushing and interdental cleaning) at the same time and in the same manner each day. Unfortunately, with subjects who live busy, stressful lives, this may be difficult to achive (Thomas 2004). Despite the fact that most individuals claim to brush their teeth at least twice a day, it is clear from both epidemiologic and clinical studies that mechanical oral hygiene procedures as performed by most subjects are insufficient to control supragingival plaque formation and to prevent gingivitis and more severe forms of periodontal disease (Sheiham & Netuveli 2002).

Brushing duration

Patients usually believe that they spend more time on toothbrushing than they actually do (Saxer *et al*. 1998). The least time spent on brushing was observed in a study carried out on English schoolchildren; in the 13 years age group, the children spent approximately 33 seconds on brushing (Macgregor & Rugg-Gunn 1985). About one third of the studies that were reviewed reported an average brushing time of less than 56 seconds whereas two thirds of the studies reported a brushing time of ≥56 seconds and <70 seconds. One investigation which used dental students as study population reported an average of 90 seconds (Ayer *et al*. 1965). The best estimate of actual manual brushing time seems to range between 30 and 60 seconds (Van der Weijden *et al*. 1993).

In reviewing the literature for studies that addressed the question whether in adult patients the duration of toothbrushing is correlated with efficacy of plaque removal five studies were identified. Three of these evaluated the use of electric toothbrushes (Van der Weijden *et al*. 1996a; McCracken *et al*. 2003, 2005). One study compared a manual toothbrush with an electric toothbrush (Preber *et al*. 1991), while one study included only manual toothbrushes (Hawkins *et al*. 1986). Results from all five studies indicate that duration of brushing is consistently correlated with the amount of plaque that is removed. In one study, toothbrushing was delivered by a dentist/dental hygienist. This study compared the effect of brushing time on plaque removal using manual and electric toothbrushes utilizing five different brushing times (30, 60, 120, 180, and 360 seconds).

This study showed that 2 minutes of electric toothbrushing can be as effective as 6 minutes of manual toothbrushing. The authors furthermore observed that at 2 minutes an optimum in plaque-removing efficacy was reached with both a manual and electric toothbrushes (Van der Weijden *et al*. 1993). Based on these observations the duration of toothbrushing should also be stressed during the toothbrushing instruction session.

Brushing filaments

Most current toothbrushes have nylon filaments. The degree of hardness and stiffness of a toothbrush depends on the filament characteristics, such as material, diameter, and length. Also the density of filaments in a tuft influences stiffness, since each filament gives support to the adjacent fiaments and each tuft gives support to adjacent tufts. Toothbrushes with thinner filaments are softer while thicker filament diameters are stiffer and less flexible. This increased stiffness will prevent the filament ends from bending back during brushing, avoiding the potential risk of damaging the gums. However, the filament must be sufficiently stiff so that during brushing enough pressure is exerted to allow proper plaque removal. Consider that a rod represents a filament of a toothbrush. Whilst brushing, a vertical upward load is exerted, which in turn exerts an effect of the same order of magnitude on the oral mucosa. The force of the brush, acting on the individual filament, is thus always as great as the load exercised by the filament on the mucosa. If the load is increased then the load on the mucosa increases to the same extent. Consequently the risk of soft tissue damage increases in that the filament's tip can penetrate into the mucosa. However, elastic rods demonstrate a peculiarity in their behavior. They suddenly fold back laterally when a certain limit load is reached. When folding back, the rod suddenly gives way elastically (without breaking) and the load on the oral mucosa diminishes abruptly. A load higher than this fold-back limit can thus not be transferred to the mucosa by the rod, via its tip. Tapered filaments (Fig. 35-3) have endings with the shape of an extreme rotational ellipsoid instead of a hemisphere. This is suggested to give the filaments very soft endings combined with a good stability of the filament corpus. Curved filaments may be more flexible and less stiff than straight filaments of equal length and diameter.

As late as 1967, most people were buying hard brushes (Fanning & Henning 1967). The shift in preference to soft brushes of specific design paralleled the change that occurred in oral health care when calculus was the prime etiologic agent in periodontal disease (Mandell 1990). The concentration on plaque, especially in the crevicular area and the attention to intrasulcular brushing strongly influenced the change from hard to soft filaments, primarily because of the concern of trauma to the gingival tissues (Niemi *et al*. 1984). The cleaning performance of a toothbrush is influenced by its degree of hardness. The toothbrush must not be too hard, to avoid damaging the gums when positioning the toothbrush. The harder the toothbrush filaments are the greater is risk of gingival abrasion (Khocht *et al*. 1993). But there is no point in using a brush with very thin filaments that merely strokes across the tooth and, as a result of the lack of load, no longer cleans the tooth surface.

Filament end-rounding

The end of a toothbrush filament can be cut bluntly or rounded. End-rounding has become increasingly common in the manufacturing process to reduce gingival abrasion (Fig. 35-4). The logic that smooth filament tips would cause less trauma than filament tips with sharp edges or jagged projections has been validated with both animal and clinical studies (Breitenmoser *et al*. 1979). Danser *et al*. (1998) evaluated two types of end-rounding, and saw an effect of end-rounding on the incidence of abrasion. The form to which the ends were rounded, however, had no effect on the level of plaque removal.

Toothbrush wear and replacement

It is generally recommended that toothbrushes be replaced before the first signs of the filaments

Fig. 35-3 Tapered toothbrush filaments.

Fig. 35-4 Filament end-rounding.

becoming worn. The useful life of an average toothbrush has been estimated to be 2–3 months. Not all patients take this advice, and evidence indicates that the average age at which a toothbrush is replaced ranges from 2.5–6 months (Bergström 1973). Common sense would suggest that a worn toothbrush with splayed or frayed filaments loses resilience and is less likely to be as effective in removing plaque than a new brush. This is why dental professionals often recommend that toothbrushes are used for a maximum of 3 months before they are they are replaced. Whilst this advice would seem reasonable, there is little actual clinical proof that this recommendation is correct. Because of variability in subjects' brushing techniques and the force applied to the teeth whilst brushing, the degree of wear varies significantly from subject to subject. It is also likely that different brushes, made from various materials, would exhibit differences in longevity. Some commercially available brushes have filaments that change color after a certain amount of use. This serves as a reminder to the patients that it is time to replace the brush.

Kreifeldt and co-workers (1980) showed that new brushes were more efficient in removing dental plaque than old brushes. They examined worn toothbrushes and observed that, as a result of wear, the filaments showed a taper, proceeding from the insertion to the free end. For example filaments were seen which tapered from 0.28 mm at one end to 0.020–0.015 mm at the free end. They concluded that among other wear factors, tapering contributed the most to loss of effectiveness. Their explanation for this observation was that as the tapering will result in a reduction of filament diameter, the brush will become softer and remove less plaque.

Since many patients use a brush for periods significantly longer than the recommended time of 3 months, it is important to know whether excessive wear is of clinical relevance. Several studies have examined this question but there is inconclusive evidence about the relationship between toothbrush wear and plaque removal. Studies with laboratory-worn toothbrushes reported that such used toothbrushes had inferior plaque removal efficacy as compared to new brushes (Kreifeldt *et al*. 1980; Warren *et al*. 2002). However, artificially worn toothbrushes may not mimic the characteristics of a naturally worn brush. In a laboratory study of the wear of toothbrushes, wear will inevitably be highly uniform and not reflect the variation in wear seen in normal toothbrush use. Most studies in which naturally worn toothbrushes were used reported no statistically significant decrease in reduction of whole-mouth plaque scores after brushing when compared to using new toothbrushes (Daly *et al*. 1996; Sforza *et al*. 2000; Tan & Daly 2002; Conforti *et al*. 2003; Van Palenstein Helderman *et al*. 2006). From this brief review of the literature it may be concluded that in contrast to what is generally thought, the wear status of a toothbrush might be less critical for maintaining good plaque control.

Electric toothbrushes (see Procedure 2)

In well motivated and properly instructed individuals who are willing to invest the necessary time and effort, mechanical measures, using traditional toothbrushes and adjunctive manual (interdental) devices, are effective in removing plaque. Maintaining a dentition close to plaque-free is, however, not easy. The electric toothbrush represents an advance that has the potential to both enhance plaque removal and patient motivation. Electric toothbrushes were introduced to the market more than 50 years ago. The first toothbrush powered by electricity was developed by Bemann & Woog in Switzerland and was introduced in the United States in 1960 as the Broxodent. In 1961 a cordless rechargeable model was introduced by General Electric (Darby & Walsh 2003). Studies of the use of these early electric tootbrushes showed that there was no difference in plaque removal when compared with a manual toothbrush and they had mixed effects on gingivitis. The consensus of the research reports on toothbrushing of the World Workshop in Periodontics in 1966 states: "*in non-dentally oriented persons, in persons not high motivated to oral health care, or in those who have difficulty in mastering suitable hand brushing technique the use of an electric brush with its standard movements may result in more frequent and better cleansing of the teeth*".

Since the 1980s, tremendous advances have been made in the technology of electrically powered toothbrushes. Various electric toothbrushes have been developed to improve the efficiency of plaque removal using increased filament velocity, brush stroke frequency, and various filament patterns and motions. Where old electric toothbrushes were using a combination of horizontal and vertical movements mimicking closely the back-and-forth motion of the traditional brushing methods, the more recent designs apply rotary motion or oscillating/rotating motion with pulsation, or have brush heads which move at high frequencies.

After reviewing many of the published reports over the past decades, it may be concluded that certain newer types of rechargeable electric toothbrushes have become more effective in removing supragingival plaque and controlling gingivitis. It is also clear that the effectiveness of particularly the low-cost battery-operated brushes are not well documented. To some extent, power brushes have overcome the limitations of the manual dexterity and skill of the user. Modern design features appear to be responsible for this (Fig. 35-5). These newer designed toothbrushes remove plaque in a shorter time than a standard manual brush (Van der Weijden *et al*. 1993, 1996a). The new generation of electric brushes have better plaque removal efficacy and gingival inflammation control in the approximal tooth surfaces

Fig. 35-5 Overview of the development of electric toothbrushes from brushes mimicking a manual toothbrush to high-frequency brushhead movement. From left to right: the Braun D3®, Rotadent®, Interplak®, Braun/Oral-B Triumph®, Sonicare Elite®.

(Egelberg & Claffey 1998). This superiority was clearly demonstrated in a study carried out on extracted teeth (Rapley & Killoy 1994). The electric toothbrush should not be considered a substitute for a specific interdental cleaning method, such as flossing, but it may offer advantages in terms of an overall approach to improved oral hygiene.

Two independent systematic reviews confirmed that oscillating rotating toothbrushes have superior efficacy over manual toothbrushes in reducing plaque and gingivitis (Sicilia *et al*. 2002; Robinson *et al*. 2005). Toothbrushes with this mode of action reduced plaque by 7% and gingival bleeding by 17% when compared with manual brushes (Robinson *et al*. 2005).

One electric toothbrush that has consistently been shown to be more effective than a manual toothbrush, both with respect to plaque removal and improvement of the gingival condition, is the original Braun Oral-B Plaque Remover (D7) (Warren & Chater 1996b). This toothbrush features a small round brush head that makes rotating and oscillating movements at a speed of 2800 oscillating rotations per minute. A further development of this brush, the Braun Oral-B Ultra Plaque Remover (D9) maintained the oscillating rotating action but at an increased speed (3600 rotations per minute). A clinical study with the D9 demonstrated equivalence in safety and a trend towards greater plaque removal when compared with the D7 (Van der Weijden *et al*. 1996b). Newer developments in the oscillating rotating brush technology add the additional high-frequency vibrations in the direction of the bristles creating three-dimensional movements during brushing. This modification was developed to enhance penetration and removal of plaque from approximal spaces of the dentition. Studies have shown the three-dimensional movements carried out by the brush are safe to use and more efficient regarding plaque removal (Danser *et al*. 1998).

Another approach in this technology was the development of sonic toothbrushes that have a high frequency of filament movement in excess of approximately 30 000 strokes per minute. Two recently introduced sonic toothbrushes are the Oral-B Sonic Complete® (SC; Oral-B Laboratories, Boston, MA, USA) rechargeable toothbrush with a side-to-side filament operating at 260 Hz, and the Philips Sonicare® Elite (SE; Philips Oral Healthcare, Snoqualmie, WA, US) based on a different technology, with a side-to-side motion also operating at a frequency of 260 Hz. Some clinical studies have shown sonic technology to be comparable or more effective than a manual toothbrush in removing plaque and reducing gingival inflammation (Johnson & McInnes 1994; Tritten & Armitage 1996; Zimmer *et al*. 2000; Moritis *et al*. 2002). Two studies using the same experimental gingivitis model compared an earlier Sonicare device and the Oral-B oscillating rotating toothbrush. In both studies the oscillating rotating brush was more effective in improving the level of gingival health (Putt *et al*. 2001; Van der Weijden *et al*. 2002a,b). This confirmed the findings of an earlier 6-week crossover study (Isaacs *et al*. 1998) where improvement in gingival condition was 8.6% greater with the oscillating rotating brush. Rosema and co-workers (2005) compared the Sonicare Elite to the Oral-B Professional Care 7000 and again found the oscillating rotating pulsation brush to be more effective. On the other hand, Tritten & Armitage (1996) compared the Sonicare advance to a traditional manual toothbrush in a 12-week parallel group study and concluded that both brushes were equally effective in reducing gingival inflammation.

Modern power toothbrushes are known to enhance long-term compliance. In a study involving periodontitis patients with persistent poor compliance, Hellstadius and co-workers (1993) found that switching from a manual to a power toothbrush reduced plaque levels and that the reduced levels were maintained over a period of between 12 and 36 months. The power brush significantly improved compliance, and patients expressed a positive attitude to the new brush. In a survey carried out in Germany most dentists stated that the time their patients spent on toothbrushing was too small (Warren 1998). Approximately half of the dentists stated that they recommend their patients to use a power toothbrush, and the vast majority of the dentists believed that changing to a power toothbrush would improve the condition of their patients' teeth and gums. Findings from a recent US practice-based study, involving a large number of subjects who switched from a manual toothbrush to the Braun Oral-B Ultra Plaque Remover (D9), confirmed the findings from the German study (Warren *et al*. 2000).

Electrically active (ionic) toothbrush

Several toothbrushes have been marketed over the years, which are designed to send a small

imperceptible electronic current through the brush head, presumedly to enhance the efficacy of the brush in plaque elimination. The electrons should reduce the H^+ ions from the organic acid in the plaque which may result in a decomposition of the bacterial plaque (Hoover *et al*. 1992). The first record of a charged toothbrush, the "Dr. Scott's Electric Toothbrush" was found in the February 1886 issue of Harper's weekly magazine. The handle of Dr. Scott's toothbrush was purportedly "charged with an electromagnetic current which acts without any shock, immediately upon the nerves and tissues of the teeth and gums . . . arresting decay . . . and restoring the natural whiteness of the enamel."

Short-term clinical studies with the use of these kinds of brushes documented a beneficial effect in terms of plaque reduction and gingivitis resolution (Hoover *et al*. 1992; Weiger 1998). Hotta and Aono (1992) studied an electrically active manual toothbrush that was designed with a piezo-electric element in the handle. This brush generates a voltage potential corresponding to the bending motion of the handle as the teeth are brushed. In this study no difference in the amount of remaining plaque after brushing was observed between the placebo and the electrically active brush. Other toothbrushes, which have a claimed 'electrochemical' effect on dental plaque, have a semiconductor of TiO_2 incorporated in the brush handle. In the presence of light, saturated low energy electrons in the wet semiconductor are transformed into high-energy electrons. An electron current of approximately 10 nA was measured to run from the semiconductor to the tooth (Weiger 1988).

Interdental cleaning

There is confusion in the literature with respect to the definitions of approximal, interproximal, interdental, and proximal sites. Commonly used indices are not suitable for assessing interdental plaque (directly under the contact area), and thereby limit interpretation of interdental plaque removal. The European Workshop on Mechanical Plaque Control in 1999 proposed the following definitions: *approximal* (proximal) areas are the visible spaces between teeth that are not under the contact area. In health these areas are small, although they may increase after periodontal attachment loss. The terms *interproximal* and *interdental* may be used interchangeably and refer to the area under and related to the contact point.

As stated above, the toothbrush does not reach the approximal surfaces of teeth as efficiently as it does for the facial, lingual, and ooclusal aspects nor does it reach into the interproximal area between adjacent teeth. Therefore measures for interdental plaque control should be selected to complement plaque control by toothbrushing (Lang *et al*. 1977; Hugoson & Koch 1979).

The interdental gingiva fills the embrasure between two teeth apical to their contact point. This is a 'sheltered' area, difficult to access, when teeth are in normal position. In populations that use a toothbrush, the interproximal surfaces of the molars and premolars are the predominant sites of residual plaque. The removal of plaque from these surfaces remains a valid objective, since in patients susceptible to periodontal diseases, gingivitis and periodontitis are usually more pronounced in this interdental area than on oral or facial aspects (Löe 1979). Dental caries also occurs more frequently in the interdental region than on oral or facial smooth surfaces. A fundamental principle of prevention is that the effect is greatest where the risk of disease is greatest. Therefore, interdental plaque removal, which cannot be achieved with the toothbrush, is of critical importance for most patients. A number of interdental cleaning methods have been developed, ranging from floss to the more recently introduced electrically powered cleaning aids. Flossing is the most universally applicable method, since it may be used effectively in nearly all clinical situations. However, not all interdental cleaning devices suit all patients or all types of dentitions. Factors such as the contour and consistency of gingival tissues, the size of the interproximal embrasure, tooth position and alignment, and the ability and motivation of the patient should be taken into consideration when recommending an interdental cleaning method. The most appropriate interdental hygiene aids must be selected for each individual patient. The selection made from the numerous commercially available devices is dependent for the most part on the size and shape of the interdental space as well as on the morphology of the proximal tooth surface. In subjects with normal gingival contours and embrasures, dental floss or tape should be recommended. At sites where soft tissue recession has become pronounced, flossing becomes progressively less effective. Then an alternative method (either woodsticks or interdental brushes) should be recommended. A review on interdental cleaning methods (Warren & Chater 1996a) concluded that all conventional devices are effective, but each method should be suited to a particular patient but also to a particular situation in the mouth (Table 35-1).

The use of dental floss, interproximal brushes, and woodsticks may also induce soft tissue damage. In most cases, however, this damage is limited to acute lesions, such as lacerations and gingival erosions (Gillette & Van House 1980). Gingival bleeding during interdental cleaning can be a result of trauma or an indication of inflammation. Patients must be aware that bleeding *per se* is not a sign that interdental cleaning should be avoided but more likely an indicator of inflammation that needs to be treated.

Dental floss and tape (see Procedure 3)

Of all the methods used for removing interproximal plaque, dental flossing is the most frequently recom-

Table 35-1 Interdental cleaning methods recommended for particular situations in the mouth

Situation	Interdental cleaning method
Intact interdental papillae; narrow interdental space	Dental floss or small woodstick
Moderate papillary recession; slightly open interdental space	Dental floss, woodstick or small interdental brush
Complete loss of papilla; wide open interdental space	Interdental brush
Wide embrasure space; diastema, extraction diastema, furcation or posterior surface of most distal molar, root concavities or grooves	Single-tufted/end-tufted brush or gauze strip

mended technique. Levi Spear Parmly, a dentist based in New Orleans, is credited as being the inventor of modern dental floss. As early as 1815 Parmly recommended teeth flossing with a piece of silk thread. Clinical studies clearly show that, when toothbrushing is used together with flossing, more plaque is removed from the proximal surfaces than by toothbrushing alone (Reitman *et al*. 1980; Kinane *et al*. 1992). Dental floss and tape – a type of broader dental floss – are most useful where the interdental papillae completely fill the embrasure space. When properly used, flossing effectively removes up to 80% of proximal plaque. Even subgingival plaque can be removed, since dental floss can be introduced 2–3.5 mm below the tip of the papilla (Waerhaug 1981b). Several types of floss (waxed, unwaxed) are available. Studies have shown no difference in the effectiveness of unwaxed versus waxed dental floss. Unwaxed dental floss is generally recommended for patients with normal tooth contacts because it slides through the contact area easily. It is the thinnest type of floss available, yet when it separates during use it covers a larger surface area of the tooth than waxed floss. Waxed floss is recommended for patients with tight proximal tooth contacts. *Ease of use* is the most important factor that influences whether patients will use floss on a daily basis. Recently, powered flossing devices have been introduced. In comparison with manual flossing no differences have been found in terms of plaque removal and gingivitis reduction, although patients preferred flossing with the automated device (Gordon *et al*. 1996).

Frequent reinstruction and reinforcement in the use of floss are necessary because flossing is a difficult skill to master. Flossing is also time-consuming. When a patient is unwilling to use dental floss alternative interdental hygiene aids should be recommended even if these are less efficient. If a patient finds a particular method or device more appealing to use, long-term compliance becomes an achievable goal. Although it is clear that flossing, when properly used, removes plaque in a very efficient manner, there is no evidence that flossing in adult patients with preserved interproximal periodontal tissues should be routinely indicated (Burt & Eklund 1999).

To facilitate flossing a special floss holder may be used. The holder may be re-used and is normally made of plastic material, durable, lightweight, and easily cleaned. Research reveals that reductions in bacterial plaque biofilm and gingivitis are equivalent with either the use of a hand flossing or flossholder. A Swedish national dental survey showed that approximately 46% of adults use woodsticks sporadically and only 12% use woodsticks daily. On the other hand, dental floss is used occasionally by 12% of adults and daily by only 2%. In other words, adults use woodsticks as an oral hygiene aid four to six times more frequently than dental floss (Axelsson 1994).

Woodsticks (see Procedure 4)

Picking our teeth may well be one of humanity's oldest habits and the toothpick one of the earliest tools. The evolution of the primitive toothpick took a second pathway in the more acquisitive societies. It became part of a personal care kit along with a depilatory tweezer and a ear wax scoop (Mandel 1990). In 1872, Silas Noble and J.P. Cooley patented the first toothpick-manufacturing machine.

The key difference between a toothpick and a woodstick (wooden stimulator/cleaner) relates to the triangular (wedge-like) design. Woodsticks should not be confused with toothpicks which are simply meant for removing food debris after a meal (Warren & Chater 1996a). Woodsticks are inserted interdentally with the base of the triangle resting on the gingival side. The tip should point occlusally or incisally and the triangles against the adjacent tooth surfaces. Triangular wedge-like woodsticks have been found to be superior in plaque removal when compared with round or rectangluar woodsticks since they fit the interdental area more snugly (Bergenholtz *et al*. 1980; Mandel 1990). Woodsticks are usually made of soft wood to prevent injury to the gingiva. The tapered form makes it possible for the patient to angle the woodstick interdentally and even clean the lingually localized interdental surfaces. Unlike floss they can be used on the concave surfaces of the tooth root. Some are hand held, while others are designed to be mounted in a handle, which helps gain access to the interdental areas in the posterior region of the mouth (Axelsson 2004).

The wood can store fluoride crystals both on the surface and in the porosities. These crystals readily dissolve when the woodstick is moistened with saliva (Axelsson 2004). During use the soft wood may become splayed. As soon as the first signs of splaying are evident the woodstick should be discarded. As stated above most patients prefer to use woodsticks

for the removal of interdental plaque. Woodsticks have the advantage that they are easy to use, and can be used throughout the day without the need for special facilities such as a bathroom or a mirror. Woodsticks may also be used in primary prevention, even in cases of poor manual dexterity, including posterior areas. To use woodsticks there must be sufficient interdental space available and in these cases woodsticks are an excellent substitute to dental floss. Although woodsticks have a good cleansing capacity in the center part of the interproximal surfaces of teeth in contact, their effect is reduced on the lingual side of these surfaces. The woodstick is somewhat difficult to use in the far posterior regions of the jaws because of the lack of accessibility and since the triangular cross section must pass into the embrassure space at a specific angle (Bassiouny & Grant 1981).

When used in healthy dentitions, woodsticks may depress the gingival margin and clean the toothsurface up to 2–3 mm subgingivally (Morch & Waerhaug 1956). Long-term use may cause a permanent loss of the papilla and opening of the embrasure which may have important esthetic implications in the anterior dentition. Woodsticks can clearly be recommended in patients with open interdental spaces as secondary prevention for periodontal diseases.

A review of the literature for studies that have addressed the question whether woodsticks used as adjunct to toothbrushing in adult patients have an effect on plaque and periodontal inflammation identified eight publications. In only one study a significant reduction in plaque scores was reported as result of the use of woodsticks (Schmid *et al*. 1976). In three studies the use of woodsticks resulted in reduction of gingival bleeding (Anaise 1976; Bassiouny & Grant 1981; Bouwsma *et al*. 1992).

Interdental brushes (see Procedure 5)

Interdental brushes were introduced in the 1960s as an alternative to woodsticks. They are effective in the removal of plaque from the proximal tooth surfaces (Bergenholtz & Olsson 1984). The interdental brush consists of soft nylon filaments twisted into a fine stainless steel wire. This 'metal' wire can prove uncomfortable for patients with sensitive root surfaces. For such patients the use of plastic-coated metal wires may be recommended. The support wire is continuous or inserted into a metal/plastic handle. Interdental brushes are manufactured in different sizes and forms The most common forms are cylindrical or conical/tapered (like a Christmas tree). The length of the bristles in cross section should be tailored to the interdental space. Appropriate interdental brushes are currently available for the smallest to the largest interdental space (Fig. 35-6). Although unconfirmed with scientific documentation, it is believed that the most effcient cleaning is achieved if the brush selected is slightly larger than the embrasure space. The brush is inserted obliquely into the interdental space, from an apical direction. Cleaning is performed with a back-and-forth motion. The interdental brush is the aid of choice when root surfaces with concavities or grooves have been exposed. The interdental brush is also the most suitable cleaning device in "through-and-through" furcation defects. Like woodsticks, interdental brushes are easy to use, although they may have some drawbacks, including the fact that different types may be needed to fit differently sized open interproximal spaces. When not properly used, interdental brushes may elicit dentin hypersensitivity. In order to minimize the risk of hard tissue abrasion interdental brushes should be used without dentifrice except in special cases and then only short-term. They can also be regularly used as a carrier to apply fluoride or antimicrobial agents, e.g. chlorhexidine gel into the interdental space to prevent caries or the recolonization of residual pockets. The brush should be discarded when the filaments become loose or deformed.

Fig. 35-6 With interdental brushes the diameter of the metal wire core is a detemining factor with respect to access. A close fit of the brushing filaments influences the cleaning ability.

Interdental brushes represent the ideal interdental cleaning tool, especially for periodontitis patients. Waerhaug (1976) showed that individuals who habitually used an interdental brush were able to maintain supragingival proximal surfaces free of plaque and to remove some subgingival plaque below the gingival margin. In a more recent study in patients with moderate to severe periodontitis Christou and coworkers (1998) showed the interdental brush to be more effective than dental floss in the removal of plaque and in promoting pocket reduction. Patients reported that the use of interdental brushes was easier than the use of dental floss. This is in agreement with previous studies (e.g. Wolffe 1976). Also the perception of efficacy was better for the interdental brushes. Significantly less patients reported problems with the use of interdental brushes. Even if efficacy of interdental brushes were not better than that of floss, the long-term use of interdental brushes

might be more easily implemented in a patient's routine than that of floss.

Single-tufted/end-tufted brush (see Procedure 6)

Single-tufted brushes are designed with smaller brush heads that have a small group of tufts or a single tuft. The tuft may be 3–6 mm in diameter and can be flat or tapered. The handle can be straight or contra-angled. Angulated handles permit easier access to lingual and palatal aspects. The filaments are directed into the area to be cleaned and activated with a rotating motion. Single-tufted toothbrushes are designed to improve access to distal surfaces of posterior molars, tipped, rotated or displaced teeth, to clean around and under fixed partial dentures, pontic, orthodontic appliances, or precission attachment, and to clean teeth affected by gingival recession and irregular gingival margin or furcation involvement.

Adjunctive aids

Dental water jet

The dental water jet was introduced in 1962. This device, also called an oral irrigator, has been demonstrated to be safe and effective. Oral irrigation has been a source of controversy within the field of periodontology. The daily use of oral irrigation has been shown to reduce dental plaque, calculus, gingivitis, bleeding, probing depth, periodontal pathogens, and host inflammatory mediators (Cutler *et al*. 2000). The strongest and most consistent evidence for the benefit of daily use of a dental water jet is the ability of the device to reduce gingivitis and bleeding. It has been reported that a pulsating stream of water is better than a continuous flow. The pulsating, hydrodynamic forces produced by irrigators can rinse away food debris from interdental spaces and plaque-retentive areas. Irrigation is not, however, a monotherapy but an adjunct designed to supplement or enhance other home care methods (brushing and flossing) intended for mechanical plaque removal (Hugoson 1978; Cutler *et al*. 2000).

Irrigation devices may be used with water or with disinfective ingredients (Lang & Raber 1982). In a study by Flemmig and co-workers (1990) it was observed that the addition of water irrigation to regular oral hygiene reduced bleeding on probing by 50% over a 6-month timeframe. The use of chlorhexidine in suboptimum concentrations (e.g. 0.06%) led to improved plaque inhibition and had an anti-inflammatory effect (Lang & Räber 1982; Flemmig *et al*. 1990). The success of pulsating irrigators with regular tips is limited in the subgingival area, and in periodontal pockets (Wennström *et al*. 1987). With specially designed tips (PikPocket: Waterpik Technologies, Inc.; Newport Beach, CA, USA), the pulsating stream of fluid may penetrate more deeply into the pocket areas (Cobb *et al*. 1988).

Tongue cleaners (see Procedure 7)

The dorsum of the tongue, with its papillary structure and furrows, harbors a great number of microorganisms (Chapter 60). It forms a unique ecologic oral site with a large surface area (Danser *et al*. 2003). The tongue is said to act as a reservoir which permits the accumulation and stagnation of bacteria and food residues (Outhouse *et al*. 2006). The tongue bacteria may serve as a source of bacterial dissemination to other parts of the oral cavity, e.g. the tooth surfaces and may contribute to dental plaque formation. Therefore, tongue brushing has been advocated as part of daily home oral hygiene together with toothbrushing and flossing (Christen & Swanson 1978). Tongue brushing has also been advocated as a component of the so-called "full-mouth disinfection" approach in the treatment of periodontitis, with the aim of reducing possible reservoirs of pathogenic bacteria (Quirynen *et al*. 2000).

Regular tongue cleaning has been used since ancient times and is still used by natives of Africa, Arabic countries, India, and South America. Many ancient religions emphasized cleanliness of the entire mouth, including the tongue. Indian people's daily ritual of oral hygiene was not only confined to brushing of the teeth but also the tongue was scraped and the mouth was rinsed with concoctions of betel leaves, cardamom, camphor or other herbs.

A large variety of tongue cleaners is commercially available. A modern tongue-scraping instrument may consist of a long strip of plastic ribbon. This is held in both hands and bent so that the edge can be pulled down over the dorsal surface of the tongue. Brushing also appears to be an easy method of cleaning the tongue providing that the gagging reflex can be controlled. In a recent systematic review it was concluded that scrapers or cleaners are more effective than toothbrushes for tongue cleaning (Outhouse *et al*. 2006). Patients should be informed that it is most important to clean the posterior portion of the tongue dorsum.

Tongue cleaning is a simple and fast procedure that helps to remove microorganisms and debris from the tongue. When tongue cleaning is practiced on a daily basis, the process becomes easier. Eventually, the patient may indeed feel "unclean" when tongue debris is not removed on a regular basis. In a study by Gross and co-workers (1975) the test group was instructed to brush their tongues as an adjunct to their normal oral hygiene measures. The members of a control group were not instructed to clean the tongue. A reduction in the presence of tongue coating was found of 40% in the test group as compared to the control group.

Some studies have shown that tongue brushing in combination with other methods of oral hygiene is

an effective method in reducing the formation of dental plaque. In contrast, Badersten and co-workers (1975) found no difference in *de novo* plaque accumulation between a 4-day period of tongue brushing and a 4-day period of no oral hygiene procedures. The authors suggested that the majority of the important plaque-forming bacteria might not originate from the tongue. Another reason for not finding an effect of tongue brushing on plaque formation may be that brushing of the posterior part of the dorsum of the tongue is difficult due to inaccesibility and discomfort.

Dentifrices

The use of a toothbrush is usually combined with a dentifrice (sold as *toothpaste*) with the purpose of facilitating plaque removal and applying agents to the tooth surfaces for therapeutic or preventive reasons (Chapter 36). In 1824, a dentist named Peabody was the first person to add soap to toothpaste. John Harris first added chalk as an ingredient to toothpaste in the 1850s. Colgate mass-produced the first toothpaste in a jar. In 1892, Dr. Washington Sheffield of Connecticut manufactured toothpaste into a collapsible tube. The traditional role of dentifrice is primarily cosmetic, in aiding the cleaning of teeth and producing fresh breath. It also makes toothbrushing more pleasant.

The studies by de la Rosa and co-workers (1979) and Stean and Forward (1980) validated the use of dentifrice since they found that there was a reduction in plaque growth after brushing with a dentifrice as opposed to brushing with water. In the course of the years many dentifrice formulations were tested and became well established because of their anti-plaque and/or anti-gingivitis properties. For additional information see Chapter 36.

Foam brushes, swabs or tooth towelettes

Tooth towelettes are being marketed as a method of plaque removal when toothbrushing is not possible. Their use is not meant to replace a daily toothbrushing regimen. Recently the I-Brush® has been introduced. This swab is mounted on the index finger of the brushing hand. It uses the agility and sensitivity of the finger. Consequently it could permit a better control over the finger pressure because the finger can actually feel the tooth and gingival surfaces and help positioning the brush for more effective scrubbing. During a 3-week clinical trial, no adverse effects were found. The results show that the finger brush removed less plaque than a regular manual toothbrush. In particular approximal plaque reduction was poor in comparison with the manual toothbrush. Based on these results, it is concluded that there is no beneficial effect of the finger brush in comparison with a regular manual toothbrush (Graveland *et al*. 2004).

Foam brushes resemble a disposable soft sponge on a stick and have been dispensed to hospital patients for intraoral cleansing and refreshing as early as the 1970s. They are particularly used for oral care in medically compromised and immunocompromised patients, to reduce the risk of oral and systemic infection (Pearson & Hutton 2002). Lefkoff and co-workers (1995) studied the effectiveness of such a disposable foam brush on plaque. In this study the regular manual toothbrush was found to be significantly more effective in retarding the accumulation of plaque from a plaque-free baseline on both facial and lingual surfaces. The foam brush did, however, show some plaque-preventive capabilities by maintaining plaque formation below 2 mm at the cervical margin of the tooth. Nevertheless, according to most authors, foam brushes should not be considered as a substitute for a regular toothbrush. In a study by Ransier and co-workers (1995) foam brushes were saturated with a chlorhexidine solution. They found the foam brush which had been soaked in chlorhexidine to be as effective as a regular toothbrush in controlling plaque and gingivitis levels. Therefore, if a toothbrush cannot be used in hospitalized patients, an alternative may be the use of chlorhexidine applied with a foam brush.

Side effects

Brushing force

Studies have shown brushing force with powered toothbrushes to be lower than that of a manual toothbrush (Van der Weijden *et al*. 1996c). This appears to be a consistent finding. There is an approximately 1.0 N difference between manual and powered toothbrushes. Recently McCracken and co-workers (2003) observed, in a range from 0.75–3.0 N, that the improvement in plaque removal, using a power toothbrush with forces in excess of 1.5 N was negligible. In a feedback study a professional brusher was asked to brush at 1.0 N, 1.5 N, 2.0 N, 2.5 N, and 3.0 N, during which the efficacy in relation of brushing force to brushing was determined. An increase in efficacy was observed with raising brushing force from 1.0 N to 3.0 N (Van der Weijden *et al*. 1996c). Hasegawa and co-workers (1992) evaluated the effect of different toothbrushing forces on plaque reduction by brushing with 100 g intervals on a scale from 100–500 g. The results of their study corroborate the findings of earlier studies that with increasing force more plaque is removed. In addition they observed that 300 g seems to be the most effective brushing force when using a manual toothbrush for both children and adults. Forces exceeding 300 g caused pain and gingival bleeding in the test patients. As shown in a manual brushing study in which efficacy was plotted against brushing force the relationship between force and efficacy appears not to be linear (Van der Weijden *et al*. 1998a). Using this particular manual toothbrush a positive correlation between efficacy and force up to 4.0 N was found. The more force was used, the more effective was the plaque removal. However

efficacy was reduced when forces above 4.0 N were used. Indeed there appeared to be a negative correlation. The hypothesis is that this negative correlation had to do with distortion of the brushing filaments. Above 4.0 N the brushing was no longer performed with the tip of the filament, but due to bending, with its side. This indicates that brushing force is not the sole factor which determines efficacy. Other factors such as action of the brush, size of the brushhead, brushing time, and manual dexterity may be of greater importance.

Excessive brushing force has been mentioned as a factor which is partly responsible for the origin of toothbrush trauma (gingival abrasion). In response to patients that use excessive force, manual and electric toothbrush manufacturers have introduced toothbrush designs, which can limit the amount of force used and thus reduce the chance of damage to soft and hard tissues. However there is no linear correlation between brushing force and abrasion. Mierau and Spindler (1989) performed a quantitative assessment of habit patterns of toothbrushing in 28 subjects and nine sessions. Least variations within each individual were observed with regard to brushing force. Brushing force ranged from 1.0–7.4 N between individuals. They did not observe any (visual) lesions from brushing in those individuals using a brushing force <2 N. If the brushing force was >2 N, co-factors such as brushing time, brushing method, and frequency of brushing appeared to be associated with acute brushing lesions. Burgett & Ash (1974) argued that the potential detrimental effect of brushing is related to the force applied at a particular point, i.e. pressure. it must be recognized that the head of a manual brush is larger than the head of the electric brush. Since the forces are given as a total of the force over the entire brush it may be that the unit pressure was less for the manual than for the electric brushes. They observed no difference in pressure between a soft manual (11.32 g/mm^2) and an electric toothbrush (11.29 g/mm^2). These data which show that the pressure for the electric and the manual brush are similar are also in agreement with findings presented by Van der Weijden and co-workers (1996c).

Toothbrush abrasion

Since various mechanical products are used in personal control of supragingival plaque, the possibility exists that some deleterious effects may appear as a consequence of these oral hygiene practices (Echeverría 1998). It has already been known for a long time that toothbrushing may have some unwanted effects on the gingiva and hard tooth tissues (Kitchin 1941). Trauma to hard tissues leads to cervical abrasion of the tooth surface. These lesions have been associated with toothbrush stiffness, the method of brushing, and brushing frequency. Cervical tooth abrasion has a multifactorial etiology, but in most cases it is the consequence of toothbrushing due to an excessive pressure of the brush and an excessive number of toothbrushing episodes/time. Both situations are probably linked to personality traits (*compulsive brushers*). Tooth wear has also been associated with toothbrush characteristics, especially related to the finishing and hardness of the filaments (Fishman 1997). It has been stated that hard tissue damage is mainly caused by the abrasives in the dentifrice, whereas lesions of the gingival tissues are caused by the toothbrush (Axelsson *et al*. 1997; Meyers *et al*. 2000).

In many instances, *tooth abrasion* is found in combination with *gingival recession*. Whereas gingival recession is associated with different etiologic/risk factors, e.g. periodontal inflammation, smoking, gingival biotype or repeated periodontal instrumentation, inadequate toothbrushing is probably the most significant one (Björn *et al*. 1981). Clinical experience does support the idea that, with improper use, toothbrushing can cause superficial damage to the gingival tissues. Patients with good oral hygiene have been found to have more gingival recession and more dental abrasion than those with poor oral hygiene. Unfortunately there are few studies in the dental literature concerning gingival lesions resulting from toothbrushing. Thus, to what extent oral hygiene procedures may traumatize the gingival tissues is not clear. Gingival abrasions as a result of brushing are often reversible localized superficial lesions. It is unlikely that gingival abrasion is induced by a single factor. One factor which has already been mentioned to be related to gingival abrasion is brushing force. In the literature, other factors have been suggested such as brushing method (e.g. Bass method), abusive toothbrush use, manual or powered toothbrushing, toothbrush grip, brush head shape, stiffness of filaments, end-rounding of toothbrush filaments, and toothbrushing frequency (Van der Weijden & Danser 2000).

Interestingly, there has been little debate on the role of dentifrice in the abrasion of soft tissues. This is somewhat surprising when abrasion of dental hard tissues is almost entirely a function of dentifrice. Detergents in dentifrice, agitated over a mucosal surface, could enhance the removal of the protective salivary glycoprotein layer and exert cytotoxic action on the overlying epithelial cells (Addy & Hunter 2003). No statistically significant difference in the incidence of gingival abrasion was found between brushing with dentifrice or without dentifrice (Versteeg *et al*. 2005) (Fig. 35-7).

Importance of instruction and motivation in mechanical plaque control

A fundamental principle for all preventive action is that the effect is greatest where the risk of development of disease is greatest. Needs-related instruction in oral hygiene should therefore intensify mechanical plaque removal on those individual teeth and surfaces that are at risk. A prerequisite for establishing needs-related toothcleaning habits is a well

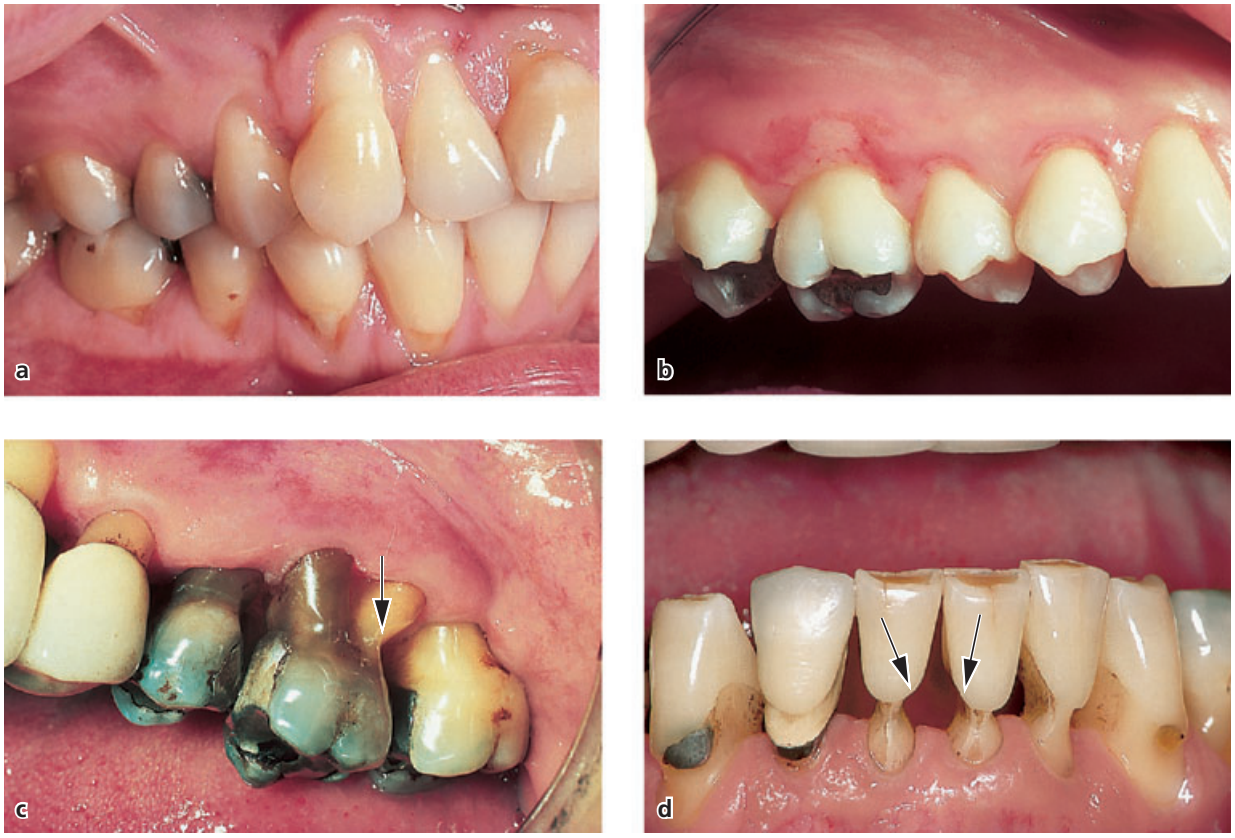


Fig. 35-7 (a) Soft tissue damage as a result of extensive toothbrushing. Note gingival recession on the buccal gingival surface of tooth 13. (b) Note multiple ulcerations of the buccal gingival margin in the right maxilla. (c,d) Hard tissue damage has resulted after extensive use of interdental brushes.

motivated, well informed, and well instructed patient (Axelsson 2004). Mechanical plaque control demands active participation of the individual subject, and therefore the establishment of proper oral home care habits is a process that involves and depends on behavioral changes to a great extent. When implementing behavioral changes, dental professionals should try to ensure that the patient recognizes his/her oral health status and the role of his/her personal oral hygiene procedures in the prevention of caries and periodontal diseases. The patient should be informed about the casual relationship that led to the disease process and should be encouraged to take responsibility for his/her own oral health. The dental team has numerous possibilities to demonstrate soft tissue alterations elicited by inflammation to the patient, and the responsible etiologic factors. Most commonly, as with sports coaching, a one-to-one professional–patient approach should be employed.

Many patients spend too little time brushing or they brush haphazardly. The importance of thorough plaque removal should be stressed. Toothbrushing instruction for a patient involves teaching what, when, where, and how. In addition, instruction should also involve a description of specific toothbrushing methods, the grasp of the brush, the sequence and amount of brushing, the areas of limited access, supplementary brushing for occlusal surfaces and the tongue. The possible detrimental effects from improper toothbrushing and variations for special condition are described (Wilkins 1999). The design of toothbrushes or a specific toothbrushing method are of secondary importance to the skills of the individual in using the brush (Frandsen 1986). The simplest, least time-consuming procedures that will effectively remove bacterial plaque and maintain oral health should be recommended. If a patient prefers a specific oral hygiene strategy the clinician can evaluate this and modify the technique to maximize effectiveness, rather than changing it. Although it is necessary to give all patients honest feedback on their plaque removal efforts, it is also important to reward a positive performance and not entertain unrealistic expectations, so that the patient will not dread each maintenance visit.

Oral hygiene instruction should also include components such as self-assessment, self-examination, self-monitoring, and self-instruction. With this purpose, several devices and chemical agents have been used in order to make dental plaque more evident to the patient. The interested patient can be informed and motivated, for example, through use of disclosing agents to visualize plaque at the gingival margin or in the interdental spaces. Disclosing agents are chemical compounds such as erythrosine, fuchsin or a fluorescein-containing dye that stains dental plaque and thus makes it fully evident to the patient, either with regular or ultraviolet light. Erythrosine

Fig. 35-8 (a) Disclosing solution is often used to identify plaque. (b) Note remaining plaque on the buccal tooth surfaces after staining. (c) After self-performed tooth cleaning, remaining plaque can be identified by the patient following rinsing with a disclosing solution.

has already been used for many years and has received an FDA approval (Arnim 1963) (Fig. 35-8).

When applied immediately before toothbrushing, the patient can identify the amount of plaque formed after the last toothbrushing episode, thus receiving an immediate feedback about his/her cleaning performance. This procedure is useful during the early phase of plaque control. Later on, the disclosing agent should be applied after toothbrushing, which allows the patient to identify those areas needing additional cleaning efforts. Disclosing solution is available in either liquid or tablet form. The liquid may offer some advantages in that the operator can ensure that all surfaces are adequately covered. The red disclosing solution remains in the mouth for some time and may temporarily stain the lips and gingiva.

Disclosing of plaque in the patient's mouth is usually not enough to establish good oral hygiene habits, however. Other factors might influence the individual to modify or determine his or her behavior. These factors may be more or less beyond the control of the dental personnel (such as social and personal factors, environmental setting, and past dental experiences) or may lie within the control of dental personnel (such as conditions of treatment, instruction, and education of the patient). All of these should be considered in the design of an individualized oral hygiene program.

A variety of methods can be used to deliver advice and instruction. The effect of various oral hygiene instruction programs, administered individually or in groups, has been evaluated in a number of clinical studies. These studies have evaluated whether instruction given during one visit only is similar to step-by-step instruction provided during several visits, or whether the use of pamphlets or video tapes is superior to self-instruction manuals and to personal instruction given by a dental professional. In a study by Renton-Harper and co-workers (1999) an instructional video for an oscillating rotating electric toothbrush was evaluated. The subjects that followed the instructional video benefited significantly and considerably in terms of plaque removal compared to subjects receiving only written instructions. Different types and amounts of feedback to the patients using disclosed plaque scores and phase contrast demonstrations have also been investigated. These studies have usually reported similar improvements in plaque and gingivitis scores, irrespective of the mode of instruction. However, these results should be interpreted with caution since the subjects participating in these studies were examined at regular intervals, and therefore it is difficult to separate the effect of repeated examinations from the effect of the instructions (Renvert & Glavind 1998).

If oral hygiene motivation, information, and instruction are combined with professional tooth cleaning the effect in terms of reduction of plaque levels and levels of gingival inflammation may persist even after 6 months. A recent systematic review concluded, based on studies ≥6 months of duration, that a single oral hygiene instruction, describing the use of a mechanical toothbrush, in addition to a single

professional "oral prophylaxis" provided at baseline, had a significant, albeit small, positive effect on the reduction of gingivitis (Van der Weijden & Hioe 2005).

Rylander and Lindhe (1997) have recommended that oral hygiene instruction be given during a series of visits allowing the possibility of giving the patient immediate feedback and reinforcing the patient in his/her home care activities. The protocol below is based on the one used in several clinical trials by Lindhe and Nyman (1975), Rosling and co-workers (1976), and Lindhe and co-workers (1982), where the role of plaque control in preventing and arresting periodontal diseases was clearly proven.

First session

1. Apply a plaque-disclosing solution to the teeth and, with aid of a hand mirror, demonstrate all sites with plaque to the patient (Fig. 35-8b). The plaque score should be recorded using a plaque control record (Fig. 35-9).
2. Ask the patient to clean the teeth using his/her traditional technique. With the aid of a hand mirror, demonstrate the results of the toothbrushing to the patient, again identifying all sites with plaque (Fig. 35-8c).
3. Without changing the technique, ask the patient to clean the surfaces with plaque.

Depending on the plaque remaining after this second toothbrushing, the dental professional should either improve the technique or introduce an alternative system of toothbrushing. In order not to overload the patient with too much information during the first session, the use of adjunctive devices for interproximal cleaning can be introduced or improved in the second session.

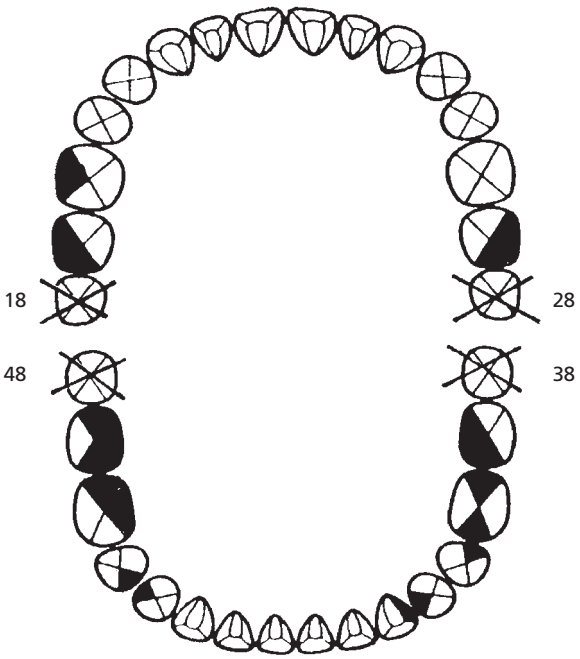


Fig. 35-9 A chart illustrating the teeth and tooth surfaces in the maxilla and mandible. The distribution of tooth surfaces with dental plaque (shadowed areas) is identified. In this case the plaque score is 17%.

Second session

1. A few days after the previous session, the disclosing solution is again applied. The results, in terms of plaque deposits, are identified in the mouth, recorded in the plaque control record, and discussed with the patient.
2. The patient is then invited to clean the teeth, according to the directions previously given in the first session, until all staining is removed. In many cases, toothbrushing instructions will need to be reinforced. Reinforcement and positive recognition should be given to the patient at the same time.

If necessary, the use of interproximal cleaning aids can now be introduced or improved.

Third and following sessions

1. One or two weeks later the same procedure used in the second session is repeated. However, the efficacy of self-performed plaque control should be evaluated and presented to the patient at each appointment. This repeated instruction, supervision, and evaluation aims to reinforce the necessary behavioral changes.

The long-term result of oral hygiene instruction is dependent on behavioral changes. Patients may fail to comply with given instructions for many reasons, ranging from unwillingness to perform oral self-care, poor understanding, lack of motivation, poor dental health beliefs, and unfavorable dental health values, to stressful life events or low socioeconomic status. Although the use of behavior-modification techniques may offer an advantage over traditional instruction techniques, there is limited research in this area to clarify the relationship between health beliefs and compliance.

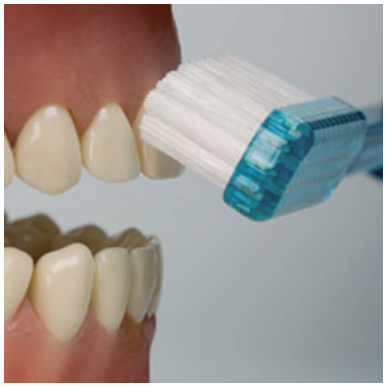
Conclusion

- Oral hygiene instruction should be tailored to each individual patient on the basis of his/her personal needs and other factors.
- The patient should be involved in the instructional process.
- An individualized maintenance program should follow the basic oral hygiene instruction.

All the illustrations for the following procedures are used with permission from *Paro Praktijk Utrecht*.

Procedure 1: Instruction for Manual Toothbrush

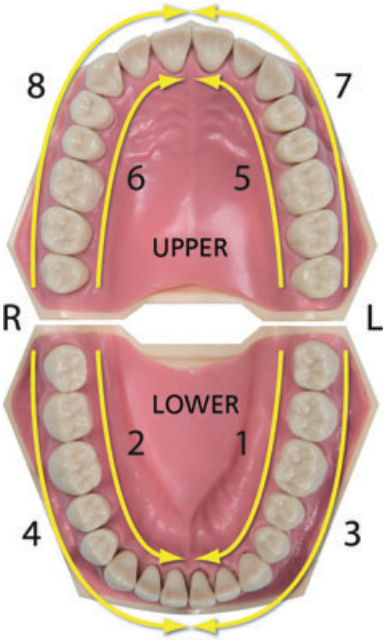
It is of utmost importance that in addition to using the correct toothpaste and also brushing for at least 2 minutes to brush the teeth in a set sequence. This prevents missing out certain areas. Areas untouched by the brush allow plaque to continue to grow. Try to choose a brush with medium or soft bristles and a small head.



Instruction

- Hold the brush firmly and place the bristles at an angle against the edge of your gums (use a 45° angle). Take care to ensure that the bristles are in contact with a small part of the gum margin.
- Place the brush against the molar or tooth at the back of the mouth and make short back and forth scrubbing movements. Brush from the back to the front of the mouth and try to overlap the strokes. Do not brush more than two teeth simultaneously. Always start at the back and work slowly forwards.
- Always hold the brush head horizontal when cleaning the outside surfaces of the teeth. It is easier to hold the head vertically when brushing the inside surfaces of the top and bottom teeth.
- Avoid too much pressure and fast movements and be aware of feeling contact with the gum margin. Also avoid brushing too vigorously thereby preventing damage to the gums.

When cleaning the teeth keep using the same sequence of brushing. For example, inside of bottom jaw left (15 seconds) inside right (15 seconds). Then left on the outside (15 seconds), followed by right on the outside (15 seconds). Repeat the same sequence in the top jaw. Finally, brush the chewing surfaces with small scrubbing movements. Replace the brush when the bristles start to splay.



Procedure 2: Instruction for the Electric Toothbrush

The importance of using a set sequence of brushing movements is also applicable when using an electric toothbrush. The question as to whether an electric brush is better than a manual one has been asked many times. Both allow to one achieve a high level of oral hygiene. However research has shown that electric toothbrushes are more efficient and many people report that they are easier to use.

Instruction

- Place the brush firmly on the hand piece. Grip the brush in the palm so that the bristles of the head are somewhat angled toward the gums (at an angle of approximately 70°). Try to allow the longer bristles to penetrate between the teeth and take care that the bristles contact your gums.
- Switch on the brush and place the head on the last tooth in the mouth (check the angle) and move the head gradually (in about 2 seconds) from the back to the front of this tooth.
- Try to follow the contour of both the tooth and the gums. Place the brush head on the next tooth and repeat this process.
- Allow the electric toothbrush to do the work. It is not necessary to press hard or make brushing movements.
- Use a timer! Many brushes will give some form of signal after 30 seconds (the apparatus stops for a moment). This is the point at which to move on to a new part of the mouth.

Remember to thoroughly clean the brush and its head when finished.

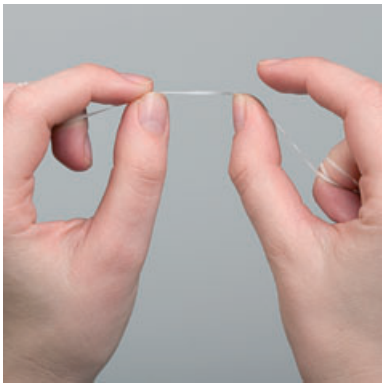
Procedure 3: Use of Dental Floss

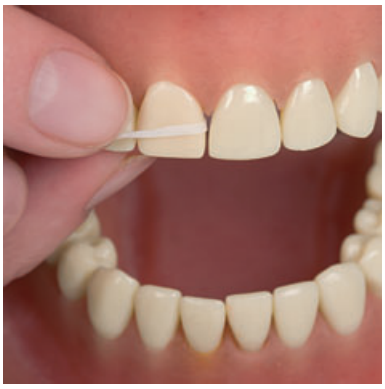
The use of dental floss has become part of oral care in addition to correct, more frequent and longer tooth brushing. Floss can be purchased in a variety of thicknesses and types and with or without a layer of wax. If there is sufficient space between the front and back teeth is it advisable to use the somewhat thicker tape than the thinner floss.

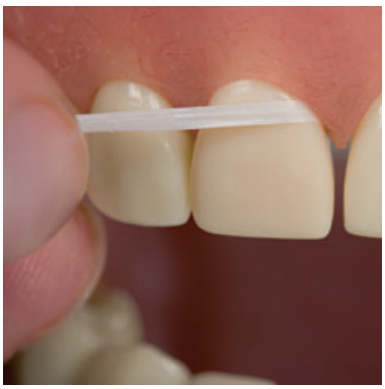
Instruction

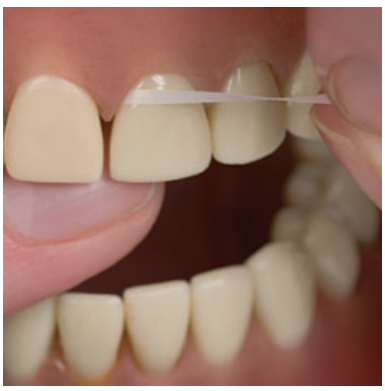
- Take approximately 40 cm of floss and wind the ends loosely around the middle finger. Allow for 10 cm between the middle fingers. Then hold the floss between the thumb and first finger so that about 3 cm remains between the thumbs.
- Using a sawing movement, allow the tightly stretched piece of floss to pass between the front and back teeth. This may be difficult where teeth are so close that the space between them is limited. Avoid allowing the floss to slip so fast between the teeth that the gums become damaged.
- Stretch the floss around one of the teeth and carefully allow it to pass just under the gum, once again with a sawing movement.
- Draw the floss up to the contact point with a sawing movement and then repeat the process on the other tooth bordering the space filled with gum tissue.
- Remove the floss from between the teeth, once again with a sawing movement and repeat this process for all the other spaces in the mouth.
- Use a clean piece of floss for each separate space by unwinding part of it from around one middle finger whilst winding it around the other middle finger.

Do not worry if at first your gums bleed slightly. This will stop after using the floss a number of times. Don't give up!

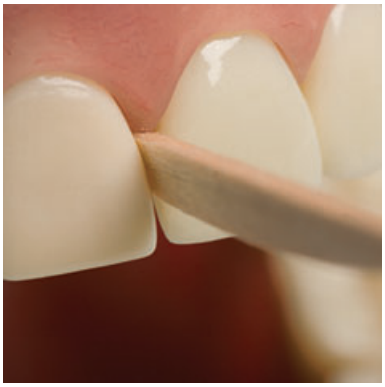


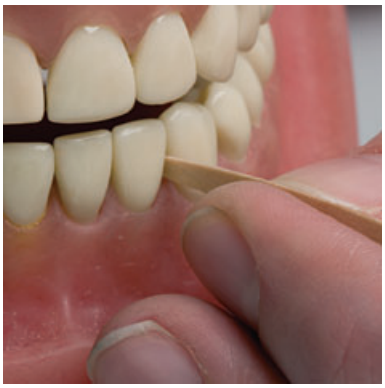


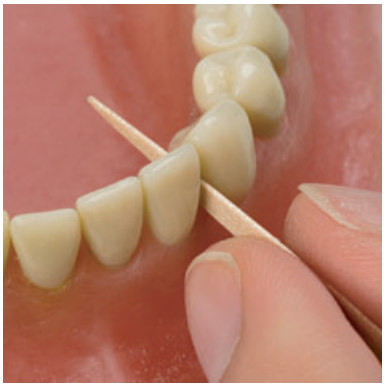




Procedure 4: Woodsticks







Most adults have sufficient space available between the incisors and molars to allow woodsticks to be used. These come in differing thicknesses and are made from wood and have a triangular cross section, mimicking the shape of the space between the teeth. Woodsticks can only be used once and are ideal when you have a few spare moments – for example when sitting in a traffic queue!

Instruction

- Hold the woodstick firmly between the thumb and first finger about halfway along its length. When possible place the other fingers for support on the chin. Moisten the tip of the woodstick by sucking on the point of it, thus making it softer and more flexible.
- Place the flat side of the woodstick (i.e. not the sharp side) against the gum. In the upper jaw the flat surface will face upwards and in the lower jaw downwards.
- Push the woodstick firmly from the outer side of the space into it until it becomes just wedged. Then pull it back slightly and push it back once again, using a light sawing motion at right angles to the outer surfaces of the teeth. Light pressure can also be applied simultaneously to the gums. Repeat this a few times, angling the woodstick so as to contact the surfaces of the teeth enclosing the space.
- When using a woodstick between the premolars and molars, close the mouth slightly to reduce tension in the cheeks making the movements easier.

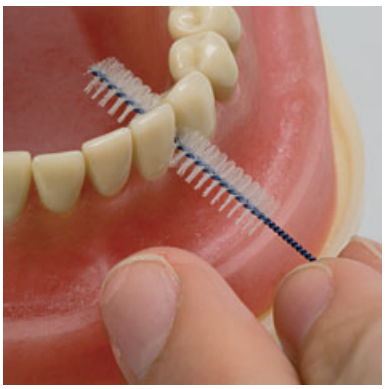
With this method, all spaces between the teeth throughout the mouth can be cleaned. Should the woodstick prick the surface of the gums with the point, angle it a little differently – in the upper jaw the point will face downwards and in the lower jaw upwards. Do not be concerned if your gums bleed a little at first – this will disappear after using the woodsticks repeatedly for a period of time.

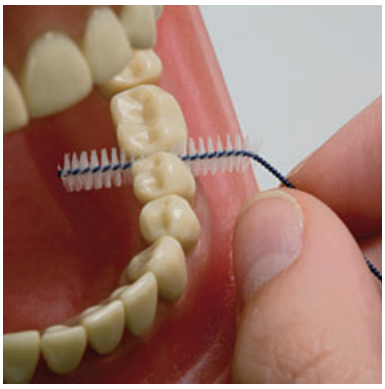
Procedure 5: Interproximal Brushes

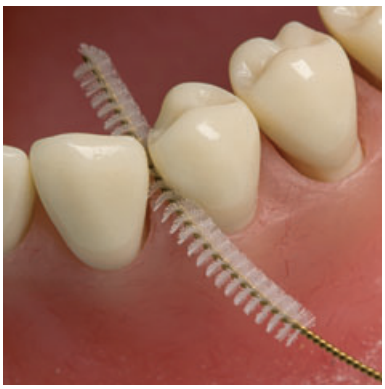
Interdental brushes are purchasable in a variety of sizes varying from small to very large. It is of importance to choose the correct diameter of the bristle part of the brush. The size of the space between the teeth determines the size of the diameter of the bristles on the brush. It is often necessary to use different size of brush within one mouth for optimal cleansing. In order to effectively remove dental plaque there should be a slight degree of resistance when the brush is moved back and forth between the teeth.

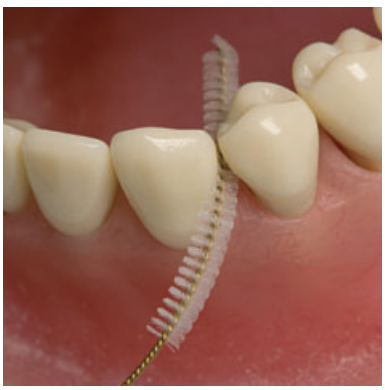
Instruction

- Always use the interdental brush *without* toothpaste
- Hold the interdental brush between the thumb and first finger just behind the bristles. Support can be achieved when necessary by placing your other fingers on your chin. Push, from the outer side of the space, the interdental brush carefully between the teeth, taking care that the brush remains at right angles to the teeth.
- Avoid scraping the centre (metal spiral part) of the brush against the teeth.
- Slide the brush in and out of the space using the full length of the bristle part of the brush. This will remove the dental plaque.
- The area of contact between the brush and the teeth can be somewhat increased by using differing angles of insertion.
- Slight pressure of the brush against the gums should be used as this will allow the bristles to penetrate a little underneath the gum margin.
- By slightly closing the mouth it will be easier to manipulate the brush as the tension in the cheeks is lessened. It may also be of help to slightly bend the brush to ease insertion.
- Cleanse all areas between the teeth where an interdental brush will fit. Rinse the interdental brushes thoroughly after use and allow them to dry out. It is often a good idea to combine the use if interdental brushes and woodsticks.







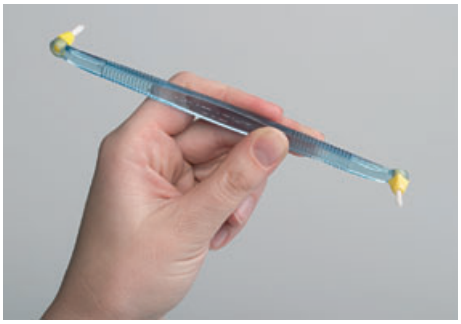


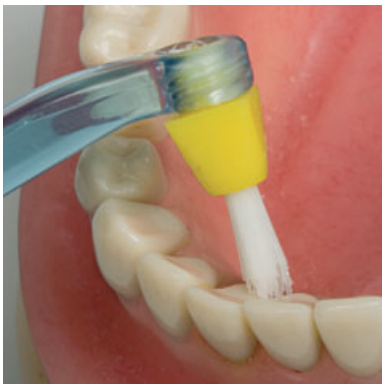
Procedure 6: Instruction for Single-Tufted/End-Tufted Brush

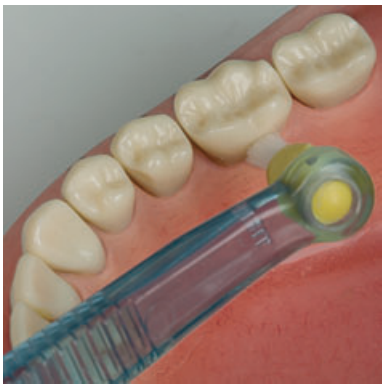
The single-tufted toothbrush is a small brush with a small, single tuft of short bristles attached to the end. The end-tufted brush has a number of small tufts attached in a similar manner. These brushes are ideal for cleansing areas of the dentition which cannot be reached with other oral hygiene aids. For example a lone standing tooth, the back surface of the last molar or tooth in the arch, wires and locks of orthodontic braces, grooves or the entrance to areas where roots split apart.

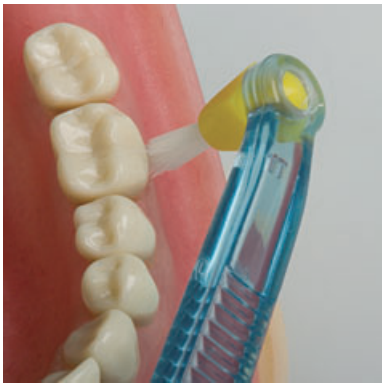
Instruction

- Hold the single-tufted brush in the same way as a pen. This prevents too much force being applied to the gums.
- Place the single-tufted brush at an angle directed toward the gums (about 45°) – this allows the bristles to reach just under the gum margin.
- Use small, rotational pencil movements.
- The bristles of the brush will then rotate under and along the gum margin. The brush should then be slowly moved along the tooth surface to cover all areas.



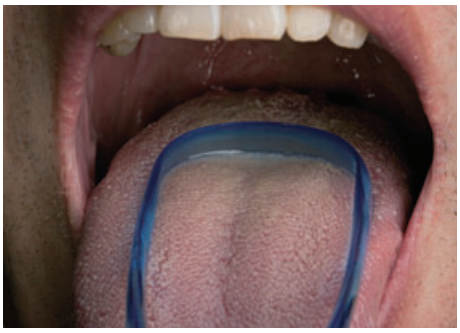






Procedure 7: Use of Tongue Cleaners

Tongue cleaning is a useful addition to the daily oral hygiene routine. Many bacteria can be found within the grooves on the back of the tongue which can cause bad breath. By brushing or scraping the tongue this problem can be markedly helped or prevented entirely. One of the problems associated with tongue cleaning is that it can stimulate a gag reflex, especially when first using this procedure. This occurs more frequently with brushing than when using a scraper. Some people find it less of a problem if they clean their tongue in the evening.



Instruction

- There are various types of tongue cleaners: the most effective seems to be one having the form of a loop.
- Extend the tongue as far as possible out of your mouth.
- Breathe calmly through your nose.
- Place the tongue cleaner as far as possible on the back of the tongue and press lightly with it so that the tongue becomes flattened.
- Ensure full contact of the tongue cleaner with the tongue.
- Pull the tongue cleaner slowly forward.
- Clean the middle part of the tongue first using the raised edge on one side of the instrument.
- Use the smooth surface of the tongue cleaner on the sides of the tongue.
- Repeat these scraping movements a number of times.
- Rinse the mouth several times.

Remember to clean the tongue cleaner thoroughly after use.

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Chapter 36

Chemical Supragingival Plaque Control

Martin Addy and John Moran

This chapter will consider the past and present status and success of chemical supragingival plaque control in the prevention of gingivitis and thereby the occurrence or recurrence of chronic periodontal diseases. Chlorhexidine, arguably the most studied agent, will be used to consider the possible applications of chemical plaque control in periodontal practice.

Classification and terminology of agents

Agents that could inhibit the development or maturation of supragingival plaque have been classified according to possible mechanisms of action (for review see Addy & Moran 1997): (1) anti-adhesive; (2) antimicrobial; (3) plaque removal; and (4) antipathogenic. The majority of agents used to control supragingival plaque are contained in "oral hygiene" products and available to the general public either directly "over the counter" or following recommendation/prescription by a dental or medical professional. Manufacturers of these products and, for that matter, published literature use a variety of terms to describe the action of these chemical agents, often interchangeably, which has tended to cause confusion. In an attempt to clarify the various descriptive terms used the European Federation of Periodontology in the 1996 European Workshop on Periodontology recommended definitions for the terminology employed for agents in chemical supragingival plaque control (Lang & Newman, 1997) as follows:

- Antimicrobial agents: chemicals that have a bacteriostatic or bactericidal effect *in vitro* that alone cannot be extrapolated to a proven efficacy *in vivo* against plaque.
- Plaque reducing/inhibitory agents: chemicals that have only been shown to reduce the quantity and/or affect the quality of plaque, which may or may not be sufficient to influence gingivitis and/or caries.
- Antiplaque agents: chemicals that have an effect on plaque sufficient to benefit gingivitis and/or caries (Addy *et al*. 1983).
- Antigingivitis agents: chemicals which reduce gingival inflammation without necessarily influencing bacterial plaque (includes anti-inflammatory agents).

The classification, terminology, and definitions are presented here because of their fundamental importance to understanding the concept of chemical

supragingival plaque control. They will be considered in greater detail however under the headings of "Approaches to chemical supragingival plaque control" and "Evaluation of chemical agents and products" and, particularly for the latter, in respect of implied and inferred claims made by manufacturers.

The concept of chemical supragingival plaque control

Epidemiologic studies revealed a peculiarly high correlation between supragingival plaque levels and chronic gingivitis (Ash *et al*. 1964), and clinical research (Löe *et al*. 1965) led to the proof that plaque was the primary etiologic factor in gingival inflammation. Subgingival plaque, derived from supragingival plaque, is also intimately associated with the advancing lesions of chronic periodontal diseases. On the basis that plaque-induced gingivitis always precedes the occurrence and recurrence of periodontitis (Lindhe 1986; Löe 1986), the mainstay of primary and secondary prevention of periodontal diseases is the control of supragingival plaque (for review see Hancock 1996). Periodontal diseases appear to occur when a pathogenic microbial plaque acts on a susceptible host (for review see Haffajee & Socransky 1994). What constitutes a pathogenic subgingival plaque has been, and continues to be, a much researched area in periodontology. In the 1996 World Workshop on Periodontology a small number of bacteria were confirmed as true pathogens with a longer list considered as putative pathogens (for reviews see Zambon 1996). Much has been learned in the intervening decade, not the least of which is the bacterial diversity of subgingival plaque in health and disease, highlighted in a number of reviews (for review see Socransky & Haffajee 2005). The possibility that viruses may be involved has also been postulated (for review see Slots 2003). If the latter postulate becomes proven an extension of the classification of chemical agents, to include antiviral, will be necessary. Interestingly, and alluded to later in this chapter, some of the antimicrobial agents used in chemical plaque control do have antiviral activity.

Susceptibility to periodontal disease is less well understood and, at this time, certainly difficult to predict and quantify, although risk factors have been identified including genetic markers (for reviews see Kinane *et al*. 2005) (see Chapters 11 and 18). The relationship of plaque levels to pathogenicity and susceptibility is also poorly understood and therefore, for any one individual, what constitutes a satisfactory level of oral hygiene cannot be stated. This aside, there is evidence which demonstrates that improving oral hygiene and gingival health, over several decades, noted in developed countries (Hugoson *et al*. 1998a), has been associated with a decreasing incidence of periodontal disease (Hugoson *et al*. 1998b). Additionally, long-term follow-up of treated periodontal disease patients has shown that success is dependent on maintaining plaque levels compatible with gingival health (Axelsson & Lindhe 1981). Supragingival plaque control is thus fundamental to the prevention and management of periodontal diseases and, with appropriate advice and instruction from professionals, is primarily the responsibility of the individual.

It could be argued that the heavy reliance on mechanical methods to prevent what are microbially associated diseases is outdated. Very few hygiene practices against microorganisms used by humans on themselves, in the home, at the workplace or in the environment rely on mechanical methods alone and some methods are only chemical. The contrary argument must be that the prevention of periodontitis, through the control of gingivitis, would require the discovery of a safe and effective agent. Also, such a preventive agent would have to be applied from an early age to a large proportion of all populations, many of whom would have low or no susceptibility to periodontal disease (for review see Papapanou 1994).

These discussions aside, chemical preventive agents, aimed at the microbial plaque, have been a feature of periodontal disease management for almost a century (for review see Fischman 1997). The consensus appears to be that the use of preventive agents should be as adjuncts and not replacements for the more conventional and accepted effective mechanical methods and only then when these appear partially or totally ineffective alone.

Mechanical tooth cleaning through toothbrushing with toothpaste is arguably the most common and potentially effective form of oral hygiene practiced by peoples in developed countries (for reviews see Frandsen 1986; Jepsen 1998); although, *per capita* in the world, wood sticks are probably more commonly used. Interdental cleaning is a secondary adjunct and would seem particularly important in individuals who, through the presence of disease, can be retrospectively assessed as susceptible (for reviews see Hancock 1996; Kinane 1998). Unfortunately, it is a fact of life that a significant proportion of all individuals fail to practice a high enough standard of plaque removal such that gingivitis is highly prevalent and from an early age (Lavstedt *et al*. 1982; Addy *et al*. 1986). This, presumably, arises either or both from a failure to comply with the recommendation to regularly clean teeth or lack of dexterity with tooth cleaning habits (Frandsen 1986). Certainly, many individuals remove only around half of the plaque from their teeth even when brushing for 2 minutes (de la Rosa *et al*. 1979). Presumably this occurs because certain tooth surfaces receive little or no attention during the brushing cycle (Rugg-Gunn & MacGregor 1978; MacGregor & Rugg-Gunn 1979). The adjunctive use of chemicals would therefore appear a way of overcoming deficiencies in mechanical tooth cleaning habits as practiced by many individuals.

Supragingival plaque control

The formation of plaque on a tooth surface is a dynamic and ordered process, commencing with the attachment of primary plaque-forming bacteria. The attachment of these organisms appears essential for initiating the sequence of attachment of other organisms such that, with time, the mass and complexity of the plaque increases (see Chapter 8). Left undisturbed, supragingival plaque reaches a quantitative and qualitative level of bacterial complexity that is incompatible with gingival health, and gingivitis ensues. Even though, as yet, the microbiology of gingivitis is poorly understood, the sequencing of plaque formation highlights how interventions may prevent the development of gingivitis. Thus, any method of plaque control, which prevents plaque achieving the critical point where gingival health deteriorates, will stop gingivitis. Unfortunately, the lack of knowledge of bacterial specificity for gingivitis does not allow targeting or the control of particular organisms except for perhaps the primary plaque formers. Plaque inhibition has, therefore, targeted plaque formation at particular points – bacterial attachment, bacterial proliferation, and plaque maturation – and these will be discussed in more detail in the later section "Approaches to chemical supragingival plaque control".

The mainstay of supragingival plaque control has been regular plaque removal using mechanical methods which, in developed countries, means the toothbrush, manual or electric, and in less well developed countries the use of wood or chewing sticks (for review see Frandsen 1986, Hancock 1996). These devices primarily access smooth surface plaque and not interdental deposits. Interdental cleaning devices include wood sticks, floss, tape, interdental brushes, and, more recently, electric interdental devices (for reviews see Egelberg & Claffey 1998; Kinane 1998). Regular mechanical tooth cleaning is directed towards maintaining a level of plaque, quantitatively and/or qualitatively, which is compatible with gingival health, and not rendering the tooth surface bacteria free. Theoretically, mechanical cleaning of teeth could prevent caries but workshops have concluded that tooth brushing *per se* and interdental cleaning as performed by the individual do not prevent caries (for review see Frandsen 1986). Clearly, but outside the scope of this chapter, the toothbrush and other mechanical devices do provide a vehicle whereby anticaries agents, such as fluoride, can be delivered to the tooth surface. Under the conditions of clinical experimentation, tooth cleaning performed once every 2 days was shown to prevent gingivitis (Lang *et al*. 1973). The professional recommendation however, has been to brush twice per day, for which there is evidence of a benefit to gingival health over less frequent cleaning with no additional benefit for more frequent brushing (for review see Frandsen 1986). Indeed, recommendations to increase the frequency of brushing more than twice daily may result in more damage to hard and soft tissues (for review see Addy & Hunter 2003). The duration of brushing is somewhat controversial given that most surveys or studies reveal an average brushing time of 60 seconds or less (Rugg-Gunn & MacGregor 1978; MacGregor & Rugg-Gunn 1979). It is worth noting that one study showed less than 50% plaque removal after 2 minutes' brushing (de la Rosa *et al.* 1979). This perhaps highlights that many individuals spend little or no time during the brushing cycle at some tooth surfaces, notably lingually (Rugg-Gunn & MacGregor 1978; MacGregor & Rugg-Gunn 1979).

Oral hygiene, oral hygiene instruction, and the effect of supragingival plaque control alone on subgingival plaque and therefore periodontal disease is the subject of other chapters. Nevertheless, some further comments on mechanical tooth cleaning are pertinent in this chapter, particularly in respect of comparative efficacy of devices. The manual toothbrush as known today, man-made filaments in a plastic head, was invented as recently as the 1930s. Evidence for such devices dates back to China, approximately 1000 years ago, re-emerging in the 1800s in Europe, but too expensive for common usage (for reviews see Fischman 1997). Numerous changes in manual toothbrush design have occurred, particularly recently, and similarly numerous claims have been made for the efficacy of individual designs. Despite this, researchers, workshop reports, and consensus views have repeatedly concluded that there is no best design of manual toothbrush nor an optimal method of tooth cleaning: the major variable being the person using the brush (for reviews see Frandsen 1986; Jepsen 1998). Limited evidence is available comparing the modern toothbrush with chewing sticks but what is available suggests similar efficacy (Norton & Addy 1989), perhaps not surprisingly if indeed the user is the important factor. Interdental cleaning is considered important particularly for those individuals who are known to be susceptible to or have periodontal disease (for reviews see Egelberg & Claffey 1998; Kinane 1998). Here again, there is little evidence supporting one interdental cleaning method over another, leaving patients and professionals to hold subjectively related preferences (for review see Kinane 1998). Electric toothbrushes of the counter-rotation type found prominence for a short time in the 1960s and 1970s but were unreliable and proven of no greater efficacy over manual brushes, except for handicapped individuals (for reviews see Frandsen 1986). More recently, ranges of new electric brushes have appeared with a variety of head, tuft, and filament actions. For these, consensus reports conclude that there is evidence for greater efficacy over manual brushes particularly when professional advice in their use is provided (for reviews see Hancock 1996; Egelberg & Claffey 1998; van der Weijden *et al*. 1998). More recently, a Cochrane systematic review concluded that only oscillating

rotating electric toothbrushes could be proven significantly more effective than manual toothbrushes in reducing plaque and gingivitis (Heanue *et al*. 2004). Despite this, there is no clear evidence that any one electric design or head motion is superior and, again, the user appears the major variable. As with manual brushes advice and instruction in the use of electric brushes can result in very high levels of plaque control (Renton Harper *et al*. 2001). Given the speed of head movement for electric versus manual brushes, there must be concerns over potential harmful effect to hard and soft tissues. In this respect, Phaneuf and co-workers (1962) hypothesized that electric brushes would produce the same or less harm, postulating that the users would apply less force. Many years later the application of less pressure to electric compared to manual brushes was proven (for review see van der Weijden *et al*. 1998). Overall, therefore, it has been concluded that the benefits of normal toothbrushing alone and as a vehicle for toothpaste with a variety of active ingredients far outweigh the potential for harm to hard and soft tissues (for review see Addy & Hunter 2003).

Chemical supragingival plaque control

History of oral hygiene products

The terminology "oral hygiene products" is recent but there is evidence dating back at least 6000 years that formulations and recipes existed to benefit oral and dental health (for reviews see Fischman 1997). This includes the written Ebers Papyrus 1500 BC containing recipes for tooth powders and mouth rinses dating back to 4000 BC. A considerable number of formulations can be attributed to the writer and scientist Hippocrates (circa 480 BC). By today's standards the early formulations appear strange if not disgusting but they were not always without logic. Thus, bodies or body parts of animals perceived to have good or continuously erupting teeth were used in the belief that they would impart health and strength to the teeth of the user. Hippocrates, for example, recommended the head of one hare and three whole mice, after taking out the intestines of two, mixing the powder derived from burning the animals with greasy wool, honey, aniseeds, myrrh, and white wine. This early toothpaste was to be rubbed on the teeth frequently.

Mouth rinses similarly contained ingredients which would have had some stimulating effect on salivary flow, breath odor masking and antimicrobial actions, albeit not necessarily formulated with all these activities in mind. Alcohol-based mouth rinses were particularly popular with the Romans and included white wine and beer. Urine, as a mouth rinse, appeared to be popular with many peoples and over many centuries. There even appeared differences in opinion, with the Cantabri and other peoples of Spain preferring stale urine, whereas Fauchard (1690–1761) in France recommended fresh urine. The Arab nations were purported to prefer children's urine and the Romans to prefer Arab urine. Anecdotal reports suggest the use of urine as a mouth rinse to this very day with individuals rinsing with their own urine. There could, indeed, be benefits to oral health from rinsing with urine by virtue of the urea content; however this has never been evaluated, and given today's Guidelines for Good Clinical Practice, it is unlikely that study protocols would receive ethical approval.

Throughout the centuries, most tooth powders, toothpastes, and mouth rinses appear to have been formulated for cosmetic reasons including tooth cleaning and breath freshening rather than the control of dental and periodontal diseases. Many formulations contained very abrasive ingredients and/or acidic substances. However, ingredients with antimicrobial properties were used, perhaps not intentionally, and included arsenic and herbal materials. Herbal extracts are, perhaps, increasingly being used in toothpastes and mouth rinses, although there are little data to support efficacy for gingivitis and none for caries. Many agents prescribed well into the twentieth century, usually as rinses, had the potential to cause local damage to tissues, if not systemic toxicity, including aromatic sulfuric acid, mercuric perchloride, carbolic acid, and formaldehyde (Dilling & Hallam 1936).

Perhaps the biggest change to toothpastes came with the chemoparasitic theory of tooth decay of W.D. Miller in 1890. The theory that organic acids were produced by oral bacteria acting on fermentable carbohydrates in contact with enamel led to both the introduction of agents into toothpaste which might influence this process, and the production of alkaline products. Shortly after, and at the beginning of the twentieth century, various potassium and sodium salts were added to toothpaste as a therapy for periodontal disease. The first half of the twentieth century saw numerous claims for toothpastes for oral health benefits, including tooth decay and periodontal disease. For example, with the early recognition that periodontal diseases were associated with microorganisms, emetin hydrochloride was added to toothpaste to treat possible amoebic infections. Perhaps with the exception of the well known essential oil mouth rinse marketed at the end of the nineteenth century, the addition of antimicrobial and/or antiseptic agents to toothpastes and mouth rinses is a relatively recent practice by manufacturers. During the nineteenth and twentieth centuries, toothpastes also became less abrasive. Interestingly, the importance of a level of abrasivity in toothpastes to the prevention of extrinsic dental stain became apparent when one manufacturer marketed a non-abrasive liquid dentifrice. The unsightly brown tooth staining that developed in many users resulted in the early removal of this product from the marketplace. Standard organizations, notably the British Standards

Institute (BSI) and the International Standards Organisation (ISO), have written standards for toothpaste (BS5136:1981, ISO11609:1995). The ISO standard for toothpaste is, at this time, under review although, as for the original standard, it is safety rather than efficacy, which is the key issue. Toxicity and abrasivity (see later under Vehicles) are important sections of the toothpaste standard although evaluations for fluoride availability are likely to feature in the next finalized toothpaste standard. An ISO standard for mouth rinses is also under preparation where the hard tissue safety issue of low pH mouth rinses is under consideration. Throughout the ages, and until relatively recently, scientific evaluations of agents and formulations for gum health were not performed and claims for efficacy appear based on anecdotal reports at best. Indeed, given the nature of many ingredients and the recipes recommended in the past for oral hygiene benefits, it is unlikely that efficacy will ever be tested. In the 6000 years history of oral hygiene products, scientific evaluation must be seen as an extremely recent event: an observation which can, of course, be applied to almost all aspects of chemoprevention and chemotherapy of human diseases. Indeed, perhaps the first ever, double-blind, randomized cross-over design clinical trial in dentistry was less than 50 years ago (Cooke & Armitage 1960).

Rationale for chemical supragingival plaque control

The epidemiologic data and clinical research (Ash *et al*. 1964; Löe *et al*. 1965) directly associating plaque with gingivitis perhaps, unfortunately, led to a rather simplistic view that regular tooth cleaning would prevent gingivitis and thereby periodontal disease. Theoretically correct, this concept did not appear to consider the multiplicity of factors which influence the ability of individuals to clean their teeth sufficiently well to prevent disease, not the least of which are those factors which affect individual compliance with advice, and dexterity in performing such tasks. The need for research into those psychosocial factors which might influence attitude to and performance in oral hygiene, was stated in a workshop report on plaque control and oral hygiene practices (Frandsen 1986) but appears not to have been heeded to this day. Moreover, and as described in other chapters, epidemiologic data suggest that not all individuals are particularly susceptible to periodontal disease. The most severe disease is accounted for by a relatively small proportion of any population and then by only a proportion of sites in their dentition (Baelum *et al*. 1986). Even accepting that a considerable proportion of middle-aged adults will have one or more sites in the dentition with moderate periodontal disease, this will be of the chronic type and a minimal threat to the longevity of their dentition (Papapanou 1994) (see Chapter 7). The prevention of chronic periodontal diseases, through improved oral hygiene practices, will therefore be grossly over-prescribed as the early identification of susceptible individuals is impossible at present.

Host susceptibility is described retrospectively in the already diseased individual but, even here, an explanation for their susceptibility, except for a few risk factors, cannot be made. These risk factors include smoking, diabetes, and polymorph defects, and possibly stress (for review see Chapters 11 and 12). Genetic markers for periodontal disease have been identified but, at present, appear to be applied retrospectively rather than prospectively (Kornman *et al*. 1997; Kinane *et al*. 2005) and the value to early onset disease has been questioned (Hodge *et al*. 2001).

One definition of periodontal disease is chronic gingivitis with loss of attachment. This is a particularly useful definition, since not only does it describe the pathogenic processes occurring but also alludes to the approach to prevent, treat or prevent recurrence of the disease. Therefore prevention through supragingival plaque control still remains the mainstay of controling gingivitis and therefore the occurrence or recurrence of periodontitis. The importance of oral hygiene to outcome and long-term success of therapy for periodontal disease is hampered by the frequent ineffectiveness of mechanical cleaning of specific sites using a toothbrush, and the limited or lack of use of interdental cleaning by many individuals. Despite the encouraging improvements in oral hygiene, gingivitis and, to some extent, periodontitis in developed countries, gingival inflammation is still highly prevalent (see Chapter 7). Taken with the microbial etiology of both gingivitis and periodontitis, this supports the concept of employing agents to control plaque which require minimal compliance and skill in their use. This is the concept that underlies chemical supragingival plaque control, but as with oral hygiene instruction in mechanical methods, it will have to be vastly over-prescribed if periodontal disease prevention is to be achieved in susceptible individuals. Chemical supragingival plaque control has thus been the subject of extensive research using scientific methodologies for 40 years. The question to be addressed here is whether a chemical or chemicals have been discovered and proven efficacious in, firstly, the prevention of gingivitis and, secondly, periodontitis.

Conclusions

- Gingivitis and periodontitis are highly prevalent diseases and prevention of occurrence or recurrence is dependent on supragingival plaque control.
- Tooth cleaning is largely influenced by the compliance and dexterity of the individual and little by design features of oral hygiene appliances and aids.

- The concept of chemical plaque control may be justified as a means of overcoming inadequacies of mechanical cleaning.
- Gingivitis is highly prevalent and from a young age in all populations, but the proportion of individuals susceptible to tooth loss through periodontal disease is small.
- Prediction of susceptibility to periodontal disease from an early age is at present impossible.
- Mechanical and/or chemical supragingival plaque control measures for prevention of periodontitis will have to be greatly over-prescribed.
- In those individuals with chronic periodontal disease, and therefore considered susceptible, a daily form of interdental cleaning must be essential to long-term treatment success.

Approaches to chemical supragingival plaque control

The well ordered and dynamic process of plaque formation is summarized in Fig. 36-1. It is apparent that this process can be interrupted, interfered with, reversed or modified at several points and before the plaque mass and/or complexity reach a level whereby gingival health deteriorates. Mechanical cleaning aims to regularly remove sufficient microorganisms to leave a "healthy plaque" present, which cannot induce gingival inflammation. Chemical agents, on the other hand, could influence plaque quantitatively and qualitatively via a number of processes and these are summarized in Fig. 36-1. The action of the chemicals could fit into four categories:

1. Antiadhesive
2. Antimicrobial
3. Plaque removal
4. Antipathogenic.

Antiadhesive agents

Antiadhesive agents would act at the pellicle surface to prevent the initial attachment of the primary plaque-forming bacteria. Such antiadhesive agents would probably have to be totally preventive in their effects, acting most effectively on an initially clean tooth surface. Antiadhesive agents do exist and are used in industry, domestically, and in the environment. Such chemicals prevent the attachment and development of a variety of biofilms and are usually described as antifouling agents. Unfortunately the chemicals found in such applications are either too toxic for oral use or ineffective against dental bacteria plaques. Nevertheless, the concept of antiadhesives continues to attract research interest (for review see Wade & Slayne 1997). To date, effective formulations or products with antiadhesive properties are not available to the general public, although the amine alcohol, delmopinol, which appears to interfere with bacterial matrix formation and therefore fits somewhere between the concepts of antiadhesion and plaque removal, has been shown effective against plaque and gingivitis (Collaert *et al*. 1992; Claydon *et al*. 1996). Were antiadhesive agents to be discovered, a secondary benefit of extrinsic stain prevention of teeth may be expected.

Antimicrobial agents

The bacterial nature of dental plaque, not surprisingly, attracted interest in prevention of plaque formation through the use of antimicrobial agents. Antimicrobial agents could inhibit plaque formation through one of two mechanisms alone or combined. The first would be the inhibition of bacterial proliferation and would be directed, as with antiadhesive agents, at the primary plaque-forming bacteria. Antimicrobial agents therefore could exert their effects either at the pellicle-coated tooth surface before the primary plaque formers attach or after attachment but before division of these bacteria. This plaque inhibitory effect would be bacteriostatic in type, with the result that the lack of bacterial proliferation would not allow attachment of subsequent bacterial types on to the primary plaque-forming bacteria. The second effect could be bactericidal, whereby the antimicrobial agent destroys all of the microorganisms either attaching or already attached to the tooth surface. Many antimicrobial agents exist which could produce this effect; however, as will be discussed, to be effective in inhibiting plaque, the bactericidal effect would have to be absolute and/or persistent.

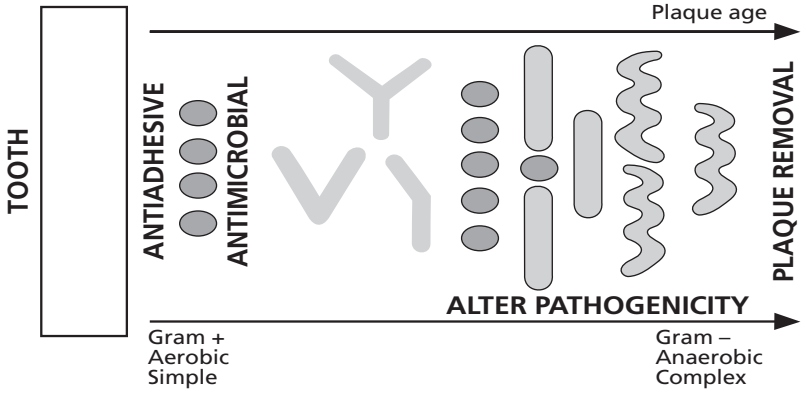


Fig. 36-1 Bacterial succession plaque formation. There is increasing mass and bacterial complexity as plaque bacteria attach and proliferate. Ideal sites of action for chemicals which might influence plaque accumulation are shown. Acknowledgment to Dr. William Wade for permission to publish this diagram.

If not, other bacteria within the oral environment would colonize the tooth surface immediately following the loss of the bactericidal effect and the biofilm would be re-established. For the most part biofilms in themselves are fairly resistant to total bactericidal effects of antimicrobial agents and, thus far, there does not appear to have been any agent discovered which effectively would sterilize the tooth surface after each application. If such an agent were found it could, of course, have potentially dangerous implications for the oral cavity since it would almost certainly destroy most of the commensal bacteria which normally colonize the oral cavity. This would open up the potential for exogenous microorganisms, with dangerous pathogenic potential, colonizing the oral cavity. In the event, it is probable that antimicrobial agents exert both a bactericidal effect followed by a bacteriostatic action of variable duration. The bactericidal effect will occur when the antimicrobial agent is at high concentration within the oral cavity and usually this will represent the time when the formulation is actually within the oral cavity. This bactericidal effect would be expected to be lost very soon after expectoration.

As will be discussed in respect of chlorhexidine, it is almost certainly the persistence of the bacteriostatic action of antimicrobial agents which accounts for their plaque-inhibitory activity. Calculations by Stralfors (1961) indicated that plaque inhibition through a bactericidal effect would require the immediate killing of 99.9% of the oral bacteria to effect a plaque-inhibitory action of significant duration. Antimicrobial agents for plaque inhibition, to date, are the only agents that have found common usage in oral hygiene products. The efficacy of these agents and products varies at the extremes (for reviews see Addy 1986; Kornman 1986; Mandel 1988; Addy *et al*. 1994; Addy & Renton-Harper 1996; Rolla *et al*. 1997; Eley 1999).

Plaque removal agents

The idea of employing a chemical agent which would act in an identical manner to a toothbrush and remove bacteria from the tooth surface, is an attractive proposition. Such an agent, contained in a mouth rinse, would be expected to reach all tooth surfaces and thereby be totally effective. For this reason, the idea of chemical plaque removal agents has attracted the terminology of "the chemical toothbrush". As with antiadhesives, there are agents, such as the hypochlorites, which might be expected to remove bacterial deposits and are commonly employed within the domestic environment. Again, such chemicals would likely be toxic were they to be applied within the oral cavity. Perhaps, the nearest success was with enzymes, directed at both pellicle, e.g. proteases, or bacterial matrices, e.g. dextranase and mutanase (for review see Kornman 1986). Again, as will be discussed, these enzymes, albeit potentially effective, lacked substantivity within the oral cavity and had local side effects.

Antipathogenic agents

It is theoretically possible that an agent could have an effect on plaque microorganisms, which might inhibit the expression of their pathogenicity without necessarily destroying the microorganisms. In some respects antimicrobial agents, which exert a bacteriostatic effect, achieve such results. At present the understanding of the pathogenesis of gingivitis is so poor that this approach has received no attention. Were our knowledge on the microbial etiology of gingivitis to improve, there exists the possibility of an alternative, but related, approach: the introduction into the oral cavity of organisms which have been modified to remove their pathogenic potential to the gingival tissues. This is not a new concept and was an approach experimented with to replace pathogenic staphylococci within the nasal cavities of surgeons with the idea of reducing the potential for wound infection caused by the operator. At present such an approach within the oral cavity for either gingivitis or caries is perhaps within the realms of science fiction.

Conclusions

- At present most antiplaque agents are antimicrobial and prevent the bacterial proliferation phase of plaque development.
- Plaque formation could be controlled by antiadhesive or plaque removal agents, but these are not, as yet, available or safe for oral use.
- Alteration of bacterial plaque pathogenicity through chemical agents or bacterial modification would require a greater understanding of the bacterial etiology of gingivitis.

Vehicles for the delivery of chemical agents

The carriage of chemical agents into the mouth for supragingival plaque control has involved a small but varied range of vehicles (for reviews see Addy 1994; Cummins 1997).

Toothpaste

By virtue of common usage the ideal vehicle for the carriage of plaque-control agents is toothpaste. A number of ingredients go to make up toothpaste and each has a role in either influencing the consistency and stability of the product or its function (for review see Forward *et al*. 1997).

The major ingredients may be classified under the following headings:

1. *Abrasives*, such as silica, alumina, dicalcium phosphate, and calcium carbonate either alone, or more usually today, in combination. Abrasives affect

the consistency of the toothpaste and assist in the control of extrinsic dental staining. The range of abrasivity of toothpaste against dental hard tissues is defined in the BSI and ISO toothpaste standards (presently under review) in an attempt to minimize tooth wear from normal toothbrushing with toothpaste. Dentine abrasion is of prime importance as the majority of abrasives used in toothpastes produce little or no wear to enamel: non-hydrated alumina being the exception. Also, toothpaste detergents produce wear to dentine (Moore & Addy 2005). Abrasivity is calculated by relating the wear of dentine (enamel) by toothpaste to a standard formulation: the relative dentine abrasivity (RDA) value (relative enamel abrasivity (REA)). For the BSI standard a calcium carbonate based abrasive formulation is used whereas for the ISO standard it is calcium pyrophosphate based. The wear of dentine, measured directly by profilometry or release of P^{52}, by the standard is considered as 100. Toothpastes, according to the two standards, can be up to twice the standard for BSI (RDA range 0–200) and two and a half times for ISO (RDA range 0–250).

2. *Detergents*: the most common detergent used in toothpaste is sodium lauryl sulfate, which imparts the foaming and "feel" properties to the product. Additionally, detergents may help dissolve active ingredients and the anionic detergent sodium lauryl sulfate has both antimicrobial and plaque inhibitory properties (Jenkins *et al*. 1991a,b). Certain toothpaste products cannot employ anionic detergents as they interact with cationic substances that may be added to the product, such as chlorhexidine, or polyvalent metal salts, such as strontium, used in the treatment of dentine hypersensitivity.
3. *Thickeners*, such as silica and gums, primarily influence the viscosity of the product.
4. *Sweeteners*, including saccharine.
5. *Humectants*, notably glycerine and sorbitol to prevent drying out of the paste once the tube has been opened.
6. *Flavors*, of which there are many but mint or peppermint are popular in the western world although rarely found in toothpaste in the Indian subcontinent where herbal flavors are more popular.
7. *Actives*, notably fluorides for caries prevention; for plaque control triclosan and stannous fluoride and, to a lesser extent, chlorhexidine have been the most studied examples. Other actives relate to different aspects of oral care including anticalculus agents (pyrophosphates), whitening agents (polyphosphates), and desensitizing agents (strontium and potassium salts).

As stated, the addition of cationic antiseptics to toothpastes is difficult but chlorhexidine has been formulated into toothpastes and shown to be effective (Yates *et al*. 1993; Sanz *et al*. 1994), although few products have reached or lasted in the marketplace.

Mouth rinses

Despite the ideal nature of the toothpaste vehicle, most chemical plaque-control agents have been evaluated and later formulated in the mouth rinse vehicle. Mouth rinses vary in their constituents but are usually considerably less complex than toothpastes. They can be simple aqueous solutions, but the need for products, purchased by the general public, to be stable and acceptable in taste usually requires the addition of flavoring, coloring, and preservatives such as sodium benzoate. Anionic detergents are included in some products but, again, cannot be formulated with cationic antiseptics such as cetylpyridinium chloride or chlorhexidine (Barkvoll *et al*. 1989). Ethyl alcohol is commonly used both to stabilize certain active ingredients and to improve the shelf-life of the product. Several concerns, not always well substantiated, have been expressed over alcohol-containing mouth rinses (for review see Eley 1999). The possible association of alcohol intake with oropharyngeal cancer, has been extended to include alcohol-containing mouth rinses. Whether these concerns are scientifically valid has not been established and separating out the well established role of smoking in these cancers is difficult, if not impossible, as is other sources of alcohol. Also, since at present there seems little support for the long-term use of mouth rinses for gingival health benefits, when mouth rinses are correctly prescribed the risk from contained alcohol is probably minuscule. This, however, does not obviate the possible risk from self-prescription, the chronic use of mouth rinses, or the ingestion of alcoholic mouth rinses by children. In the latter case, toxicity has been reported. Additionally, alcohol may adversely affect the physical properties of some esthetic restoration materials. Sensibly the prescription or recommendation of alcohol-containing mouth rinses would seem inappropriate to known alcoholics or to those individuals whose religion or culture forbids the intake of alcohol. The proportion of alcohol is usually less than 10% but some rinses have in excess of 20% alcohol. Some manufacturers are now producing alcohol-free mouth rinses.

Spray

Spray delivery of chemical plaque-control agents has attracted both research interest and the development of products by some manufacturers in some countries. Sprays have the advantage of focusing delivery on the required site. The dose is clearly reduced and for antiseptics such as chlorhexidine this has taste advantages. When correctly applied, chlorhexidine sprays were as effective as mouth rinses for plaque inhibition, although there was no reduction in staining (Francis *et al*. 1987a; Kalaga *et al*. 1989a). Chlorhexidine sprays were found particularly useful for plaque

control in physically and mentally handicapped groups (Francis *et al*. 1987a,b; Kalaga *et al*. 1989b).

Irrigators

Irrigators were designed to spray water, under pressure, around the teeth. As such they only removed debris, with little effect on plaque deposits (for review see Frandsen 1986). Antiseptics and other chemical plaque-control agents, such as chlorhexidine, have been added to the reservoir of such devices. A variety of dilutions of chlorhexidine has been employed to good effect (Lang & Raber 1981) but again with the incumbent local side effects of this agent.

Chewing gum

Over a relatively short period there has been interest in employing chewing gum to deliver a variety of agents for oral health benefits. Also, there appear to be significant benefits to dental health through the use of sugar-free chewing gum. Unfortunately, chewing gums alone appear to have little in the way of plaque-control benefits particularly at sites prone to gingivitis (Hanham & Addy 2001). They can reduce occlusal plaque deposits (Addy *et al*. 1998), but whether this is directly relevant to the prevention of fissure caries has not been proven, indeed is unlikely. Nonetheless, the vehicle has been used to deliver chemical agents such as chlorhexidine and, when used as an adjunct to normal toothbrushing, reduced plaque and gingivitis levels have been shown (Ainamo & Etemadzadeh 1987; Smith *et al*. 1996).

Varnishes

Varnishes have been employed to deliver antiseptics including chlorhexidine, but the purpose has been to prevent root caries rather than as a reservoir for plaque control throughout the mouth.

Conclusions

- Many vehicles may be used to deliver antiplaque agents but most information relates to mouth rinses and toothpaste.
- Toothpaste appears the most practical and cost-effective method for chemical plaque control for most individuals.
- In formulating antiplaque agents into toothpaste, potential inactivation by other ingredients must be considered.
- Minority groups, such as the handicapped, may benefit from other delivery systems.

Chemical plaque control agents

Over a period of nearly four decades there has been quite intense interest in the use of chemical agents to control supragingival plaque and thereby gingivitis. The number and variation of chemical agents evaluated are quite large but most have antiseptic or antimicrobial actions and success has been extremely variable. It is important to emphasize that formulations based on antimicrobial agents provide a considerably greater preventive than therapeutic action. The most effective agents inhibit the development of plaque and gingivitis but are limited or slow to affect established plaque and gingivitis. Were they available, antiadhesive agents would similarly be expected to provide preventive rather than therapeutic effects. Plaque removal agents, on the other hand, would almost certainly provide both preventive and therapeutic actions. Chemical plaque-control agents have been the subject of many detailed reviews since 1980 (Hull 1980; Addy 1986; Kornman 1986; Mandel 1988; Gjermo 1989; Addy *et al*. 1994; Heasman & Seymour 1994; Jackson 1997; Eley 1999). Based on knowledge derived from chlorhexidine (for review see Jones 1997), the most effective plaque-inhibitory agents in the antiseptic or antimicrobial group are those showing persistence of action in the mouth measured in hours. Such persistence of action, sometimes termed substantivity (Kornman 1986), appears dependent on several factors:

1. Adsorption and prolonged retention on oral surfaces including, importantly, pellicle-coated teeth
2. Maintenance of antimicrobial activity once adsorbed primarily through a bacteriostatic action against the primary plaque-forming bacteria
3. Minimal or slow neutralization of antimicrobial activity within the oral environment or slow desorption from surfaces.

The latter concepts will be discussed later under chlorhexidine.

Antimicrobial activity of antiseptics *in vitro* is not a reliable predictor of plaque-inhibitory activity *in vivo* (Gjermo *et al*. 1970, 1973). Early studies on a number of antiseptics revealed similar antimicrobial profiles but a large variation in clinical effects. For example, compared to chlorhexidine, the cationic quaternary ammonium compound, cetylpyridinium chloride, has a similar antimicrobial profile *in vitro* (Gjermo *et al*. 1970, 1973; Roberts & Addy 1981) and is initially adsorbed in the mouth to a considerably greater extent (Bonesvoll & Gjermo 1978). The persistence of action of cetylpyridinium chloride is, however, much shorter than chlorhexidine (Schiott *et al*. 1970; Roberts & Addy, 1981), and plaque inhibition is considerably less (for review see Mandel 1988). Several reasons may explain these apparent anomalies, including poor retention of cetylpyridinium chloride within the oral cavity (Bonesvoll & Gjermo 1978), reduced activity once adsorbed, and neutralization in the oral environment (Moran & Addy 1984), or a combination of these factors. Attempts to improve efficacy of cetylpyridinium chloride can, of course, include increasing the frequency of use, but this is likely to incur compliance problems and side effects (Bonesvoll & Gjermo 1978). Alternatively,

Table 36-1 Groups of agents used in the control of dental plaque and/or gingivitis

Group	Example of agents	Action	Used now/product
Antibiotics	Penicillin Vancomycin Kanamycin Niddamycin Spiromycin	Antimicrobial	No
Enzymes	Protease Lipase Nuclease Dextranase Mutanase	Plaque removal	No
	*Glucose oxidase *Amyloglucosidase	Antimicrobial	*Yes Toothpaste
Bisbiguanide antiseptics	*Chlorhexidine Alexidine Octenidine	Antimicrobial	*Yes Mouthrinse Spray Gel Toothpaste Chewing gum Varnish
Quaternary ammonium compounds	*Cetylpyridinium chloride *Benzalconium chloride	Antimicrobial	*Yes Mouthrinse
Phenols and essential oils	*Thymol *Hexylresorcinol *Ecalyptol *Triclosan+	*Antimicrobial +Anti-inflammatory	*Yes Mouthrinse Toothpaste
Natural products	*Sanguinarine	Antimicrobial	No
Fluorides	(*)Sodium fluoride (*)Sodium monofluoro-phosphate *Stannous fluoride+ +Amine fluoride	*Antimicrobial () minimal + ?	+*Yes Toothpaste Mouthrinse +Gel
Metal salts	*Tin+ *Zinc Copper	Antimicrobial	*Yes Toothpaste Mouthrinse +Gel
Oxygenating agents	*Hydrogen peroxide *Sodium peroxyborate *Sodium peroxycarbonate	Antimicrobial ? plaque removal	*Yes Mouthrinse
Detergents	*Sodium lauryl sulfate	Antimicrobial ? plaque removal	*Yes Toothpaste Mouthrinse
Amine alcohols	Octapinol Delmopinol	Plaque matrix Inhibition	No Yes Toothpaste Mouthrinse
Salicylanide	Salifluor	Antimicrobial and anti-inflammatory	No

substantivity could be improved by combining antimicrobials or using agents to increase the retention of antimicrobials (Gaffar *et al*. 1992). Individual groups of compounds, together with the specific agents within the group, are listed in Table 36-1 and discussed below.

Systemic antimicrobials including antibiotics

(For reviews see Addy 1986; Kornman 1986)

Despite evidence for efficacy in preventing caries and gingivitis or resolving gingivitis, the opinion today is

that systemic antimicrobials should not be used either topically or systemically as preventive agents against these diseases. The risk-to-benefit ratio is high and even systemic antimicrobial use in the treatment of adult periodontitis is open to debate (for reviews see Slots & Rams 1990; Addy & Martin 2003) (see Chapter 42). Thus, systemic antimicrobials have their own specific side effects not all of which can be avoided by topical application. Perhaps of greatest importance is the development of bacterial resistance within human populations, for example methicillin-resistant *Staphylococcus aureus* (MRSA), which causes serious and life-threatening wound infections, particularly within hospitalized patients.

Enzymes

(For reviews see Addy 1986)

Enzymes fall into two groups. Those in the first group are not truly antimicrobial agents but more plaque removal agents in that they have the potential to disrupt the early plaque matrix, thereby dislodging bacteria from the tooth surface. In the late 1960s and early 1970s enzymes such as dextranase, mutanase and various proteases were thought to be a major breakthrough in dental plaque control that might prevent the development of both caries and gingivitis. Such agents, unfortunately, had poor substantivity and were not without unpleasant local side effects, notably mucosal erosion. The second group of enzymes employed glucose oxidase and amyloglucosidase to enhance the host defense mechanism. The aim was to catalyse the conversion of endogenous and exogenous thiocyanate to hypothiocyanite via the salivary lactoperoxydase system. Hypothiocycanite produces inhibitory effects upon oral bacteria, particularly streptococci, by interfering with their metabolism. This approach is a theoretical possibility and the chemical processes can be produced in the laboratory. A toothpaste product containing the enzymes and thiocyanate was produced but equivocal results for benefits to gingivitis were obtained and there are no convincing long-term studies of efficacy.

Bisbiguanide antiseptics

(For reviews see Addy 1986; Addy *et al*. 1994; Kornman 1986; Gjermo 1989; Jones 1997; Eley 1999)

Chlorhexidine is thus far the most studied and effective antiseptic for plaque inhibition and the prevention of gingivitis. Consequent upon the original publication (Löe & Schiott 1970), chlorhexidine arguably represents the nearest that research has come to identifying a chemical agent that could be used as a replacement for, rather than an adjunct to, mechanical oral hygiene practices. Other bisbiguanides such as alexidine and octenidine have less or similar activity, respectively, to chlorhexidine but bring with them no improvement in local side effects and have less toxicity data available. Chlorhexidine has thus remained the only bisbiguanide used in a number of vehicles and available in commercial products. In view of the importance of this antiseptic within preventive dentistry, a separate section later in the chapter will be devoted to considering its activity and usage in the mouth.

Quaternary ammonium compounds

(For reviews see Mandel 1988; Eley 1999)

Benzalconium chloride and, more particularly, cetylpyridinium chloride are the most studied of this family of antiseptics. Cetylpyridinium chloride is used in a wide variety of antiseptic mouth rinse products, usually at a concentration of 0.05%. At oral pH these antiseptics are monocationic and adsorb readily and quantitatively, to a greater extent, than chlorhexidine to oral surfaces (Bonesvoll & Gjermo 1978). The substantivity of cetylpyridinium chloride however appears to be only 3–5 hours (Roberts & Addy 1981) due either to loss of activity once adsorbed or rapid desorption. Cetylpyridinium chloride in mouth rinses has some chemical plaque-inhibitory action but evidence for gingivitis benefits is equivocal, particularly when formulations are used alongside toothbrushing with toothpaste. Home use studies, given the large number of rinse products containing this antiseptic, are surprisingly few. Those available, with one exception, failed to demonstrate any adjunctive benefits to toothbrushing with toothpaste. The one exception (Allen *et al*. 1998) was peculiar in that there was a lack of the expected Hawthorne effect in the control group (see section "Evaluation of chemical agents and products" later in this chapter) and the plaque reduction in the active group, 28%, was as great as seen in no brushing chemical plaque inhibition studies. As will be discussed, it is not unusual to find chemicals that provide modest, even moderate, plaque inhibition in no brushing studies but fail to show effects in adjunctive home use studies. This occurs because the range over which to show a benefit of the chemical is limited by the mechanical oral hygiene practices of the study subjects. Additionally, the plaque-inhibitory properties of cetylpyridinium chloride are reduced by toothpaste used before or after the rinse (Sheen *et al*. 2001, 2003). This may explain why a pre-brushing cetylpyridinium mouth rinse offered no adjunctive benefit to mechanical plaque control (Moran & Addy 1991). The efficacy of cetylpyridinium chloride can be increased by doubling the frequency of rinsing to four times per day (Bonsvoll & Gjermo 1978), but this increases local side effects, including tooth staining, and would probably affect compliance. Mouth rinses combining cetylpyridinium chloride with chlorhexidine are available and compare well with established chlorhexidine products (Quirynen *et al*. 2001, 2005). Whether the cetylpyridinium chloride actually contributes to the

activity of the chlorhexidine cannot be assessed. A slow-release system and lozenges have been used to deliver cetylpyridinium chloride but provided no greater plaque inhibition than the cetylpyridinium mouth rinse and significantly less than a chlorhexidine rinse (Vandekerchove *et al*. 1995). Interestingly, in this study, the lozenges produced the most dental staining. There is limited information on quaternary ammonium compounds in toothpastes and very few products are available.

Phenols and essential oils

(For reviews see Mandel 1988; Jackson 1997; Eley 1999)

Phenols and essential oils have been used in mouth rinses and lozenges for many years. One mouth rinse formulation dates back more than 100 years and, although not as efficacious as chlorhexidine, has antiplaque activity supported by a number of short- and long-term home use studies. This mouth rinse product may reduce gingivitis via both a plaque-inhibitory action and an anti-inflammatory action possibly due to an anti-oxidative activity (Firalti *et al*. 1994). The data from home use studies led the American Dental Association to accept the product as an aid to home oral hygiene measures (for review see Eley 1999). When compared directly with chlorhexidine one 6-month study has demonstrated equivalent effects on plaque and gingivitis but without the inherent side effects of chlorhexidine (Charles *et al*. 2004). Nevertheless, the pH of the product is low (pH 4.3) and has been shown *in vitro* and *in situ* to cause erosion of dentine and enamel respectively, albeit to a considerably less degree than orange juice (Addy *et al*. 1991; Pontefract *et al*. 2001). Combining essential oils with cetylpyridinium chloride has been attempted and with promising results from initial studies (Hunter *et al*. 1994).

The non-ionic antimicrobial triclosan, a trichlora-2-hydroxy phenyl ether, is usually considered to belong to the phenol group and has been widely used over many years in a number of medicated products including antiperspirants and soaps. More recently, it has been formulated into toothpaste and mouth rinses and, for the former, has accumulated an impressive amount of literature, some of which is conflicting. In simple solutions, at relatively high concentrations (0.2%) and dose (20 mg twice per day), triclosan has moderate plaque-inhibitory action and antimicrobial substantivity of around 5 hours (Jenkins *et al*. 1991a,b). The dose response against plaque of triclosan alone is relatively flat (Jenkins *et al*. 1993), although significantly greater benefits are obtained at 20 mg doses twice daily compared to 10 mg doses. In terms of plaque inhibition, a 0.1% triclosan concentration (10 mg dose twice per day) was considerably less effective than a 0.01% chlorhexidine mouth rinse (1 mg twice per day) (Jenkins *et al*. 1994).

The activity of triclosan appears to be enhanced by the addition of zinc citrate or the co-polymer, polyvinylmethyl ether maleic acid (for review see Gaffar *et al*. 1992). The co-polymer appears to enhance the retention of triclosan whereas the zinc is thought to increase the antimicrobial activity. Only triclosan toothpastes with the co-polymer or zinc citrate have shown antiplaque activity in long-term home use studies (for review see Jackson 1997). Some home use studies showed little or no effect for one or other of the products on plaque alone, gingivitis alone or both compared to the control paste or conventional fluoride toothpaste (Palomo *et al*. 1994; Kanchanakamol *et al*. 1995; Renvert & Birkhed 1995; Binney *et al*. 1996; Owens *et al*. 1997a). Triclosan toothpastes appear to provide greater gingivitis benefits in some studies than plaque reductions and this could be explained by a possible anti-inflammatory action for this agent (Barkvoll & Rolla 1994).

More recently, long-term studies have suggested that triclosan-containing toothpaste can reduce the progress of periodontitis, although the effects have been considered small (Rosling *et al*. 1997; Ellwood *et al*. 1998). Mouth rinses containing triclosan and the co-polymer are available, with some evidence of adjunctive benefits to oral hygiene and gingival health when used alongside normal tooth cleaning (Worthington *et al*. 1993). This latter study was again interesting with, unusually, no clear Hawthorne effect in the control group. Other studies on the plaque inhibitory properties of a triclosan/co-polymer mouth rinse showed effects significantly less than those of an essential oil mouth rinse product (Moran *et al*. 1997).

Natural products

(For review see Mandel 1988; Eley 1999)

Herb and plant extracts have been used in oral hygiene products for many years if not centuries. Unfortunately, there are few data available and such toothpaste products provide no greater benefits to oral hygiene and gingival health than do conventional fluoride toothpaste (Moran *et al*. 1991). The plant extract sanguinarine has been used in a number of formulations. Zinc salts are also incorporated, which makes it difficult to evaluate the efficacy of sanguinarine alone. Even when it is combined with zinc, however, data are equivocal for benefits (Moran *et al*. 1988, 1992a; Quirynen *et al*. 1990). Some positive findings were reported for the combined use of sanguinarine/zinc toothpaste and mouth rinses (Kopczyk *et al*. 1991), but the benefit-to-cost ratio must be low. Importantly and very recently, sanguinarine-containing mouth rinses have been shown to increase the likelihood of oral precancerous lesions almost ten-fold even after cessation of mouth rinse use. The manufacturer of the most well known product has replaced sanguinarine in the mouth rinses with an alternative agent. More recently, tea tree oil

has been suggested to be of value when topically delivered with positive effects at reducing gingival inflammation (Sookoulis & Hirsch 2004) but as yet no conclusive evidence for effects on plaque accumulation.

Fluorides

The caries-preventive benefits for a number of fluoride salts are well established but the fluoride ion has no effect against the development of plaque and gingivitis. Amine fluoride and stannous fluoride provide some plaque-inhibitory activity, particularly when combined; however, the effects appear to be derived from the non-fluoride portion of the molecules. A mouth rinse product containing amine fluoride and stannous fluoride is available and there is some evidence from home use studies of efficacy against plaque and gingivitis (Brecx *et al*. 1990, 1992), but less so than chlorhexidine.

Metal salts

(For reviews see Addy *et al*. 1994; Jackson 1997)

Antimicrobial actions including plaque inhibition by metal salts have been appreciated for many years, with most research interest centered on copper, tin, and zinc. Results have been somewhat contradictory but appear dependent on the metal salt used, its concentration, and frequency of use. Essentially, polyvalent metal salts alone are effective plaque inhibitors at relatively high concentration when taste and toxicity problems may arise. Stannous fluoride is an exception but is difficult to formulate into oral hygiene products because of stability problems, with hydrolysis occurring in the presence of water. Stable anhydrous gel and toothpaste products are available with evidence of efficacy against plaque and gingivitis (Beiswanger *et al*. 1995; Perlich *et al*. 1995). Stannous pyrophosphate at 1% has been added to some stannous fluoride toothpaste to good effect (Svatun 1978). Indeed, it appears that the concentration of available stannous ions is the most significant factor in determining efficacy (Addy *et al*. 1997). Dental staining, however, occurs with stannous formulations and appears to occur by the same mechanism as for chlorhexidine and other cationic antiseptics, involving interaction with dietary chromogens (for reviews see Addy & Moran 1995; Watts & Addy 2001). Combining metal salts with other antiseptics produces added plaque and gingivitis inhibitory effects, for example zinc and hexetidine (Saxer & Muhlemann 1983) and, as already described, zinc and triclosan. Copper also causes dental staining but is not available in oral hygiene products. Zinc, at low concentration, has no side effects and is used in a number of toothpastes and mouth rinses; however, alone it has little effect on plaque (Addy *et al*. 1980) except at higher concentrations. Zinc salts nevertheless, may be of value at reducing volatile sulfur compounds associated with oral malodor (Rosing *et al*. 2002).

Oxygenating agents

(For review see Addy *et al*. 1994)

Oxygenating agents have been used as disinfectants in various disciplines of dentistry, including endodontics and periodontics. Hydrogen peroxide has been employed for supragingival plaque control and more recently has become important as bleach in tooth whitening. Similarly, peroxyborate may be used in the treatment of acute ulcerative gingivitis (Wade *et al*. 1966). Products containing peroxyborate and peroxycarbonate were, until recently, available in Britain and Europe with evidence of antimicrobial and plaque-inhibitory activity (Moran *et al*. 1995). There are little data from long-term home use studies and such evaluations would seem warranted before conclusions about true antiplaque activity can be drawn.

Detergents

Detergents, such as sodium lauryl sulfate, are common ingredients in toothpaste and mouth rinse products. Besides other qualities and, for that matter, side effects, detergents such as sodium lauryl sulfate have antimicrobial activity (Jenkins *et al*. 1991b) and probably provide most of the modest plaque-inhibitory action of toothpaste (Addy *et al*. 1983). Alone, sodium lauryl sulfate was shown to have moderate substantivity, measured at between 5 and 7 hours, and plaque-inhibitory action similar to triclosan (Jenkins *et al*. 1991a,b). Detergent-only formulations are not available and no long-term evaluations have been performed.

Amine alcohols

This group of compounds does not truly fit into an antimicrobial or antiseptic category; indeed they exhibit minimal effects against microbes. Of these morpholinoethenol derivatives, octopinol was the first to be shown effective as an antiplaque agent but was withdrawn for toxicologic reasons. Delmopinol followed and at 0.1% and 0.2% in mouth rinses was shown to be effective against plaque and gingivitis in short-term no oral hygiene and long-term home use studies (Collaert *et al*. 1992; Moran *et al*. 1992b; Claydon *et al*. 1996; Hase *et al*. 1998; Lang *et al*. 1998). Arguably, the short-term no oral hygiene studies showed plaque inhibition closer to chlorhexidine than any other previous agent (Moran *et al*. 1992b). Recently, the data from eight studies from seven independent research groups in five European countries using a 0.2% delmopinol mouth rinse as an adjunct to normal oral hygiene practices were subjected to a meta-analysis. Delmopinol, one of the very few chemical plaque-control agents to be subjected to

such analyses, was shown to be a significantly effective adjunct for reducing the plaque burden and severity of gingivitis (Addy *et al*. 2007). The data for gingivitis in several studies met the efficacy criteria for gingivitis reduction of the American Dental Association. The mode of action of delmopinol can be debated but appears to be an interference with plaque matrix formation, reducing the adherence of the primary plaque-forming bacteria of the successional bacteria (Simonsson *et al*. 1991a,b). If correct, delmopinol would closest fit classification as an antiadhesive agent. Side effects include tooth discoloration, transient numbness of the tongue, and burning sensations in the mouth (Claydon *et al*. 1996; Hase *et al*. 1998; Lang *et al*. 1998). Interestingly, the staining was considerably less than with chlorhexidine, rarely reported by study participants and easily removed. In these adjunctive studies discontinuations were considerably less with delmopinol than chlorhexidine. Rinses containing 0.2% delmopinol are available in some countries.

Salifluor

(For review see Eley 1999)

Salifluor, a salicylanide with both antibacterial and anti-inflammatory properties, has been studied for its effects of plaque inhibition and retardation of onset of gingivitis (Furuichi *et al*. 1996). To improve oral retention and to maximize adsorption, Gantrez (PVM/MA) has been incorporated in salifluor toothpaste and mouth rinse formulations. Perhaps surprisingly, salifluor has not been extensively evaluated, since initial 4-day plaque regrowth studies and 14-day gingivitis studies have suggested equivalent efficacy to a 0.12% chlorhexidine mouth rinse (Furuichi *et al*. 1996). In spite of this evidence to suggest the potential value of the chemical as an antiplaque agent, further long-term studies have yet to be carried out.

Acidified sodium chlorite

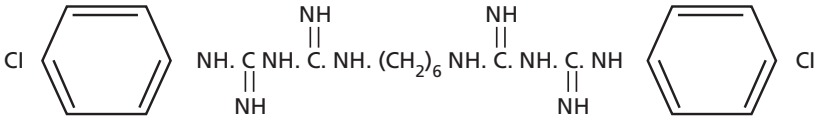
(For review see Yates *et al*. 1997)

This agent does not sit well with any particular group listed in Table 36-1; however, depending on the acid chosen and the conditions of the reaction between the acid and the sodium chlorite, a varied and complex range of reaction products can ensue. Under ideal conditions for antimicrobial benefits sodium chlorite is reacted with a protic acid to produce chlorous acid, which then liberates a range of higher oxidant species but contains minimal amounts of chlorine dioxide. These higher oxidant species have a broad range of antimicrobial action against bacteria, fungi, yeast, and viruses, and products are available in the US within the veterinary and food industry, both as a preventive for mastitis in cows and for the preservation of frozen poultry. Experimental mouth rinses have been tested in short-term plaque regrowth studies and salivary bacterial count investigations (Yates *et al*. 1997). Surprisingly, given that the acid and sodium chlorite are mixed immediately before rinsing, and that the duration of the chemical reaction would be limited to the rinsing time, three experimental formulations were shown to be as good as chlorhexidine against plaque regrowth and showed the same substantivity as chlorhexidine. Although not tested in longer-term studies, side effects, particularly staining and alteration of taste, would appear unlikely with the acidified sodium chlorite mouth rinses. Unfortunately, the low pH of the formulations would be expected to cause some dental erosion and this has been proven in studies *in situ* (Pontefract *et al*. 2001). Such erosion, which was found comparable to that of orange juice *in situ*, would tend to obviate the long-term continuous use of such agents. Acidified sodium chlorite mouth rinses, however, could find application in preventive dentistry similar to those to be described for chlorhexidine (see later in this chapter). The erosive effects would not, in short- to medium-term use, reach clinically significant levels. To date no commercial products are available.

Other antiseptics

(For review see Addy 1986)

A number of antiseptics/antimicrobial agents have been studied for plaque inhibition. Most have been found to have little or no effect *in vivo*; a few have been formulated in mouth rinse products including povidone iodine and hexetidine. Povidone iodine at 1% has a substantivity of only 60 minutes (Addy & Wright 1978) and lacks appreciable plaque-inhibitory activity (Addy *et al*. 1977) or action in acute infections such as acute ulcerative gingivitis (Addy & Llewelyn 1978), for which it is recommended. Povidone iodine is largely without side effects but as a rinse has potential to affect thyroid function adversely (Wray *et al*. 1978). Hexetidine, a saturated pyrimidine, at 0.1% was shown to have limited plaque-inhibitory action (Bergenholtz & Hanstrom 1974) and no evidence for antiplaque activity when used as an adjunct for oral hygiene (Chadwick *et al*. 1991). The action of hexetidine against plaque appears enhanced by zinc salts (Saxer & Muhlemann 1983) but data are derived only from short-term studies. Side effects for hexetidine include tooth staining and mucosal erosion, although both are uncommon (Bergenholtz & Hanstrom 1974). Nevertheless, mucosal erosion is markedly increased in incidence if the concentration is raised to 0.14% (Bergenholtz & Hanstrom 1974). A mouth rinse product containing 0.1% hexetidine is available in some European countries. Recent studies have shown favorable effects on plaque and gingivitis (Sharma *et al*. 2003; Ernst *et al*. 2005) and when compared to 0.1% chlorhexidine, less tendency for stain production (Ernst *et al*. 2005).



1,6–di (4–chlorophenyldiguanido) hexane

Fig. 36-2 Chlorhexidine molecule.

Conclusions

- Effective antimicrobial antiplaque agents show prolonged persistence of action in the mouth (substantivity). Chlorhexidine is the most effective antiplaque agent to date. Stannous fluoride and triclosan oral hygiene products are available with proven antiplaque activity. The long established mouth rinse, based on essential oils, has some evidence for adjunctive antiplaque activity.
- The limited information on natural products, for example herbal formulations, is not encouraging and the root extract sanguinarine has been withdrawn because of the potential to cause precancerous oral lesions.
- The amine alcohol, delmopinol, is an effective antiplaque agent and products are becoming available.
- Acidified sodium chlorite appears as effective as chlorhexidine against plaque but the acidic nature of the rinse may obviate oral hygiene products ever coming to the marketplace.
- Combinations of agents sometimes provide additive or synergistic action, but with the exception of triclosan, few products are available.

Chlorhexidine

Chlorhexidine is available in three forms, the digluconate, acetate, and hydrochloride salts. Most studies and most oral formulations and products have used the digluconate salt, which is manufactured as a 20% V/V concentrate. Digluconate and acetate salts are water soluble but hydrochloride is very sparingly soluble in water. Chlorhexidine was developed in the 1940s by Imperial Chemical Industries, England, and marketed in 1954 as an antiseptic for skin wounds. Later, the antiseptic was more widely used in medicine and surgery including obstetrics, gynecology, urology, and presurgical skin preparation for both patient and surgeon. Use in dentistry was initially for presurgical disinfection of the mouth and in endodontics. The first definitive study on chlorhexidine was performed by Löe and Schiott (1970). This study showed that rinsing for 60 seconds twice per day with 10 ml of a 0.2% (20 mg dose) chlorhexidine gluconate solution in the absence of normal tooth cleaning, inhibited plaque regrowth and the development of gingivitis. Numerous studies followed, such that chlorhexidine is one of the most investigated compounds in dentistry (for reviews see Jones 1997; Eley 1998). Chlorhexidine is a bisbiguanide antiseptic, being a symmetrical molecule consisting of four chlorophenyl rings and two biguanide groups connected by a central hexamethylene bridge (Fig. 36-2). The compound is a strong base and dicationic at pH levels above 3.5, with two positive charges on either side of a hexamethylene bridge. Indeed, it is the dicationic nature of chlorhexidine, making it extremely interactive with anions, which is relevant to its efficacy, safety, local side effects, and difficulties with formulation in products.

Toxicology, safety, and side effects

The cationic nature of chlorhexidine minimizes absorption through the skin and mucosa, including from the gastrointestinal tract. Systemic toxicity from topical application or ingestion is therefore not reported, nor is there evidence of teratogenicity in the animal model. Even in intravenous infusion in animals, chlorhexidine is well tolerated and this has occurred accidentally in humans without serious consequences. Hypersensitivity reactions including anaphylaxis have been reported in fewer than 10 people in Japan and resulted from the application of non-proprietary chlorhexidine products to sites other than the mouth. There was insufficient information to confirm that the reactions were actually due to chlorhexidine. Neurosensory deafness can occur if chlorhexidine is introduced into the middle ear and the antiseptic should not be placed in the outer ear in case the eardrum is perforated. The antiseptic has a broad antimicrobial action, including a wide range of Gram-positive and Gram-negative bacteria (Wade & Addy 1989). It is also effective against some fungi and yeasts including *Candida*, and some viruses including HBV and HIV. Bacterial resistance has not been reported with long-term, oral use or evidence of super-infection by fungi, yeasts or viruses. Long-term oral use resulted in a small shift in the flora towards the less sensitive organisms but this was rapidly reversible at the end of the 2-year study (Schiott *et al*. 1976).

In oral use as a mouth rinse, chlorhexidine has been reported to have a number of local side effects (Flotra *et al*. 1971). These side effects are:

1. Brown discoloration of the teeth and some restorative materials and the dorsum of the tongue (Figs. 36-3 and 36-4).
2. Taste perturbation where the salt taste appears to be preferentially affected (Lang *et al*. 1988) to leave food and drinks with a rather bland taste.
3. Oral mucosal erosion (Fig. 36-5). This appears to be an idiosyncratic reaction and concentration

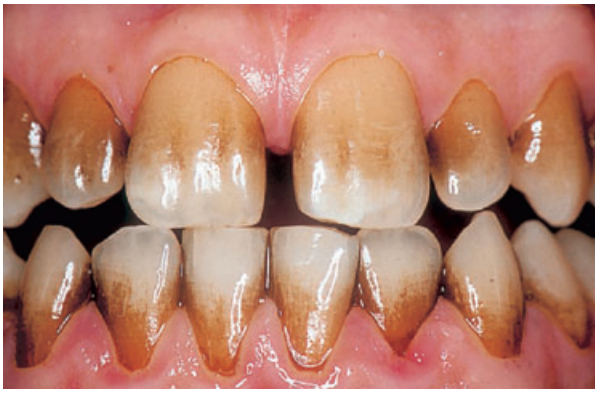


Fig. 36-3 Brown discoloration of the teeth of an individual rinsing twice a day for 3 weeks with a 0.2% chlorhexidine mouth rinse.

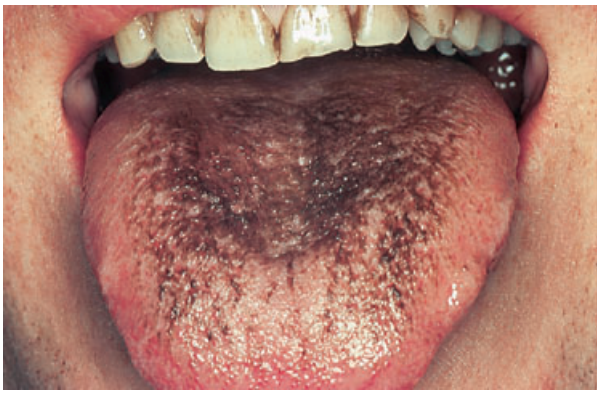


Fig. 36-4 Brown discoloration of the tongue of an individual rinsing twice a day for 2 weeks with a 0.2% chlorhexidine mouth rinse.

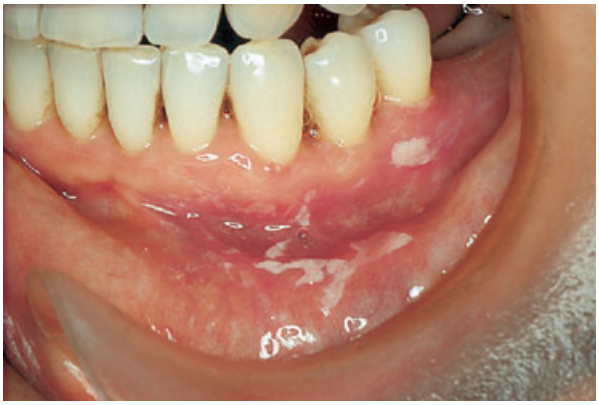


Fig. 36-5 Mucosal erosion occurring following a few days of rinsing twice a day with a 0.2% chlorhexidine mouth rinse.

dependent. Dilution of the 0.2% formulation to 0.1%, but rinsing with the whole volume to maintain dose, usually alleviates the problem. Erosions are rarely seen with 0.12% rinse products used at 15 ml volume.

4. Unilateral or bilateral parotid swelling (Fig. 36-6). This is an extremely rare occurrence and an explanation is not available.
5. Enhanced supragingival calculus formation. This effect may be due to the precipitation of salivary proteins on to the tooth surface, thereby increasing pellicle thickness and/or precipitation of inorganic salts on to or into the pellicle layer.

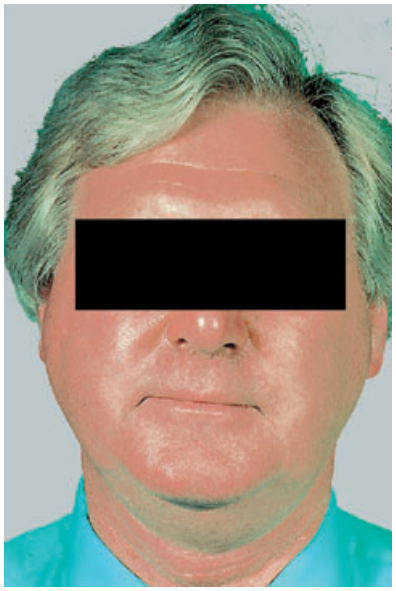


Fig. 36-6 Bilateral parotid swelling following a few days of rinsing with a 0.2% chlorhexidine mouth rinse.

Chlorhexidine also has a bitter taste, which is difficult to mask completely.

Chlorhexidine staining

The mechanisms proposed for chlorhexidine staining can be debated (Eriksen *et al*. 1985; for reviews see Addy & Moran 1995; Watts & Addy 2001) but have been proposed as:

1. Degradation of the chlorhexidine molecule to release parachloraniline
2. Catalysis of Maillard reactions
3. Protein denaturation with metal sulfide formation
4. Precipitation of anionic dietary chromogens.

Degradation of chlorhexidine to release parachloraniline appears not to occur on storage or as a result of metabolic processes. Also, alexidine, a related bisbiguanide, does not have parachloraniline groups, yet causes staining identical to that of chlorhexidine. Non-enzymatic browning reactions (Maillard reactions) catalyzed by chlorhexidine are a theoretical possibility; however, evidence is indirect, circumstantial or inconclusive (Eriksen *et al*. 1985). The theory does not consider the fact that other antiseptics and metals such as tin, iron, and copper also produce dental staining. Protein denaturation produced by chlorhexidine with the interaction of exposed sulfide radicals with metal ions is also theoretically possible but there is no direct evidence to support this concept. Again, the theory does not take into account similar staining by other antiseptics and metal ions. Laboratory and clinical studies also could

not reproduce this process (for reviews see Addy & Moran 1985; Watts & Addy 2001). Precipitation of anionic dietary chromogens by cationic antiseptics, including chlorhexidine and polyvalent metal ions as an explanation for the phenomenon of staining by these substances, is supported by a number of well controlled laboratory and clinical studies (for reviews see Addy & Moran 1995; Watts & Addy 2001). Thus, the locally bound antiseptics or metal ions on mucosa or teeth can react with polyphenols in dietary substances to produce staining. Beverages such as tea, coffee, and red wine are particularly chromogenic, but other foods and beverages will interact to produce various colored stains. These reactions between chlorhexidine and other cationic antiseptics and polyvalent metal ions with chromogenic beverages can be performed within the test tube. Interestingly, most of the precipitates formed between polyvalent metal ions and chromogens have the same color as their sulfide salts. It is for this reason that original theories considered that staining, seen in individuals exposed to these polyvalent metal ions, usually in the workplace, was due to metal sulfide formation. Again, laboratory and clinical experiments have failed to produce such interactions.

It is perhaps the staining side effect that limits long-term use of chlorhexidine in preventive dentistry (Flotra *et al*. 1971) and occurs with all correctly formulated products including gels, toothpastes, and sprays. Indeed, the staining side effect can be used to assess patient compliance in the use and activity of formulations. In the latter case laboratory and clinical studies on staining have revealed a proprietary chlorhexidine mouth rinse product to be inactive (Renton-Harper *et al*. 1995). Interestingly, this particular chlorhexidine product was reformulated in the UK to produce an active formulation (Addy *et al*. 1991), but the manufacturers maintained the original formulation within France when both laboratory and clinical studies confirmed markedly reduced potential of the product to cause staining in the laboratory, and plaque inhibition in the clinic (Renton-Harper *et al*. 1995). Recently, a chlorhexidine product with an anti-discoloration system (ADS) was launched in Europe. A clinical study purporting to show reduced staining had significant drawbacks in design and presentation (Bernadi *et al*. 2004). A laboratory study found no difference in staining potential (Addy *et al*. 2005) and a plaque regrowth study showed significantly reduced plaque inhibition for the ADS rinse (Arweiler *et al*. 2006). The old adage concerning chlorhexidine products appears to still hold true: "If it does not stain it does not work".

Mechanism of action

(For reviews see Addy 1986; Jenkins *et al*. 1988)

Chlorhexidine is a potent antibacterial substance but this alone does not explain its antiplaque action. The antiseptic binds strongly to bacterial cell membranes. At low concentration this results in increased permeability with leakage of intracellular components including potassium. At high concentration, chlorhexidine causes precipitation of bacterial cytoplasm and cell death. In the mouth chlorhexidine readily adsorbs to surfaces including pellicle-coated teeth. Once adsorbed, and unlike some other antiseptics, chlorhexidine shows a persistent bacteriostatic action lasting in excess of 12 hours (Schiott *et al*. 1970). Radio-labelled chlorhexidine studies suggest a slow release of the antiseptic from surfaces (Bonesvoll *et al*. 1974a,b) and this was suggested to produce a prolonged antibacterial milieu in the mouth (Gjermo *et al*. 1974). The methods used, however, could not determine the activity of the chlorhexidine, which was almost certainly attached to the salivary proteins and desquamating epithelial cells and therefore unavailable for action. Consistent with the original work and conclusions (Davies *et al*. 1970), a more recent study and review suggested that plaque inhibition is derived only from the chlorhexidine adsorbed to the tooth surface (Jenkins *et al*. 1988). It is possible that the molecule attaches to pellicle by one cation leaving the other free to interact with bacteria attempting to colonize the tooth surface. This mechanism would, therefore, be similar to that associated with tooth staining. It would also explain why anionic substances, such as sodium lauryl sulfate based toothpastes, reduce the plaque inhibition of chlorhexidine if used shortly after rinses with the antiseptic (Barkvoll *et al*. 1989). Indeed, a more recent study has demonstrated that plaque inhibition by chlorhexidine mouth rinses is reduced if toothpaste is used immediately before or immediately after the rinse (Owens *et al*. 1997b). These inhibitory effects on chlorhexidine activity by substances such as toothpastes can be modeled using the chlorhexidine tea staining method, which shows reduced staining activity by the chlorhexidine solutions resulting from an interaction with toothpaste (Sheen *et al*. 2001).

Plaque inhibition by chlorhexidine mouth rinses appears to be dose related (Jenkins *et al*. 1994) such that similar effects to that seen with the more usual 10 ml, 0.2% solution (20 mg) can be achieved with high volumes of low-concentration solutions (Lang & Ramseier-Grossman 1981). It is worth noting, however, that not inconsiderable plaque inhibition is obtained with doses as low as 1–5 mg twice daily (Jenkins *et al*. 1994). Also, and relevant to the probable mechanism of action, topically applying 0.2% solutions of chlorhexidine only to the tooth surface, including by the use of sprays, produces the same level of plaque inhibition as rinsing with the full 20 mg dose (Addy & Moran 1983; Francis *et al*. 1987a; Jenkins *et al*. 1988; Kalaga *et al*. 1989a).

Chlorhexidine products

Chlorhexidine has been formulated into a number of products.

Mouth rinses

Aqueous alcohol solutions of 0.2% chlorhexidine were first made available for mouth rinse products for twice daily use in Europe in the 1970s. A 0.1% mouth rinse product also became available; however questions were raised over the activity of the 0.1% product and in some countries the efficacy of this product is less than would be expected from a 0.1% solution (Jenkins *et al*. 1989). Later, in the US, a 0.12% mouth rinse was manufactured but to maintain the almost optimum 20 mg doses derived from 10 ml of 0.2% rinses, the product was recommended as a 15 ml rinse (18 mg dose). The studies revealed equal efficacy for 0.2% and 0.12% rinses when used at appropriate similar doses (Segreto *et al*. 1986). More recently alcohol-free chlorhexidine rinses have become available, some formulated with the inclusion of 0.05% CPC. Such formulations have been shown to possess equivalent effects at inhibiting plaque and gingivitis compared to alcohol-containing chlorhexidine rinses but with better taste acceptability with the non-alcoholic rinse (Quirynen *et al*. 2001; Van Strydonck *et al*. 2005)

Gel

A 1% chlorhexidine gel product is available and can be delivered on a toothbrush or in trays. The distribution of the gel by toothbrush around the mouth appears to be poor and preparations must be delivered to all tooth surfaces to be effective (Saxen *et al*. 1976).

In trays the chlorhexidine gel was found to be particularly effective against plaque and gingivitis in handicapped individuals (Francis *et al*. 1987a). The acceptability of this tray delivery system to the recipients and the carers was found to be poor (Francis *et al*. 1987b). More recently, 0.2% and 0.12% chlorhexidine gels have become available.

Sprays

Sprays containing 0.1% and 0.2% chlorhexidine are commercially available in some countries. Studies with the 0.2% spray have revealed that small doses of approximately 1–2 mg delivered to all tooth surfaces produces similar plaque inhibition to a rinse with 0.2% mouth rinses (Kalaga *et al*. 1989a). Sprays appear particularly useful for the physically and mentally handicapped groups, being well received by individuals and their carers (Francis *et al*. 1987a,b; Kalaga *et al*. 1989b).

Toothpaste

(For review see Yates *et al*. 1993)

Chlorhexidine is difficult to formulate into toothpaste for reasons already given and early studies produced variable outcomes for benefits to plaque and gingivitis. More recently, a 1% chlorhexidine toothpaste with and without fluoride was found to be superior to the control product for the prevention of plaque and gingivitis in a 6-month home use study (Yates *et al*. 1993). Stain scores however, were markedly increased as was supragingival calculus formation, and the manufacturer did not produce a commercial product. For a short time a commercial product was available, having been shown to be efficacious for both plaque and gingivitis (Sanz *et al*. 1994). Although effective, chlorhexidine products based on toothpaste and sprays produce similar tooth staining to mouth rinses and gels; taste disturbance, mucosal erosion, and parotid swellings tend to be less or have never been reported.

Varnishes

Chlorhexidine varnishes have been used mainly for prophylaxis against root caries rather than an antiplaque depot for chlorhexidine in the mouth.

Slow-release vehicles

A chlorhexidine chip has been produced commercially for placement into periodontal pockets as an adjunct to scaling and root planning. This will be discussed in Chapter 42.

Conclusions

- Chlorhexidine to date is the proven most effective antiplaque agent, for which commercial products are available to the public.
- Chlorhexidine is free from systemic toxicity in oral use, and microbial resistance and super-infection do not occur.
- Local side effects are reported which are mainly cosmetic problems.
- The antiplaque action of chlorhexidine appears dependent on prolonged persistence of antimicrobial action in the mouth (substantivity).
- A number of vehicles for delivering chlorhexidine are available, but mouth rinses are most commonly recommended.
- Extrinsic dental staining and perturbation of taste are variably the two side effects of chlorhexidine mouth rinse usage, which limit acceptability to users and the long-term employment of this antiseptic in preventive dentistry.

Clinical uses of chlorhexidine

Despite the excellent plaque inhibitory properties of chlorhexidine, widespread and prolonged use of the agent is limited by local side effects. Moreover, because of the cationic nature of the chlorhexidine and therefore its poor penetrability, the antiseptic is of limited value in the therapy of established oral conditions including gingivitis, and is much more valuable in the preventive mode. A number of

clinical uses, some well researched, have been recommended for chlorhexidine (for reviews see Gjermo 1974; Addy 1986; Addy & Renton-Harper 1996; Addy & Moran 1997; Eley 1999).

As an adjunct to oral hygiene and professional prophylaxis

Oral hygiene instruction is a key factor in the treatment plan for patients with periodontal disease and as part of the maintenance program following treatment. Adequate plaque control by periodontal patients is therefore essential to successful treatment and the prevention of recurrence of the disease. Chlorhexidine should therefore increase the improvement in gingival health through plaque control, particularly following professional prophylaxis to remove existing supra- and immediately subgingival plaque. There is, however, a potential disadvantage of using such an effective chemical plaque-control agent at this stage of the periodontal treatment plan. Thus, following oral hygiene instruction, it is normal, usually by the use of indices, to quantify the improvement in plaque control by patients so instructed and, in particular, the improvement at specific sites, which previously had been missed by individual patients. By virtue of the excellent plaque-control effects of chlorhexidine, the response to oral hygiene instruction cannot be accurately assessed since the antiseptic will overshadow any deficiencies in mechanical cleaning. Indeed, as the original research demonstrated, with chlorhexidine mouth rinse patients could maintain close to zero levels of plaque following a professional prophylaxis without using any form of mechanical oral hygiene (Löe & Schiott 1970). Nevertheless, chlorhexidine mouth rinse may be of value in maintaining oral hygiene following scaling and root planing when adequate tooth brushing may be compromised by post-treatment soreness or sensitivity.

Post oral surgery including periodontal surgery or root planing

Chlorhexidine may be used post-operatively since it offers the advantage of reducing the bacterial load in the oral cavity and preventing plaque formation at a time when mechanical cleaning may be difficult because of discomfort. In periodontal surgery, periodontal dressings have largely been replaced by the use of chlorhexidine preparations, in particular mouth rinses, since healing is improved and discomfort reduced (Newman & Addy 1978, 1982). Regimens vary but chlorhexidine should be used immediately post treatment and for periods of time until the patient can re-institute normal oral hygiene. Depending on the appointment schedule, chlorhexidine could be used throughout the treatment phase and for periods of weeks after completion of the treatment plan. If dressings are used, chlorhexidine is of limited value to the post-operative site since it does not penetrate beneath the periodontal dressings (Pluss *et al*. 1975). Although chlorhexidine rinses are probably used after root planing by many clinicians, evidence of therapeutic benefit has only recently been published (Faveri *et al*. 2006).

The idea of full-mouth disinfection using chlorhexidine both supra- and subgingivally as an adjunct to scaling and root planing has been assessed by one group in a number of papers since 1995 (for review see Quirynen *et al*. 2006). In the event, few adjunctive benefits could be shown (for review see Apatzidou 2006). It appeared that the more dominant factor was the time over which the non-surgical treatment plan was completed. Thus, root planing performed totally within 24 hours was more effective than root planing completed over more conventional periods of several weeks (Quirynen *et al*. 2006). Similar clinical research however, showed no difference between root planing completed within 24 hours compared to within several weeks (Apatzidou & Kinane 2004).

For patients with jaw fixation

Oral hygiene is particularly difficult when jaws are immobilized by such methods as intermaxillary fixation. Chlorhexidine mouth rinses have been shown markedly to reduce the bacterial load, which tends to increase during jaw immobilization, and to improve plaque control (Nash & Addy 1979). The more recent trend to use sub-dermal or sub-mucosal plates to stabilize bony fragments probably impedes oral hygiene procedures to a lesser degree, providing there are no oral mucosal lacerations. The influence of these factors on oral hygiene and therefore the role of chlorhexidine formulation has never been investigated.

For oral hygiene and gingival health benefits in the mentally and physically handicapped

Chlorhexidine has been found particularly useful in institutionalized mentally and physically handicapped groups, improving both oral hygiene and gingival health (Storhaug 1977). Spray delivery of 0.2% solutions was found particularly useful and acceptable to patients and care workers (Francis *et al*. 1987a,b; Kalaga *et al*. 1989b).

Medically compromised individuals predisposed to oral infections

A number of medical conditions predispose individuals to oral infections, notably candidiasis. Chlorhexidine is effective as an anticandidal agent but is most useful when combined with specific anticandidal drugs, such as nystatin or amphotericin B (Simonetti *et al*. 1988). Indications for chlorhexidine use combined with anticandidal drugs have been for the prevention of oral and systemic infections in the

immunocompromised, including those with blood dyscrasias, those receiving chemotherapy and/or radiotherapy, and notably bone marrow transplant patients (Ferretti *et al*. 1987, 1988; Toth *et al*. 1990). The value of chlorhexidine appears greatest when initiated before oral or systemic complications arise. A chlorhexidine spray was also found to produce symptomatic/psychologic oral care benefits in the terminally ill (Jobbins *et al*. 1992).

High-risk caries patients

Chlorhexidine rinses or gels can reduce considerably the *Streptococcus mutans* counts in individuals who are caries prone. Additionally, and interestingly, chlorhexidine appears synergistic with sodium fluoride and combining chlorhexidine and fluoride rinses appears beneficial to such at-risk individuals (Dolles & Gjermo 1980). Sodium monofluorophosphate on the other hand, reduces the effect of chlorhexidine and probably *vice versa* (Barkvoll *et al*. 1988). A chlorhexidine rinse product with sodium fluoride has recently become available.

Recurrent oral ulceration

Several studies have shown that chlorhexidine mouth rinses and chlorhexidine gels reduce the incidence, duration, and severity of recurrent minor aphthous ulceration (for review see Hunter & Addy 1987). The mechanism of action is unclear but may relate to a reduction in contamination of ulcers by oral bacteria, thereby reducing the natural history of the ulceration. Regimens have included three times daily use of chlorhexidine products for several weeks. Interestingly, one study showed that triclosan rinses reduce the incidence of recurrent mouth ulcers (Skaare *et al*. 1996). There have been no controlled studies of chlorhexidine in the management of major aphthous ulceration or other oral erosive or ulcerative conditions, although anecdotally chlorhexidine appears ineffective. Again, this may reflect the low therapeutic potential of this and other antiseptics, and the considerable amount of proteinacious material associated with these lesions which would both tend to inactivate chlorhexidine and block access to underlying microorganisms (Roberts & Addy 1981). A similar explanation may be propounded for the failure of chlorhexidine mouth rinses in treatment of acute necrotizing ulcerative gingivitis (periodontitis) (Addy & Llewelyn 1978): further evidence for the lack of absorption into tissues and biofilms of this cationic antiseptic.

Removable and fixed orthodontic appliance wearers

Plaque control in the early stages of orthodontic appliance therapy may be compromised and chlorhexidine can be prescribed for the first 4–8 weeks. Additionally, chlorhexidine has been shown to reduce the number and severity of traumatic ulcers during the first 4 weeks of fixed orthodontic therapy (Shaw *et al*. 1984).

Denture stomatitis

Chlorhexidine has been recommended in the treatment of *Candida*-associated infections; however, in practice even applying chlorhexidine gel to the fitting surfaces of dentures produces, in many cases, slow and incomplete resolution of the condition. Again, chlorhexidine is less effective in the therapeutic mode and it is more advantageous to treat denture stomatitis with specific anticandidal drugs and then employ chlorhexidine to prevent recurrence. The denture itself can be usefully sterilized from *Candida* by soaking in chlorhexidine solutions (Olsen 1975).

Oral malodor

Rinsing with chlorhexidine as with other antiseptic mouth rinses containing CPC, triclosan, and essential oils, has been suggested to be of value in reducing halitosis. Reductions in volatile sulphur compounds and morning malodor have been noted with all these chemicals (Carvalho *et al*. 2004).

Immediate pre-operative chlorhexidine rinsing and irrigation

This technique can be used immediately prior to operative treatment, particularly when air polishing, ultrasonic scaling or high-speed instruments are to be used. Such pre-operative rinsing markedly reduces the bacterial load and contamination of the operative area, operator, and staff (Worral *et al*. 1987). Additionally, in susceptible patients, irrigation of chlorhexidine around the gingival margin reduces the incidence of bacteremia (MacFarlane *et al*. 1984). This should be seen, however, only as an adjunct to appropriate systemic antimicrobial prophylaxis. Chlorhexidine mouth rinsing now features as an adjunct to antibiotic prophylaxis in the new UK guidelines.

Subgingival irrigation

Numerous antimicrobial agents have been used as subgingival irrigants in the management and treatment of periodontal diseases (for reviews see Wennstrom 1992, 1997). Alone, irrigation with antimicrobial agents produces effects little different from using saline, and they are of short duration, suggesting that the action is a washing-out effect. Irrigation combined with root planing appears to provide no adjunctive benefits.

Conclusions

- There is a significant number of indications for the use of chlorhexidine in preventive dentistry, most

of which rely on the antimicrobial properties of the antiseptic and its duration of action.
- The most valuable chemical plaque-control uses of chlorhexidine are in the short to medium term when mechanical tooth cleaning is not possible, difficult or inadequate and during which time local side effects are likely to be minimized.
- Chlorhexidine is more effective as a preventive rather than a therapeutic agent and therefore must be of questionable value as a subgingival adjunct in the treatment of periodontitis (see Chapter 42).

Evaluation of chemical agents and products

(For reviews see Addy *et al*. 1992; Addy 1995; Moss *et al*. 1995; Addy & Moran 1997)

The number and use of oral hygiene products has grown enormously in recent years and, as an example, hundreds of millions of pounds per year are spent on oral hygiene products in the UK and presumably billions worldwide. There can be no doubt that the oral hygiene industries, through their collaboration and research with the dental profession and their promotion of their products have, in no small way, contributed to the improvement in dental health seen in many countries. Claims for efficacy of oral hygiene products, however, are frequently made and it is essential that these are supported by scientific evidence. Without such evidence the profession and the public may be confused or misled. The dental profession is, however, faced with a large number of oral hygiene products supported by huge quantities of varied promotional literature and media advertising, which makes impossible, in many cases, any valid judgment or assessment of the efficacy or value of individual products to specific patient groups or the public as a whole. Even those with specialized interest, and research experience in specific aspects of oral hygiene product evaluation, must find validation, based on published literature, a daunting task. This is made all the more difficult since what constitutes proof of efficacy is not generally agreed even amongst so-called experts. Few countries of the world have central control over what evidence is required before efficacy claims can be made and there are very few guidelines suggesting requirements for proof of efficacy for oral hygiene products.

The scientific evaluation of dental products, and for that matter, preventive and therapeutic agents in medicine as a whole, is a relatively modern concept but today must be the backbone on which to base claims of efficacy. Anecdotal and case reports, uncontrolled studies and data listed as "held on file" by manufacturers, whilst interesting, should not be used as the basis for efficacy claims. Blind, randomized, controlled clinical and laboratory studies must be the methods used today to obtain data on the activity of agents, formulations, and products. Terminology and phraseology in product claims also needs to be carefully reviewed and assessed. Perhaps the greatest area for criticism must be the implied claim by the manufacturer and/or the inferences left to be drawn, from promotional material, by the dental profession or public. A classic scenario for which there is precedence can be stated as follows: A is the cause of B, C reduces A, leaving the inference to be drawn that C can control B. Perhaps nowhere is this more apparent than in the use of agents which are known to control plaque, and therefore it can be implied, without evidence, they must control gingivitis. The now familiar claim would be "this product reduces plaque, the major cause of gum disease". Similarly, creative arithmetic is not infrequently used to give inflated impressions of efficacy. Proportional differences, rather than actual differences, are not infrequently quoted, as are percentages of percentages giving hundreds of percent improvements over another product or control, yet the actual benefit is a fraction of the scoring index used. Finally, "piggy back" claims are not uncommon, when a known active ingredient is formulated into a new product and equivalent efficacy to established products is assumed. It would seem reasonable here to repeat the definitions for the terminology for oral hygiene products, agreed at the European Workshop on Periodontology in 1996 which defined certain terms (Lang & Newman 1997):

- *Antimicrobial agents*: chemicals that have a bacteriostatic or bactericidal effect *in vitro* that alone cannot be extrapolated to a proven efficacy *in vivo* against plaque.
- *Plaque reducing/inhibitory agents*: chemicals that have only been shown to reduce the quantity and/or affect quality of plaque, which may or may not be sufficient to influence gingivitis and/or caries.
- *Antiplaque agents*: chemicals that have an effect on plaque sufficient to benefit gingivitis and/or caries.
- *Antigingivitis agents*: chemicals which reduce gingival inflammation without necessarily influencing bacterial plaque (includes anti-inflammatory agents).

Thus, the fact that antimicrobial agents such as antiseptics kill or inhibit the growth of bacteria does not necessarily mean they will be effective plaque inhibitors (Gjermo *et al*. 1970). Also, the mere incorporation of a known antiplaque agent into a formulation is not a guarantee of efficacy because inactivation by other ingredients may occur.

This section looks at methods that have been used to test oral hygiene products both in the laboratory and the clinic. No one protocol can provide all the answers, and research and development of agents into products is a step-by-step process, hopefully culminating in a body of evidence proving efficacy, beyond doubt, of a final product. Methods *in vitro* and *in vivo* will be summarized but animal testing

will not be discussed except to acknowledge that the use of animals is still necessary in drug development, in understanding the mode of action of drugs and, particularly, in evaluating safety from a toxicologic point of view. The evaluation of oral hygiene products on animals, however, particularly for efficacy, must be questioned on a number of scientific and moral grounds.

Most laboratory and clinical methods have been developed to test antimicrobial agents but methodologies are available, or present ones could be modified, to study potential antiadhesive and plaque removal chemicals (for reviews see Addy *et al*. 1992; Addy 1995; Addy & Moran 1997).

Studies *in vitro*

Bacterial tests

Antimicrobial tests, including minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and kill curves, can be determined. These tests indicate the antibacterial activity and antimicrobial spectrum of agents and formulations against a range of oral bacteria. Continuous culture techniques can also be used but they may not provide more meaningful data. It is likely that, with technologic advances, laboratory models to accurately replicate the plaque biofilm will become available to test chemical plaque-control agents. At present, antimicrobial tests *in vitro* primarily only indicate activity, or lack of it, and they are very poor predictors *per se* of effects on plaque *in vivo*. This is because, so far, methods do not provide particularly reliable information on the substantivity of the antimicrobial agent. Nevertheless, antimicrobial tests are valuable for a variety of reasons. With few exceptions, agents without activity *in vitro* will not provide activity *in vivo*. The additive or negative effects of ingredient mixtures can be determined. The availability of active ingredients incorporated in the product can be assessed. The adverse influence of the oral environment can be modeled; for example, the influence of saliva or proteins on the antibacterial activity of agents can be tested.

Uptake measurements

One aspect of substantivity is adsorption of antimicrobials and other potential plaque-inhibitory agents on to surfaces. This can be quantified using a variety of substrates such as hydroxyapatite, dentine, enamel, acrylic, and other polymers. The influence of other factors or agents on the uptake of a particular agent can also be assessed. Such data are of interest but must be interpreted with caution since they only measure uptake, not activity once adsorbed. Nevertheless, desorption of an agent from such surfaces can be measured by a variety of analytical techniques, thereby giving some indication of both the adsorption profile and the subsequent substantivity of the agent to the substrate surface.

Other methods

Activity or availability of an ingredient in a formulation can be measured or assessed. Methods include chemical analyses; however, some methods chemically extract the agent from the formulation in its entirety and therefore do not necessarily demonstrate that it is freely available and active within the formulation. For the cationic antiseptics and polyvalent metal salts, their potential to bind dietary chromogens from beverages such as tea can be used to assess the possibility that they may cause staining *in vivo*. More usefully, the test method can be employed to determine and compare the availability of the same ingredient in different formulations. Such methods have shown considerable differences in availability of chlorhexidine and cetylpyridinium chloride in apparently similar mouth rinses (Addy *et al*. 1995). Moreover, how other oral hygiene products might interfere with the activity of chemical plaque-control agents, such as toothpaste with chlorhexidine and cetylpyridinium chloride, has given surprisingly accurate predictions of clinical outcome (Owens *et al*. 1997b; Sheen *et al*. 2001, 2003). Again, these methods give little indication of substantivity and therefore the staining method *in vitro* cannot be used to compare different agents for propensities to cause staining *in vivo*. For example, a 0.05% cetylpyridinium chloride mouth rinse produces comparable tea staining on a substrate surface to a 0.2% chlorhexidine mouth rinse, yet clinically the amount of staining reported for chlorhexidine is considerably greater than that for cetylpyridinium chloride and this can be explained by the fact that the substantivity of the former is greater than that of the latter.

Study methods *in vivo*

A considerable number of protocols have been developed to evaluate potential antiplaque agents and products. Ideally, because of the number of ingredients and more particularly formulations, a step-by-step pyramid approach is taken. Thus initially, study designs are used which permit, if necessary, the screening of relatively large numbers of agents and formulations and on relatively small numbers of subjects.

Depot studies

Retention of agents in the mouth may be measured by determining the amount expectorated versus the known dose (the buccal retention test) or by measuring plaque and saliva levels of the agent over time. Such retention assessments can be misleading because retention is only one aspect of substantivity and the measurement techniques do not provide information

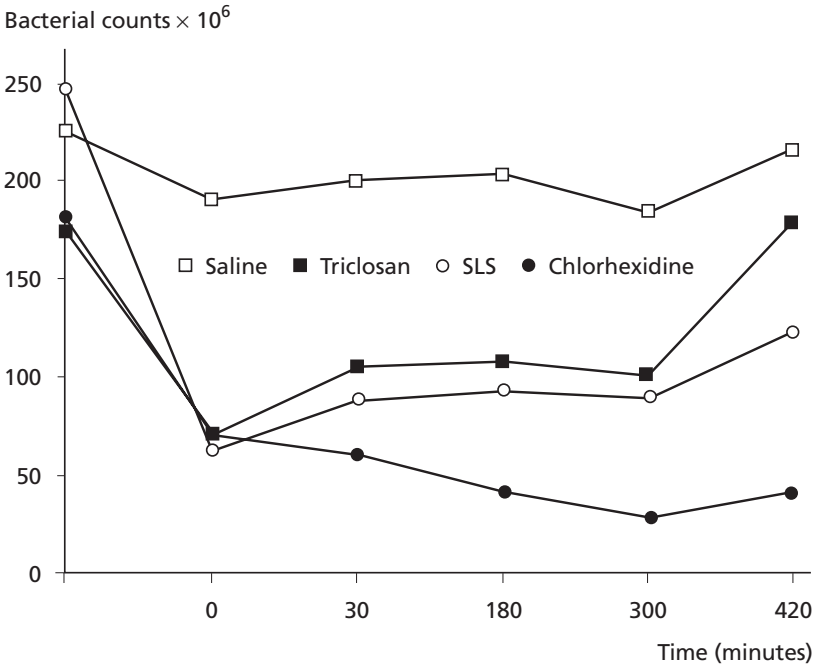


Fig. 36-7 Salivary bacterial counts over time following mouth rinsing with chlorhexidine, saline, sodium lauryl sulfate, and triclosan. Following a single rinse with chlorhexidine, sodium lauryl sulfate, and triclosan there is an immediate large reduction in bacterial counts. This continues and persists to the 420-minute endpoint of the study for chlorhexidine (positive control) with a tendency for counts to revert towards baseline for triclosan and sodium lauryl sulfate. With saline (placebo control), there is little change in counts over time.

on the activity of the retained agents. Moreover, the buccal retention test does not distinguish drug absorption from adsorption nor determine how much is swallowed. Thus, for example, studies using radiolabeled chlorhexidine purported to demonstrate slow release from oral surfaces and this occurred over a protracted period of time (Bonesvoll *et al*. 1974a,b). However, saliva derived from subjects following rinsing with chlorhexidine only provided antimicrobial activity for up to 3 hours following rinsing (Addy & Wright 1978). This is clearly markedly less than the known substantivity or persistence of action of chlorhexidine in the mouth of at least 12 hours (Schiott *et al*. 1970). It is likely, therefore, that the initial desorption studies using a radiolabel were merely detecting chlorhexidine adsorbed to desquamating oral surfaces, particularly the mucosa.

Antimicrobial tests

For antimicrobial agents only, salivary bacterial count assessments are much more indicative of substantivity and are predictive of antiplaque action for the same agents. The method involves measuring salivary bacterial counts before, and at time points, after a single rinse with the agent (Fig. 36-7) and was first described for chlorhexidine (Schiott *et al*. 1970). In the case of toothpaste, the product can be either brushed or rinsed as an aqueous slurry (Addy *et al*. 1983; Jenkins *et al*. 1990). Agents and products produce variable reductions in counts ranging from none, as with water, to greater than 90%, as with chlorhexidine. More importantly, the duration of reduction from baseline varies from minutes to hours. Thus, povidone iodine only reduces counts for approximately 1 hour, cetylpyridinium chloride for 3 hours (Roberts & Addy 1981), whereas chlorhexidine produces such effects for over 12 hours (Schiott *et al*. 1970). Toothpastes generally show reductions in counts between 3 and 5 hours, probably largely due to contained detergents and/or specific ingredients such as triclosan (Addy *et al*. 1989).

Experimental plaque studies

Short-term plaque regrowth studies are perhaps the most commonly used clinical experiments to screen chemical oral hygiene products. They have the advantage of assessing the chemical action of the formulation divorced from the indeterminate variable of toothbrushing. Typically, plaque regrowth from a zero baseline and the influence of the test agent is recorded. Originally used for mouth rinses, the method has been modified for toothpaste by delivering the formulation in a tray applied to the teeth (Etemadzadeh *et al*. 1985) or as a slurry rinse (Addy *et al*. 1983). Studies are usually cross-over, allowing many formulations to be evaluated against suitable controls. Study periods range from 24 hours to several days, usually 4–5 days (Harrap 1974; Addy *et al*. 1983). A negative control such as water and a positive control such as chlorhexidine may be used (Fig. 36-8). These help to position the activity of the test formulations between the extremes. Also, because the results from these controls can be predicted, their use tends to confirm or otherwise the conduct of these blind, randomized study designs.

Experimental gingivitis studies

Experimental gingivitis studies (Löe & Schiott 1970) are based on the original experimental gingivitis in man protocol first used to demonstrate the direct etiologic relationship between plaque and gingivitis

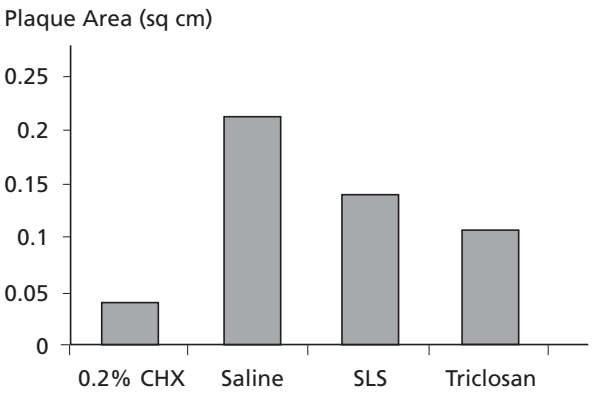


Fig. 36-8 Plaque area following the use of chlorhexidine, saline, sodium lauryl sulfate, and triclosan mouth rinses after 4-day periods. Considerable plaque inhibition was afforded by chlorhexidine (positive control) when toothcleaning was suspended. Both sodium lauryl sulfate and triclosan show significant plaque-inhibitory action compared to saline (placebo control) albeit significantly less than chlorhexidine.

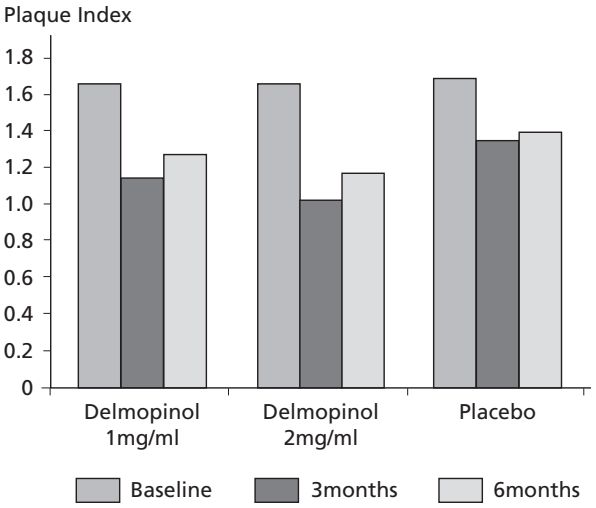


Fig. 36-9 A 6-month study of delmopinol rinses as adjuncts to oral hygiene. Significant improvements in plaque scores are seen in the delmopinol mouth rinse groups at 3 and 6 months compared to placebo. A Hawthorne effect of improved toothcleaning irrespective of the treatment is apparent in the placebo group, particularly at 3 months, although this is still present at 6 months.

(Löe *et al*. 1965). This latter original study did not return subjects to zero baseline plaque scores or gingival health, whereas most subsequent methods, to evaluate oral hygiene products, have taken this approach with baseline parameters. Study periods usually range from 12, but more particularly 19–28 days. In the absence of normal tooth cleaning, the development of plaque and gingivitis are recorded under the influence of test and control formulations. Studies may be either cross-over or parallel.

Home use studies

For chemical oral hygiene products and usually toothpastes and mouth rinses, the final evaluation requires that they are shown to be effective against plaque and, more particularly, gingivitis, when used along with normal mechanical tooth cleaning. Studies can be over days or weeks but usually, in accordance with guidelines such as those for the American Dental Association (Council of Dental Therapeutics 1985), they need to be 6 months or longer, particularly since safety needs to be assessed (Fig. 36-9). Most studies are parallel in design. Protocols have used two approaches. One is perhaps more therapeutic in concept whereby subjects have to exhibit a certain level of plaque and/or gingivitis before entry (Johansen *et al*. 1975). The other is more preventive in concept and there is a pre-study period in which subjects with gingivitis receive prophylaxis and instruction to improve their gingival health. Those satisfactorily responding are entered, and change in gingival health is monitored in the test and control groups (Stephen *et al*. 1990).

Several factors tend to confound home use studies of oral hygiene products and may mask a proven chemical antiplaque action determined from short-term plaque and experimental gingivitis studies. Most important is the so-called Hawthorne effect where subjects knowingly involved in oral hygiene studies improve their tooth cleaning (Fig. 36-9). Secondly, baseline prophylaxes are commonly given and the influence of this on the subsequent gingivitis levels is not known. In mouth rinse studies used as adjuncts to tooth cleaning, there is the potential of interaction between toothpaste and mouth rinse, which could be additive but in most cases is more likely negative for effects on mouth rinse ingredients (Owens *et al*. 1997b; Sheen *et al*. 2001, 2003). Compliance in home use studies can also be a problem and difficult to determine accurately. In short-term studies compliance can be guaranteed through supervision but this is difficult in home use studies although was achieved, in part, in a series of delmopinol studies (for review see Addy *et al*. 2007). Finally, particularly in toothpaste studies, the control product will have some inherent plaque-inhibitory action consequent upon ingredients such as detergents (Addy *et al*. 1983). If the appropriate control products have been used in the screening plaque inhibitory and experimental gingivitis models this should not pose a problem. However, there is no doubt, and this will be discussed, that the choice of control toothpaste, used to compare an active toothpaste, could considerably influence the outcome and therefore the conclusions concerning a potential antiplaque toothpaste.

Clinical trial design considerations

Clinical trials involving human patients, subjects or healthy volunteers in many countries must now conform to the Guidelines for Good Clinical Practice (ICH 1996) including the Declaration of Helsinki (World Medical Association 1996). The Declaration of

Helsinki was introduced primarily to protect the well-being of the participants. The Guidelines for Good Clinical Practice are broadly concerned with all aspects of a clinical trial and, in particular, the ethical requirements, the design and conduct of the trial, data collection and record keeping, data analysis, and reporting of the findings. As a result, the Guidelines not only also protect the interests of the participants but of those organizing, supporting, and conducting the trials. An important additional purpose of the Guidelines is to limit the possibility of falsification of data. Requirements of ethical committees will vary locally, nationally, and internationally; however, common to all is a need for a detailed protocol covering all aspects of the clinical trial, subject or patient information, and consent. Written indemnification and/or insurance cover from the appropriate source or sources for the subjects or patients is required, although the details may vary both nationally and internationally. For example, in the UK most ethical committees would adopt the indemnification principles as set out by the Association of British Pharmaceutical Industries.

The basic requirements of a clinical trial are that it should be blind, randomized, and suitably controlled. These three aspects of clinical trial design are intimately related and are there to remove, limit or allow adjustment for possible influences that might confound the outcome of a clinical trial and thereby reduce or completely obviate the scientific value of any particular study. These three design features will be discussed individually.

Blindness

The term "blindness" is for obvious reasons not universally accepted and alternatives include "masking" or "masked". All clinical studies must be, at least, single, examiner blind. Single blindness requires that any investigator collecting data from the patients or subjects should not know the identity of the treatments used by any particular individual. Single blindness should eliminate bias in data collection. Examiner blindness, however, can be compromised to a variable degree if a particular treatment produces changes within the oral cavity, which can be perceived by the examiner. Such an example could be extrinsic staining of the teeth and/or oral mucosa by chlorhexidine formulations. The use of objective measures, which reduce or remove the requirement for subjective judgment, by the examiner, can improve the likelihood of single blindness. Unfortunately, such objective methods are not common to the recording of plaque, gingivitis, and periodontal disease parameters.

Double blindness is the ideal when neither the examiner nor subject or patient is aware of the treatment being used by the individual. Numerous factors will influence whether the subjects or patients can be maintained totally blind to their treatment(s), including whether the study is parallel or cross-over (to be discussed later), prior experience with treatments, and the presentation, taste, and appearance of the treatments, particularly controls. Subject blindness, although ideal, is less important where the treatment outcome measures are out of the immediate control of the subject, e.g. plaque accumulation and gingivitis; assuming, that is, that lack of subject blindness does not influence compliance. Subject blindness becomes highly important where the subject is required to make a valid judgment of the effects of the treatment, for example the effects of treatments on symptoms such as pain. The term "triple blindness" is used by some investigators and relates to the blindness of the individual analyzing the data to the identity of the treatments. Thus, the data are analyzed using the treatment codes e.g. treatments A, B, and C. The identities of A, B, and C are only revealed once the statistical tests have been completed.

Randomization

The order in which treatments are received by each subject in a cross-over study, or into which treatment group subjects are placed in a parallel study, should be according to a randomized schedule. Randomization provides several important safety aspects to the study design in that firstly it is an essential part of examiner blindness. Secondly, in a cross-over study randomization should remove the potential confounding effects of the order of product use, the so-called period effects. Thirdly, the use of balanced randomization designs allows for potential carry-over effects of treatments in cross-over design studies (Newcombe *et al*. 1995). Finally, where the effects of a treatment on a disease state are to be assessed, randomization improves the chances that parallel treatment groups should be as similar as possible in baseline disease levels and, if relevant, demographic data. Randomization schedules, which use subject matching for demographic and disease status or stratification for level of disease, can be employed to improve balancing of parallel groups.

Controls

The use of appropriate control treatments is essential to the evaluation of the benefits of a particular agent or product. Without such controls, studies essentially become no more than case report data at best and anecdotal at worst, particularly when specific treatment is evaluated alone for effects on various parameters. The choice of controls, however, can vary depending on the aim of the study and the level of evaluation of an agent or product within a program of research. The choice of controls could therefore be one or more of the following:

- *Placebo control*. Here the control is a substance without any expected pharmacologic action, e.g. water. This is useful when assessing a new agent or positioning an agent or formulation between a positive or benchmark control. Placebo controls are particularly valuable where a condition or symptom

may be perceived by the subject or patient to have improved, so-called placebo response, or where a condition appears to improve naturally over time, the so-called regression to the mode. Both of these phenomena are common to studies of the treatment of dentine hypersensitivity where pain is a primary outcome measure, but they are, of course, unlikely to occur in studies where the outcome measure are levels of plaque and gingivitis.

- *Minus active control (negative control)*. This type of control is commonly employed to determine whether an agent provides activity over and above its vehicle. It is particularly useful in the initial assessment of formulations such as toothpastes which have included a new active. In the later stages of development, perhaps at the product level, the use of minus active controls in home use studies is of less value since minus active controls are not normally used by the general public.
- *Bench mark control*. This term is usually used to define a control which is a commercially available product commonly used by the general public. Such controls would appear more sensible for home use studies rather than minus active products when, for example, a new toothpaste product is formulated to promote gingival health benefits. In this case it would seem reasonable to determine whether efficacy is superior to conventional fluoride toothpaste rather than the minus active toothpaste.
- *Positive control*. Positive control is an agent or formulation presently considered the most effective agent available. In this case chlorhexidine mouth rinse is arguably considered the "gold" standard antiplaque agent and is frequently used as the positive control by which to compare and position the efficacy of agents and formulations. Usually a chlorhexidine mouth rinse is used as the positive control in the early no oral hygiene study protocols.

Depending on the aims and constraints of a clinical study, more than one of the aforementioned controls may be used; for example, in the short-term studies it is not unusual to position an agent or formulation for plaque and gingivitis efficacy between a positive control, chlorhexidine, and a placebo, water.

Study groups

Study designs for oral hygiene products are usually either parallel or cross-over. Parallel group studies require that each individual uses only one of the formulations (active or control) throughout the duration of the study. Parallel designs can be used for any of the previously described oral hygiene study methods; however they are more commonly used when the study duration is protracted to weeks or months. Parallel designs require that the study groups are large in number to provide sufficient power for statistical analysis. Indeed, the power of any particular study to demonstrate a statistically significant difference between treatments should be calculated prior to the study, although this may be compromised by lack of data as to the likely outcome or by difficulty in deciding the clinical relevance of any difference found. Advice from a statistician is important and group sizes can be calculated based on expected differences between test and control formulations. It must be remembered that small differences can be found statistically significant merely by using large group sizes.

Cross-over studies randomly allocate subjects to use all of the agents or formulations under test. Since each individual acts as their own control, paired statistical analytical techniques mean that the power to detect differences is markedly increased compared to parallel designs, and thereby the total study cohort of subjects can be relatively small. Furthermore, a considerable number of formulations can be compared, although this will be limited by the duration of each study period which, in itself, will have a knock-on effect on acceptability to and compliance of the subjects. Cross-over studies require a wash-out period between each treatment period and this will depend on the known, or expected, carry-over effect of a treatment or a condition into the next period. Random incomplete block designs can be used, in which each subject only uses so many of the agents under test.

The relationship between statistical significance and clinical significance is always difficult to resolve (for review see Addy & Newcombe 2005). Statistical significance is a mathematical concept which, with varying levels of probability, supports the idea that any difference between treatments is not due to chance. Clinical significance, on the other hand, is conceptual and attempts to define the benefit to the patient of any particular treatment. Unlike some branches of medicine and surgery, in periodontology, clinical significance is particularly difficult to define because the usual outcome variables are not absolute. Thus, treatment effects on plaque and/or gingivitis indices, unless approaching 100%, cannot be translated with any certainty to the initiation or progress of periodontitis and certainly not to tooth loss. Clinical significance could be:

1. *Bench mark equivalent*: when a formulation performs as well as an established formulation or product.
2. *Bench mark superior*: when a formulation performs significantly better than an established formulation.
3. *Disease related*: when a formulation has an effect on an etiologic factor such that the related signs or symptoms of the associated disease are reduced to a significantly greater extent than the control, e.g. plaque reduction which reduced gingivitis to a greater extent than control.
4. *Positive*: when a formulation produced the effect significantly greater than the most effective agent

today, e.g. the antiplaque effect is greater than chlorhexidine.

5. *Proportional superiority*: when from the outset of a study a minimum percentage improvement over the control group is set down as clinically significant.

Conclusions

- Terminology concerning oral hygiene products needs to be standardized and defined.
- Efficacy claims, which are implied, or rely on inferences to be drawn, should be avoided.
- Studies *in vitro* can provide supportive data to clinical investigations but cannot stand alone as proof of efficacy *in vivo*.
- Research and development of oral hygiene products needs to be step-by-step processed, making available a body of knowledge supporting the efficacy of a final formulation.
- Clinical proof should be largely dependent on data from blind, randomized, controlled clinical trials conducted to the Guideline for Good Clinical Practice (GCP).
- In reporting clinical trials the clinical significance of the finding should be considered.
- Statistical significance should not necessarily be taken as proof *per se* of the benefit of an oral hygiene product to the general public.
- Clinical outcome, when possible, should be evaluated against side effects and the cost–benefit ratio should be determined.
- Where possible, systematic reviews with meta-analyses need to be conducted to prove the efficacy of agents and products for the control of supragingival plaque.

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Chapter 37

Non-surgical Therapy

Noel Claffey and Ioannis Polyzois

Introduction

It is generally accepted that the goal of the initial periodontal treatment is to restore the biological compatibility of periodontally diseased root surfaces, thus halting the process of the disease. Figure 37-1 illustrates the role and sequencing of non-surgical therapy in the management of most periodontitis patients.

Non-surgical therapy aims to eliminate both living bacteria in the microbial biofilm and calcified biofilm microorganisms from the tooth surface and adjacent soft tissues. Complete elimination of such pathogenic microorganisms is perhaps over-ambitious. However a reduction in inflammation of the periodontium due to a lesser bacterial load leads to beneficial clinical changes. In addition, non-surgical therapy aims to create an environment in which the host can more effectively prevent pathogenic microbial recolonization using personal oral hygiene methods.

This chapter outlines the various methods used in non-surgical therapy, such as hand instrumentation, ultrasonic and sonic scalers, and ablative laser therapy. Their respective merits and shortcomings and their clinical efficacy will be discussed. The chapter will attempt to identify realistic prognostic outcomes of therapy when taking into consideration factors such as different methods of instrumentation, different root surfaces, and varying degrees of periodontitis.

Re-evaluation of the initial clinical response to non-surgical therapy as well as consideration of modifiable risk factors allows the clinician to formulate an ongoing treatment plan tailored to the individual.

Detection and removal of dental calculus

Periodontitis is strongly associated with the presence of dental calculus on root surfaces. It has been suggested that the rough surface of calculus does not in itself induce inflammation but that the deleterious effect of calculus relates to its ability to provide an ideal surface for microbial colonization (Waerhaug 1952). It has also been demonstrated that epithelial adherence to subgingival calculus can occur following its disinfection with chlorhexidine (Lisgarten & Ellegaard 1973). Thus, a rationale for the removal of calculus relates to eliminating, as far as possible, surface irregularities harboring pathogenic bacteria.

Microbes giving rise to and colonizing the surface of dental calculus have been shown to produce lipopolysaccharides (LPS). These potent triggers of host response mechanisms were thought to be present within calculus and underlying cementum. For this reason it was thought necessary to remove not only calculus but also underlying cementum. However later evidence suggested that removal of tooth substance was not necessary. Ground sections of extracted periodontally involved teeth were examined. LPS was detected on cementum which had been previously exposed to the periodontal pocket. LPS also extended 1 mm into the surrounding connective tissue attachment. On no occasion was LPS seen penetrating into sub-surface cementum (Hughes & Smales 1986). These conclusions were further supported by animal and human studies which demonstrated that removal of superficial plaque on subgingival calculus resulted in the healing of periodontal lesions and the maintenance of health,

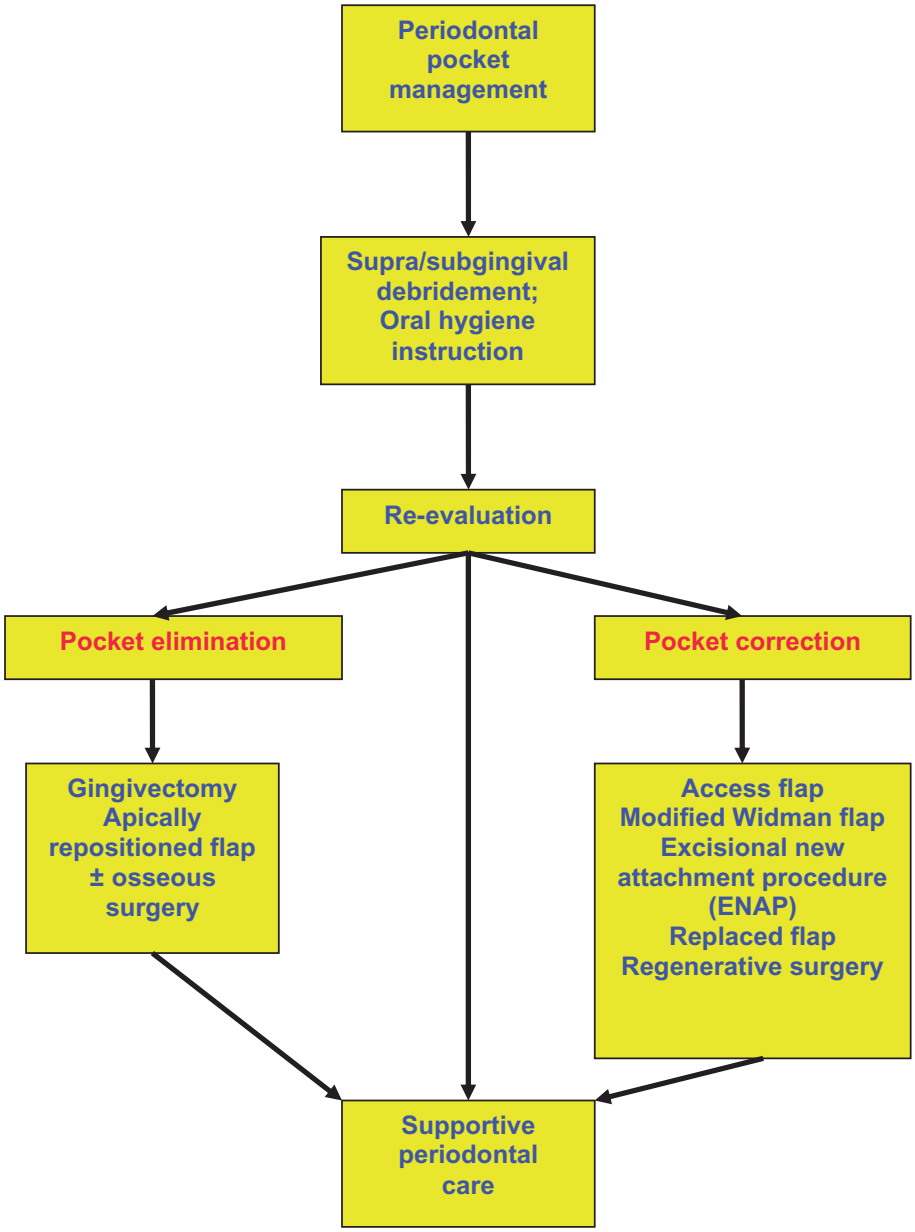

Fig. 37-1 Schematic representation of a typical treatment regimen for periodontitis patient management.

provided supragingival hygiene was meticulous (Nyman *et al*. 1986, 1988; Mombelli *et al*. 1995). From a clinical standpoint, minimizing the total volume of dental calculus present seems to be desirable. However, aggressive tooth substance removal does not seem warranted.

Factors that may influence complete calculus removal include the extent of disease, anatomic factors, the skill of the operator, and the instruments used. Waerhaug (1978) suggested that in more than 90% of cases, deposits of plaque and calculus remained in sites with pocket depths (PD) >5 mm following scaling and root planing. Similar conclusions were reported by Rabbani *et al*. (1981) and Magnusson *et al*. (1984). Brayer *et al*. (1989) investigated inter-operator variability performing non-surgical root debridement, comparing operators of two different levels of experience. It was found that the more experienced clinician achieved a superior level of calculus removal.

Although Caffesse *et al*. (1986) found more residual calculus following non-surgical root debridement compared to root debridement as part of a surgical procedure, 50% or more of surfaces with PD >7 mm showed residual calculus irrespective of methodology. Buchanan and Robertson (1987) found more residual calculus following non-surgical treatment on molar and premolar tooth surfaces than non-molar teeth. They also demonstrated that over 60% of molar sites had residual calculus following closed root debridement. These findings may reflect increased difficulty in achieving successful root debridement in posterior areas in the mouth in addition to the more complicated anatomy of multi-rooted teeth.

Matia *et al*. (1986) noted no difference in the quality of root debridement following evaluation of ultra-

sonic, sonic or hand instrumentation. However none of the sites treated were totally free of calculus.

The agreement between clinicians in the detection of residual subgingival calculus has been found to be low. Furthermore microscopic studies have demonstrated that even if calculus is not detected clinically it may yet be present on a microscopic level. Nonetheless from a practical standpoint if calculus is detected clinically the site is more likely to display ongoing inflammation (Sherman *et al*. 1990).

Methods used for non-surgical root surface debridement

Scaling is a procedure which aims at the removal of plaque and calculus from the tooth surface. Depending on the location of deposits, scaling is performed by supragingival and/or subgingival instrumentation. Root planing denotes a technique of instrumentation by which the "softened cementum" is removed and the root surface is made "hard" and "smooth". However, on the basis of evidence already discussed, excessive tooth substance removal is not warranted and so perhaps the term root debridement is more appropriate. Root debridement may therefore be defined as the removal of plaque and/or calculus from the root surface without the intentional removal of tooth structure.

Non-surgical periodontal treatment may be carried out using a variety of methods including hand instruments, sonic and ultrasonic scalers reciprocating instruments, and ablative laser therapy.

Hand instrumentation

Hand instrumentation allows good tactile sensation while minimizing the risk of contaminated aerosol production. However, it tends to be more time consuming than other methods and, if aggressively performed, hand instrumentation can lead to excessive tooth substance removal. In addition, hand instrumentation is more technique sensitive and requires correct and frequent instrument sharpening.

Access to furcations and the base of deep pockets is limited compared to some machine-driven instruments which have been designed to access narrow apertures and relatively inaccessible areas (Leon *et al*. 1987; Oda & Ishikawa 1989; Dragoo *et al*. 1992; Takacs *et al*. 1993; Yukna *et al*. 1997; Kocher *et al*. 1998, 2001; Beuchat *et al*. 2001). Recently however, modified curettes with extended shanks for deep pockets and mini-bladed curettes for narrow pockets have been developed to improve efficacy of scaling and root planing in difficult areas (Singer *et al*. 1992; Landry *et al*. 1999).

Hand instruments

A hand instrument is composed of three parts: the working part (the blade), the shank, and the handle (Fig. 37-2). The cutting edges of the blade are centered over the long axis of the handle in order to give the instrument proper balance. The blade is often made of carbon steel, stainless steel or tungsten carbide.

Curettes are instruments used for both scaling and root debridement (Fig. 37-3). The working part of the curette is the spoon-shaped blade which has two curved cutting edges. The two edges are united by the rounded toe. The curettes are usually made "double-ended" with mirror-turned blades. The length and angulation of the shank as well as the dimensions of the blade differ between different brands of instruments.

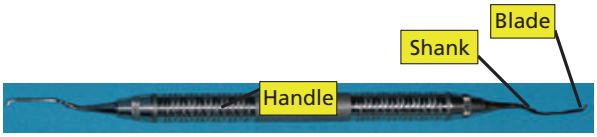

Fig. 37-2 A curette demonstrating the handle, shank, and blade.

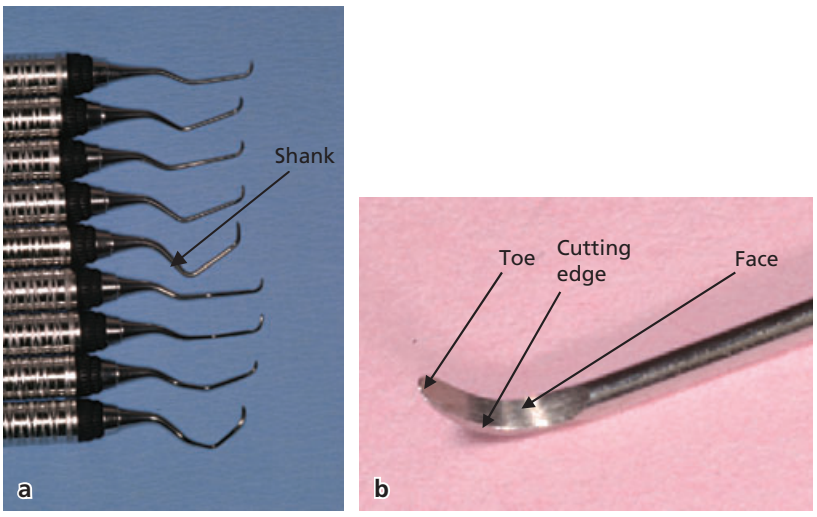

Fig. 37-3 (a) Selections of curettes with varying shank configurations to facilitate debridement of different areas of the dentition. (b) The working end of a curette demonstrating rounded toe, face, and cutting edge.

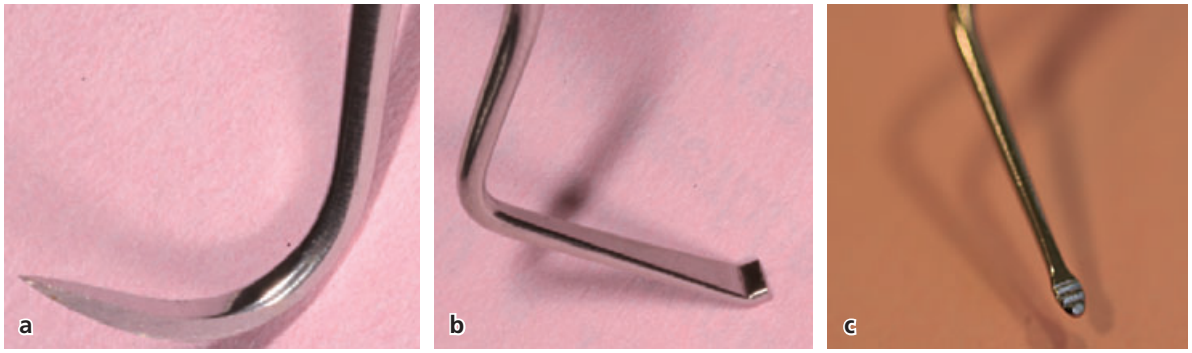

Fig. 37-4 (a) Sickle scaler. (b) Hoe. (c) File.

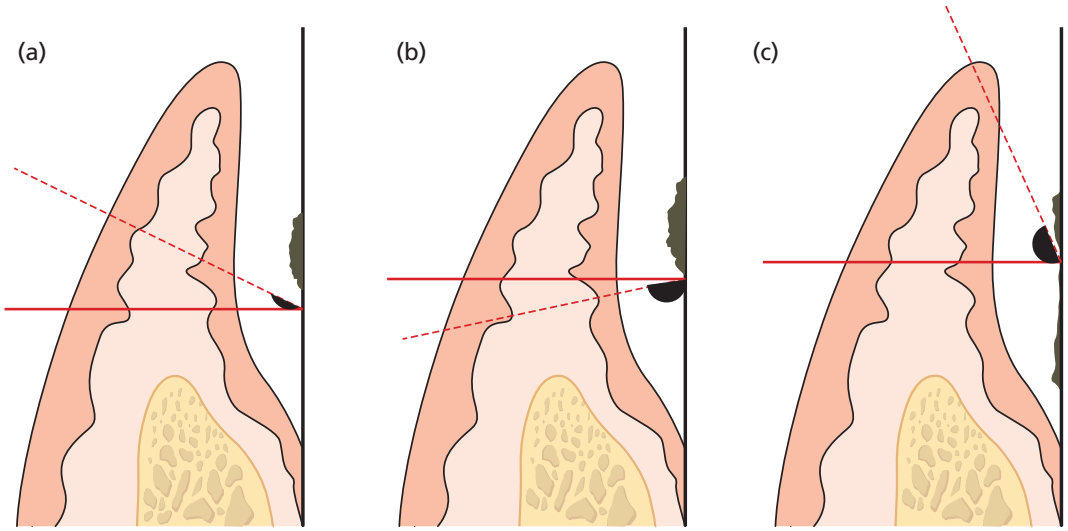

Fig. 37-5 The effect of different angulations of the cutting edge of the curette to the tooth surface. (a) Correct angle of application. (b) Too obtuse angulation resulting in ineffective calculus removal and the possibility of cratering the surface. (c) Too acute angulation resulting in ineffective calculus removal and burnishing of the calculus deposits.

The sickle is manufactured with either a curved or a straight blade which has a triangular cross section and two cutting edges. The "facial" surface between the two cutting edges is flat in the lateral direction but may be curved in the direction of its long axis. The "facial" surface converges with the two lateral surfaces of the blade. Sickles are mainly used for supragingival debridement or scaling in shallow pockets (Fig. 37-4a).

The hoe has only one cutting edge. The blade is turned at a 100° angle to the shank with the cutting edge bevelled at a 45° angle. The blade can be positioned at four different inclinations in relation to the shank: facial, lingual, distal, and mesial. The hoe is mainly used for supragingival scaling (Fig. 37-4b). Periodontal files can be useful for smoothing roots in areas of stubborn deposits (Fig. 37-4c).

Principles of curette use

Perhaps the most widely used instrument type for subgingival debridement is the curette. The angulation of the cutting edge of the curette to the tooth surface influences the efficiency of debridement. The optimal angle between the cutting edge and the tooth is approximately 80° (Fig. 37-5a). Too obtuse an angle, as shown in Fig. 37-5b, will result in cratering and consequent roughening of the root surface. Too acute an angle, as shown in Fig. 37-5c, will result in ineffective removal and burnishing of subgingival calculus deposits.

Subgingival instrumentation should preferably be performed under local anesthesia. The root surface of the diseased site is explored with a probe to identify (1) the probing depth, (2) the anatomy of the root surface (irregularities, root furrows, open furcation, etc.), and (3) the location of the calcified deposits.

The instrument is held in a modified pen grasp and the blade inserted into the periodontal pocket with the face of the blade parallel to and in light contact with the root surface. It is important that all root surface instrumentation is performed with a proper finger rest. This implies that one finger – the third or the fourth – must act as a fulcrum for the movement of the blade of the instrument. A proper finger rest serves to (1) provide a stable fulcrum, (2) permit optimal angulation of the blade, and (3) enable the use of wrist–forearm motion. The finger rest must

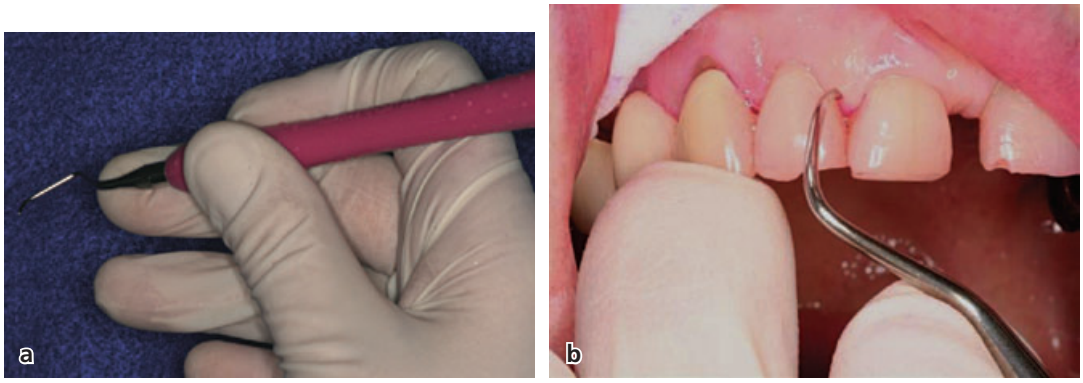

Fig. 37-6 Illustrations of (a) a modified pen grasp and (b) a finger rest in close proximity to the area of instrumentation.

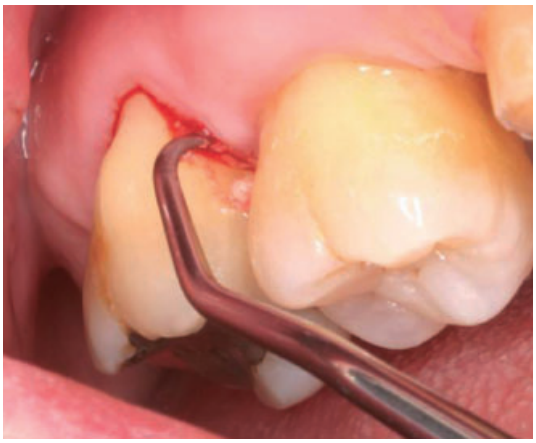

Fig. 37-7 Illustration of the shank of the curette held parallel to the long axis of the tooth during instrumentation of a posterior site.

be secured as close as possible to the site of instrumentation to facilitate controlled use of the instrument (Fig. 37-6).

After the base of the periodontal pocket has been identified with the lower edge of the blade, the instrument is turned into a proper "cutting" position: i.e. the shank is parallel to the long axis of the tooth (Fig. 37-7). The grasp of the instrument is tightened somewhat, the force between the cutting edge and the root surface is increased, and the blade is moved in a coronal direction. Strokes must be made in different directions to cover all aspects of the root surface (crosswise, back and forth) but, as stated above, strokes should always start from an apical position and be guided in a coronal direction. The probe is inserted in the pocket again and the surface of the root assessed anew for the presence of calculus.

Frequent sharpening of the cutting edge of the instrument is necessary to obtain efficient calculus removal (Fig. 37-8a). The angle between the face and the back of curettes must be maintained at approximately 70° during sharpening (Fig. 37-8b). Any greater angle will result in dulling of the cutting edge. A more acute angle results in a fragile and easily worn cutting edge.

Sonic and ultrasonic scalers

A common alternative to hand instrumention for non-surgical periodontal therapy is the use of sonic and ultrasonic scalers. Sonic scalers use air pressure to create mechanical vibration that in turn causes the instrument tip to vibrate; the frequencies of vibration ranging from 2000–6000 Hz (Gankerseer & Walmsley 1987; Shah *et al*. 1994). Ultrasonic scalers convert electrical current to mechanical energy in the form of high-frequency vibrations at the instrument tip; the vibration frequencies ranging from 18 000–45 000 Hz. There are two types of ultrasonic scalers, magnetostrictive and piezoelectric. In piezoelectric scalers the alternating electrical current causes a dimensional change in the hand piece which is transmitted to the working tip as vibrations. The pattern of vibration at the tip is primarily linear. In magnetostrictive scalers the generated electrical current produces a magnetic field in the handpiece that causes the insert to expand and contract along its length and in turn causes the insert to vibrate. The pattern of vibration at the tip is elliptical. Modified sonic and ultrasonic scaler tips, e.g. tiny, thin, periodontal probe type, and diamond coated, have been developed for use in deep pockets (Drisko *et al*. 2000).

Recently, ultrasonic instruments using a working frequency of 25 kHz and a coupling at the head of the handpiece to transfer energy indirectly to the working tip have been developed. These instruments are cooled by a water-based medium containing polishing particles of various sizes dependent on therapeutic indication. The amount of contaminated aerosol is said to be reduced compared to other ultrasonic or sonic scalers. This system has been advocated for the treatment of periodontitis and peri-implantitis, as well as minimal invasive preparation of tooth structures. This development has been shown to be equally effective as conventional methods (Sculean *et al*. 2004).

Reciprocating instruments

Few studies have been carried out to investigate the efficacy of reciprocating instruments. Results demon-

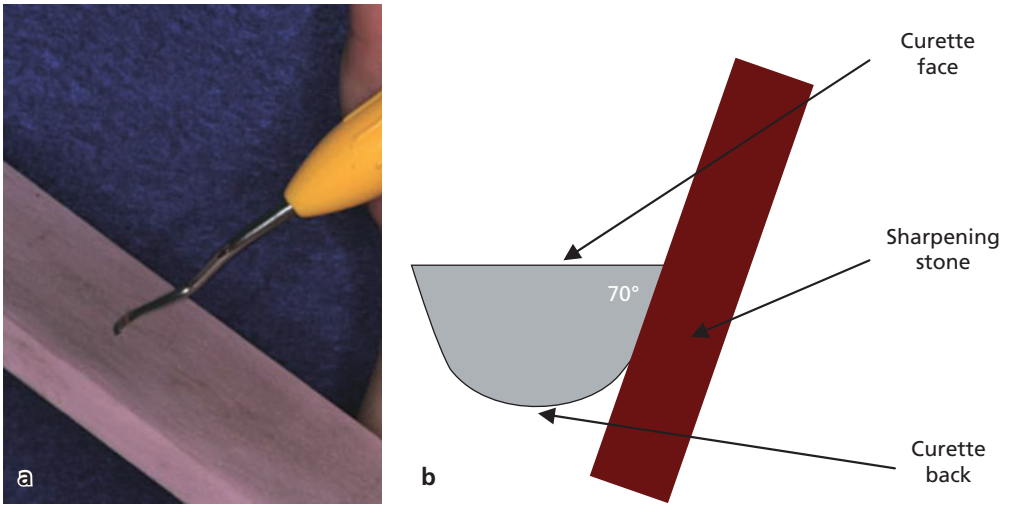

Fig. 37-8 (a) The angulation of the sharpening stone in relation to the curette shank. (b) The angle between the flat surface of the sharpening stone and the cutting edge of the curette.

strated that they produce an equivalent clinical outcome compared to hand, sonic or ultrasonic scalers. The use of reciprocating instruments is less time consuming than hand instrumentation and results in less root surface loss (Obeid *et al*. 2004; Obeid & Bercy 2005). Further evidence is awaited to support their widespread use.

Ablative laser therapy

Ablative laser therapy targets both the soft and hard tissues of the periodontium. It has bacteriocidal and detoxification effects and can remove the epithelium lining and granulation tissue within the periodontal pocket which may potentially improve healing. Considering the possibility of bacterial invasion into the soft tissues of pockets, this effect could be an important factor in the treatment of moderate to deep pockets. However, studies have shown that curettage of granulation tissues had no added benefit over scaling and root planing (Lindhe & Nyman 1985; Ramfjord *et al*. 1987). Laser therapy is capable of removing plaque and calculus with extremely low mechanical stress and no formation of a smear layer on root surfaces. In addition the use of lasers may allow access to sites that conventional mechanical instruments cannot reach.

Various types of lasers such as carbon dioxide lasers, Er:YAG lasers, and Nd:YAG lasers are currently in use. Carbon dioxide lasers, when used with relatively low energy output in a pulsed and/or defocused mode, have root conditioning, detoxification, and bacteriocidal effects on contaminated root surfaces. However, at low energy outputs they are unable to remove calculus. Er:YAG lasers are capable of effectively removing calculus from the root surface. Er:YAG laser irradiation energy is absorbed by water and organic components of the biological tissues which causes their evaporation resulting in heat generation, water vapour production, and thus an increase in internal pressure within the calculus deposits. The resulting expansion within the calculus causes its separation from the root surface.

Choice of debridement method

It has been demonstrated that hand, sonic, and ultrasonic scalers produce similar periodontal healing response with respect to probing pocket depths, bleeding on probing, and clinical attachment level (Badersten *et al*. 1981, 1984; Lindhe & Nyman 1985; Kalkwarf *et al*. 1989; Loos *et al*. 1987; Copulos *et al*. 1993; Yukna *et al*. 1997; Kocher *et al*. 2001; Obeid *et al*. 2004; Wennstrom *et al*. 2005; Christgau *et al*. 2006). With respect to time spent, several studies have shown that debridement time spent per tooth may be reduced when ultrasonic or sonic scalers used compared to hand scalers (Copulos *et al*. 1993; Boretti *et al*. 1995; Tunkel *et al*. 2002; Wennstrom *et al*. 2005; Christgau *et al*. 2006). Regarding root surface loss, sonic and ultrasonic scalers have been shown to produce less tooth surface loss compared to hand scalers (Ritz *et al*. 1991; Schmidlin *et al*. 2001).

In contrast to hand instrumentation, the use of sonic and ultrasonic scalers is less technique sensitive, requires less time to complete, and removes less root surface cementum. It has been shown to provide better access to deep pockets and furcation areas (Kocher *et al*. 1998; Beuchat *et al*. 2001). In addition the flushing action of water used in sonic and ultrasonic scalers removes, to a certain extent, debris and bacteria from the pocket area. However, tactile sensation is reduced, and there is production of contaminated aerosols (Harrel *et al*. 1998; Barnes *et al*. 1998; Rivera-Hidalgo *et al*. 1999; Timmerman *et al*. 2004). Some patients may find the vibration, sound, and water spray uncomfortable.

It has been demonstrated that the use of lasers produces results comparable to scaling and root planing (Schwarz *et al*. 2001). However, no adjunctive

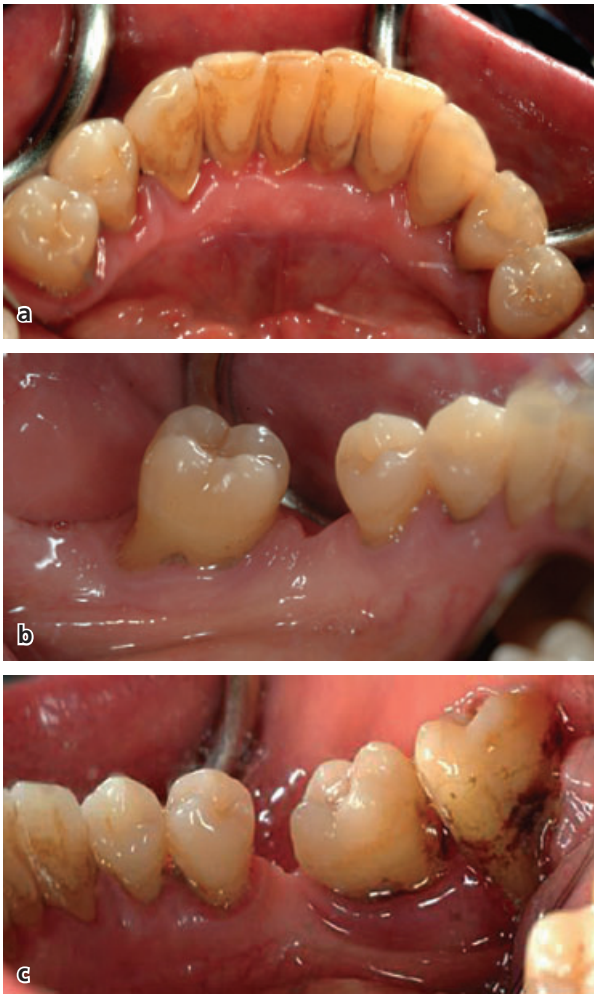

Fig. 37-9 Lingual view of mandibular teeth of patient with untreated periodontitis prior to periodontal therapy.

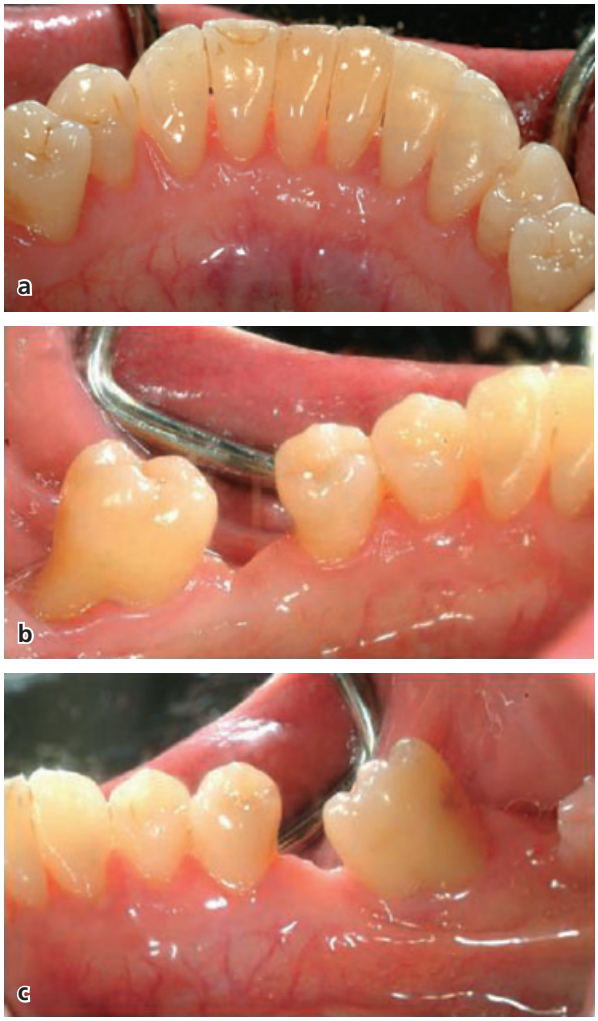

Fig. 37-10 Lingual view of mandibular teeth of patient 3 months following initial non-surgical therapy.

benefit of the use of lasers over scaling and root planing alone has been demonstrated (Schwarz *et al*. 2003; Ambrosini *et al*. 2005). Inadvertent irradiation and reflection from shiny metal surfaces may cause damage to patient's eyes, throat, and oral tissues other than the targeted area. In addition there is also a risk of excessive tissue destruction by direct ablation and thermal side effects. Also the high cost of the laser apparatus is a drawback for many clinicians.

Figures 37-9 and 37-10 demonstrate the effects of non-surgical therapy.

The influence of mechanical debridement on subgingival biofilms

Supra- and subgingival debridement results in the mechanical disruption of the plaque biofilm and remains the "gold standard" modality for periodontal treatment. Removal of subgingival plaque and calculus deposits through subgingival debridement exposes the cementum, root dentine, and pocket epithelium for novel colonization. Species which may have thrived in the subgingival environment of the diseased pocket may find the new habitat less hospitable. A decreased concentration of microbial products and tissue breakdown products, and a decrease in the flow of gingival crevicular fluid, along with a more neutral subgingival biofilm pH may encourage the growth of less pathogenic bacterial species. Also a decrease in pocket depth as a result of a resolution of inflammation, decreased oedema, and a re-adaptation of apical junctional epithelium favors the recolonization of more aerobic species.

Following treatment the subgingival habitat may be repopulated by microorganisms which originate from: residual subgingival plaque deposits (Ramberg *et al*. 1994; Dahan *et al*. 2004); radicular dentinal tubules or cementum (Daly *et al*. 1982; Adriaens *et al*. 1988; Giuliana *et al*. 1997); pocket epithelium and connective tissues (Slots & Rosling 1983); supragingival plaque deposits (Magnusson *et al*. 1984; Ximenez-Fyvie *et al*. 2000); subgingival deposits of adjacent teeth and from other intraoral soft tissue sites (von Troil-Linden *et al*. 1996).

Subgingival debridement has been observed to result in a decrease in the total number of micro-

organisms present in subgingival sites and a shift in the relative proportion of different microbial species within the subgingival plaque biofilm. A decrease in the total bacterial count for sites of 3 mm or greater depth, from $91 \pm 11 \times 10^5$ to $23 \pm 6 \times 10^5$, has been observed immediately following subgingival debridement (Teles *et al*. 2006). Although pre-debridement subgingival microbial counts are restored in 4–7 days post debridement (Sharawy *et al*. 1966), the impact of subgingival debridement on the composition of subgingival plaque biofilms, although often transient, is more long lasting.

Subgingival debridement has been observed to result in a decrease in the mean counts and number of sites colonized by *P. gingivalis*, *A. actinomycetemcomitans*, *Pr. intermedia* (Shiloah & Patters 1994), *T. forsythia*, and *Tr. denticola* (Darby *et al*. 2005) several weeks following subgingival debridement. The persistence of *A. actinomycetemcomitans* and *P. gingivalis* following subgingival debridement is attributed to the ability of these microorganisms to invade the pocket epithelium and connective tissues (Slots & Rosling 1983; Renvert *et al*. 1990; Shiloah & Patters 1994). Haffajee *et al*. (1997) found that the only species to be significantly affected in prevalence and mean counts 3 months following non-surgical periodontal therapy were *B. forsythus*, *P. gingivalis*, and *Tr. denticola*.

An increase in the proportions of Gram-positive aerobic cocci and rods following subgingival debridement is associated with health (Cobb 2002). Haffajee *et al*. (2006) reported an increase in proportion of streptococci (including *S. gordonni*, *S. mitis*, *S. oralis*, and *S. sanguinis*) and *Actinomyces* spp., *E. corrodens*, and *G. morbillarum* post subgingival debridement.

Microorganisms do not exist in isolation in the subgingival environment, but rather as members of communities. Socransky *et al*. (1998) identified groups of organisms which were commonly found together and subdivided microorganisms into complexes accordingly. Members of the red and orange complexes are most commonly identified at sites displaying signs of periodontitis. A re-emergence of species of the red and orange complex 3–12 months post debridement may be associated with ongoing attachment loss at these sites (Haffajee *et al*. 2006).

In the absence of appropriate home care, the re-establishment of the pretreatment microflora as well as the rebound of clinical improvements due to treatment will occur in a matter of weeks (Magnusson *et al*. 1984; Loos *et al*. 1988; Sbordone *et al*. 1990). In the absence of professional maintenance an increase in the prevalence and counts of periodontopathogens is to be expected (Renvert *et al*. 1990; Shiloah & Patters 1994). Following supra- and subgingival debridement and appropriate home care the re-establishment of a pathogenic subgingival microflora and an associated rebound in clinical parameters may occur in localized sites (Beikler *et al*. 2004).

Implication of furcation involvement

Once attachment loss has progressed to the furcation area of multi-rooted teeth, patient-performed home care and professionally performed subgingival debridement become more difficult (Wylam *et al*. 1993). Microbial communities may develop relatively undisturbed in this sheltered anatomic site and increasingly anaerobic and virulent microbes may thrive.

Loos *et al*. (1988) observed that while subgingival debridement resulted in improvements in clinical and microbiologic parameters over a 1-year period post debridement, sites with furcation involvement consistently demonstrated higher microbial counts and greater proportions of suspected periodontopathogens. Generally clinical improvement was found to be less pronounced in furcation sites than in other locations (Loos *et al*. 1989). Nordland *et al*. (1987) and Claffey and Egelberg (1994) observed that the frequency of continued probing attachment loss was considerably greater in furcation-involved sites compared with all other sites. Consequently, teeth with furcation involvement may be viewed with some caution with respect to long-term prognosis.

Pain and discomfort following non-surgical therapy

It has been demonstrated that tissue trauma occurs during non-surgical periodontal therapy (Claffey *et al*. 1988). This trauma can trigger local mechanoreceptors and polymodal nociceptors, the activation of which leads to the release of chemicals, such as prostaglandins, bradykinin, and histamine, and ultimately to the perception of pain in the central nervous system.

Clinical studies referring to pain experience after non-surgical therapy are limited. Quantifying pain is difficult as it cannot be measured directly. Pain perception to a similar stimulus is highly variable from individual to individual. Pain may be measured using visual analogue scales whereby the patient is asked to indicate their level of pain by a mark on a gradated scale from no pain to the most severe pain imaginable.

Pihlstrom *et al*. (1999) reported that patients experienced pain of significant duration and magnitude following scaling and root planning. Pain was reported to peak in intensity between 2 and 8 hours post therapy and on average lasted for 6 hours. Almost 25% of patients self-medicated to relieve pain after treatment.

In addition to pain resulting from soft tissue trauma, patients may also experience root sensitivity following non-surgical therapy. Good oral hygiene measures resulting in low plaque scores prior to commencement of non-surgical periodontal therapy have been shown to decrease root dentin sensitivity.

Despite this, root dentin sensitivity can be a side effect of thorough root planing. Tammaro *et al*. (2000) demonstrated only moderate increases in root dentin sensitivity in most patients with only a small portion of patients experiencing more extreme sensitivity. Patients with sensitive teeth prior to treatment had higher levels of sensitivity following treatment. Although a reduction in the intensity of root dentin sensitivity over 4 weeks was noted, the number of sensitive teeth remained unchanged.

Clinical trials have shown anxiety, depression, and stress to be related to pain perception. Kloostra *et al*. (2006) investigated these factors with regard to non-surgical as well as surgical periodontal therapy and concluded that psychosocial factors may influence pain experience and the need for medication after therapy.

In a further clinical trial concerned with patients' experience of pain during diagnosis and non-surgical treatment of periodontitis it was demonstrated that pain experience during diagnostic instrumentation correlated significantly with pain experience during root instrumentation (van Steenberghe *et al*. 2004). One third of patients took analgesic medication after non-surgical treatment. However approximately half of the total number of patients complained of gingival soreness and pain and two thirds even experienced problems while eating.

Pain during and after periodontal diagnosis and non-surgical therapy seems to be on average mild to moderate and transient in nature. Nevertheless, some patients experience significant pain during treatment. Patients' psychosocial factors such as anxiety may influence the intensity of the pain experienced. Moreover recognition of this anxiety may be the first step in the management of pain in such patients (Chung *et al*. 2003). There is some first evidence that preemptive analgesics (ibruprofen arginine) may have some beneficial effect and help the patient to have a much more positive experience during periodontal treatment (Ettlin *et al*. 2006).

Re-evaluation

Healing following non-surgical therapy is almost complete at 3 months. However a slower ongoing but limited healing can continue for up to 9 or more months following the treatment (Badersten *et al*. 1984). Re-evaluation is a vital stage in a periodontal treatment plan. At re-evaluation the effectiveness of treatment previously carried out is evaluated and the nature of further therapy, if needed, is established.

Measurements are made at baseline and again at 3 months as a method of evaluation of periodontal status and effectiveness of therapy. Measurements include plaque scores, bleeding on probing, suppuration on probing, probing pocket depth, recession, probing attachment level, and assessment of mobility. These are usually recorded at four to six sites around each tooth.

Interpretation of probing measurements at re-evaluation

Probing depth is defined as the distance from the gingival margin to the base of the periodontal pocket measured in millimeters using a periodontal probe. Probing attachment level change is utilized to assess events occurring at the base of the periodontal pocket. Measurements are made at different times from a fixed point, such as from a stent margin or cemento-enamel junction to the base of the pocket. It is generally accepted that any improvement in probing attachment level is not a result of connective tissue reattachment but due to a re-adaptation of the junctional epithelium at the base of the pocket (Fig. 37-11). Probing depth change is a combination of recession and the change in probing attachment level

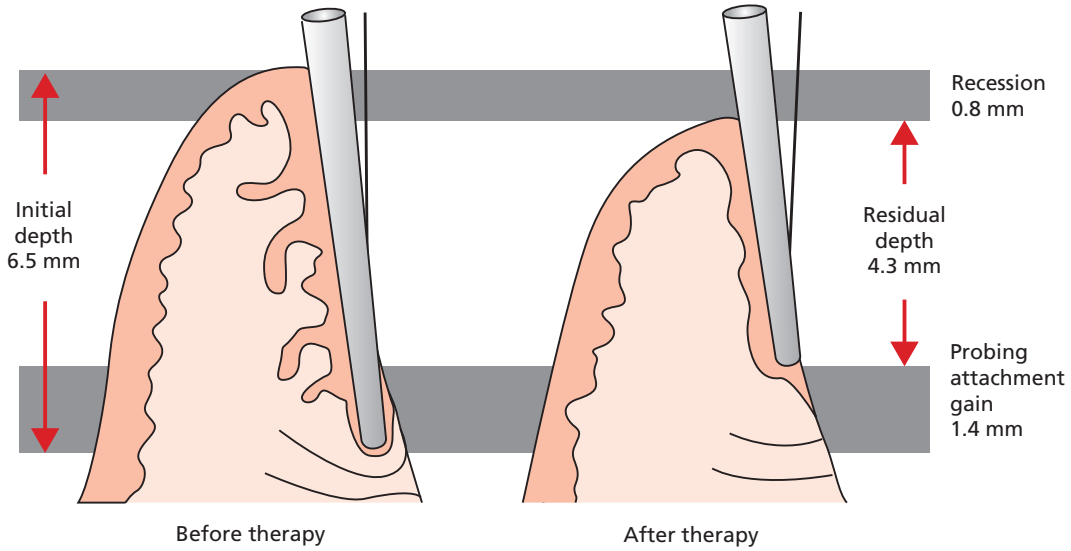

Fig. 37-11 Schematic illustration of the healing occurring in deep pockets following initial therapy (adapted from Fowler *et al*. 1982).

due to events occurring at the base of the periodontal pocket.

On average the change in pocket depth seen following treatment for deeper pockets is a combination of recession at the gingival margin due to resolution of inflammation and a tightening of the junctional epithelium at the base of the pocket. Moreover the reduced bleeding on probing scores found after treatment may reflect the increased resistance to probe penetration into the connective tissue.

Average changes in measurements due to non-surgical therapy

Tables 37-1 and 37-2 present mean changes in plaque scores, bleeding scores, probing depths, and probing attachment levels which were generally observed in studies of mean changes from baseline to re-evaluation. However the use of mean results of pooled sites can mask deterioration or improvement at individual sites.

It is important to appreciate that the extent of the initial probing depth has a marked influence on probing depth changes due to treatment. For example, for shallow pockets, non-surgical treatment results in loss of probing attachment, whereas in deep pockets there is a marked gain of probing attachment. It has been shown that there is an initial loss of probing attachment due to instrumentation trauma for pockets of all initial probing depths. However in the deeper sites this loss is reversed upon resolution of inflammation (Claffey *et al*. 1988).

Interpretation of longitudinal changes at individual sites

Difficulties arise in detecting individual sites with ongoing destruction due to the following reasons:

Table 37-1 Estimations generally observed in studies, of improvements in plaque and bleeding scores for sites of different initial probing depths after a single episode of supra- and subgingival instrumentation

Initial probing depth (mm)	Plaque	Bleeding
≤3.5	≈ 50% → 10%	≈ 55% → 15%
4–6.5	≈ 80% → 15%	≈ 80% → 25%
≥7	≈ 90% → 25%	≈ 90% → 30%

Table 37-2 Mean changes (mm) generally observed in studies in probing depth, probing attachment levels, and gingival recession after a single episode of supra- and subgingival instrumentation

Initial probing depth (mm)	Probing depth	Probing attachment level	Recession
≤3.5	0	–0.5	0.5
4–6.5	1–2	0–1	0–1
≥7	2–3	1–2	1–2

- Lack of reproducibility of probing measurements. Factors influencing the reproducibility of probing measurements include: probing force, probe tip diameter, angulation of probe, position in the mouth, probing depth itself and the inflammatory status of the tissues. A similar lack of reproducibility has been reported following recordings made by the same examiner at different time points (intra-examiner) and recordings taken by different examiners at the same time points (inter-examiner). Badersten *et al*. (1984) demonstrated that duplicate probing measurements were exactly the same in only 30–40% of cases when looking at both inter-examiner and intra-examiner reproducibility. Differences of 2 mm or more were noted in 5–7% of recordings. Therefore, such probing attachment level changes at individual sites cannot be relied upon to indicate true disease progression.
- As discussed above variations in probing attachment levels may simply reflect changes in the inflammatory status at the base of the pocket rather than true connective tissue loss or gain.

With these points in mind, in order to identify sites with ongoing connective tissue loss, probing measurements should be interpreted with caution. Various methods have been reported in the literature to address this problem. One method is to demand a high threshold of change before indicating a site as deteriorating. Others include the application of statistical methods, such as regression analysis, to a series of longitudinal measurements.

Prediction of outcome and evaluation of treatment

It would be of great benefit to the clinician to be able to predict the outcome of treatment prior to therapy and also to identify at re-evaluation the sites likely to continue to deteriorate. Prediction and evaluation must be considered both at a patient level and a site level. On a patient level, the extent of baseline bleeding scores, probing attachment loss, and probing depths have been found to relate to future probing attachment loss in untreated patients (Halazonetis *et al*. 1989; Lindhe *et al*. 1989; Haffajee *et al*. 1991). In patients treated with non-surgical therapy without the use of local anesthetic, baseline scores of attachment loss were also seen to relate to the risk of further loss of attachment (Grbic *et al*. 1991; Grbic & Lamster 1992). On a patient level, the number of sites greater then 6 mm at re-evaluation bears a direct relationship to future periodontal breakdown (Claffey & Egelberg 1995).

On a site level, bleeding on probing is, at best, a moderate predictor of future attachment loss (Badersten *et al*. 1990; Claffey *et al*. 1990). On the other hand, absence of bleeding on probing has been demonstrated as a useful indicator of health (Lang *et al*. 1990). Claffey *et al*. (1990) found that deep residual

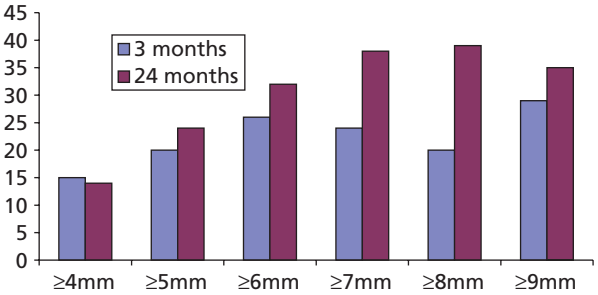

Fig. 37-12 Diagnostic predictability of residual probing depths at 3 months and 12 months following non-surgical treatment of advanced periodontitis. Diagnostic predictability is the percentage of sites with a certain feature, for instance with a deep probing depth at 3 or 6 months, which show attachment loss at a later time point.

probing depth was of limited predictive value when observed over short periods (Fig. 37-12). However, over the longer term, deep residual sites appeared to be more indicative of further attachment loss, particularly if combined with bleeding on probing. This emphasizes the need for ongoing monitoring to identify such sites and instigate appropriate intervention.

Full-mouth disinfection

Traditionally non-surgical treatment of periodontitis involves a series of appointments separated by perhaps a week or more. Each appointment typically involves root debridement of a quadrant depending on disease severity. In 1995 Quirynen *et al*. introduced the concept of total mouth disinfection as a new treatment strategy. It involved full-mouth scaling and root debridement within a 24-hour treatment period, subgingival irrigation (repeated three times within 10 minutes) with 1% chlorhexidine gel, tongue brushing with 1% chlorhexidine gel, and mouth rinsing with 0.2% chlorhexidine. This full-mouth disinfection protocol aimed to reduce the bacterial load in pockets and intraoral niches to minimize the risk of reinfection of the treated pockets from areas harboring pathogenic bacteria. Quirynen *et al*. (1995) showed that full-mouth disinfection yielded better periodontal treatment results on a short-term basis compared to conventional treatment.

Subsequent studies (Bollen *et al*. 1996, 1998; Vandekerckhove *et al*. 1996; Mongardini *et al*. 1999; Quirynen *et al*. 1999, 2000; De Soete *et al*. 2001) concluded that the full-mouth disinfection protocol resulted in clinical and microbiologic improvements comparable to the traditional technique of treatment in patients with advanced chronic periodontitis.

Many recent studies report varying degrees of efficacy of full-mouth disinfection protocol (Apatzidou & Kinane 2004). However, the full-mouth disinfection treatment approach has been promoted as a more efficient way of treating chronic periodontitis patients (Koshy *et al*. 2004; Wennstrom *et al*. 2005).

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Part 12: Additional Therapy

Chapter 38

Periodontal Surgery: Access Therapy

Jan L. Wennström, Lars Heijl, and Jan Lindhe

Introduction

Since most forms of periodontal disease are plaque-associated disorders, it is obvious that surgical access therapy can only be considered as adjunctive to cause-related therapy (see Chapters 34 to 37). Therefore, the various surgical methods described below should be evaluated on the basis of their potential to facilitate removal of subgingival deposits and self-performed plaque control and thereby enhance the long-term preservation of the periodontium.

The decision concerning what type of periodontal surgery should be performed and how many sites should be included is usually made after the effect of initial cause-related measures has been evaluated. The time lapse between termination of the initial cause-related phase of therapy and this evaluation may vary from 1 to 6 months. This routine has the following advantages:

- Removal of calculus and bacterial plaque will eliminate or markedly reduce the inflammatory cell infiltrate in the gingiva (edema, hyperemia, flabby tissue consistency), thereby making assessment of the "true" gingival contours and pocket depths possible.
- Reduction of gingival inflammation makes the soft tissues more fibrous and thus firmer, which facilitates surgical handling of the soft tissues. The propensity for bleeding is reduced, making inspection of the surgical field easier.
- A better basis for a proper assessment of the prognosis has been established. The effectiveness of the patient's home care, which is of decisive importance for the long-term prognosis, can be properly evaluated. Lack of effective self-performed infection control will often mean that the patient should be excluded from surgical treatment.

Techniques in periodontal pocket surgery

Over the years, several different surgical techniques have been described and used in periodontal therapy. A superficial review of the literature in this area may give the reader a somewhat confusing picture of the specific objectives and indications relevant for various surgical techniques. It is a matter of historic interest that the first surgical techniques used in periodontal therapy were described as means of gaining access to diseased root surfaces. Such access could be accomplished without excision of the soft tissue pocket ("open-view operations"). Later, procedures were described by which the "diseased gingiva" was excised (gingivectomy procedures).

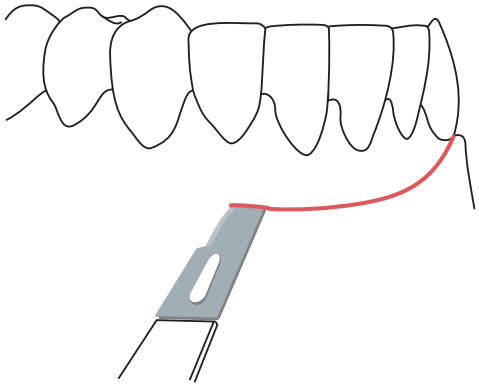

Fig. 38-1 Gingivectomy. The straight incision technique (Robicsek 1884).

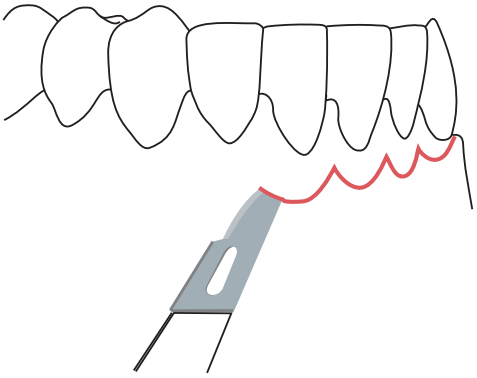

Fig. 38-2 Gingivectomy. The scalloped incision technique (Zentler 1918).

The concept that not only inflamed soft tissue but also "infected and necrotic bone" had to be eliminated called for the development of surgical techniques by which the alveolar bone could be exposed and resected (flap procedures). Other concepts such as (1) the importance of maintaining the mucogingival complex (i.e. a wide zone of gingiva) and (2) the possibility for regeneration of periodontal tissues have also prompted the introduction of "tailor-made" surgical techniques.

In the following, surgical procedures will be described which represent important steps in the development of the surgical component of periodontal therapy.

Gingivectomy procedures

The surgical approach as an alternative to subgingival scaling for pocket therapy was already recognized in the latter part of the nineteenth century, when Robicsek (1884) pioneered the so-called *gingivectomy* procedure. Gingivectomy was later defined by Grant *et al*. (1979) as being "the excision of the soft tissue wall of a pathologic periodontal pocket". The surgical procedure, which aimed at "pocket elimination", was usually combined with recontouring of the diseased gingiva to restore physiologic form.

Robicsek (1884) and, later, Zentler (1918) described the gingivectomy procedure in the following way. The line to which the gum is to be resected is determined first. Following a straight (Robicsek) (Fig. 38-1) or scalloped (Zentler) (Fig. 38-2) incision, first on the labial and then on the lingual surface of each tooth, the diseased tissue should be loosened and lifted out by means of a hook-shaped instrument. After elimination of the soft tissue, the exposed alveolar bone should be scraped. The area should then be covered with some kind of antibacterial gauze or be painted with disinfecting solutions. The result obtained should include eradication of the deepened periodontal pocket and formation of an area which can be kept clean more easily.

Technique

The gingivectomy procedure as it is employed today was described in 1951 by Goldman.

- When the dentition in the area scheduled for surgery has been properly anesthetized, the depths of the pathological pockets are identified with a conventional periodontal probe (Fig. 38-3a). At the level of the bottom of the pocket, the gingiva is pierced with the probe and a bleeding point is produced on the outer surface of the soft tissue (Fig. 38-3b). The pockets are probed and bleeding points produced at several location points around each tooth in the area. The series of bleeding points produced describes the depth of the pockets in the area scheduled for treatment and is used as a guideline for the incision.
- The primary incision (Fig. 38-4), which may be made by a scalpel (blade No. 12B or 15; Bard-Parker®) in either a Bard-Parker handle or an angulated handle (e.g. a Blake's handle), or a Kirkland knife No. 15/16, should be planned to give a thin and properly festooned margin of the remaining gingiva. Thus, in areas where the gingiva is bulky, the incision must be placed at a level more apical to the level of the bleeding points than in areas with a thin gingiva, where a less accentuated bevel is needed. The beveled incision is directed towards the base of the pocket or to a level slightly apical to the apical extension of the junctional epithelium. In areas where the interdental pockets are deeper than the buccal or lingual pockets, additional amounts of buccal and/or lingual (palatal) gingiva must be removed in order to establish a "physiologic" contour of the gingival margin. This is often accomplished by initiating the incision at a more apical level.
- Once the primary incision is completed on the buccal and lingual aspects of the teeth, the interproximal soft tissue is separated from the interdental periodontium by a secondary incision using an Orban knife (No. 1 or 2) or a Waerhaug knife (No. 1 or 2; a saw-toothed modification of the Orban knife) (Fig. 38-5).

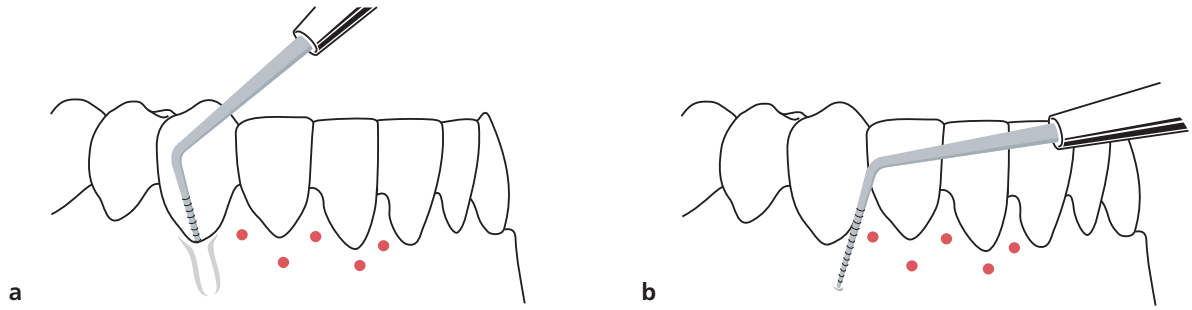

Fig. 38-3 Gingivectomy. Pocket marking. (a) An ordinary periodontal probe is used to identify the bottom of the deepened pocket. (b) When the depth of the pocket has been assessed an equivalent distance is delineated on the outer aspect of the gingiva. The tip of the probe is then turned horizontally and used to produce a bleeding point at the level of the bottom of the probeable pocket.

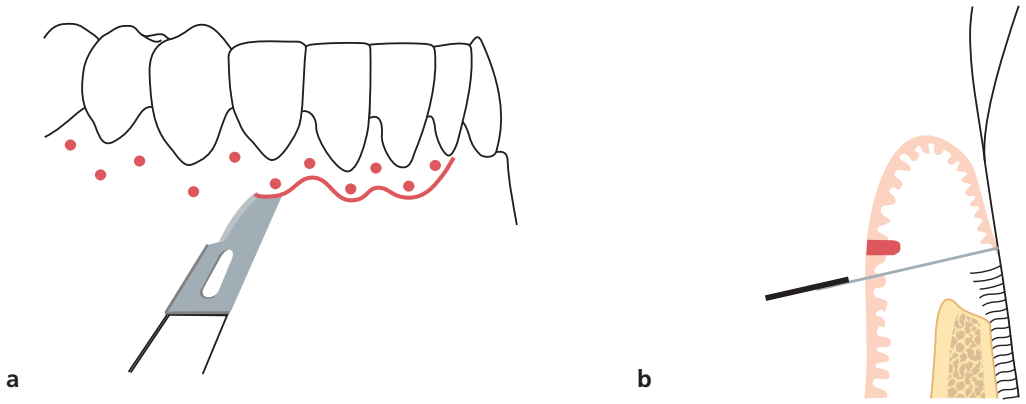

Fig. 38-4 Gingivectomy. (a) The primary incision. (b) The incision is terminated at a level apical to the "bottom" of the pocket and is angulated to give the cut surface a distinct bevel.

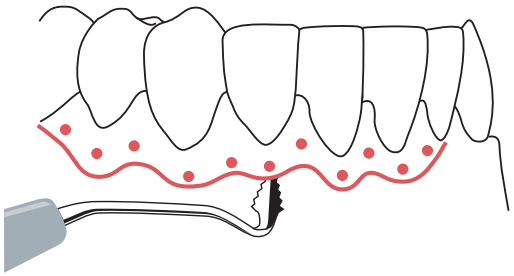

Fig. 38-5 Gingivectomy. The secondary incision through the interdental area is performed with the use of a Waerhaug knife.

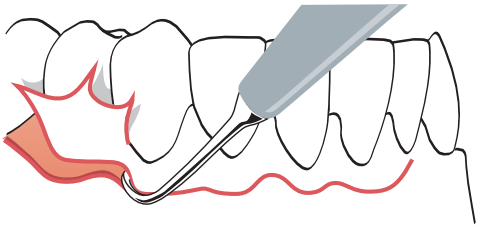

Fig. 38-6 Gingivectomy. The detached gingiva is removed with a scaler.

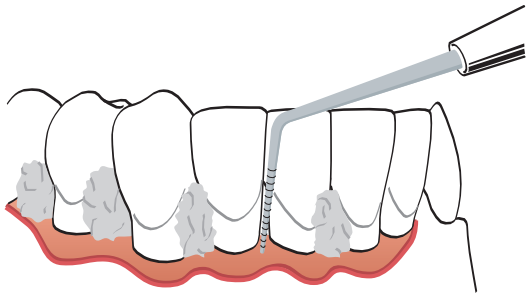

Fig. 38-7 Gingivectomy. Probing for residual pockets. Gauze packs have been placed in the interdental spaces to control bleeding.

- The incised tissues are carefully removed by means of a curette or a scaler (Fig. 38-6). Remaining tissue tabs are removed with a curette or a pair of scissors. Pieces of gauze packs often have to be placed in the interdental areas to control bleeding. When the field of operation is properly prepared, the exposed root surfaces are carefully scaled and planed.
- Following meticulous debridement, the dentogingival regions are probed again to detect any remaining pockets (Fig. 38-7). The gingival contour is checked and, if necessary, corrected by means of knives or rotating diamond burs.
- To protect the incised area during the period of healing, the wound surface must be covered by a periodontal dressing (Fig. 38-8). The dressing should be closely adapted to the buccal and lingual wound surfaces as well as to the interproximal spaces. Care should be taken not to allow the

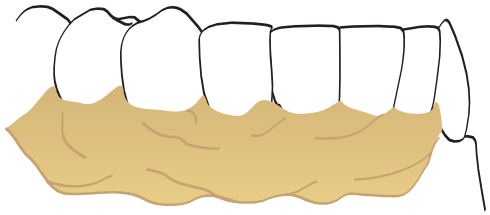

Fig. 38-8 Gingivectomy. The periodontal dressing has been applied and properly secured.

dressing to become too bulky, since this is not only uncomfortable for the patient, but also facilitates dislodgement of the dressing.

- The dressing should remain in position for 10–14 days. After removal of the dressing, the teeth must be cleaned and polished. The root surfaces are carefully checked and remaining calculus removed with a curette. Excessive granulation tissue is eliminated with a curette. The patient is instructed to clean properly the operated segments of the dentition, which now have a different morphology compared to the pre-operative situation.

Flap procedures

The original Widman flap

In 1918 Leonard Widman published one of the first detailed descriptions of the use of a flap procedure for pocket elimination. In his article "The operative treatment of pyorrhea alveolaris" Widman described a mucoperiosteal flap design aimed at removing the pocket epithelium and the inflamed connective tissue, thereby facilitating optimal cleaning of the root surfaces.

Technique

- Sectional releasing incisions were first made to demarcate the area scheduled for surgery (Fig. 38-9). These incisions were made from the mid-buccal gingival margins of the two peripheral teeth of the treatment area and were continued several millimeters out into the alveolar mucosa. The two releasing incisions were connected by a gingival incision, which followed the outline of the gingival margin and *separated the pocket epithelium and the inflamed connective tissue from the non-inflamed gingiva*. Similar releasing and gingival incisions, if needed, were made on the lingual aspect of the teeth.
- A mucoperiosteal flap was elevated to expose at least 2–3 mm of the marginal alveolar bone. The collar of inflamed tissue around the neck of the teeth was removed with curettes (Fig. 38-10) and the exposed root surfaces were carefully scaled. Bone recontouring was recommended in order to achieve an ideal anatomic form of the underlying alveolar bone (Fig. 38-11).

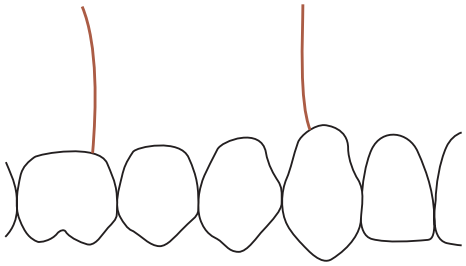

Fig. 38-9 Original Widman flap. Two releasing incisions demarcate the area scheduled for surgical therapy. A scalloped reverse bevel incision is made in the gingival margin to connect the two releasing incisions.

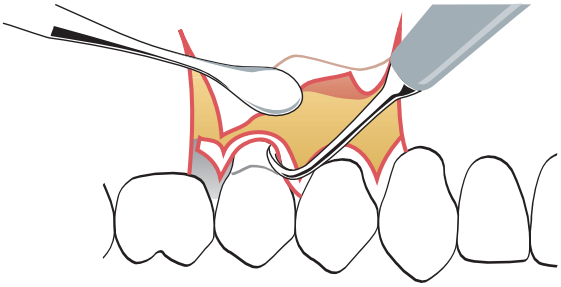

Fig. 38-10 Original Widman flap. The collar of inflamed gingival tissue is removed following the elevation of a mucoperiosteal flap.

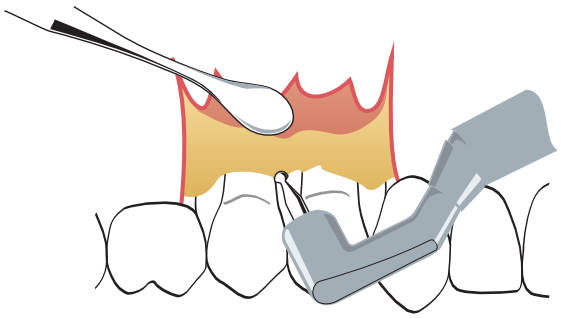

Fig. 38-11 Original Widman flap. By bone recontouring, a "physiologic" contour of the alveolar bone may be re-established.

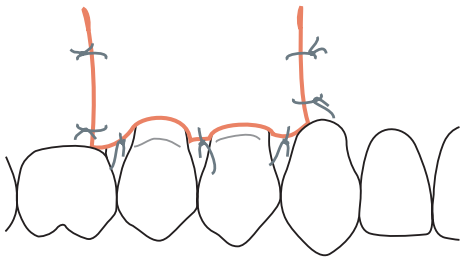

Fig. 38-12 Original Widman flap. The coronal ends of the buccal and lingual flaps are placed at the alveolar bone crest and secured in this position by interdentally placed sutures.

- Following careful debridement of the teeth in the surgical area, the buccal and lingual flaps were laid back over the alveolar bone and secured in this position with interproximal sutures (Fig. 38-12). Widman pointed out the importance of placing

the soft tissue margin at the level of the alveolar bone crest, so that no pockets would remain. The surgical procedure resulted in the exposure of root surfaces. Often the interproximal areas were left without soft tissue coverage of the alveolar bone.

The main advantages of the "*original Widman flap*" procedure in comparison to the gingivectomy procedure included, according to Widman (1918):

- Less discomfort for the patient, since healing occurred by primary intention
- It was possible to re-establish a proper contour of the alveolar bone in sites with angular bony defects.

The Neumann flap

Only a few years later, Neumann (1920) suggested the use of a flap procedure, which in some respects was different from that originally described by Widman.

Technique

- According to the technique suggested by Neumann, an intracrevicular incision was made through the base of the gingival pockets and the entire gingiva (and part of the alveolar mucosa) was elevated in a mucoperiosteal flap. Sectional releasing incisions were made to demarcate the area of surgery.
- Following flap elevation, the inside of the flap was curetted to remove the pocket epithelium and the granulation tissue. The root surfaces were subsequently carefully "cleaned". Any irregularities of the alveolar bone were corrected to give the bone crest a horizontal outline.
- The flaps were then trimmed to allow both an optimal adaptation to the teeth and a proper coverage of the alveolar bone on both the buccal/lingual (palatal) and the interproximal sites. With regard to pocket elimination, Neumann (1920) pointed out the importance of removing the soft tissue pockets, i.e. replacing the flap at the crest of the alveolar bone.

The modified flap operation

In a publication from 1931 Kirkland described a surgical procedure to be used in the treatment of "periodontal pus pockets". The procedure was called the *modified flap operation*, and is basically an access flap for proper root debridement.

Technique

- In this procedure incisions were made intracrevicularly through the bottom of the pocket (Fig. 38-13) on both the labial and the lingual aspects of the interdental area. The incisions were extended in a mesial and distal direction.

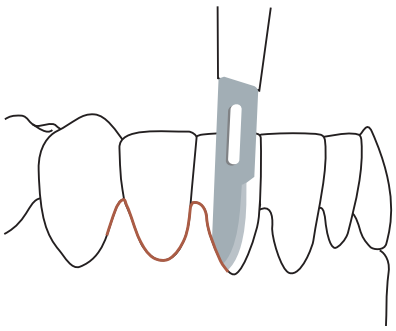

Fig. 38-13 Modified flap operation (the Kirkland flap). Intracrevicular incision.

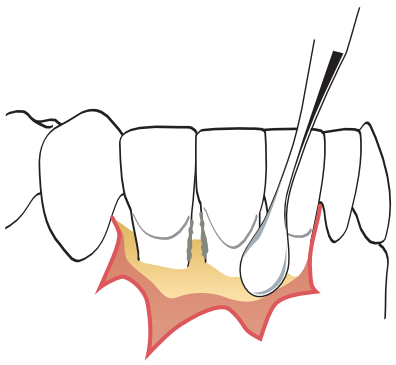

Fig. 38-14 Modified flap operation (the Kirkland flap). The gingiva is retracted to expose the "diseased" root surface.

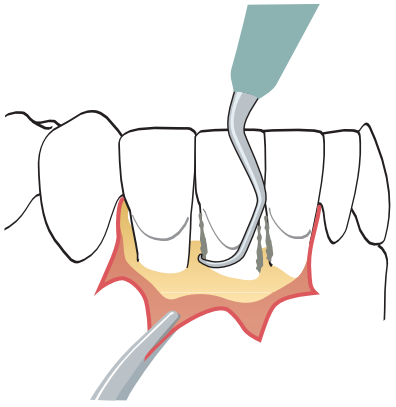

Fig. 38-15 Modified flap operation (the Kirkland flap). The exposed root surfaces are subjected to mechanical debridement.

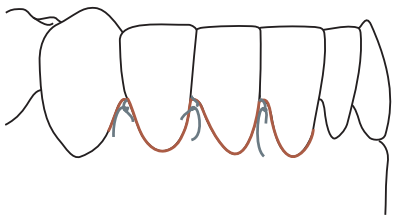

Fig. 38-16 Modified flap operation (the Kirkland flap). The flaps are replaced to their original position and sutured.

- The gingiva was retracted labially and lingually to expose the diseased root surfaces (Fig. 38-14) which were carefully debrided (Fig. 38-15). Angular bony defects were curetted.
- Following the elimination of the pocket epithelium and granulation tissue from the inner surface of the flaps, these were *replaced* to their original position and secured with interproximal sutures (Fig. 38-16). Thus, no attempt was made to reduce the pre-operative depth of the pockets.

In contrast to the *original Widman flap* as well as the *Neumann flap*, the *modified flap operation* did not include (1) extensive sacrifice of non-inflamed tissues and (2) apical displacement of the gingival margin. The method could be useful in the anterior regions of the dentition for esthetic reasons, since the root surfaces were not markedly exposed. Another advantage of the *modified flap operation* was the potential for bone regeneration in intrabony defects which frequently occurred according to Kirkland (1931).

The main objectives of the flap procedures so far described were to:

- Facilitate the debridement of the root surfaces as well as the removal of the pocket epithelium and the inflamed connective tissue
- Eliminate the deepened pockets (the *original Widman flap* and the *Neumann flap*)
- Cause a minimal amount of trauma to the periodontal tissues and discomfort to the patient.

The apically repositioned flap

In the 1950s and 1960s new surgical techniques for the removal of soft and, when indicated, hard tissue periodontal pockets were described in the literature. The importance of maintaining *an adequate zone of attached gingiva* after surgery was now emphasized. One of the first authors to describe a technique for the preservation of the gingiva following surgery was Nabers (1954). The surgical technique developed by Nabers was originally denoted "repositioning of attached gingiva" and was later modified by Ariaudo and Tyrrell (1957). In 1962 Friedman proposed the term *apically repositioned flap* to describe more appropriately the surgical technique introduced by Nabers. Friedman emphasized the fact that, at the end of the surgical procedure, the entire complex of the soft tissues (gingiva and alveolar mucosa) rather than the gingiva alone was displaced in an apical direction. Thus, rather than excising the amount of gingiva which would be in excess after osseous surgery (if performed), the whole muco-gingival complex was maintained and repositioned apically. This surgical technique was used on buccal surfaces in both upper and lower jaws and on lingual surfaces in the lower jaw, while an excisional technique had to be used on the palatal aspect of maxillary teeth where the lack of alveolar mucosa made it impossible to reposition the flap in an apical direction.

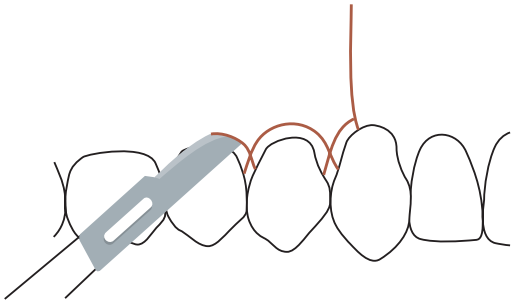

Fig. 38-17 Apically repositioned flap. Following a vertical releasing incision, the reverse bevel incision is made through the gingiva and the periosteum to separate the inflamed tissue adjacent to the tooth from the flap.

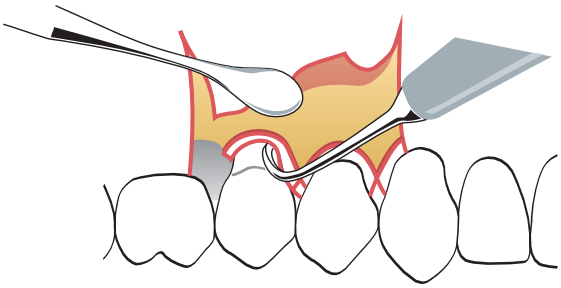

Fig. 38-18 Apically repositioned flap. A mucoperiosteal flap is raised and the tissue collar remaining around the teeth, including the pocket epithelium and the inflamed connective tissue, is removed with a currette.

Technique

According to Friedman (1962) the technique should be performed in the following way:

- A reverse bevel incision is made using a scalpel with a Bard-Parker blade (No. 12B or No. 15). How far from the buccal/lingual gingival margin the incision should be made is dependent on the pocket depth as well as the thickness and the width of the gingiva (Fig. 38-17). If pre-operatively the gingiva is thin and only a narrow zone of keratinized tissue is present, the incision should be made close to the tooth. The beveling incision should be given a scalloped outline, to ensure maximal interproximal coverage of the alveolar bone when the flap subsequently is repositioned. Vertical releasing incisions extending out into the alveolar mucosa (i.e. past the muco-gingival junction) are made at each of the end points of the reverse incision, thereby making apical repositioning of the flap possible.
- A full-thickness mucoperiosteal flap including buccal/lingual gingiva and alveolar mucosa is raised by means of a mucoperiosteal elevator. The flap has to be elevated beyond the muco-gingival line in order to be able later to reposition the soft tissue apically. The marginal collar of tissue, including pocket epithelium and granulation tissue, is removed with curettes (Fig. 38-18), and

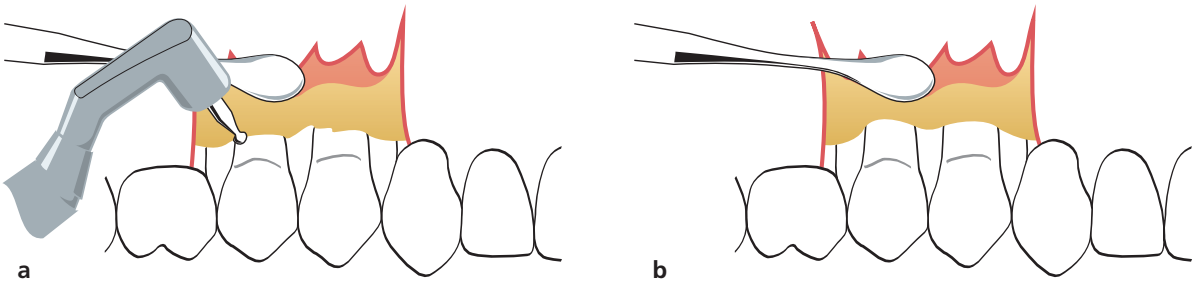

Fig. 38-19 Apically repositioned flap. Osseous surgery is performed with the use of a rotating bur (a) to recapture the physiologic contour of the alveolar bone (b).

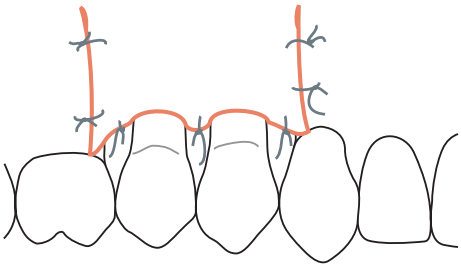

Fig. 38-20 Apically repositioned flap. The flaps are repositioned in an apical direction to the level of the recontoured alveolar bone crest and retained in this position by sutures.

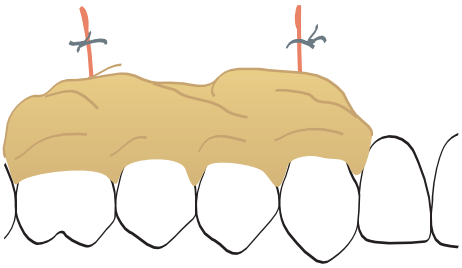

Fig. 38-21 Apically repositioned flap. A periodontal dressing is placed over the surgical area to ensure that the flaps remain in the correct position during healing.

the exposed root surfaces are carefully scaled and planed.

- The alveolar bone crest is recontoured with the objective of recapturing the normal form of the alveolar process but at a more apical level (Fig. 38-19). The osseous surgery is performed using burs and/or bone chisels.
- Following careful adjustment, the buccal/lingual flap is repositioned to the level of the newly recontoured alveolar bone crest and secured in this position (Fig. 38-20). The incisional and excisional technique used means that it is not always possible to obtain proper soft tissue coverage of the denuded interproximal alveolar bone. A periodontal dressing should therefore be applied to protect the exposed bone and to retain the soft tissue at the level of the bone crest (Fig. 38-21). After healing, an "adequate" zone of gingiva is preserved and no residual pockets should remain.

To handle periodontal pockets on the palatal aspect of the maxillary teeth, Friedman described a modification of the "apically repositioned flap", which he termed the *beveled flap*:

- In order to prepare the tissue at the gingival margin to follow the outline of the alveolar bone crest properly, a conventional mucoperiosteal flap is first resected (Fig. 38-22).
- The tooth surfaces are debrided and osseous recontouring is performed (Fig. 38-23).
- The palatal flap is subsequently replaced and the gingival margin is prepared and adjusted to the alveolar bone crest by a secondary scalloped and beveled incision (Fig. 38-24). The flap is secured in this position with interproximal sutures (Fig. 38-25).

Among a number of suggested advantages of the *apically repositioned flap* procedure, the following have been emphasized:

- Minimum pocket depth post-operatively
- If optimal soft tissue coverage of the alveolar bone is obtained, the post-surgical bone loss is minimal
- The post-operative position of the gingival margin may be controlled and the entire muco-gingival complex may be maintained.

The sacrifice of periodontal tissues by bone resection and the subsequent exposure of root surfaces (which may cause esthetic and root sensitivity problems) were regarded as the main disadvantages of this technique.

The modified Widman flap

Ramfjord and Nissle (1974) described the *modified Widman flap* technique that is also recognized as the *open flap curettage* technique. It should be noted that, while the *original Widman flap* technique included both apical displacement of the flaps and osseous recontouring (elimination of bony defects) to obtain proper pocket elimination, the *modified Widman flap* technique is not intended to meet these objectives.

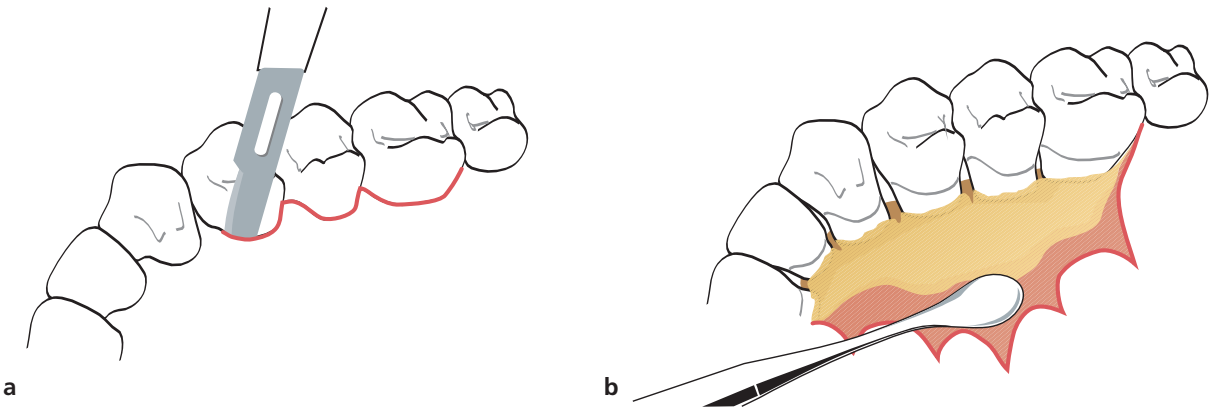

Fig. 38-22 Bevelled flap. A primary incision is made intracrevicularly through the bottom of the periodontal pocket (a) and a conventional mucoperiosteal flap is elevated (b).

Fig. 38-23 Bevelled flap. Scaling, root planing, and osseous recontouring are performed in the surgical area.

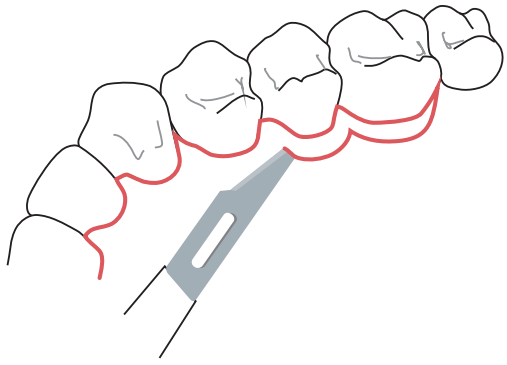

Fig. 38-24 Bevelled flap. The palatal flap is replaced and a secondary, scalloped, reverse bevel incision is made to adjust the length of the flap to the height of the remaining alveolar bone.

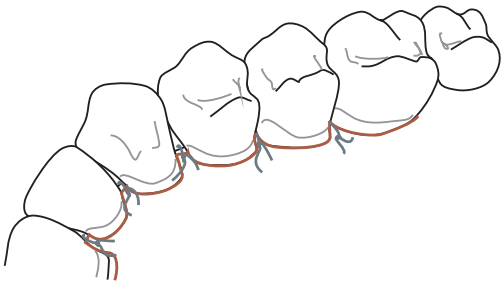

Fig. 38-25 Bevelled flap. The shortened and thinned flap is replaced over the alveolar bone and in close contact with the root surfaces.

Technique

- According to the description by Ramfjord and Nissle (1974) the *initial incision* (Fig. 38-26), which may be performed with a Bard-Parker knife (No. 11), should be parallel to the long axis of the tooth and placed approximately 1 mm from the buccal gingival margin in order to properly separate the pocket epithelium from the flap. If the pockets on the buccal aspects of the teeth are less than 2 mm deep or if esthetic considerations are important, an intracrevicular incision may be made. Furthermore, the scalloped incision should be extended as far as possible in between the teeth, to allow maximum amounts of the interdental gingiva to be included in the flap. A similar incision technique is used on the palatal aspect. Often, however, the scalloped outline of the initial incision may be accentuated by placing the knife at a distance of 1–2 mm from the mid-palatal surface of the teeth. By extending the incision as far as possible in between the teeth, sufficient amounts of tissue can be included in the palatal flap to allow for proper coverage of the interproximal bone when the flap is sutured. Vertical releasing incisions are not usually required.
- Buccal and palatal full-thickness flaps are carefully elevated with a mucoperiosteal elevator. The flap elevation should be limited and allow only a few millimeters of the alveolar bone crest to become exposed. To facilitate the gentle separation of the collar of pocket epithelium and granulation tissue from the root surfaces, an intracrevicular incision is made around the teeth (*second incision*) to the alveolar crest (Fig. 38-27).
- A *third incision* (Fig. 38-28) made in a horizontal direction and in a position close to the surface of

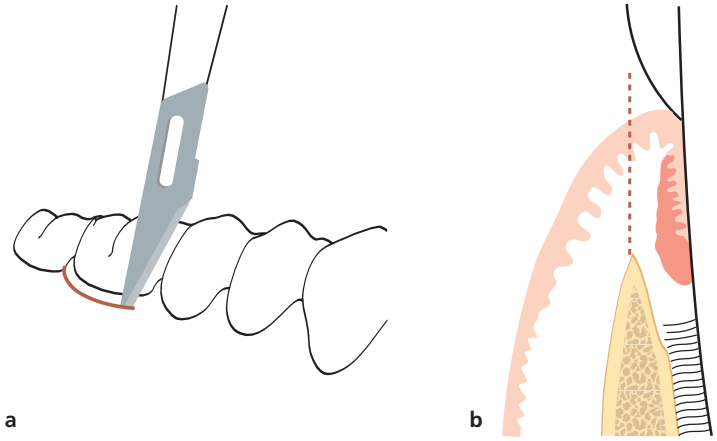

Fig. 38-26 Modified Widman flap. The initial incision is placed 0.5–1 mm from the gingival margin (a) and parallel to the long axis of the tooth (b).

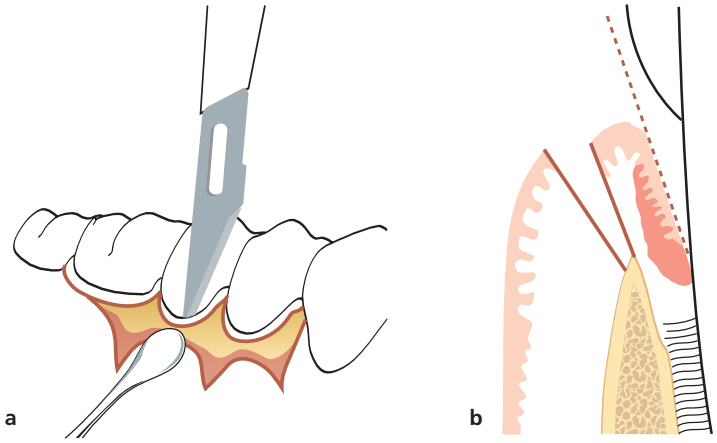

Fig. 38-27 Modified Widman flap. Following careful elevation of the flaps, a second intracrevicular incision (a) is made to the alveolar bone crest (b) to separate the tissue collar from the root surface.

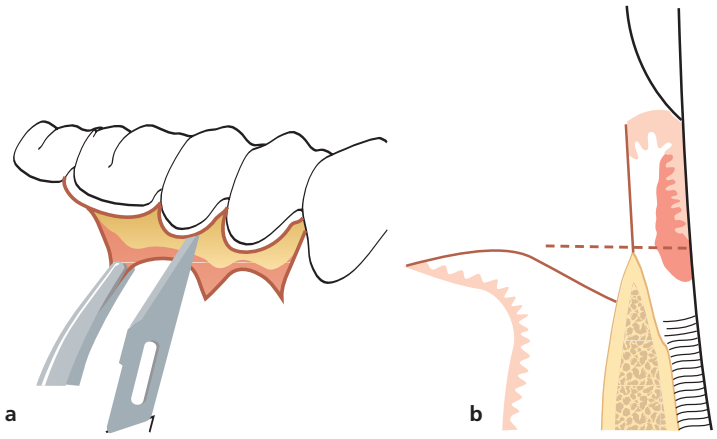

Fig. 38-28 Modified Widman flap. A third incision is made perpendicular to the root surface (a) and as close as possible to the bone crest (b), thereby separating the tissue collar from the alveolar bone.

the alveolar bone crest separates the soft tissue collar of the root surfaces from the bone.

- The pocket epithelium and the granulation tissues are removed by means of curettes. The exposed roots are carefully scaled and planed, except for a narrow area close to the alveolar bone crest in which remnants of attachment fibers may be preserved. Angular bony defects are carefully curetted.
- Following the curettage, the flaps are trimmed and adjusted to the alveolar bone to obtain complete coverage of the interproximal bone (Fig. 38-29). If this adaptation cannot be achieved by soft tissue recontouring, some bone may be removed from the outer aspects of the alveolar process in order to facilitate the all-important flap adaptation. The flaps are sutured together with individual interproximal sutures. Surgical dressing may be placed over the area to ensure close adaptation of the flaps to the alveolar bone and root surfaces. The dressing, as well as the sutures, is removed after 1 week.

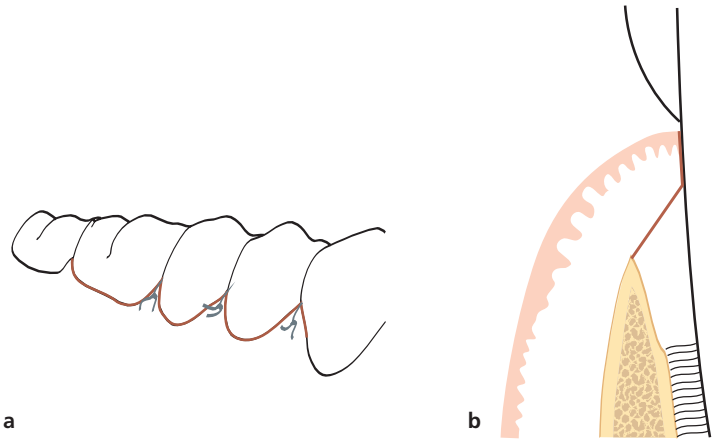

Fig. 38-29 Modified Widman flap. (a) Following proper debridement and currettage of angular bone defects, the flaps are carefully adjusted to cover the alveolar bone and sutured. (b) Complete coverage of the interdental bone as well as close adaptation of the flaps to the tooth surfaces should be accomplished.

The main advantages of the *modified Widman flap* technique in comparison to other procedures previously described are, according to Ramfjord and Nissle (1974):

- The possibility of obtaining a close adaptation of the soft tissues to the root surfaces
- The minimum of trauma to which the alveolar bone and the soft connective tissues are exposed
- Less exposure of the root surfaces, which from an esthetic point of view is an advantage in the treatment of anterior segments of the dentition.

The papilla preservation flap

In order to preserve the interdental soft tissues for maximum soft tissue coverage following surgical intervention involving treatment of proximal osseous defects, Takei *et al*. (1985) proposed a surgical approach called *papilla preservation technique*. Later, Cortellini *et al*. (1995b, 1999) described modifications of the flap design to be used in combination with regenerative procedures. For esthetic reasons, the papilla preservation technique is often utilized in the surgical treatment of anterior tooth regions.

Technique

- According to the description by Takei *et al*. (1985) the *papilla preservation flap technique* is initiated by an intra-sulcular incision at the facial and proximal aspects of the teeth without making incisions through the interdental papillae (Fig. 38-30a). Subsequently, an intra-sulcular incision is made along the lingual/palatal aspect of the teeth with a semilunar incision made across each interdental area. The semilunar incision should dip apically at least 5 mm from the line angles of the teeth, which will allow the interdental tissue to be dissected from the lingual/palatal aspect so that it can be elevated intact with the facial flap. In situations where an osseous defect has a wide extension into the lingual/palatal area, the semilunar incision may be placed on the facial aspect of the interdental area to have the papillae included with the lingual/palatal flap.
- A curette or interproximal knife is used to free the interdental papilla carefully from the underlying hard tissue. The detached interdental tissue is pushed through the embrasure with a blunt instrument (Fig. 38-30b).
- A full-thickness flap is reflected with a periosteal elevator on both facial and lingual/palatal surfaces. The exposed root surfaces are thoroughly scaled and root planed and bone defects carefully curetted (Fig. 38-31).
- While holding the reflected flap, the margins of the flap and the interdental tissue are scraped to remove pocket epithelium and excessive granulation tissue. In anterior areas, the trimming of granulation tissue should be limited in order to maintain the maximum thickness of tissue.
- The flaps are repositioned and sutured using cross mattress sutures (Fig. 38-32). Alternatively, a direct suture of the semilunar incisions can be done as the only means of flap closure. A surgical dressing may be placed to protect the surgical

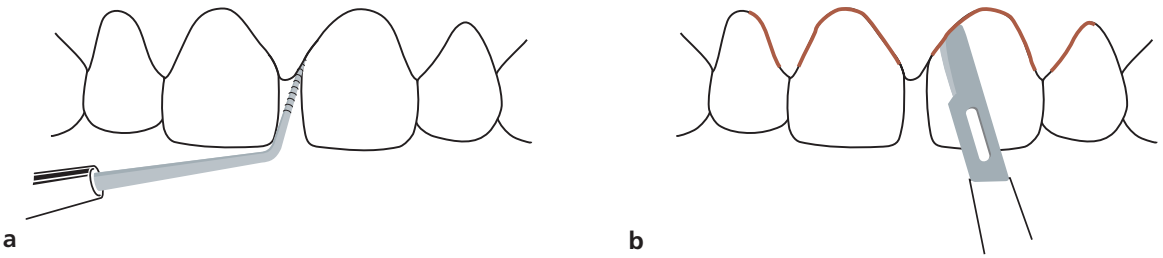

Fig. 38-30 Papilla preservation flap. Intracrevicular incisions are made at the facial and proximal aspects of the teeth.

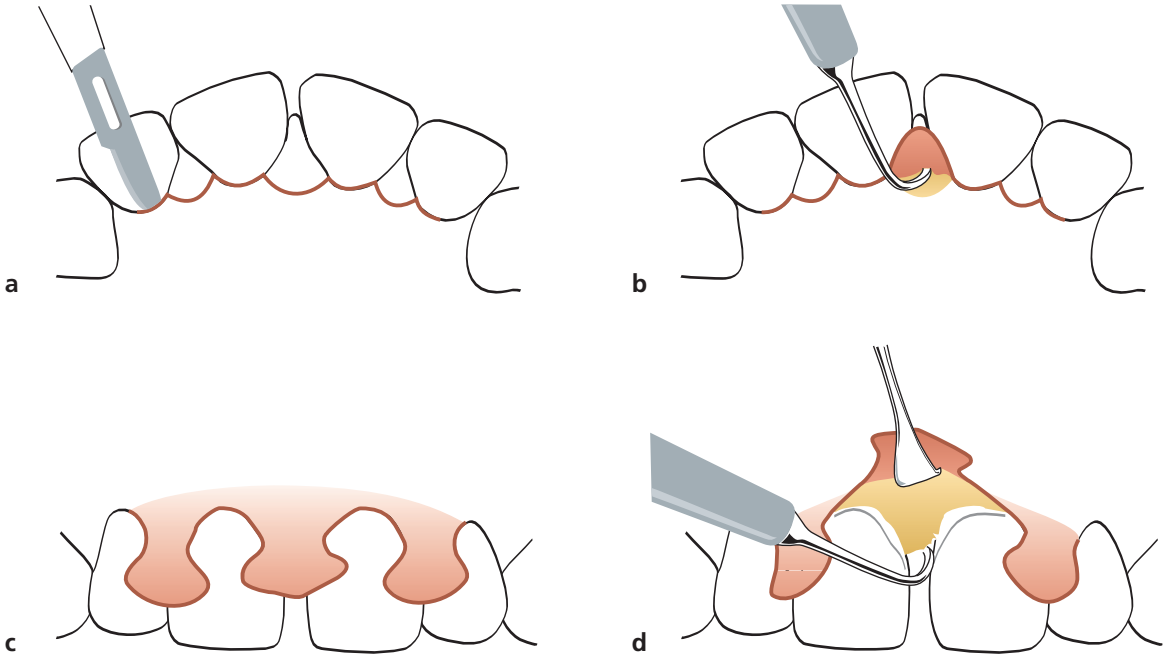

Fig. 38-31 Papilla preservation flap. (a) An intracrevicular incision is made along the lingual/palatal aspect of the teeth with a semilunar incision made across each interdental area. (b) A curette or a papilla elevator is used to carefully free the interdental papilla from the underlying hard tissue. (c,d) The detached interdental tissue is pushed through the embrasure with a blunt instrument to be included in the facial flap.

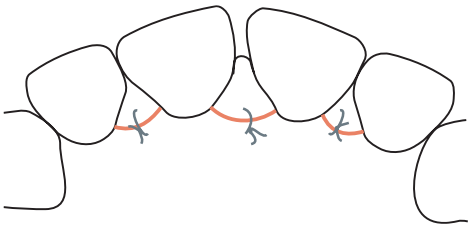

Fig. 38-32 Papilla preservation flap. The flap is replaced and sutures are placed on the palatal aspect of the interdental areas.

area. The dressing and sutures are removed after 1 week.

Regenerative procedures

In the 1980s treatment of periodontal pockets was given a new dimension when it was shown that, with specific surgical handling of the periodontal wound, a significant amount of new connective tissue attachment is achievable following surgical treatment (Nyman *et al*. 1982; Bowers *et al*. 1989).

Obtaining periodontal regeneration has always been a major challenge to the periodontist and several approaches to periodontal regeneration have been used throughout the years. The earliest attempts involved various bone-grafting procedures, such as the use of autogenous grafts from both extraoral and intraoral donor sites, allogenic marrow grafts, and non-decalcified/decalcified lyophilized bone grafts, or "implant" procedures utilizing slowly resorbable tricalcium phosphate and non-resorbable, non-porous hydroxyapatite. Other approaches to periodontal regeneration involved the use of citric acid for root surface demineralization or the use of methods for improved root surface biocompatibility or to enhance cellular responses.

The use of physical barriers, such as membranes (non-biodegradable or biodegradable), to retard or prevent apical migration of epithelium as well as exclude gingival connective tissue from the healing wound, formed the basis for the concept known as "guided tissue regeneration" (Gottlow *et al*. 1986). The procedure can be described as a coronally repositioned flap procedure without bone recontouring, with the adjunctive use of a membrane tightened to the tooth to cover the exposed root surface and adjacent intrabony defect before repositioning the soft tissue flaps.

In the late 1990s a new approach to periodontal regeneration was presented, which involves the use of a derivative of enamel matrix proteins (Hammarström 1997; Heijl *et al*. 1997). These proteins are involved in the embryogenesis of cementum, periodontal ligament, and supporting bone, and when applied to the exposed root surface facing an intrabony periodontal defect they mediate regeneration of a new attachment apparatus. The surgical procedure is performed as a coronally repositioned flap procedure without bone recontouring. Before repositioning of the soft tissue flaps, the exposed roots are treated with EDTA for removal of the "smear layer", followed by the application of the derivative of enamel matrix proteins.

Various regenerative procedures for surgical treatment of periodontal lesions, as well as the biologic

basis for periodontal regeneration, are discussed in detail in Chapters 25 and 43.

Distal wedge procedures

In many cases the treatment of periodontal pockets on the distal surface of distal molars is complicated by the presence of bulbous tissues over the tuberosity or by a prominent retromolar pad. The most direct approach to pocket elimination in such cases in the maxillary jaw is the gingivectomy procedure. The incision is started on the distal surface of the tuberosity and carried forward to the base of the pocket of the distal surface of the molar (Fig. 38-33).

However, when only limited amounts of keratinized gingiva are present, or none at all, or if a distal angular bony defect has been diagnosed, the bulbous tissue should be reduced in size rather than being removed *in toto*. This may be accomplished by the *distal wedge procedure* (Robinson 1966). This technique facilitates access to the osseous defect and makes it possible to preserve sufficient amounts of gingiva and mucosa to achieve soft tissue coverage.

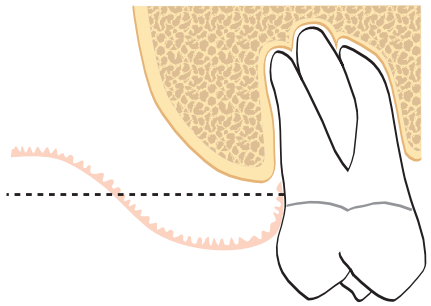

Fig. 38-33 Distal wedge procedure. Simple gingivectomy incision (broken line) can be used to eliminate a soft tissue pocket and adjacent fibrous tissue pad behind a maxillary molar.

Technique

- Buccal and lingual incisions are made in a vertical direction through the tuberosity or retromolar pad to form a triangular wedge (Fig. 38-34a). The facial and lingual incisions should be extended in a mesial direction along the buccal and lingual surfaces of the distal molar to facilitate flap elevation.
- The facial and lingual walls of the tuberosity or retromolar pad are deflected and the incised wedge of tissue is dissected and separated from the bone (Fig. 38-34b).
- The walls of the facial and lingual flaps are then reduced in thickness by undermining incisions (Fig. 38-34c). Loose tags of tissue are removed and the root surfaces are scaled and planed. If necessary, the bone is recontoured.
- The buccal and lingual flaps are replaced over the exposed alveolar bone, and the edges trimmed to avoid overlapping wound margins. The flaps are secured in this position with interrupted sutures (Fig. 38-34d). The sutures are removed after approximately 1 week.

The original distal wedge procedure may be modified according to individual requirements. Some commonly used modifications of the incision

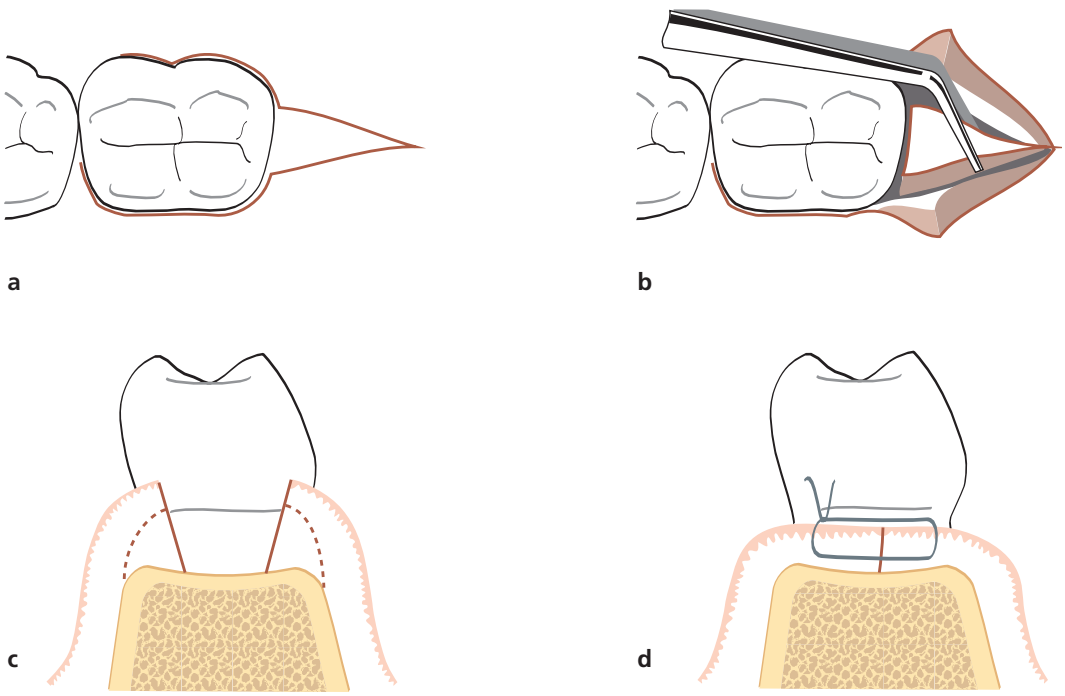

Fig. 38-34 Distal wedge procedure. (a) Buccal and lingual vertical incisions are made through the retromolar pad to form a triangle behind a manibular molar. (b) The triangular-shaped wedge of tissue is dissected from the underlying bone and removed. (c) The walls of the buccal and lingual flaps are reduced in thickness by undermining incisions (broken lines). (d) The flaps, which have been trimmed and shortened to avoid overlapping wound margins, are sutured.

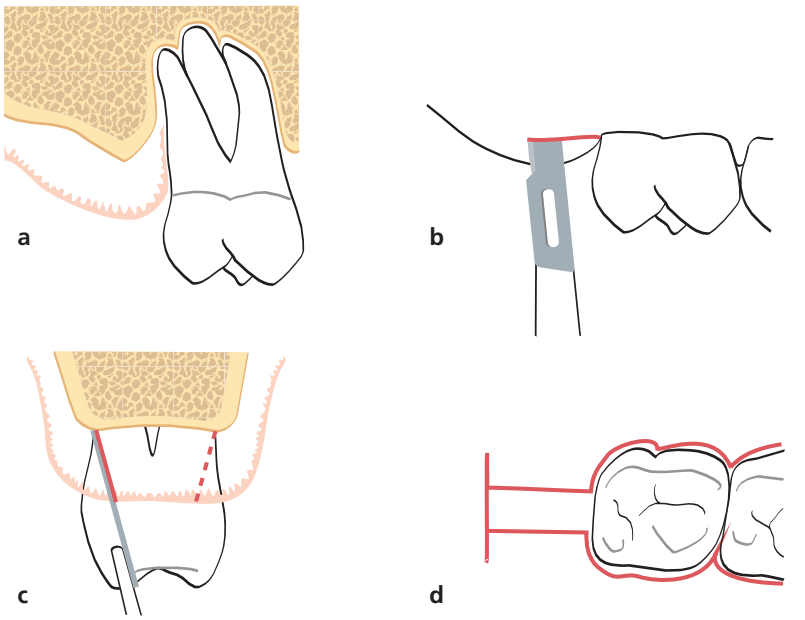

Fig. 38-35 Modified distal wedge procedure. A deep periodontal pocket combined with an angular bone defect at the distal aspect of a maxillary molar (a). Two parallel reverse bevel incisions, one buccal and one palatal, are made from the distal surface of the molar to the posterior part of the tuberosity (b–d), where they are connected with a bucco-lingual incision (d). The buccal and palatal incisions are extended in a mesial direction along the buccal and palatal surfaces of the molar to facilitate flap elevation.

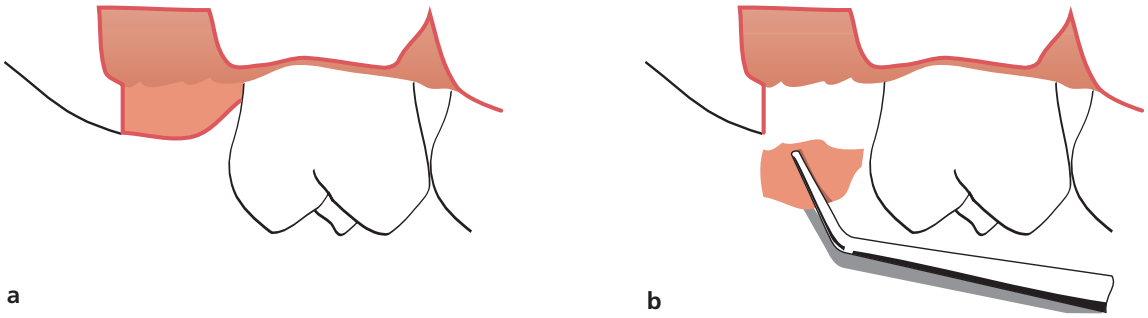

Fig. 38-36 Modified distal wedge procedure. Buccal and palatal flaps are elevated (a) and the rectangular wedge is released from the tooth and underlying bone by sharp dissection and then removed (b).

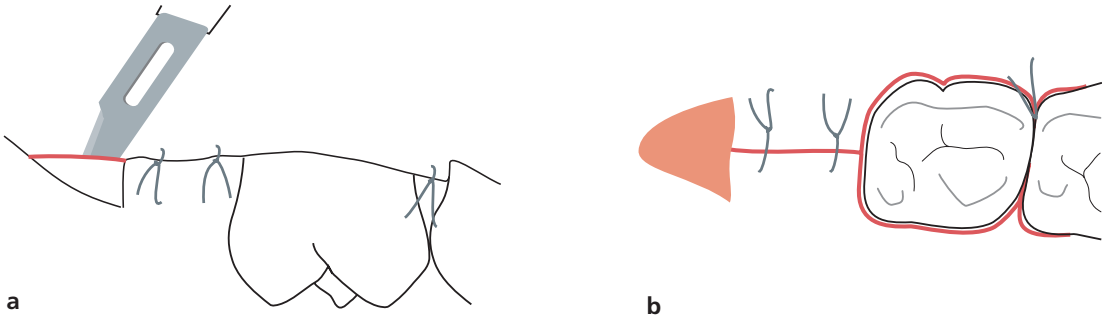

Fig. 38-37 Modified distal wedge procedure. Following bone recontouring and root debridement, the flaps are trimmed and shortened to avoid overlapping wound margins and sutured (a,b). A close soft tissue adaptation should be accomplished to the distal surface of the molar. The remaining fibrous tissue pad distal to the bucco-lingual incision line is "levelled" by the use of a gingivectomy incision.

technique are illustrated in Figs. 38-35 to 38-38, all having the goals of eliminating the deep pocket and achieving mucosal coverage of the remaining periodontium.

Osseous surgery

The principles of osseous surgery in periodontal therapy were outlined by Schluger (1949) and Goldman (1950). They pointed out that alveolar bone loss caused by inflammatory periodontal disease often results in an uneven outline of the bone crest. Since, according to these authors, the gingival contour is closely dependent on the contour of the underlying bone as well as the proximity and anatomy of adjacent tooth surfaces, the elimination of soft tissue pockets often has to be combined with osseous reshaping and the elimination of osseous craters and

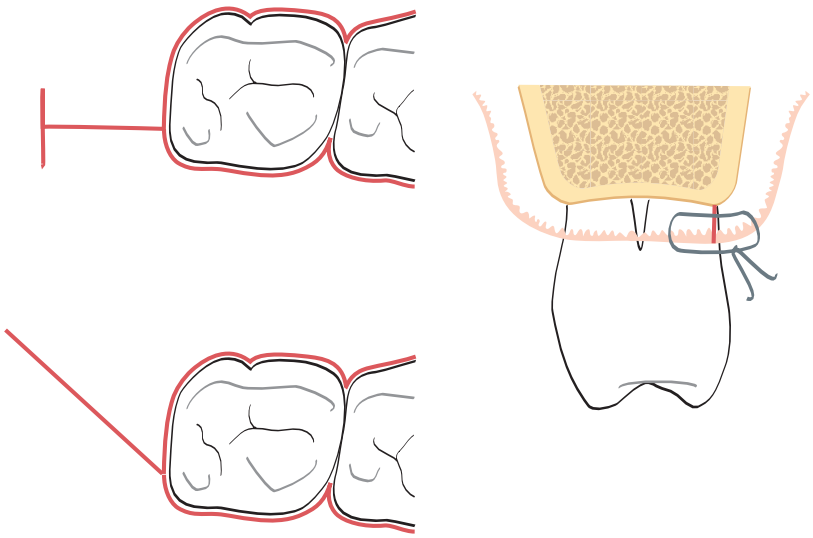

Fig. 38-38 Modified incision techniques in distal wedge procedures. To ensure optimal flap adaptation at the furcation site the incision technique may be modified. The amount of attached keratinized tissue present as well as the accessibility to the retromolar area has to be considered when placing the incision.

angular bony defects to establish and maintain shallow pockets and optimal gingival contour after surgery.

Osteoplasty

The term *osteoplasty* was introduced by Friedman in 1955. The purpose of osteoplasty is to create a physiologic form of the alveolar bone *without* removing any "supporting" bone. Osteoplasty therefore is a technique analogous to gingivoplasty. Examples of osteoplasty are the thinning of thick osseous ledges and the establishment of a scalloped contour of the buccal (lingual and palatal) bone crest (Fig. 38-39). In flap surgery without bone recontouring, interdental morphology may sometimes preclude optimal mucosal coverage of the bone post-surgically, even if pronounced scalloping of soft tissue flaps is performed. In such a situation removal of non-supporting bone by vertical grooving to reduce the facio-lingual dimension of the bone in the interdental areas may facilitate flap adaptation, thereby reducing the risk of bone denudation as well as reducing the risk of ischemic necrosis of unsupported mucosal flaps due to flap margin deficiencies.

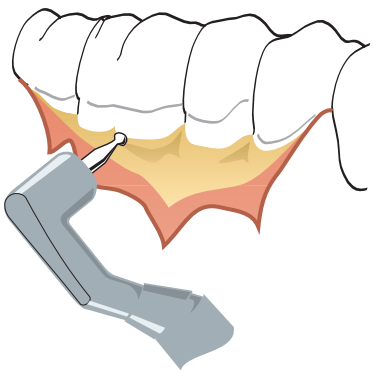

Fig. 38-39 Osteoplasty. Thick osseous ledges in a mandibular molar region area are eliminated with the use of a round bur to facilitate optimal flap adaptation.

Removal of non-supporting bone may sometimes also be required to gain access for intrabony root surface debridement. The leveling of interproximal craters and the elimination (or reduction) of bony walls of circumferential osseous defects are often referred to as "osteoplasty" since usually no resection of supporting bone is required (Fig. 38-40).

Ostectomy

In *ostectomy* supporting bone, i.e. bone directly involved in the attachment of the tooth, is removed to reshape deformities caused by periodontitis in the marginal and interdental bone. Ostectomy is considered to be an important part of surgical techniques aimed at pocket elimination. As a general rule, however, care must be exercised when supporting bone is to be removed.

After exposing the alveolar bone by elevation of a flap, buccal and/or lingual crater walls are reduced to the base of the osseous defect using bone chisels and bone rongeurs (Fig. 38-41). A round bur or a diamond stone under continuous saline irrigation

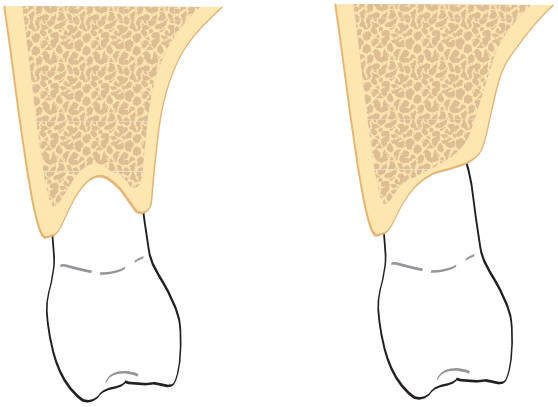

Fig. 38-40 Osteoplasty. Levelling of an interproximal bone crater through the removal of the palatal bone wall. For esthetic reasons the buccal bone wall is maintained to support the height of the soft tissue.

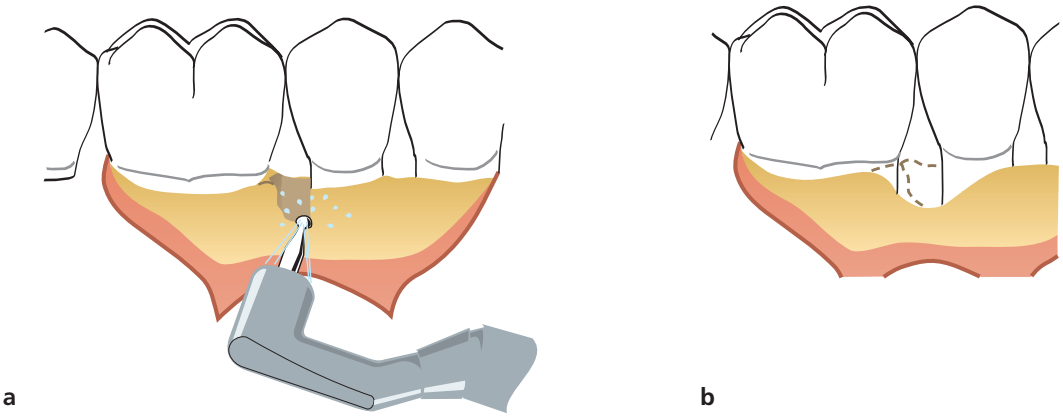

Fig. 38-41 Ostectomy. (a) A combined one- and two-wall osseous defect on the distal aspect of a mandibular bicuspid has been exposed following reflection of mucoperiosteal flaps. Since esthetics is not a critical factor to consider in the posterior tooth region of the mandible, the bone walls are reduced to a level close to the base of the defect using rotating round burs under continuous saline irrigation. (b) The osseous recontouring completed. Note that some supporting bone has to be removed from the buccal and lingual aspect of both the second bicuspid and the first molar in order to provide a hard tissue topography which allows a close adaptation of the covering soft tissue flap.

can also be used. If bone resection has been carried out in the interdental area, the buccal and lingual/palatal bone margins may subsequently have to be recontoured to compensate for discrepancies in bone height resulting from the interdental bone resection (Fig. 38-41b). It is considered important to remove the small peaks of bone, which often remain in the area of the line angles. The objective of bone surgery is thus to establish a "physiologic" anatomy of the alveolar bone, but at a more apical level.

General guidelines for periodontal surgery

Objectives of surgical treatment

Traditionally, *pocket elimination* has been the main objective of periodontal therapy. The removal of the pocket by surgical means served two purposes: (1) the pocket, which established an environment conducive to progression of periodontal disease, was eliminated and (2) the root surface was made accessible for scaling and for self-performed tooth cleaning after healing.

While these objectives cannot be entirely discarded today, the necessity for pocket elimination in periodontal therapy has been challenged. During recent years our understanding of the biology of the periodontium, the pathogenesis of periodontal disease and the healing capacity of the periodontium has markedly increased. This new information has thus formed the basis for a more differentiated understanding of the role played by periodontal surgery in the preservation of teeth.

In the past, *increased pocket depth* was the main indication for periodontal surgery. However, pocket depth is no longer as unequivocal a concept as it used to be. The *probeable depth*, i.e. the distance from the gingival margin to the point where tissue resistance stops further periodontal probe penetration, may only rarely correspond to the "true" depth of the pocket (see Chapter 26). Furthermore, regardless of the accuracy with which pockets can be measured, there is no established correlation between probeable pocket depths and the presence or absence of active disease. This means that symptoms other than increased probing depth should be present to justify surgical therapy. These include clinical signs of inflammation, especially exudation and bleeding on probing (to the bottom of the pockets), as well as aberrations of gingival morphology. Finally, the fact that proper infection control, maintained by the patient, is a decisive factor for a good prognosis (Rosling *et al*. 1976a; Nyman *et al*. 1977; Axelsson & Lindhe 1981) must be considered prior to the initiation of surgery.

In conclusion, the main objective of periodontal surgery is to contribute to the long-term preservation of the periodontium by facilitating plaque removal and infection control, and periodontal surgery can serve this purpose by:

- Creating accessibility for proper professional scaling and root planing
- Establishing a gingival morphology which facilitates the patient's self-performed infection control.

In addition to this, periodontal surgery may aim at regeneration of periodontal attachment lost due to destructive disease. (New attachment procedures in periodontal therapy are discussed in Chapter 43.)

Indications for surgical treatment

Impaired access for scaling and root planing

Scaling and root planing are methods of therapy that are difficult to master. The difficulties in

accomplishing proper debridement increase with (1) increasing depth of the periodontal pockets, (2) increasing width of the tooth surfaces, and (3) the presence of root fissures, root concavities, furcations, and defective margins of dental restorations in the subgingival area.

Provided a correct technique and suitable instruments are used, it is usually possible properly to debride pockets up to 5 mm deep (Waerhaug 1978; Caffesse *et al*. 1986). However, this 5 mm limit cannot be used as a universal rule of thumb. Reduced accessibility and the presence of one or several of the above-mentioned impeding conditions may prevent proper debridement of shallow pockets, whereas at sites with good accessibility and favorable root morphology, proper debridement can be accomplished even in deeper pockets (Badersten *et al*. 1981; Lindhe *et al*. 1982a).

It is often difficult to ascertain by clinical means whether subgingival instrumentation has been properly performed. Following scaling, the root surface should be smooth – roughness will often indicate the presence of remaining subgingival calculus. It is also important to monitor carefully the gingival reaction to subgingival debridement. If inflammation persists and if bleeding is elicited by gentle probing in the subgingival area, the presence of subgingival deposits should be suspected (Fig. 38-42). If such symptoms are not resolved by repeated subgingival instrumentation, surgical treatment should be performed to expose the root surfaces for proper cleaning.

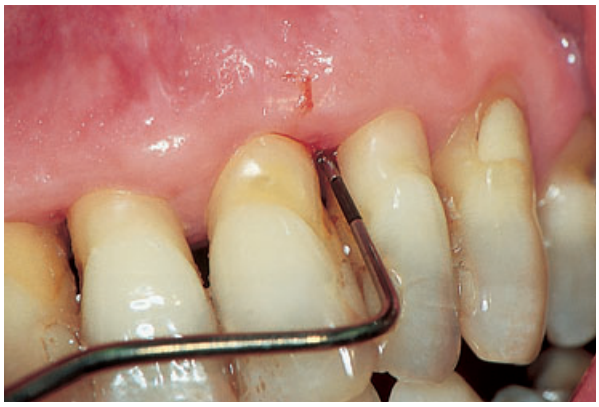

Fig. 38-42 Evaluation following non-surgical instrumentation reveals persistent signs of inflammation, bleeding following pocket probing and probing depth ≥6 mm. Flap elevation to expose the root surface for proper cleaning should be considered.

Impaired access for self-performed plaque control

The level of infection control that can be maintained by the patient is determined not only by his/her interest and dexterity but also, to some extent, by the morphology of the dentogingival area. The patient's responsibility in an infection-control program must obviously include the cleansing of the supragingival tooth surfaces and the marginal part of the gingival sulcus. This means that the tooth area coronal to the gingival margin and at the entrance to the gingival sulcus should be the target for the patient's home care efforts.

Pronounced gingival hyperplasia and gingival craters (Fig. 38-43) are examples of morphologic aberrations, which may impede proper home care. Likewise, the presence of restorations with defective marginal fit or adverse contour and surface characteristics at the gingival margin may seriously compromise plaque removal.

By the professional treatment of periodontal disease, the dentist prepares the dentition in such a way that home care can be effectively managed. At the completion of treatment, the following objectives should have been met:

- No sub- or supragingival dental deposits
- No pathologic pockets (no bleeding on probing to the bottom of the pockets)
- No plaque-retaining aberrations of gingival morphology

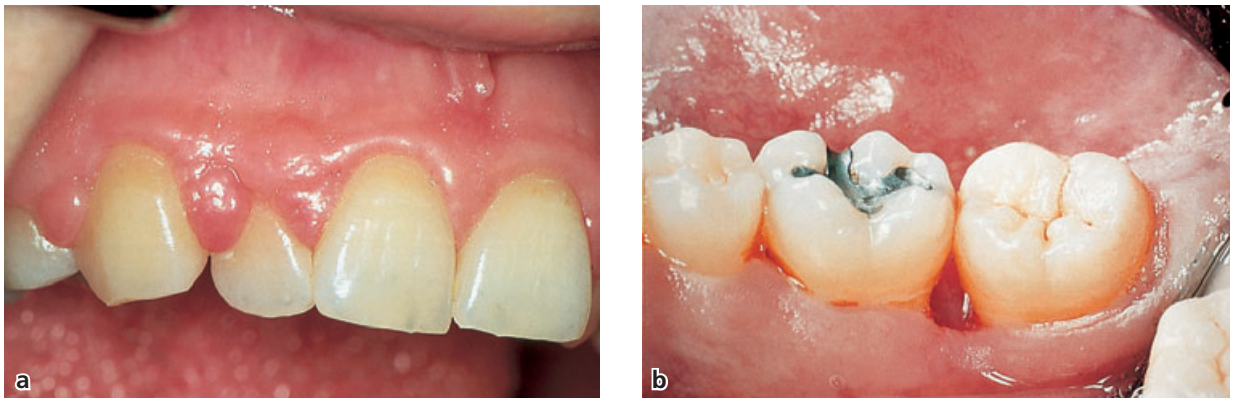

Fig. 38-43 Examples of gingival aberrations, (a) gingival enlargement and (b) proximal soft tissue crater, which favor plaque retention and thereby impede the patient's plaque control.

- No plaque-retaining parts of restorations in relation to the gingival margin.

These requirements lead to the following indications for periodontal surgery:

- Accessibility for proper scaling and root planing
- Establishment of a morphology of the dentogingival area conducive to infection control
- Pocket depth reduction
- Correction of gross gingival aberrations
- Shift of the gingival margin to a position apical to plaque-retaining restorations
- Facilitate proper restorative therapy.

Contraindications for periodontal surgery

Patient cooperation

Since optimal post-operative infection control is decisive for the success of periodontal treatment (Axelsson & Lindhe 1981), a patient who fails to cooperate during the cause-related phase of therapy should not be exposed to surgical treatment. Even though short-term post-operative infection control entails frequent professional treatments, the long-term responsibility for maintaining good oral hygiene must rest with the patient. Theoretically, even the poorest oral hygiene performance by a patient may be compensated for by frequent recall visits for supportive therapy (e.g. once a week), but it is unrealistic to consider larger groups of patients being maintained in this manner. A typical recall schedule for periodontal patients involves professional consultations for supportive periodontal therapy once every 3–6 months. Patients who cannot maintain satisfactory oral hygiene over such a period should normally be considered unsuited for periodontal surgery.

Cardiovascular disease

Arterial hypertension does not normally preclude periodontal surgery. The patient's medical history should be checked for previous untoward reactions to local anesthesia. Local anesthetics free from or low in adrenaline may be used and an aspirating syringe should be adopted to safeguard against intravascular injection.

Angina pectoris does not normally preclude periodontal surgery. The drugs used and the number of episodes of angina may indicate the severity of the disease. Premedication with sedatives and the use of local anesthesia low in adrenaline are often recommended. Safeguards should be adopted against intravascular injection.

Myocardial infarction patients should not be subjected to periodontal surgery within 6 months following hospitalization, and thereafter only in cooperation with the physician responsible for the patient.

Anticoagulant treatment implies increased propensity for bleeding. Periodontal surgery should be scheduled first after consultation with the patient's physician to determine whether modification of the anticoagulant therapy is indicated. In patients on moderate levels of anticoagulation and only requiring minor surgical treatment, no alteration of their anticoagulant therapy may be required. To keep the prothrombin time within a safety level for hemorrhage control during surgery in patients with higher levels of anticoagulation, adjustments of the anticoagulant drug therapy usually needs to be initiated 2–3 days prior to the dental appointment. Anticoagulation may be safely resumed immediately after the periodontal surgical procedure since several days are needed for full anticoagulation to return. Aspirin and other non-steroidal anti-inflammatory drugs should not be used for post-operative pain control since they increase bleeding tendency. Furthermore, tetracyclines are contraindicated in patients on anticoagulant drugs due to interference with prothrombin formation (Fay & O'Neil 1984).

Rheumatic endocarditis, *congenital heart lesions*, and *heart/vascular implants* involve risk for transmission of bacteria to heart tissues and heart implants during the transient bacteremia that follows manipulation of infected periodontal pockets. In patients with these conditions, as well as in patients at risk of hematogenous total prosthetic joint infection (for the first 2 years following joint placement), probing, scaling and root planing (including placement of antimocribial devices and prophylactic cleaning of implants and teeth where bleeding is anticipated), surgery and tooth extraction should be preceded by prescription and administration of an appropriate antibiotic at a high dose (American Dental Association – Position Statement on Antibiotic Prophylaxis 2003) and antiseptic mouth rinsing (0.2% chlorhexidine). According to the recommendations by the American Heart Association (Advisory Statement 1997), 2 grams of amoxicillin administrated orally 1 hour before the treatment is an adequate regimen. If the patient is allergic to penicillin, clindamycin (600 mg) orally 1 hour before the treatment is recommended as alternative. No second doses are recommended for any of the above dosing regimens. Tetracyclines and erythromycin are not recommended for prophylactic cardiovascular antibiotic coverage.

Organ transplantation

In organ transplantation medications are used to prevent transplant rejection. The drug of choice today is cyclosporine A, a potent immunosuppressant drug. The adverse effects seen following cyclosporine A treatment include an increased risk for gingival enlargement as well as hypertension. In addition, hypertension seen in renal transplant recipients is often treated with calcium channel blockers. These

antihypertensive agents have also been associated with gingival enlargement. As in patients on phenytoin therapy, gingival enlargement in patients on cyclosporine A therapy or on antihypertensive therapy with calcium blockers may be corrected by means of periodontal surgery. However, due to the strong propensity for recurrence, the use of intensified conservative periodontal therapy to prevent gingival enlargement in susceptible patients should be encouraged.

Prophylactic antibiotics are recommended in transplant patients taking immunosuppressive drugs, and the patient's physician should be consulted before any periodontal therapy is performed. In addition, antiseptic mouth rinsing (0.2% chlorhexidine) should precede the surgical treatment.

Blood disorders

If the medical history includes blood disorders, the exact nature of these should be ascertained. Patients suffering from *acute leukemias*, *agranulocytosis*, and *lymphogranulomatosis* must *not* be subjected to periodontal surgery. *Anemias* in mild and compensated forms do not preclude surgical treatment. More severe and less compensated forms may entail lowered resistance to infection and increased propensity for bleeding. In such cases, periodontal surgery should only be performed after consultation with the patient's physician.

Hormonal disorders

Diabetes mellitus entails lowered resistance to infection, propensity for delayed wound healing, and predisposition for arteriosclerosis. Well compensated patients may be subjected to periodontal surgery provided precautions are taken not to disturb dietary and insulin routines.

Adrenal function may be impeded in patients receiving large doses of corticosteroids over an extended period. These conditions involve reduced resistance to physical and mental stress, and the doses of corticosteroid may have to be altered during the period of periodontal surgery. The patient's physician should be consulted.

Neurologic disorders

Multiple sclerosis and *Parkinson's disease* may, in severe cases, make ambulatory periodontal surgery impossible. Paresis, impaired muscular function, tremor, and uncontrollable reflexes may necessitate treatment under general anesthesia.

Epilepsy is often treated with *phenytoin* that, in approximately 50% of cases, may mediate the formation of gingival enlargement. These patients may, without special restrictions, be subjected to periodontal surgery for correction of the enlargement. There is, however, a strong propensity for recurrence of the enlargement, which in many cases can be countered by intensifying plaque control.

Smoking

Although smoking negatively affects wound healing (Siana *et al*. 1989), it may not be considered as a contraindication for surgical periodontal treatment. The clinician should be aware, however, that less resolution of probing pocket depth and smaller improvement in clinical attachment may be observed in smokers than in non-smokers (Preber & Bergström 1990; Ah *et al*. 1994; Scabbia *et al*. 2001; Labriola *et al*. 2005).

Local anesthesia in periodontal surgery

Traditional views of pain and discomfort as an inevitable consequence of dental procedures, in particular surgical procedures (including scaling and root planing) and extractions, are no longer accepted by patients. Pain management is an ethical obligation and will improve patient satisfaction in general (e.g. increased confidence and improved cooperation) as well as patient recovery and short-term functioning after oral/periodontal surgical procedures. In order to prevent pain during the performance of a periodontal surgical procedure, the entire area of the dentition scheduled for surgery, the teeth as well as the periodontal tissues, require proper local anesthesia.

Mechanism of action

Local anesthesia is defined as a loss of feeling or sensation that is confined to a certain area of the body. All local anesthetics have a common mechanism of action. To produce their effect they block the generation and propagation of impulses along nerve fibers. Such impulses are transmitted by rapid depolarization and repolarization within the nerve axons. These changes in polarity are due to the passage of sodium and potassium ions across the nerve membrane through ionic channels within the membrane. Local anesthetics prevent the inward movement of sodium ions, which initiate depolarization, and as a consequence the nerve fiber cannot propagate any impulse. The potassium efflux, on the other hand, is influenced very little and there is no change in the resting potential. The mechanisms behind the activity of the local anesthetics are not fully understood, but the most plausible theory is that the lipid-soluble free base form of the local anesthetic, which is the form that penetrates biologic membranes most easily, penetrates the connective tissue to reach the axons and diffuses across the lipid membrane into the axon. Inside the axon the drug interacts with specific receptor sites on or within the sodium channels to exert an inhibitory effect on sodium influx and, consequently, on impulse conduction.

Dental local anesthetics

Anesthetics from the chemical group amino-amides, for example lidocaine, mepivacaine, prilocaine, and articaine, are more potent and significantly less allergenic than amino-esters (e.g. procaine and tetracaine) and have therefore replaced esters as the "gold standard" for dental local anesthetics.

Due to the specific need for bone penetration, dental local anesthetics contain high concentrations of the active agent. Although most amide local anesthetics may cause local vasoconstriction in low concentrations, the clinically used concentrations in dental solutions will cause an increase in the local blood flow. Significant clinical effects of this induced vasodilatation are an increased rate of absorption, thus decreasing the duration of anesthesia. Major benefits can therefore be obtained by adding relatively high concentrations of vasoconstrictors (e.g. epinephrine >1 : 200 000 or >5 mg/ml) to dental local anesthetic solutions; the duration is considerably prolonged, the depth of anesthesia may be enhanced, and the peak concentrations of the local anesthetic in blood can be reduced. Furthermore, in periodontal surgery incorporation of adrenergic vasoconstrictors into the local anesthetic is of considerable value to allow for only minimal bleeding during surgery (to avoid considerable blood loss, to visualize the surgical site, and shorten the time spent on the procedure maintaining surgical quality). As a matter of fact, the use of a dental local anesthetic without a vasoconstrictor during a periodontal surgical procedure is counterproductive because the vasodilating properties of such a local anesthetic will increase bleeding in the area of surgery.

Vasoconstrictors and local hemostasis

Epinephrine is the vasoconstrictor of choice for local hemostasis and is most commonly used in a concentration of 1 : 80 000 (12.5 mg/ml). However, 1 : 100 000 epinephrine also provides excellent hemostasis and most periodontists are unable to detect a clinical difference between the two concentrations. It therefore seems prudent to use the least concentrated form of epinephrine that provides clinically effective hemostasis (i.e. the 1 : 100 000 concentration).

Although the cardiovascular effects of the usually small amounts of epinehrine used during a periodontal surgical procedure are of little practical concern in most individuals, accidental intravascular injections, unusual patient sensitivity and unanticipated drug interactions (or excessive doses), can result in potentially serious outcomes. It must also be understood that the use of epinephrine for hemostasis during periodontal surgery has some potential drawbacks. Epinephrine will produce a rebound vasodilatation after the vasoconstriction has worn off leading to increased risk for bleeding in the immediate postoperative period. There is a greater potential for such undesirable delayed hemorrhage following the use of 1 : 80 000 epinephrine than after the use of 1 : 100 000.

Post-operative pain may increase and wound healing may be delayed when adrenergic vasoconstrictors are used because of local ischemia with subsequent tissue acidosis and accumulation of inflammatory mediators. Furthermore, the possibility of an ischemic necrosis of surgical flaps infiltrated with an adrenergic vasoconstrictor (especially if norepinephrine is used instead of epinephrine) cannot be discounted. For these reasons as well as for the possibility of systemic reactions eluded to above, dental local anesthetics containing adrenergic vasoconstrictors for hemostasis should be infiltrated *only* as needed and *not* merely by habit.

Felypressin, another commonly used vasoconstrictor, appears to act preferentially on the venous side of the microcirculation and is not very active in constricting the arteriolar circulation. Felypressin is therefore not nearly as effective as adrenergic vasoconstrictors in limiting hemorrhage during a surgical procedure.

Individual variability in response to dental local anesthetics

Although it is possible for the periodontist to choose from a broad spectrum of dental local anesthetics to achieve the expected clinical action, there is a number of other factors (i.e. not related to the drug) that can affect the drug action in a single patient. During clinical conditions the variability in response to dental local anesthetics administered can be expected to be great, for example with regard to depth and duration of anesthesia. The reasons for the great variation have not been adequately explained but have to be accepted as the variation may have significant implications in periodontal surgical procedures. A list of possible factors that may cause anesthetic failures include:

- Accuracy in administration of the drug
- Anatomic variation between patients (e.g. in elderly patients with bone resorption)
- Status of the tissues at the site of injection (vascularity, inflammation)
- General condition of patient
- Psychologic factors.

Inaccuracy in administration is a major factor causing anesthetic failures. Although not particularly significant in infiltration anesthesia, the mandibular block is a prime example of a technique in which duration of anesthesia is greatly influenced by accuracy of injection.

The general condition of the patient as well as psychologic factors may also affect the anticipated duration of action. Infection, stress or pain will usually lead to decreased duration of anesthesia,

while an increase in the patient's own defense mechanisms against pain perception by, for example, release of endogenous endorphins, may provide for improved depth and/or duration of anesthesia.

Techniques for anesthesia in periodontal surgery

Injections of dental local anesthetics prior to a periodontal surgical procedure may be routine for the dentist, but is often a most unpleasant experience for the patient. Reassurance and psychologic support are essential and will increase the patient's confidence in his dentist. To create a relaxed atmosphere and to decrease the patient's fear in an unusual situation is of course also a useful way of increasing the patient's own defense mechanisms against pain perception (e.g. release of endogenous endorphins).

Anesthesia for periodontal surgery is obtained by nerve block and/or by local infiltration. In cases of flap surgery, complete anesthesia must be attained before commencing the operation, as it may be difficult to supplement the anesthesia after the bone surface has been exposed. In addition, the pain elicited by needle insertion can be significantly reduced if the mucosa at the puncture site is anesthetized in advance by the use of a suitable topical ointment or spray.

Local infiltration may have a greatly decreased rate of success in areas where inflammation remains in the periodontal tissues, in spite of optimal conservative periodontal therapy and good oral hygiene. The suggested reason being that tissue pH tends to be low in inflamed areas and anesthetic solutions are less potent at low pH because there is a greater proportion of charged cation molecules than of the uncharged base molecules. Because of this, diffusion of the local anesthetic into the axoplasm is slower with subsequent delayed onset and decreased efficacy. Another more recent hypothesis suggests that NGF (nerve growth factor) released during tissue inflammation will induce sprouting or proliferation of sensory nerve endings expressing a different (sub-) type of sodium channel than is expressed in normal tissues. Our presently used dental local anesthetics may not be selective enough for proper interaction with these sodium channel subtypes to induce anticipated anesthesia.

Local anesthesia in the mandible

As a rule, analgesia of the teeth and the soft and hard tissues of the mandible should be obtained by a mandibular block and/or a mental block. In the anterior region of the mandible, canines and incisors can often be anesthetized by infiltration, but there are often anastomoses over the midline. These anastomoses must be anaesthetized by bilateral infiltration, or by bilateral mental blocks. The buccal soft tissues of the mandible are anesthetized by local infiltration or by blocking the buccal nerve. Local infiltration, performed as a series of injections in the buccal fold of the treatment area, has of course the added advantage of providing a local ischemic effect if a suitable anesthetic is used.

The lingual periodontal tissues must also be anesthetized. This is accomplished by blocking the lingual nerve and/or by infiltration in the floor of the mouth close to the site of operation. If necessary to obtain proper ischemia, and only then, supplementary injections may be made in the interdental papillae (intraseptal injections).

Local anesthesia in the maxilla

Local anesthesia of the teeth and buccal periodontal tissues of the maxilla can easily be obtained by injections in the muco-gingival fold of the treatment area. If larger areas of the maxillary dentition are scheduled for surgery, repeated injections (in the muco-gingival fold) have to be performed, e.g. at the central incisor, canine, second premolar, and second molar. In the posterior maxillary region a tuberosity injection can be used to block the superior alveolar branches of the maxillary nerve. However, because of the vicinity to the pterygoid venous plexus, this type of block anesthesia is not recommended due to the risk of intravenous injection and/or hematoma formation.

The palatal nerves are most easily anesthetized by injections made at right angles to the mucosa and placed around 10 mm apical to the gingival margin adjacent to teeth included in the operation. In cases of advanced bone loss, the pain produced by injecting into the non-resilient palatal mucosa can be minimized if the injections are performed from the buccal aspect, i.e. through the interdental gingiva. Sometimes blocks of the nasopalatine nerves and/or the greater palatine nerves can be applied. Supplementary blocking of the greater palatine nerve should be considered, especially for periodontal surgery involving molars.

Instruments used in periodontal surgery

General considerations

Surgical procedures used in periodontal therapy often involve the following measures (instruments):

- Incision and excision (periodontal knives)
- Deflection and re-adaptation of mucosal flaps (periosteal elevators)
- Removal of adherent fibrous and granulomatous tissue (soft tissue rongeurs and tissue scissors)
- Scaling and root planing (scalers and curettes)
- Removal of bone tissue (bone rongeurs, chisels, and files)
- Root sectioning (burs)

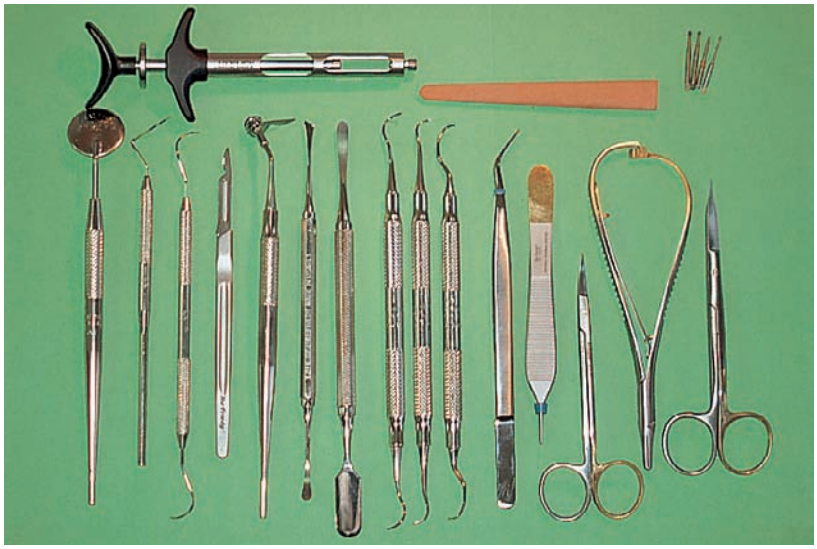

Fig. 38-44 Set of instruments used for periodontal surgery and included in a standard tray.

- Suturing (sutures and needle holders, suture scissors)
- Application of wound dressing (plastic instruments).

The set of instruments used for the various periodontal surgical procedures should have a comparatively simple design. As a general rule, the number and varieties of instruments should be kept to a minimum. In addition to particular instruments used for periodontal treatment modalities, equipment and instruments generally used in oral surgery are often needed. Within each category of surgical instruments used for periodontal therapy there are usually several brands available, varying in form and quality, leaving ample room for individual preferences.

The instruments should be stored in sterile "ready-to-use" packs or trays. Handling, storing, and labeling of surgical instruments and equipment must be managed in such a way that interchanging of sterile and non-sterile items is prevented.

It is also important that the instruments are kept in good working condition. The maintenance routine should ensure that scalers, curettes, knives with fixed blades, etc., are sharp and the hinges of scissors, rongeurs, and needle holders are properly lubricated. Spare instruments (sterile) should always be available to replace instruments found to be defective or accidentally contaminated.

The instrument tray

Instrument trays for periodontal surgery may be arranged in several ways. Different trays can be used for different procedures or a standard tray can be used for all procedures supplemented with the particular instruments that are needed for a specific procedure.

A commonly used standard tray combines the basic set of instruments used in oral surgery and a few periodontal instruments. The instruments listed below are often found on such a standard tray (Fig. 38-44):

- Mouth mirrors
- Graduated periodontal probe/explorer
- Handles for disposable surgical blades (e.g. Bard-Parker handle)
- Mucoperiosteal elevator and tissue retractor
- Scalers and curettes
- Cotton pliers
- Tissue pliers (*ad modum* Ewald)
- Tissue scissors
- Needle holder
- Suture scissors
- Plastic instrument
- Hemostat
- Burs.

Additional equipment may include:

- Syringe for local anesthesia
- Syringe for irrigation
- Aspirator tip
- Physiologic saline
- Drapings for the patient
- Surgical gloves, surgical mask, surgeon's hood.

Surgical instruments

Knives

Knives are available with fixed or replaceable blades. The advantage of the fixed blade versions is that the blade can be given any desired shape and orientation in relation to the handle. A disadvantage is that such instruments need frequent resharpening. Figure 38-45 shows examples of knives with fixed blades.

New disposable blades are always sharp. They can be rapidly replaced if found defective. The cutting edge of the blades normally follows the long axis of

Fig. 38-45 Examples of gingivectomy knives with fixed blades. From left to right: Kirkland 15/16, Orban 1/2, and Waerhaug 1/2.

Fig. 38-47 A universal 360° handle for disposable blades, which allows the mounting of the blade in any angulated position of choice.

Fig. 38-46 Disposable blades which can be mounted in various types of handles. The shape of the blades are from left to right: No. 11, No. 12, No. 12D, No. 15, and No. 15C.

Fig. 38-48 Examples of double-ended sickle scalers and curettes useful for root debridement in conjunction with periodontal surgery. From left to right: Curette SG 215/16C Syntette, Sickle 215-216 Syntette, and mini-curette SG 215/16MC.

the handle, which limits their use. However, knives with disposable blades fitted at an angle to the handle are also available. Disposable blades are manufactured in different shapes (Fig. 38-46). When mounted in ordinary handles (Bard-Parker®), they are used for releasing incisions in flap operations and mucogingival surgery and for reverse bevel incisions where access is obtainable. Special handles (Fig. 38-47) make it possible to mount blades in angulated positions, which facilitate the use of such knives for both gingivectomy excisions and reverse bevel incisions.

Scalers and curettes

Scaling and root planing in conjunction with periodontal surgery take place on exposed root surfaces. Access to the root surfaces for debridement may therefore be obtained with the use of comparatively sturdy instruments (Fig. 38-48). Tungsten carbide curettes and scalers with durable cutting edges are often used when "access" is not a problem. Rotating fine-grained diamond stones (Fig. 38-49) may be used

Fig. 38-49 A set of burs useful in periodontal surgery. The rotating fine-grained diamond stones may be used for debridement of infrabony defects. The round burs are used for bone recontouring.

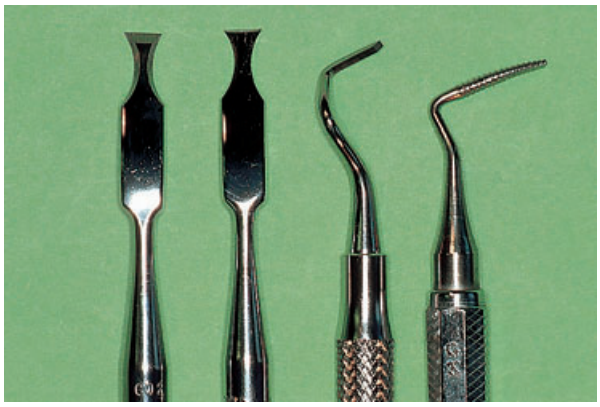

Fig. 38-50 Examples of instruments used for bone recontouring. From left to right: Bone chisels Ochsenbein no. 1 and 2 (Kirkland 13K/13KL), Bone chisel Ochsenbein no. 3, and Schluger curved file no. 9/10.

within infrabony pockets, root concavities, and entrances to furcations.

Instruments for bone removal

Sharp bone chisels or bone rongeurs (Fig. 38-50) cause the least tissue damage and should be employed whenever access permits. With reduced access, surgical burs or files may be used. The burs should operate at low speed and ample rinsing with sterile physiologic saline should ensure cooling and removal of tissue remnants.

Instruments for handling flaps

The proper healing of the periodontal wound is critical for the success of the operation. It is therefore important that the manipulations of soft tissue flaps are performed with the minimum of tissue damage. Care should be exercised in the use of periosteal elevators when flaps are deflected and retracted for optimal visibility. Surgical pliers and tissue retractors that pierce the tissues should not be used in the marginal area of the flaps. Needle holders with small beaks and atraumatic sutures should be used.

Additional equipment

Hemorrhage is rarely a problem in periodontal surgery. The characteristic oozing type of bleeding can normally be controlled by a pressure pack (sterile gauze moistened with saline). Bleeding from small vessels can be stopped by clamping and tying using a hemostat and resorbable sutures. If the vessel is surrounded by bone, bleeding may be stopped by crushing the nutrient canal in which the vessel runs with a blunt instrument.

Sterile physiologic saline is used for rinsing and moistening the field of operation and for cooling when burs are employed. The saline solution may be kept in a sterile metal cup on the instrument tray and may be applied to the wound by means of a sterile disposable plastic syringe and a needle with a blunt tip.

Visibility in the field of operation is secured by using effective suction. The lumen of the aspirator tip should have a smaller diameter than the rest of the tube, in order to prevent clogging.

The patient's head may be covered by autoclaved cotton drapings or sterile disposable plastic/paper drapings. The surgeon and all assistants should wear sterile surgical gloves, surgical mask, and surgeon's hood.

Selection of surgical technique

Many of the technical problems experienced in periodontal surgery stem from the difficulties in accurately assessing the degree and type of breakdown that has occurred prior to surgery. Furthermore, at the time of surgery, previously undiagnosed defects may be recognized or some defects may have a more complex outline than initially anticipated. Since each of the surgical procedures described above is designed to deal with a specific situation or to meet a certain objective, it must be understood that in most patients no single standardized technique alone can be applied when periodontal surgery is undertaken. Therefore, in each surgical field, different techniques are often used and combined in such a way that the overall objectives of the surgical part of the periodontal therapy are met. As a general rule, surgical modalities of therapy that preserve or induce the formation of periodontal tissue should be preferred over those that resect or eliminate tissue.

General indications for various surgical techniques

Gingivectomy

The obvious indication for gingivectomy is the presence of deep supra-alveolar pockets. In addition, the gingivectomy technique can be used to reshape abnormal gingival contours such as gingival craters and gingival hyperplasias (Fig. 38-43). In such cases the technique is often termed *gingivoplasty*.

Gingivectomy is usually not considered suitable in situations where the incision will lead to the removal of the entire zone of gingiva. This is the case when the bottom of the probeable pocket to be excised is located at or below the mucogingival junction. As an alternative in such a situation, an *internal beveled gingivectomy* may be performed (Fig. 38-51). Furthermore, since the gingivectomy procedure is aimed at the complete elimination of the periodontal pocket, the procedure cannot be used in periodontal sites where infrabony lesions or bony craters are present.

These limitations, combined with the development in recent years of surgical methods which have a broader field of application, have led to less frequent use of gingivectomy in the treatment of periodontal disease.

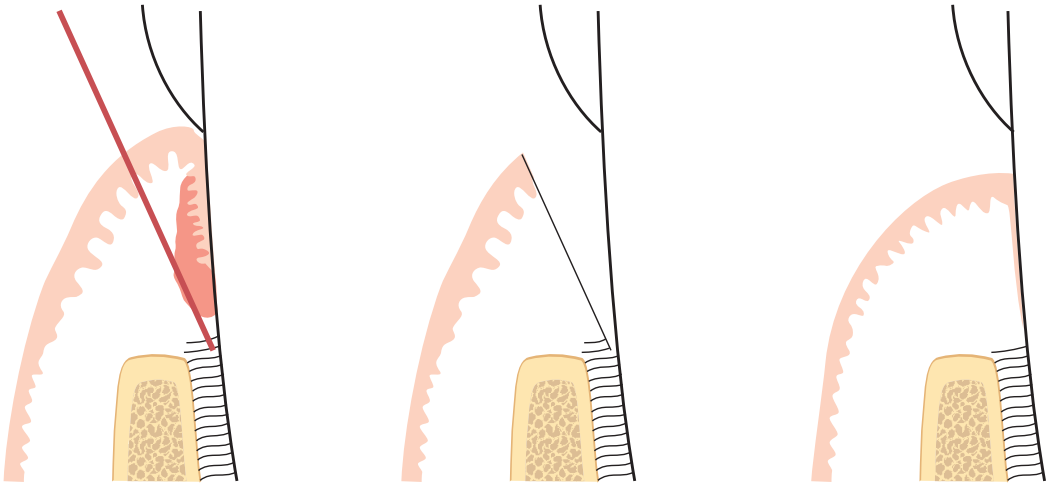

Fig. 38-51 Internal beveled gingivectomy. Schematic illustration of the incision technique in case of the presence of only a minimal zone of gingiva.

Flap operation with or without osseous surgery

Flap operations can be used in all cases where surgical treatment of periodontal disease is indicated. Flap procedures are particularly useful at sites where pockets extend beyond the muco-gingival border and/or where treatment of bony lesions and furcation involvements is required.

The advantages of flap operations include:

- Existing gingiva is preserved
- The marginal alveolar bone is exposed whereby the morphology of bony defects can be identified and the proper treatment rendered
- Furcation areas are exposed, the degree of involvement and the "tooth–bone" relationship can be identified
- The flap can be repositioned at its original level or shifted apically, thereby making it possible to adjust the gingival margin to the local conditions
- The flap procedure preserves the oral epithelium and often makes the use of surgical dressing superfluous
- The post-operative period is usually less unpleasant to the patient when compared to gingivectomy.

Treatment decisions for soft and hard tissue pockets in flap surgery

Classifications of different flap modalities used in the treatment of periodontal disease often make distinctions between methods involving the marginal tissues and those involving the muco-gingival area and, further, between tissue-eliminating/resective varieties and tissue-preserving/reconstructive types (access flaps for debridement). Such classifications appear less than precise since several techniques are often combined in the treatment of individual cases, and since there is no clear-cut relationship between disease characteristics and selection of surgical methods. From a didactic point of view it seems more appropriate to discuss surgical therapy with regard to how to deal with (1) the soft tissue component and (2) the hard tissue component of the periodontal pocket at a specific tooth site (Fig. 38-52).

Soft tissue pockets

The description of the various flap procedures reveals that, depending on the surgical technique used, the soft tissue flap should either be apically positioned at the level of the bone crest (original Widman flap, Neumann flap, and apically repositioned flap) or maintained in a coronal position (Kirkland flap, modified Widman flap, and papilla preservation flap) at the completion of the surgical intervention. The maintenance of the pre-surgical soft tissue height is of importance from an esthetic point of view, particularly in the anterior tooth region. However, long-term results from clinical trials have shown that major differences in the final position of the soft tissue margin are not evident between surgical procedures involving coronal and apical positioning of the flap margin. The reported difference in final positioning of the gingival margin between surgical techniques is attributed to osseous recontouring (Townsend-Olsen *et al*. 1985; Lindhe *et al*. 1987; Kaldahl *et al*. 1996; Becker *et al*. 2001). In many patients it may be of significance to position the flap coronally in the anterior tooth region in order to give the patient a prolonged time of adaptation to the inevitable soft tissue recession. In the posterior tooth region, however, an apical position should be the standard.

Independent of flap position, the goal should be to achieve complete soft tissue coverage of the alveolar bone, not only at buccal/lingual sites but also in proximal sites. It is therefore of utmost importance to carefully plan the incisions in such a way that this goal can be achieved at the termination of the surgical intervention.

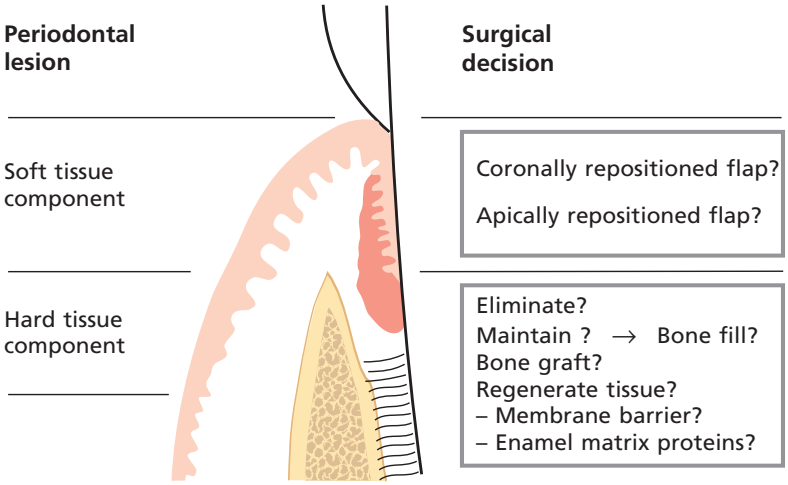

Fig. 38-52 Surgical decisions. Treatment decisions with respect to the soft and the hard tissue component of a periodontal pocket.

Hard tissue pockets

During conventional periodontal surgery one would usually opt for the conversion of an intrabony defect into a suprabony defect, which then is eliminated by apical repositioning of the soft tissues. Osseous recontouring of angular bony defects and craters are excisional techniques, which should be used with caution and discrimination. However, the therapist is often faced with the dilemma of deciding whether or not to eliminate an angular bony defect. There are a number of factors that should be considered in the treatment decision, such as:

- Esthetics
- Tooth/tooth site involved
- Defect morphology
- Amount of remaining periodontium.

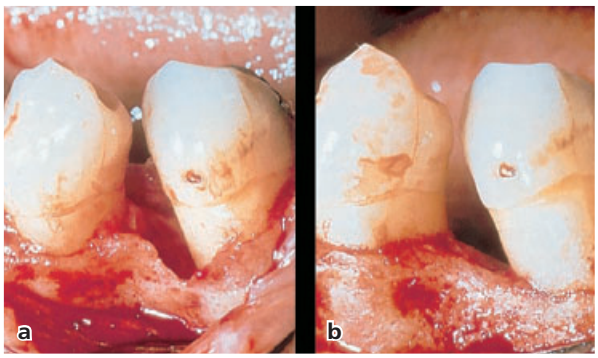

Fig. 38-53 Illustration of the amount of crestal bone resorption that may take place following a modified Widman flap procedure without bone recontouring. (a) View of the area at time of initial surgical treatment. (b) At the re-entry operation performed after 6 months of healing.

Since alveolar bone supports the soft tissue, an altered bone level through recontouring will result in recession of the soft tissue margin. For esthetic reasons one may therefore be restrictive in eliminating proximal bony defects in the anterior tooth region. For example, in the case of an approximal crater it may often be sufficient to reduce/eliminate the bone wall on the lingual side of the crater, thereby maintaining the bone support for the soft tissue on the facial aspect (Fig. 38-40). In favor of esthetics one may even have to compromise the amount of bone removal and accept that some pocket depth will remain in certain situations. In addition to esthetics, the presence of furcations may limit the extent to which bone recontouring can be performed.

Defect morphology is a variable of significance for repair/regeneration during healing (Rosling *et al*. 1976a; Cortellini *et al*. 1993, 1995a). While two- and, especially, three-wall defects may show great potential for repair/regeneration, one-wall defects and approximal craters will rarely result in such good healing. Further, the removal of intrabony connective tissue/granulation tissue during a surgical procedure will always lead to crestal resorption of bone, especially in sites with thin bony walls. This results in reduction of the vertical dimensions of the bone tissue at the site (Fig. 38-53). Thus, the potential for bone fill following a compromise in regard to osseous surgery is greater in areas with thick, non-supporting bone.

The various treatment options available for the hard tissue defect may include:

- Elimination of the osseous defect by resection of bone (osteoplasty and/or ostectomy)
- Maintenance of the area without osseous resection (hoping for some type of periodontal repair, e.g. bone fill leading to gain of clinical attachment)
- Compromising the amount of bone removal and accepting that a certain pocket depth will remain
- An attempt to improve healing through the use of a regenerative procedure
- Extract the involved tooth if the bony defect is considered too advanced.

After careful consideration, indications for osseous surgery in conjunction with apical repositioning of flaps may also include subgingival caries,

perforations or root fractures in the coronal third of the root as well as inadequate retention for fixed prosthetic restorations due to a short clinical crown (crown-lengthening procedures). The "crown lengthening" needed in such cases is performed by removing often significant amounts of supporting bone and by recontouring. A "biologic width" of approximately 3 mm between the alveolar bone crest to be established and the anticipated restoration margin must be ensured for successful results (Brägger *et al*. 1992; Herrero *et al*. 1995; Pontoriero & Carnevale 2001).

Root surface instrumentation

Before incisions are made to excise or elevate the soft tissue, a careful examination should be carried out to identify at which tooth sites periodontal lesions remain. Only tooth sites with signs of pathology (bleeding following pocket probing) should be subjected to root instrumentation following surgical exposure. Further, at these sites root surface instrumentation should be limited to that part of the root that will be covered by the soft tissue following flap replacement and suturing. This is an important consideration since instrumentation of the supragingival portion of the root may lead to post-surgical root hypersensitivity, which in turn may impede proper oral hygiene measures. Before root instrumentation is executed, therefore, remaining granulation tissue must be removed, bone recontouring is carried out, if indicated, and the post-surgical soft tissue level is determined. If the intention is to reposition the flap apically at the level of the bone crest, only approximately 3 mm of the root surface coronal to the bone crest has to be carefully scaled and root planed, whereas if the flap is to be positioned coronally the entire exposed root has to be instrumented.

The root instrumentation can be performed with hand or ultrasonic instruments according to the operator's preferences. Ultrasonic (sonic) instrumentation offers the additional benefits of improved visibility due to the irrigating effect of the cooling water. For root instrumentation within intrabony defects, root concavities, and entrances to furcations, the use of rotating fine-grained diamond stones may be used.

Root surface conditioning/biomodification

An important consideration in periodontal surgery is to make the exposed root surface biologically compatible with a healthy periodontium. This so-called conditioning includes removing bacteria, endotoxins, and other antigens found within the cementum–dentin of a pathologically exposed root. In addition to scaling and root planing, agents such as citric acid/orthophosphoric acid, tetracycline, and EDTA are used for root surface conditioning. Root surface conditioning/biomodification by means of an etching procedure may serve several purposes:

- Removal of the smear layer following mechanical debridement
- Demineralization of the root surface (citric acid)
- Selective removal of hydroxyapatite and exposure of the collagenous matrix of the root surface (EDTA)
- Local delivery of antimicrobial compound (tetracycline HCL)
- Inhibition of collagenolytic activity (tetracycline HCL)
- Enhancing cellular responses
- Preventing of epithelial down-growth
- Improving retention of different biomolecules to exposed collagen
- To express a cementoblast phenotype for colonizing cells.

It should be noted that etching of a root surface with an agent operating at a low pH, e.g. citric acid or orthophosphoric acid, might exert immediate necrotizing effects on the surrounding periodontal ligament and other periodontal tissues, whereas agents operating at a neutral pH (e.g. EDTA) do not seem to have this negative effect (Blomlöf & Lindskog 1995a,b).

Although *in vitro* results have indicated possible benefits of the use of root surface conditioning/biomodification agents through enhanced cellular responses during wound healing, the usefulness of acids as well as other chemical agents for conditioning of root surfaces in conjunction with conventional periodontal surgery has been questioned (Blomlöf *et al*. 2000). Histologic evidence indicates that healing following root surface conditioning with acids or other chemical agents is generally dominated by a long junctional epithelium or connective tissue attachment without evidence of new cementum formation. However, root surface biomodification must still be regarded as an important method to facilitate regeneration. Thus, in this treatment the root represents one of the wound margins and must provide an appropriate surface for cell attachment, colonization, and proliferation.

Suturing

When a flap procedure has been employed it is important to ensure that, at the end of surgery, the flaps are placed in the intended position and that the flaps are properly adapted to each other and to the tooth surfaces. Preferably, full coverage of the buccal/lingual (palatal) and interdental alveolar bone should be obtained by full (primary) closure of the soft tissue flaps. If this can be achieved, healing by first intention results and post-operative bone resorption is minimal. Therefore, prior to suturing, the flap margins should be trimmed to properly fit the buccal and lingual (palatal) bone margin as well as the interproximal areas; excessive soft tissue must be removed. If the amount of flap tissue present is insufficient to

cover the interproximal bone, the flaps at the buccal or lingual aspects of the teeth must be recontoured and, in some cases, even displaced coronally.

Following proper trimming, the flaps are secured in the correct position by sutures. Sutures should not interfere with incision lines and must not pass through the tissues near the flap margins or too close to a papilla, because this may result in tearing of the tissues. The use of non-irritating, mono-filamentous materials is recommended. These materials are non-resorbable and extremely inert, do not adhere to tissues, and are therefore easy to pull out. "Wicking", the phenomenon of bacteria moving along or within multi-stranded suture materials, particularly silk, is also avoided. The dimensions usually preferred are 4/0 to 5/0, but even finer suture material (6/0 or 7/0) may be used, particularly in conjunction with periodontal micro- and plastic surgical procedures. Sutures are removed after 7–14 days.

Since the flap tissue following the final preparation is thin, either curved or straight non-traumatic needles (eyeless), with a small diameter, should be used. Such needles are available as rounded (non-cutting) or with different cutting edges. In the latter case, a reverse-cutting needle should be selected.

Suturing technique

The three most frequently used sutures in periodontal flap surgery are:

- Interrupted interdental sutures
- Suspensory sutures
- Continuous sutures.

The *interrupted interdental suture* (Fig. 38-54) provides a close interdental adaptation between the buccal and lingual flaps with equal tension on both units. This type of suture is therefore not recommended when the buccal and lingual flaps are repositioned at different levels. When this technique of suturing is employed, the needle is passed through the buccal flap from the external surface, across the interdental area and through the lingual flap from the internal surface, or vice versa. When closing the suture, care must be taken to avoid tearing the flap tissues.

In order to avoid having the suture material between the mucosa and the alveolar bone in the interdental area, an alternative technique in the use of the interrupted interdental suture can be used if the flaps have not been elevated beyond the mucogingival line (Fig. 38-55). With the use of a curved needle the suture is anchored in the attached tissue on the buccal aspect of the proximal site, the suture brought to the lingual side through the proximal sites, and anchored in the attached tissue on the lingual side. The suture is then brought back to the starting point and tied (Fig. 38-55b). Hence, the suture will be lying on the surface of the interdental tissue,

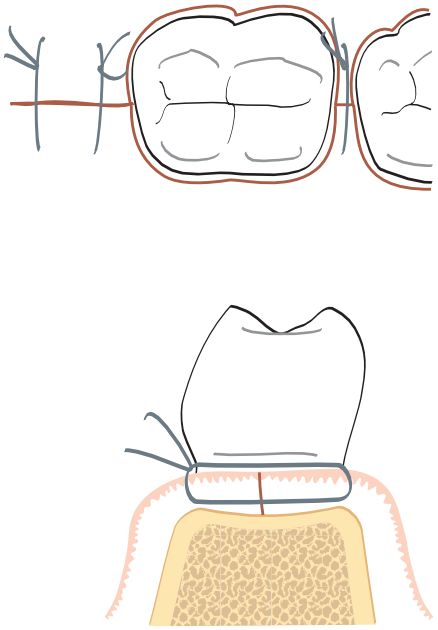

Fig. 38-54 Suturing. Interrupted interdental suture.

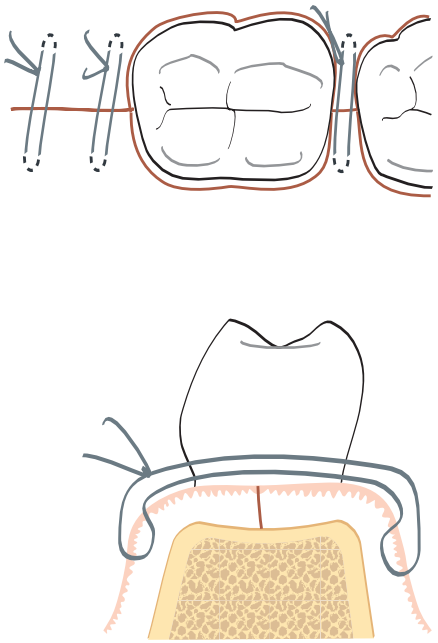

Fig. 38-55 Suturing. Modified interrupted interdental suture. Note that with this suturing technique the suture is laying on the surface of the interdental tissue keeping the soft tissue flaps in close contact with the underlying bone.

keeping the soft tissue flaps in close contact with the underlying bone.

In regenerative procedures, which usually require a coronal advancement of the flap, a *modified mattress suture* may be used to secure close flap adaptation (Fig. 38-56). The needle is passed through the buccal flap from the external surface, across the interdental area and through the lingual flap from the internal surface. The suture is run back to the buccal side by passing the needle through the lingual and buccal flaps. Thereafter, the suture is brought through the approximal site coronally to the tissue, passed

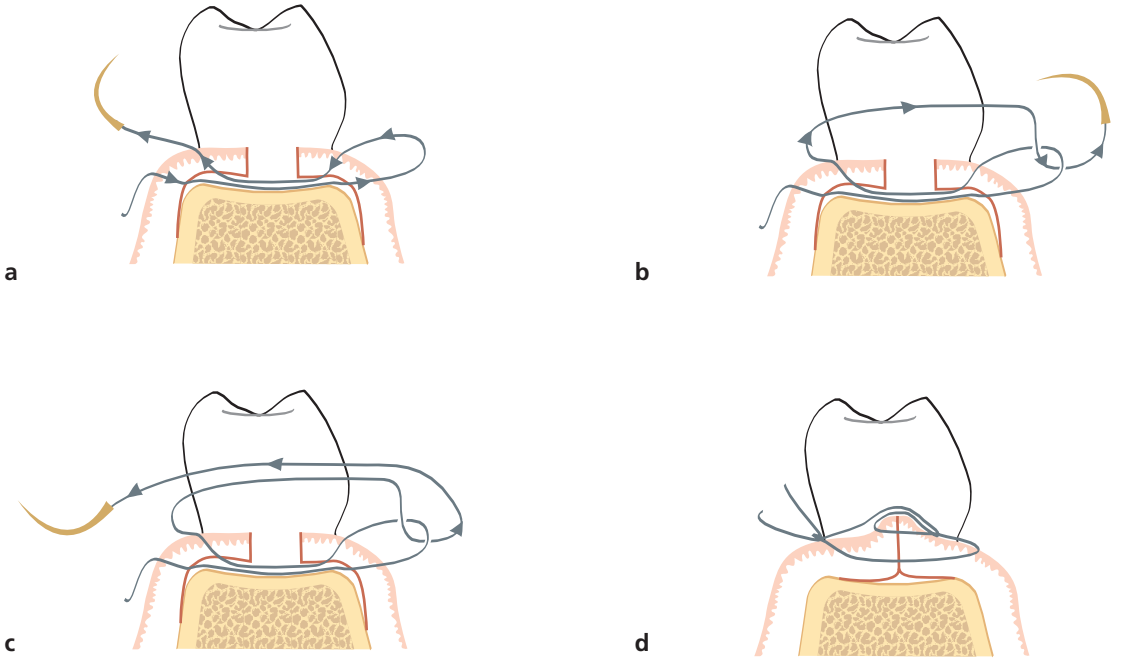

Fig. 38-56 Suturing. Modified mattress suture.

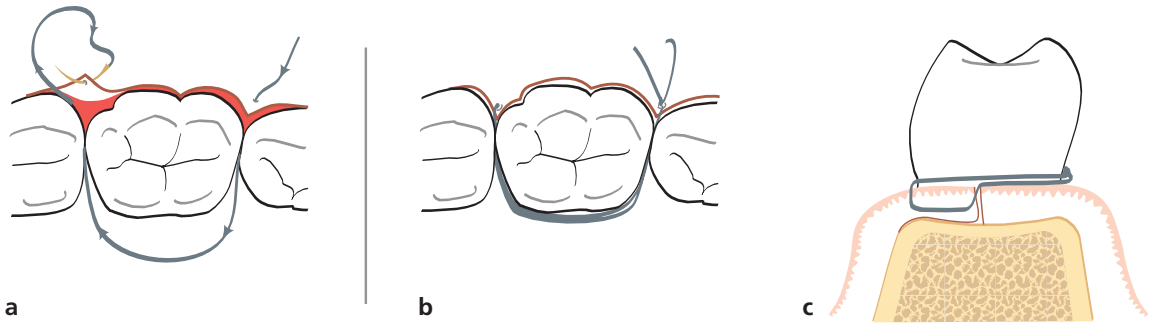

Fig. 38-57 Suturing. Suspensory suture.

through the loop of the suture on the lingual aspect, and then brought back to the starting point on the buccal side and tied.

The *suspensory suture* (Fig. 38-57) is used primarily when the surgical procedure is of limited extent and involves only the tissue of the buccal or lingual aspect of the teeth. It is also the suture of choice when the buccal and lingual flaps are repositioned at different levels. The needle is passed through the buccal flap from its external surface at the mesial side of the tooth, the suture is placed around the lingual surface of the tooth and the needle is passed through the buccal flap on the distal side of the tooth (Fig. 38-57a). The suture is brought back to the starting point via the lingual surface of the tooth and tied (Figs. 38-57b,c). If a lingual flap has been elevated as well, this is secured in the intended position using the same technique.

The *continuous suture* (Fig. 38-58) is commonly used when flaps involving several teeth are to be repositioned apically. When flaps have been elevated on both sides of the teeth, one flap at a time is secured

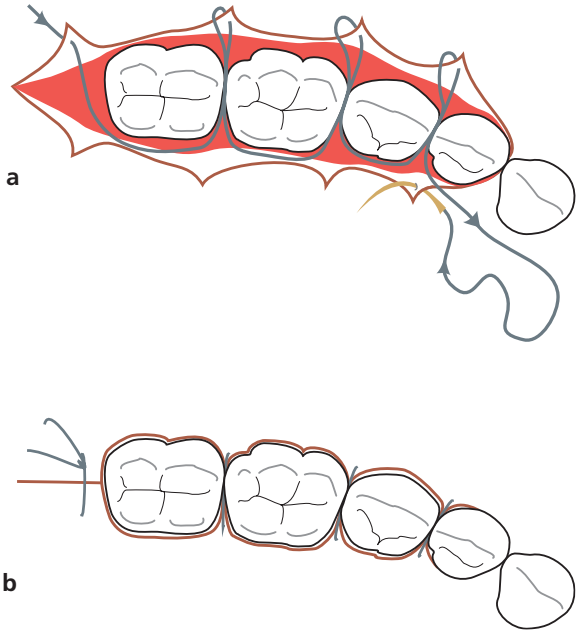

Fig. 38-58 Suturing. Continuous suture.

in its correct position. The suturing procedure is started at the mesial/distal aspect of the buccal flap by passing the needle through the flap and across the interdental area. The suture is laid around the lingual surface of the tooth and returned to the buccal side through the next interdental space. The procedure is repeated tooth by tooth until the distal/mesial end of the flap is reached. Thereafter, the needle is passed through the lingual flap (Fig. 38-58a), with the suture laid around the buccal aspect of each tooth and through each interproximal space. When the suturing of the lingual flap is completed and the needle has been brought back to the first interdental area, the positions of the flaps are adjusted and secured in their proper positions by closing the suture (Fig. 38-58b). Thus, only one knot is needed.

Periodontal dressings

Periodontal dressings are mainly used:

- To protect the wound post-surgically
- To obtain and maintain a close adaptation of the mucosal flaps to the underlying bone (especially when a flap has been repositioned apically)
- For the comfort of the patient.

In addition, periodontal dressings can prevent post-operative bleeding during the initial phase of healing and, if properly placed in the operated segment (especially interproximally), prevent the formation of excessive granulation tissue.

Periodontal dressings should have the following properties:

- The dressing should be soft, but still have enough plasticity and flexibility to facilitate its placement in the operated area and to allow proper adaptation.
- The dressing should harden within a reasonable time.
- After setting, the dressing should be sufficiently rigid to prevent fracture and dislocation.
- The dressing should have a smooth surface after setting to prevent irritation to the cheeks and lips.
- The dressing should preferably have bacteriocidal properties to prevent excessive plaque formation.
- The dressing must not detrimentally interfere with healing.

It has been suggested that antibacterial agents should be incorporated in periodontal dressings to prevent bacterial growth in the wound area during healing. Results from clinical studies and *in vitro* evaluation of the antibacterial properties of various periodontal dressings, however, suggest that the antibacterial activity of most commercial dressings probably is exhausted long before the end of the 7–14-day period during which the dressing is frequently maintained in the operated segment (O'Neil 1975; Haugen *et al*. 1977).

Mouth rinsing with antibacterial agents such as chlorhexidine does not prevent the formation of plaque *under* the dressing (Plüss *et al*. 1975) and should therefore not be regarded as a means to improve or shorten the period of wound healing. On the other hand, results from clinical studies as well as clinical experience suggest that a periodontal dressing may often be unnecessary or even undesirable after periodontal flap procedures and may be usefully replaced by rinsing with chlorhexidine only (Sanz *et al*. 1989; Vaughan & Garnick 1989).

A commonly used periodontal dressing is Coe-Pak™ (Coe Laboratories Inc., Chicago, IL, USA), which is supplied in two tubes. One tube contains oxides of various metals (mainly zinc oxide) and lorothidol (a fungicide). The second tube contains non-ionizing carboxylic acids and chlorothymol (a bacteriostatic agent). Equal parts from both tubes are mixed together immediately prior to insertion. Adding a retarder can prolong the setting time of the dressing.

A light-cured dressing, e.g. Barricaid™ (Dentsply International Inc., Milford, DE, USA), is useful in the anterior tooth region and particularly following muco-gingival surgery, because it has a favorable esthetic appearance and it can be applied without dislocating the soft tissue. However, the light-cured dressing is not the choice of dressing for situations where the flap has to be retained apically, due to its soft state before curing.

Cyanoacrylates have also been used as periodontal dressings with varying success. Dressings of the cyanoacrylate type are applied in a liquid directly on to the wound, or sprayed over the wound surface. Although the application of this kind of dressing is simple, its properties often do not meet clinical demands, which is why its use is rather limited at present.

Application technique

- Ensure that bleeding from the operated tissues has ceased before the dressing material is inserted.
- Carefully dry teeth and soft tissue before the application for optimal adherence of the dressing.
- Moisten the surgical gloves to avoid the material sticking to the fingertips.
- When using the Coe-Pak™ dressing material, the interproximal areas are filled first. Thin rolls of the dressing, adjusted in length to cover the entire field of operation, are then placed against the buccal and lingual surfaces of the teeth. The rolls are pressed against the tooth surfaces and the dressing material is forced into the interproximal areas. Coe-Pak™ may also be applied to the wound surfaces by means of a plastic syringe. It is important to ensure that dressing material is never introduced between the flap and the underlying bone or root surface.

- The surface of the dressing is subsequently smoothened and excess material is removed with a suitable instrument. The dressing should not cover more than the apical third of the tooth surfaces. Furthermore, interference of the dressing with muco-gingival structures (e.g. vestibular fold, frenula) should be carefully checked to avoid displacement of the dressing during normal function.

The light-cured dressing (Barricaid™) is preferably applied with the supplied syringe, adjusted and then cured by light. It is important to dry teeth and soft tissue carefully before application for optimal adherence. Excess of dressing material can easily be removed following curing with a knife or finishing burs in a low-speed handpiece.

Post-operative pain control

In order to minimize post-operative pain and discomfort for the patient, surgical handling of the tissues should be as atraumatic as possible. Care should be taken during surgery to avoid unnecessary tearing of the flaps, to keep the bone moistened, and to secure complete soft tissue coverage of the alveolar bone at suturing. With a carefully performed surgical procedure most patients will normally experience only minimal post-operative problems. The pain experience is usually limited to the first days following surgery and of a level that in most patients can be adequately controlled with normally used drugs for pain control. However, it is important to recognize that pain threshold level is subjective and may vary between individuals. It is also important to give the patient information about the post-surgical sequence and that uncomplicated healing is the common event. Further, during the early phase of healing, the patient should be instructed to avoid chewing in the area subjected to surgical treatment.

Post-surgical care

Post-operative plaque control is the most important variable in determining the long-term result of periodontal surgery. Provided proper post-operative infection control levels are established, most surgical treatment techniques will result in conditions that favor the maintenance of a healthy periodontium. Although there are other factors of a more general nature affecting surgical outcome (e.g. the systemic status of the patient at time of surgery and during healing), disease recurrence is an inevitable complication, regardless of surgical technique used, in patients not given proper post-surgical and maintenance care.

Since self-performed oral hygiene is often associated with pain and discomfort during the immediate post-surgical phase, regularly performed professional tooth cleaning is a more effective means of mechanical infection control following periodontal surgery. In the immediate post-surgical period self-performed rinsing with a suitable antiplaque agent, e.g. twice daily rinsing with 0.1–0.2% chlorhexidine solution, is recommended. Although an obvious disadvantage with the use of chlorhexidine is the staining of teeth and tongue, this is usually not a deterrent for compliance. Nevertheless, it is important to return to and maintain good mechanical oral hygiene measures as soon as possible. This is especially important since rinsing with chlorhexidine, in contrast to properly performed mechanical oral hygiene, is not likely to have any influence on subgingival recolonization of plaque.

Maintaining good post-surgical wound stability is another important factor affecting the outcome of some types of periodontal flap surgery. If wound stability is judged an important part of a specific procedure, the procedure itself as well as the post-surgical care must include measures to stabilize the healing wound (e.g. adequate suturing technique, protection from mechanical trauma to the marginal tissues during the initial healing phase). If a muco-periosteal flap is replaced rather than repositioned apically, early apical migration of gingival epithelial cells will occur as a consequence of a break between root surface and healing connective tissue. Hence, maintenance of a tight adaptation of the flap to the root surface is essential and one may therefore consider keeping the sutures in place for longer than the 7–10 days usually prescribed following standard flap surgery.

Following suture removal, the surgically treated area is thoroughly irrigated with a dental spray and the teeth are carefully cleaned with a rubber cup and polishing paste. If the healing is satisfactory for starting mechanical tooth cleaning, the patient is instructed in gentle brushing of the operated area using a toothbrush that has been softened in hot water. Toothpicks are prescribed for cleaning the interdental area. In this early phase following surgical treatment the use of interdental brushes is abandoned due to the risk of traumatizing the interdental tissues. Visits are scheduled for supportive care at 2-week intervals to monitor the patient's plaque control closely. During this post-operative maintenance phase, adjustments of the methods for optimal self-performed mechanical cleaning are made depending on the healing status of the tissues. The time interval between visits for supportive care may gradually be increased, depending on the patient's plaque control standard.

Outcome of surgical periodontal therapy

Healing following surgical pocket therapy

Gingivectomy

Within a few days following excision of the inflamed gingival soft tissues coronal to the base of the peri-

odontal pocket, epithelial cells start to migrate over the wound surface. The epithelialization of the gingivectomy wound is usually complete within 7–14 days following surgery (Engler *et al*. 1966; Stahl *et al*. 1968). During the following weeks a new dentogingival unit is formed (Fig. 38-59). The fibroblasts in the supra-alveolar tissue adjacent the tooth surface proliferate (Waerhaug 1955) and new connective tissue is laid down. If the wound healing occurs in the vicinity of a plaque-free tooth surface, a free gingival unit will form which has all the characteristics of a normal free gingiva (Hamp *et al*. 1975). The height of the newly formed free gingival unit may vary not only between different parts of the dentition but also from one tooth surface to another due to primarily anatomic factors.

The re-establishment of a new, free gingival unit by coronal regrowth of tissue from the line of the "gingivectomy" incision implies that sites with so-called "zero pockets" only occasionally occur following gingivectomy. Complete healing of the gingivectomy wound takes 4–5 weeks, although by clinical inspection the surface of the gingiva may appear to be healed already after approximately 14 days (Ramfjord *et al*. 1966). Minor remodeling of the alveolar bone crest may also occur post-operatively.

The apically repositioned flap

Following osseous surgery for elimination of bony defects and the establishment of "physiologic contours" and repositioning of the soft tissue flaps to the level of the alveolar bone, healing will occur primarily by first intention, especially in areas where proper soft tissue coverage of the alveolar bone has been obtained. During the initial phase of healing, bone resorption of varying degrees almost always occurs in the crestal area of the alveolar bone (Fig. 38-60)

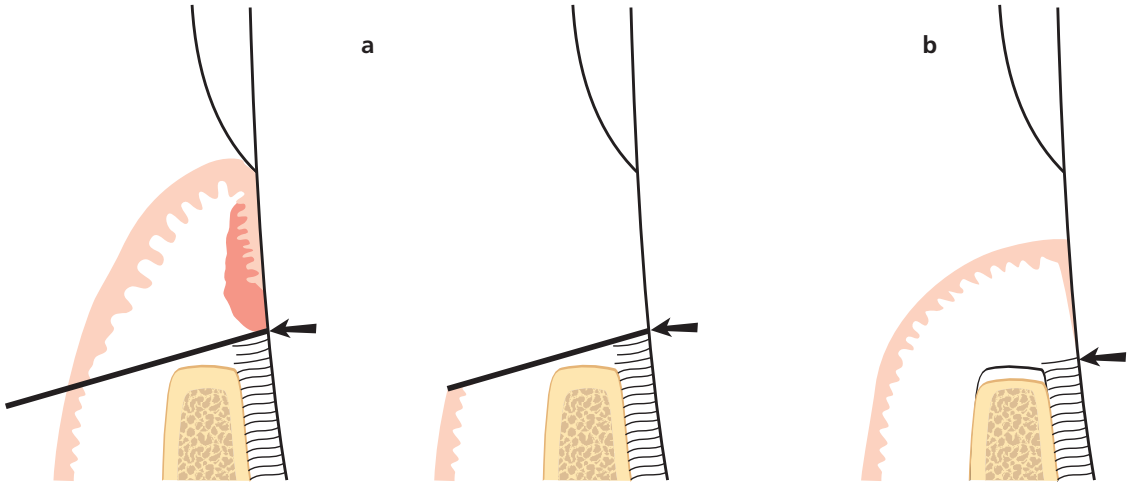

Fig. 38-59 Gingivectomy. Dimensional changes as a result of therapy. (a) The pre-operative dimensions. The black line indicates the location of the primary incision, i.e. the suprabony pocket is eliminated with the gingivectomy technique. (b) Dimensions following proper healing. Minor resorption of the alveolar bone crest as well as some loss of connective tissue attachment may occur during the healing.

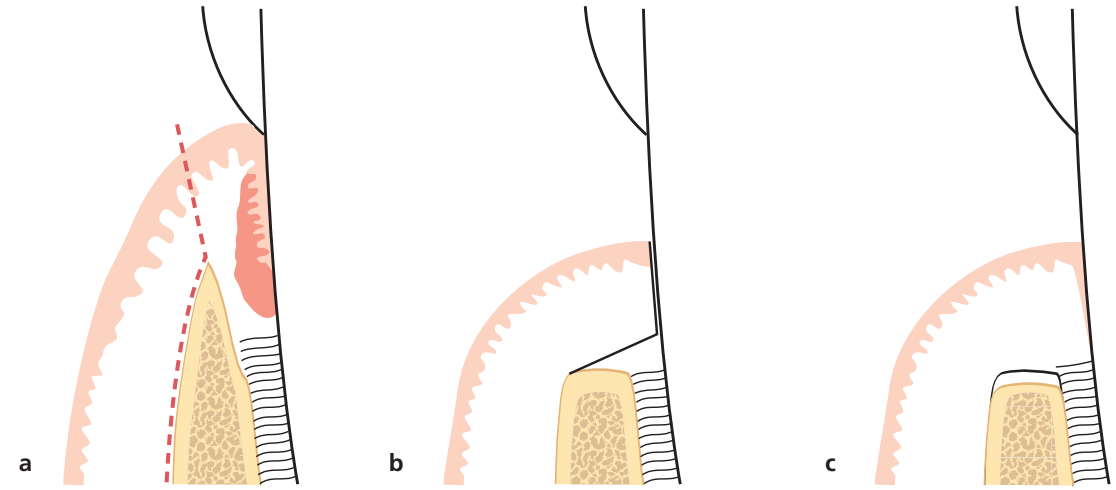

Fig. 38-60 Apically repositioned flap. Dimensional changes. (a) The pre-operative dimensions. The broken line indicates the border of the elevated mucoperiosteal flap. (b) Bone recontouring has been completed and the flap repositioned to cover the alveolar bone. (c) Dimensions following healing. Minor resorption of the marginal alveolar bone has occurred as well as some loss of connective tissue attachment.

(Ramfjord & Costich 1968). The extent of the reduction of the alveolar bone height resulting from this resorption is related to the thickness of the bone in each specific site (Wood *et al*. 1972; Karring *et al*. 1975).

During the phase of tissue regeneration and maturation a new dentogingival unit will form by coronal growth of the connective tissue. This regrowth occurs in a manner similar to that which characterized healing following gingivectomy.

The modified Widman flap

If a "modified Widman flap" procedure is carried out in an area with a deep infrabony lesion, bone repair may occur within the boundaries of the lesion (Rosling *et al*. 1976a; Polson & Heijl 1978). However, crestal bone resorption is also seen. The amount of bone fill obtained is dependent upon (1) the anatomy of the osseous defect (e.g. a three-walled infrabony defect often provides a better mould for bone repair than two- or one-walled defects), (2) the amount of crestal bone resorption, and (3) the extent of chronic inflammation, which may occupy the area of healing. Interposed between the regenerated bone tissue and the root surface, a long junctional epithelium is always found (Fig. 38-61) (Caton & Zander 1976; Caton *et al*. 1980). The apical cells of the newly formed junctional epithelium are found at a level on the root that closely coincides with the presurgical attachment level.

Soft tissue recession will take place during the healing phase following a modified Widman flap procedure. Although the major apical shift in the position of the soft tissue margin will occur during the first 6 months following the surgical treatment (Lindhe *et al*. 1987), the soft tissue recession may often continue for a time period of more than 1 year. Among factors influencing the degree of soft tissue recession as well as the time period for soft tissue remodeling are the initial height and thickness of the supracrestal flap tissue and the amount of crestal bone resorption.

Clinical outcome of surgical access therapy in comparison to non-surgical therapy

Surgical treatment of periodontal lesions mainly serves the purpose of (1) creating accessibility for proper professional debridement of the infected root surfaces and (2) establishing a gingival morphology that facilitates the patient's self-performed plaque control, in order to enhance the long-term preservation of the dentition. Hence, the amount of tooth loss would be the most relevant criterion in an evaluation of the relative importance of surgical access therapy in the overall treatment of periodontal disease. However, this would require studies with extremely long follow-up periods and, therefore, other criteria are commonly used to evaluate the efficacy of periodontal therapy, even if these may only be considered as surrogate end-points. The most commonly used outcome criteria in clinical research have been resolution of gingivitis (bleeding on probing), probing pocket depth reduction, and clinical attachment level change. An additional variable often of concern is gingival recession, since this outcome variable may affect the patient's overall appreciation of the treatment result. With regard to changes in probing attachment levels, it should be recalled that healing following conventional surgical access therapy consistently results in the formation of a junctional epithelium to a level on the root that closely coincides with the presurgical attachment level. Hence, when

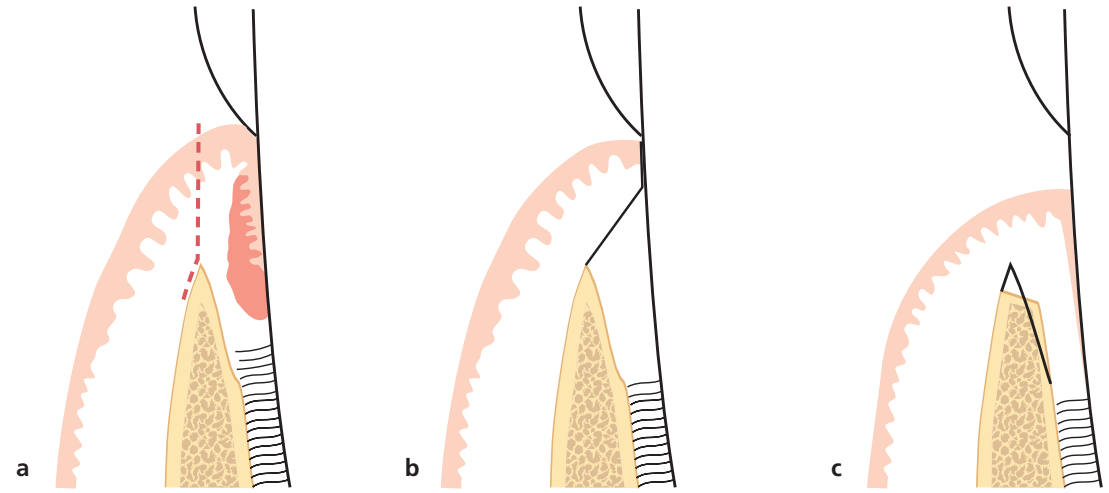

Fig. 38-61 Modified Widman flap. Dimensional changes. (a) The pre-operative dimensions. The broken line indicates the border of the elevated mucoperiosteal flap. (b) Surgery (including currettage of the angular bone defect) is completed with the mucoperiosteal flap repositioned as close as possible to its presurgical position. (c) Dimensions following healing. Osseous repair as well as some crestal bone resorption can be expected during healing with the establishment of a "long" junctional epithetium interposed between the regenerated bone tissue and the root surface. An apical displacement of the soft tissue margin has occurred.

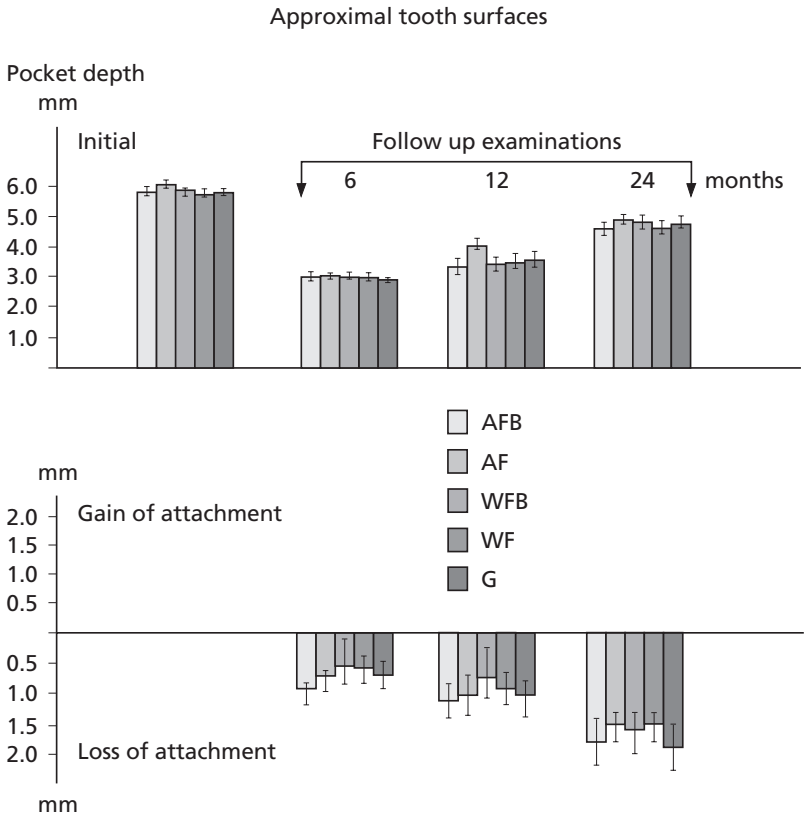

Fig. 38-62 Average approximal pocket depth at the initial examination and 6, 12, and 24 months after surgery (top) and alterations in approximal attachment levels from the initial examination immediately prior to surgery to the re-examinations 6, 12, and 24 months post-operatively (bottom). Note that only areas with pockets that at the initial examination had a depth of 3 mm or more are included in the analysis. I = standard error; AFB = apically repositioned flap with bone recontouring; AF = apically repositioned flap; WFB = modified Widman flap with bone recontouring; WF = modified Widman flap; G = gingivectomy including curettage of bone defects. (Data from Nyman *et al.* 1977.)

evaluating the outcome of various therapeutic approaches the magnitude of *gain* of clinical attachment may be of less importance since it mainly is a measure of "pocket closure". Instead maintained probing attachment levels or further loss should be focused on as the pertinent outcome variable.

Pioneering contributions to the understanding of the relative importance of the surgical component of periodontal therapy were generated by the classical longitudinal studies by the Michigan group (Ramfjord and co-workers) and the Gothenburg group (Lindhe and co-workers). Subsequently, several other clinical research centers contributed with important data regarding the efficacy of surgical access therapy in comparison to non-surgical periodontal therapy. The topic has been extensively reviewed in several recent publications (e.g. Kaldahl *et al*. 1993; Palcanis 1996) and some of the general conclusions from these reviews will be highlighted below.

Plaque accumulation

An important factor to consider in the evaluation of the relative effect of the surgical component of periodontal therapy is the standard of post-operative infection control. Nyman *et al*. (1977) reported on a clinical study in which the patients received only a single episode of oral hygiene instruction before the surgical treatment and no specific post-operative supportive care. As a consequence both plaque and gingival indices remained relatively high during the 2 years of post-operative follow-up. Independent of surgical technique used, the patients showed a rebound of pocket depths to more or less pre-treatment levels and further deterioration of clinical attachment levels at both proximal and lingual tooth sites (Fig. 38-62). In contrast, in a parallel study in which the patients received repeated oral hygiene instructions and professional tooth-cleaning once every 2 weeks during the post-operative period (Rosling *et al*. 1976b), the patients maintained the surgically reduced pocket depth throughout the 2-year follow-up period and clinical attachment level gains were observed for most of the surgical procedures evaluated (Fig. 38-63). The fact that the standard of post-operative oral hygiene is decisive for the outcome of surgical pocket therapy is further underlined by data from a 5-year longitudinal study by Lindhe *et al*. (1984), which showed that patients with a high standard of infection control maintained clinical attachment levels and probing depth reductions following treatment more consistently than patients with poor plaque control. On the other hand, professional tooth cleaning, including subgingival scaling every 3 months, may partly compensate for the negative effects of variations in self-performed plaque control (Ramfjord *et al*. 1982; Isidor & Karring 1986).

With regard to post-treatment plaque accumulation, there is no evidence to suggest that differences exist between non-surgical or surgical treatment or between various surgical procedures. In addition, most studies have shown that the magnitude of gingivitis resolution is not influenced by the treatment modality.

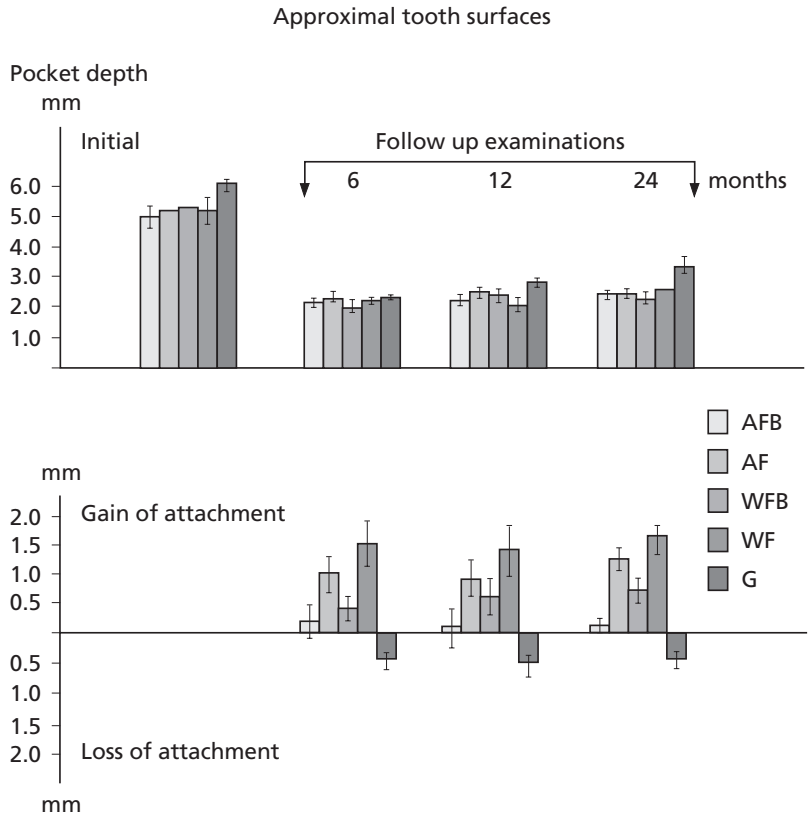

Fig. 38-63 Average approximal pocket depth at the initial examination and 6, 12, and 24 months after surgery (top) and alterations in approximal attachment levels from the initial examination immediately prior to surgery to the re-examinations 6, 12, and 24 months post-operatively (bottom). Note that only areas with pockets that at the initial examination had a depth of 3 mm or more are included in the analysis. I = standard error; AFB = apically repositioned flap with bone recontouring; AF = apically repositioned flap; WFB = modified Widman flap with bone recontouring; WF = modified Widman flap; G = gingivectomy including curettage of bone defects. (Data from Rosling *et al.* 1976b.)

Probing pocket depth reduction

All surgical procedures result in a decrease in probing pocket depths with greater reduction occurring at initially deeper sites (Knowles *et al.* 1979; Lindhe *et al.* 1984; Ramfjord *et al.* 1987; Kaldahl *et al.* 1996; Becker *et al.* 2001). Furthermore, surgical therapy generally creates greater short-term reduction of probing depth than non-surgically performed scaling and root planing. Flap surgery with bone recontouring (pocket elimination surgery) usually results in the most pronounced short-term pocket reduction. Long-term (5–8 years) results show various outcomes. Some studies reported greater probing depth reduction following surgery while others reported no differences in relation to non-surgical therapy. Also, the magnitude of the initial probing depth reduction shows a tendency to decrease with time, independent of treatment modality.

Clinical attachment level change

In sites with shallow initial probing depth, both short- and long-term data demonstrate that surgery creates a greater loss of clinical attachment than non-surgical treatment, whereas in sites with initially deep pockets (≥7 mm), a greater gain of clinical attachment is generally obtained (Knowles *et al.* 1979; Lindhe *et al.* 1984; Ramfjord *et al.* 1987; Kaldahl *et al.* 1996; Becker *et al.* 2001) (Fig. 38-64). When clinical attachment levels following surgery with and without osseous resection were compared, either no difference was found between therapies, or flap surgery without osseous resection produced a greater gain. In addition, there was no difference in the longitudinal maintenance of clinical attachment levels between sites treated non-surgically and those treated surgically, with or without osseous resection.

Based on data generated from a clinical trial comparing non-surgical and surgical (modified Widman flap) approaches to root debridement, Lindhe *et al.* (1982b) developed the concept of *critical probing depth* in relation to clinical attachment level change. For each treatment approach, the clinical attachment change was plotted against the initial pocket depth and regression lines were calculated (Fig. 38-65). The point where the regression line crossed the horizontal axis (initial probing depth) was defined as the *critical probing depth* (CPD), i.e. the level of pocket depth below which clinical attachment loss would occur as the result of the treatment procedure performed. The CPD was consistently found to be greater for the surgical approach than for the non-surgical treatment. Furthermore, at incisors and premolars the surgical therapy showed superior outcome only when the initial probing depth was greater than 6–7 mm, while at molars the corresponding cut-off point was 4.5 mm. The interpretation of the latter finding would be that, in the molar tooth regions, the surgical approach to root debridement offers advantages over the non-surgical approach. This interpretation is supported by the observation that inferior results are obtained by non-surgical therapy in molars compared to single-rooted teeth (Nordland *et al.*

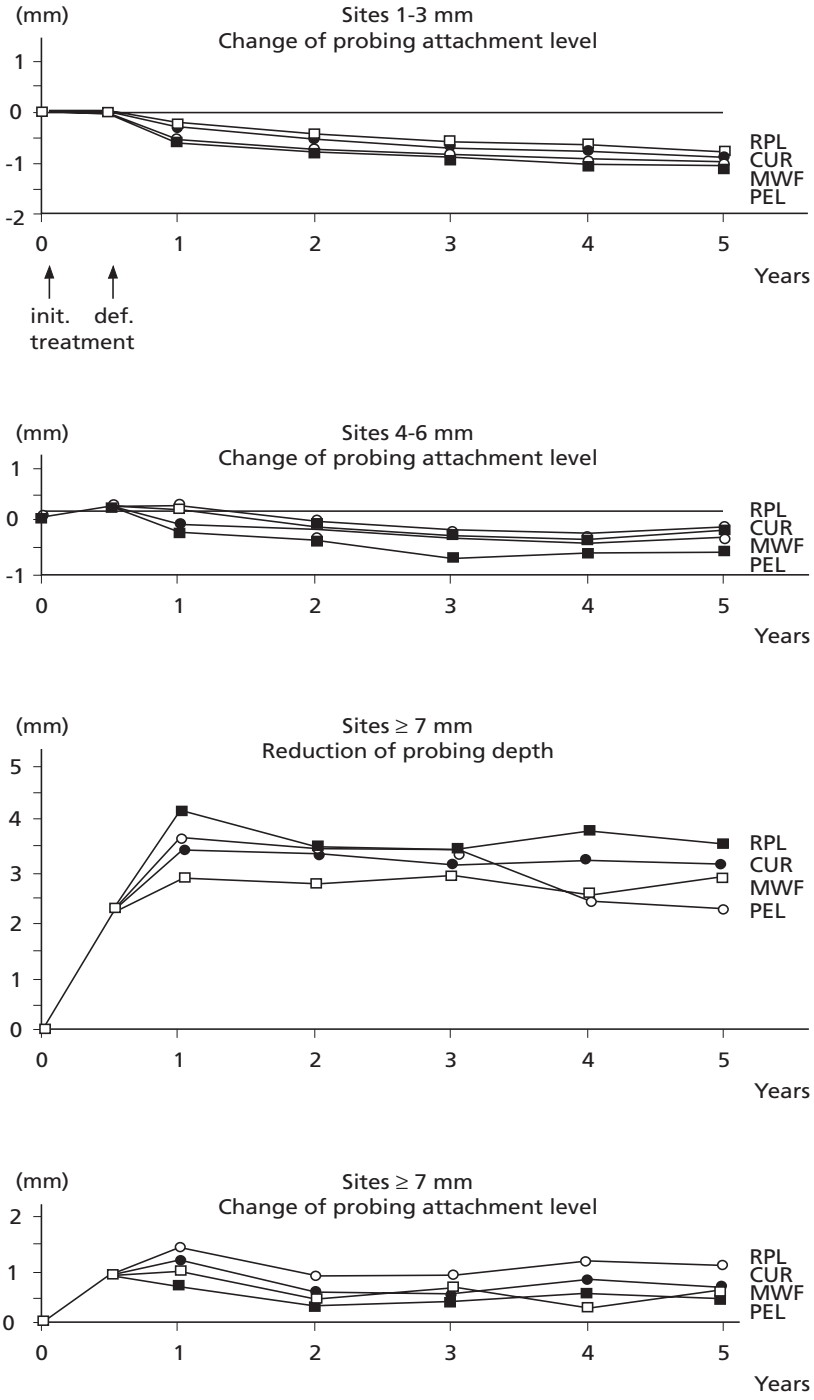

Fig. 38-64 Longitudinal evaluation of four treatment modalities in the three categories of initial probing depth; 1–3 mm, 4–6 mm and ≥7 mm. RPL = scaling and root planning; CUR = subgingival curettage; MWF = modified Widman flap; PEL = pocket elimination surgery. (Data from Ramfjord *et al*. 1987, presented by Egelberg 1995.)

1987; Loos *et al*. 1988). Also data generated from studies comparing closed and open root debridement in furcation sites favor surgical access therapy in the treatment of molar tooth regions (Matia *et al*. 1986).

The removal of the pocket epithelium and the soft tissue lesion by curettage (Echeverria & Caffesse 1983; Ramfjord *et al*. 1987) or surgical excision (Lindhe & Nyman 1985) is not a prerequisite for proper healing of the treated periodontal site. In the study by Lindhe and Nyman (1985) three treatment modalities were used, i.e. excision of the soft tissue lesion during flap surgery (modified Widman flap procedure), surgery without removal of the soft tissue lesion (Kirkland flap), and non-surgical scaling and root planing. The 1-year follow-up examination revealed about 1 mm of gain in clinical attachment level for all three procedures. Thus, deliberate excision of the soft tissue lesion did not improve the healing result.

Gingival recession

Gingival recession is an inevitable consequence of periodontal therapy. Since it occurs primarily as a result of resolution of the inflammation in the periodontal tissues, it is seen both following non-surgical and surgical therapy. Irrespective of treatment modality used, initially deeper pocket sites will experience

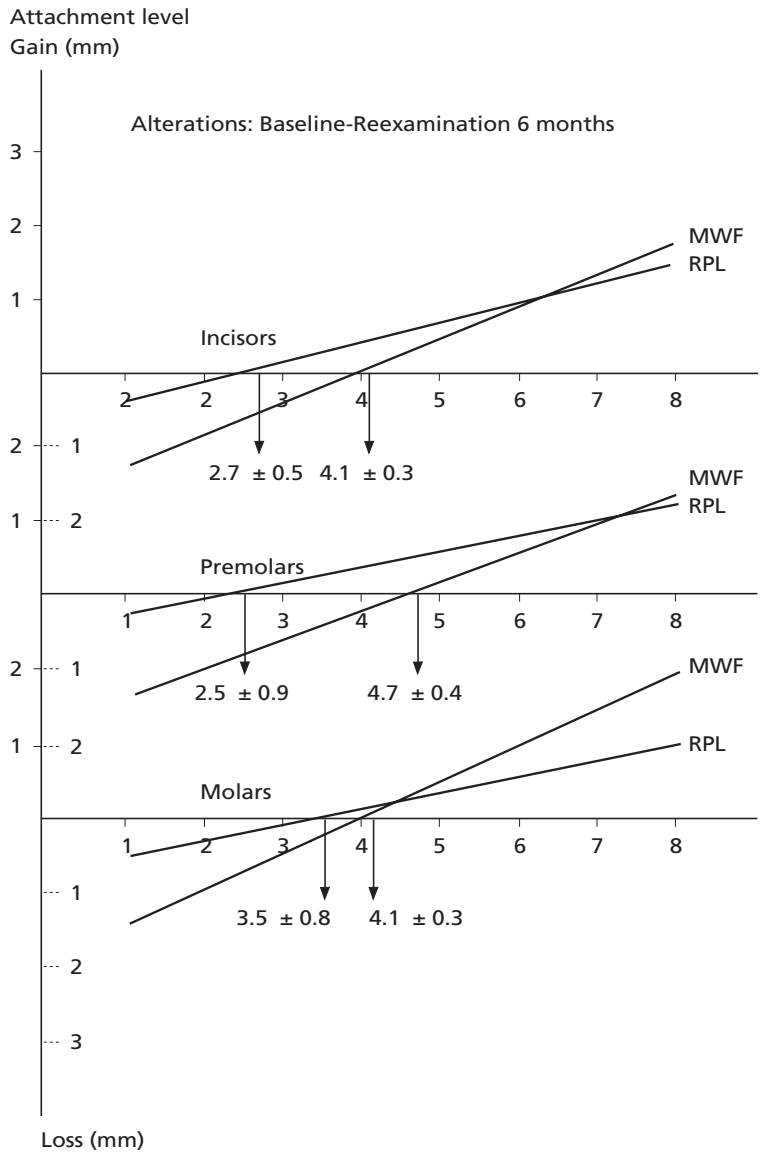

Fig. 38-65 Diagram illustrating the gain and loss of clinical attachment (Y-axis) at incisors, premolars, and molars, calculated from measurements taken prior to and 6 months after treatment. RPL = scaling and root planning; MWF = modified Widman flap surgery. The non-surgical approach (RPL) consistently yielded lower critical probing depth (CPD) values than the surgical approach. (Data from Lindhe *et al*. 1982b.)

more pronounced signs of recession of the gingival margin than sites with shallow initial probing depths (Badersten *et al*. 1984; Lindhe *et al*. 1987; Becker *et al*. 2001).

A general finding in short-term follow-up studies of periodontal therapy is that non-surgically performed scaling and root planing causes less gingival recession than surgical therapy, and that surgical treatment involving osseous resection results in the most pronounced recession. However, data obtained from long-term studies reveal that the initial differences seen in amount of recession between various treatment modalities diminish over time due to a coronal rebound of the soft tissue margin following surgical treatment (Kaldahl *et al*. 1996; Becker *et al*. 2001) (Fig. 38-66). Lindhe and Nyman (1980) found that after an apically repositioned flap procedure the buccal gingival margin shifted to a more coronal position (about 1 mm) during 10–11 years of maintenance. In interdental areas denuded following surgery, van der Velden (1982) found an upgrowth of around 4 mm of gingival tissue 3 years after surgery, while no significant change in attachment levels was observed. A similar finding was reported by Pontoriero and Carnevale (2001) 1 year after an apically positioned flap procedure for crown lengthening.

Bone fill in angular bone defects

The potential for bone formation in angular defects following surgical access therapy has been demonstrated in a number of studies. Rosling *et al*. (1976a) studied the healing of two- and three-wall angular bone defects following a modified Widman flap procedure, including careful curettage of the bone defect and proper root debridement, in 24 patients with multiple osseous defects. Following active treatment, patients assigned to the test group received supportive periodontal care once every 2 weeks for a 2-year period, while the patients in the control group were only recalled once a year for prophylaxis. Re-examination carried out 2 years after therapy demonstrated that the patients who had been subjected to the inten-

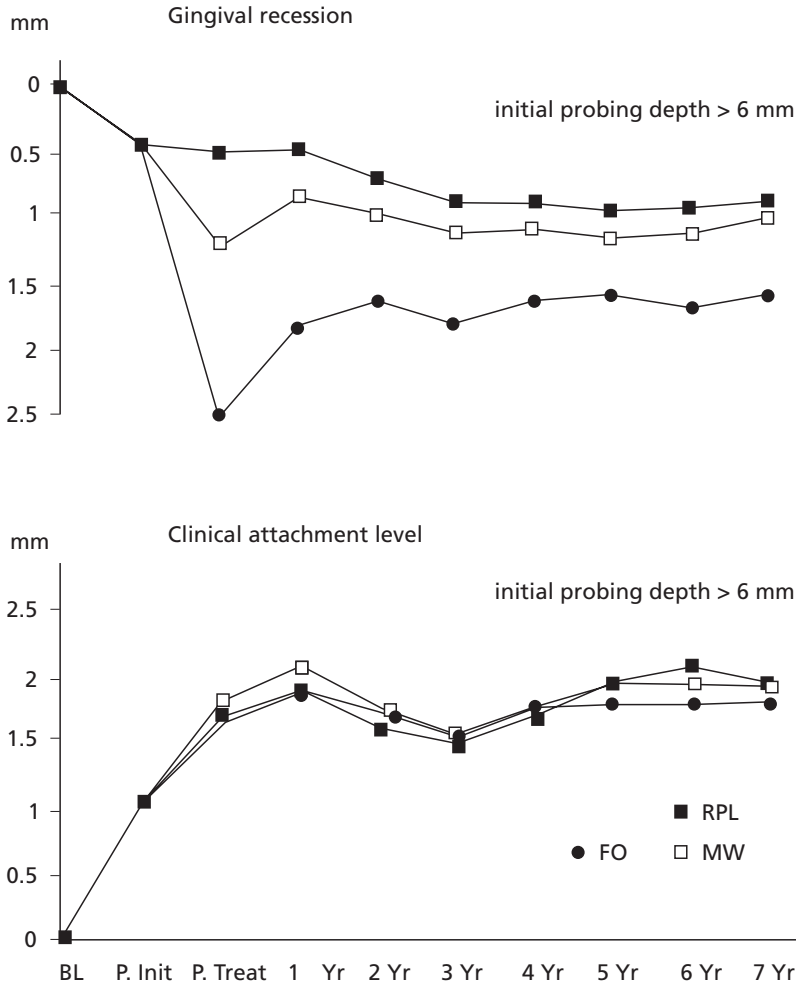

Fig. 38-66 Longitudinal changes over 7 years in recession (top diagram) and clinical attachment levels (bottom diagram) at sites with initial probing pocket depth of >6 mm following three different periodontal treatment modalities. RPL = scaling and root planning; MWF = modified Widman flap procedure; FO = flap and osseous surgery. (Data from Kaldahl *et al*. 1996.)

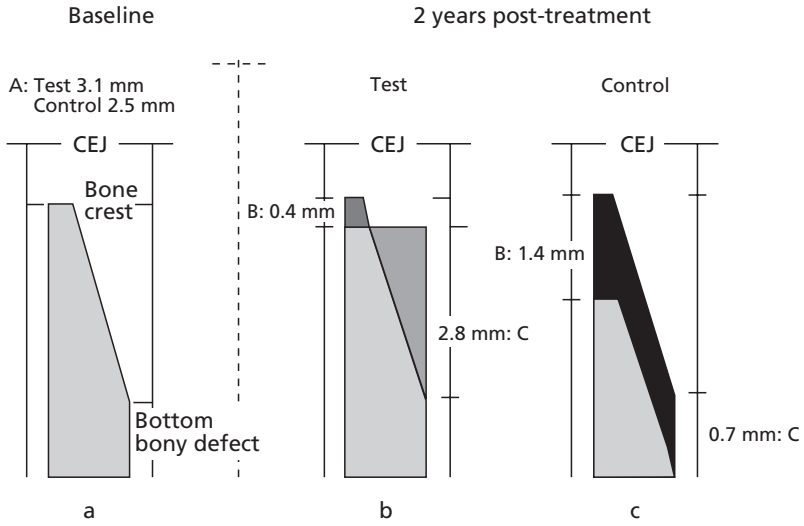

Fig. 38-67 Schematic drawing illustrating alterations in the level of the marginal bone crest and the level of the bottom of the bone defects in the test and control groups of the study by Rosling *et al*. (1976a). Distance A denotes the depth of the bone defects at the initial examination; test group 3.1 mm, control 2.5 mm. Distance B denotes resorption of the alveolar crest (b,c), which amounted to 0.4 mm in the test patients (b) and 1.4 mm in the controls (c). Distance C denotes gain or loss of bone in the apical portion of the defect. There was a refill of bone in the test patients (b) amounting to 2.8 mm, whereas a further 0.7 mm loss of bone occurred in the control patients (c).

sive professional tooth-cleaning regimen had experienced a mean gain of clinical attachment in the angular bone defects amounting to 3.5 mm. Measurements performed on radiographs revealed a marginal bone loss of 0.4 mm, but the remaining portion of the original bone defect (2.8 mm) was refilled with bone (Fig. 38-67). All the 124 bone defects treated were completely resolved. In the control group most of the sites treated showed signs of recurrent periodontitis, including further loss of clinical attachment and alveolar bone. Similar healing results were reported by Polson and Heijl (1978). They treated 15 defects (two- and three-wall) in nine patients using a modified Widman flap procedure. Following curettage of the bone defect and root planing, the flaps were closed to achieve complete soft tissue coverage of the defect area. All patients were enrolled in a professional tooth-cleaning program. The healing was evaluated

at a re-entry operation 6–8 months after the initial surgery. Eleven of the 15 defects had resolved completely. The healing was characterized by a combination of coronal bone regeneration (77% of the initial depth of the defects) and marginal bone resorption (18%). The authors concluded that intrabony defects might predictably remodel after surgical debridement and establishment of optimal plaque control.

The results from the studies referred to demonstrate that a significant bone fill may be obtained in two- and three-wall intrabony defects at single-rooted teeth, provided the post-operative supportive care is of very high quality. Two recent reviews (Laurell *et al*. 1998; Lang 2000), focusing on the outcome of surgical access therapy in angular bone defects, give additional information regarding expected bone regeneration in angular defects following open-flap debridement (modified Widman flap). In the review by Laurell *et al*. (1998) 13 studies were included representing a total of 278 treated defects with a mean depth of 4.1 mm. The weighted mean bone fill in the angular defects amounted to 1.1 mm. Lang (2000) reported an analysis of 15 studies providing data generated from radiographic assessments of the healing of 523 angular bone defects. The analysis yielded a weighted mean of 1.5 mm of bone gain. Since the included studies in these reviews showed great variability in bone fill, one may assume that the standard of post-surgical plaque control varied between the studies. As shown in the study by Rosling *et al*. (1976a), meticulous post-surgical plaque control and close professional supervision of the patients are critical for optimal healing conditions. One also has to consider that the potential for bone fill may differ depending on the morphology of the angular bone defect. Most angular defects appear as combinations of one-, two- and three-wall defects and whereas the two- and three-wall component of an angular bone defect may show great potential for bone fill during healing, the one-wall component will rarely demonstrate this type of healing.

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Chapter 39

Treatment of Furcation-Involved Teeth

Gianfranco Carnevale, Roberto Pontoriero, and Jan Lindhe

Detailed knowledge of the morphology of the multi-rooted teeth and their position in the dental arch is a fundamental prerequisite for a proper understanding of problems which may occur when such teeth become involved in destructive periodontal disease. The first part of this chapter therefore includes a brief description of some important anatomic features of the root complexes and related structures of premolars and molars.

Terminology

Root complex is the portion of a tooth that is located apical to the cemento-enamel junction (CEJ), i.e. the portion that normally is covered with a root cementum. The root complex may be divided into two parts: the *root trunk* and the *root cone(s)* (Fig. 39-1).

The *root trunk* represents the *undivided region* of the root. The height of the root trunk is defined as the distance between the CEJ and the separation line (furcation) between two root cones (roots). Depending on the position of the separation line the height of the root trunk may vary from one surface to the next in one given molar or premolar.

The *root cone* is included in the *divided region* of the root complex. The root cone (root) may vary in size and position and may at certain levels be connected to or separated from other root cones. Two or more root cones make up the *furcated region* of the root complex (Fig. 39-2a). The *furcation* is the area located between individual root cones.

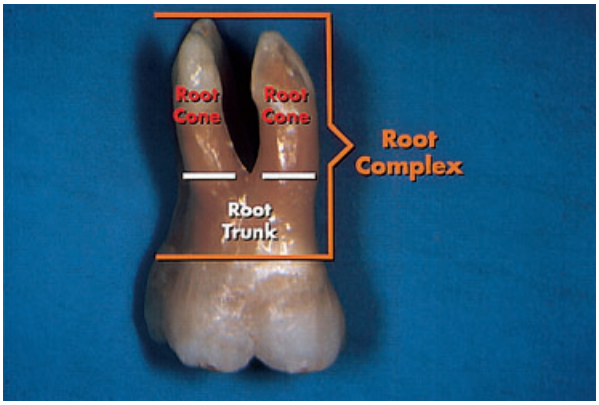

Fig. 39-1 Root complex of a maxillary molar. The root complex is separated into one undivided region: the root trunk, and one divided region: the (three) root cones.

The *furcation entrance* is the transitional area between the undivided and the divided part of the root (Fig. 39-2a,b). The *furcation fornix* is the roof of the furcation (Fig. 39-2b).

The d*egree of separation* is the angle of separation between two roots (cones) (Fig. 39-3a). *Divergence* is the distance between two roots; this distance normally increases in apical direction (Fig. 39-3a). The *coefficient of separation* is the length of the root cones in relation to the length of the root complex (Fig. 39-3b).

Fusion between divergent root cones may occur. The fusion may be complete or incomplete. In the

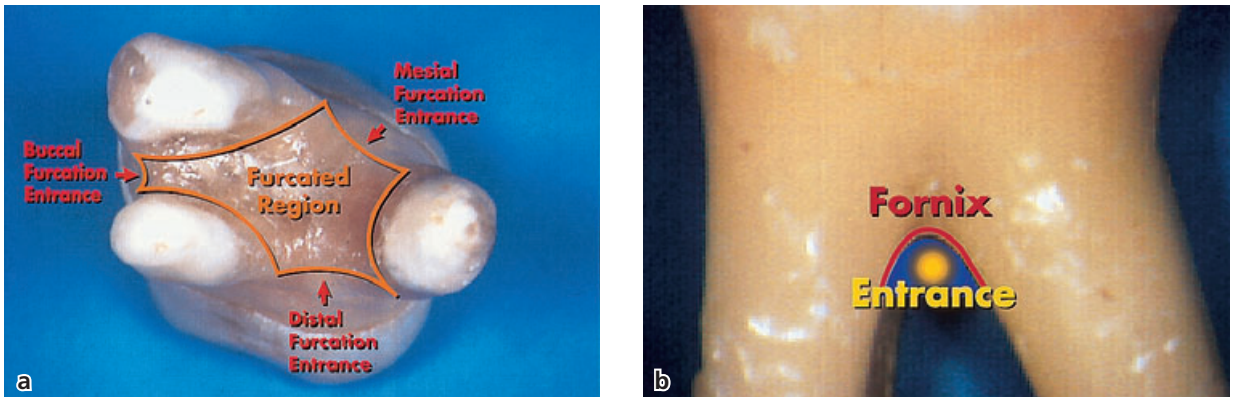

Fig. 39-2 (a) Apical-occlusal view of a maxillary molar where the three root cones make up the furcated region and the three furcation entrances. (b) A buccal view of the furcation entrance and of its roof.

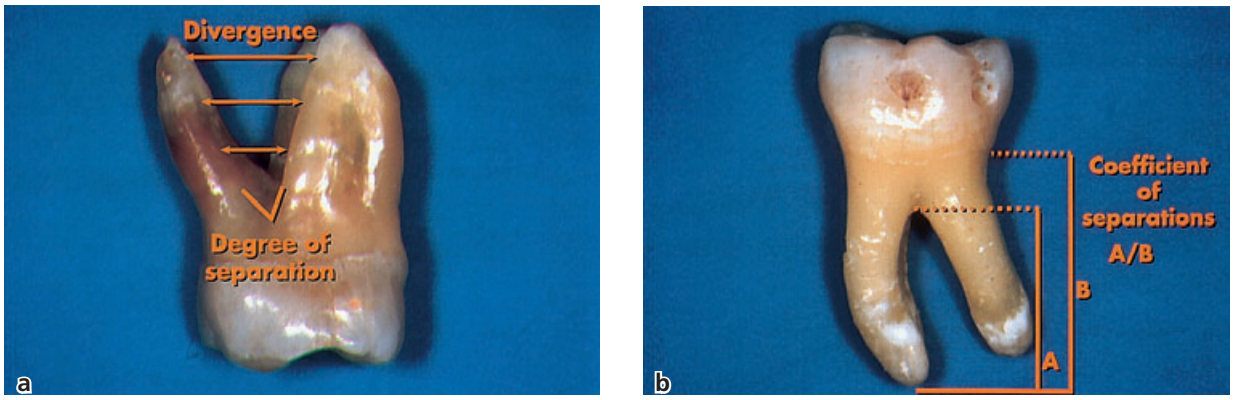

Fig. 39-3 (a) Photograph illustrating the angle (degree) of separation and the divergence between the mesio-buccal and the palatal roots of a maxillary molar. (b) The coefficient of separation (A/B) of the illustrated mandibular molar is 0.8 (A = 8 mm; B = 10 mm).

case of an incomplete fusion, the root cones may be fused in the area close to the CEJ but separated in a more apical region of the root complex.

Anatomy

Maxillary molars

As a general rule the maxillary first molar, in all respects – crown and individual roots – is larger than the second molar, which in turn is larger than the third molar.

The first and second molars most often have three roots; one mesio-buccal, one disto-buccal, and one palatal. The mesio-buccal root is normally vertically positioned while the disto-buccal and the palatal roots are inclined. The disto-buccal root projects distally and the palatal root projects in palatal direction (Fig. 39-4). The cross sections of the distobuccal and the palatal roots are generally circular. The palatal root is generally wider in the mesio-distal than in the bucco-palatal direction. The distal surface of the mesio-buccal root has a concavity which is about 0.3 mm deep (Bower 1979a,b). This concavity gives the cross section of the mesio-buccal root an "hour-glass" configuration (Fig. 39-5).

The three furcation entrances of the maxillary first and second molars vary in width and are positioned at varying distances apical to the CEJ. As a rule, the first molar has a shorter root trunk than the second molar. In the first molar the mesial furcation entrance is located about 3 mm from the CEJ, while the buccal is 3.5 mm and the distal entrance about 5 mm apical to the CEJ (Abrams & Trachtenberg 1974; Rosenberg 1988). This implies that the furcation fornix is inclined; in the mesiodistal plane the fornix is comparatively close to the CEJ at the mesial but closer to the apex at the distal surface. The buccal furcation entrance is narrower than its distal and mesial counterparts.

The degree of separation between the roots and their divergence decreases from the first to the second, and from the second to the third maxillary molar.

The mesio-buccal root of the first molar is frequently located more buccally in the arch than the disto-buccal root. If the buccal bone plate is thin, the mesio-buccal root frequently projects through the outer surface of the alveolar bone and bone fenestrations and/or dehiscences may occur.

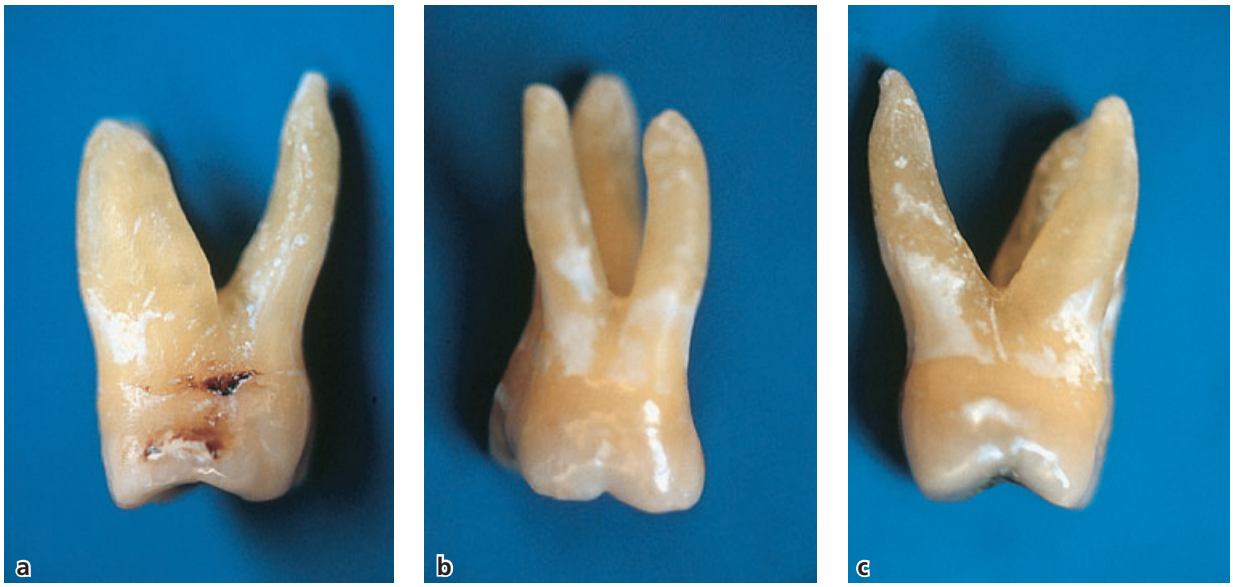

Fig. 39-4 Furcation entrances (a, mesial; b, buccal; c, distal) and the position of the roots of a maxillary first molar.

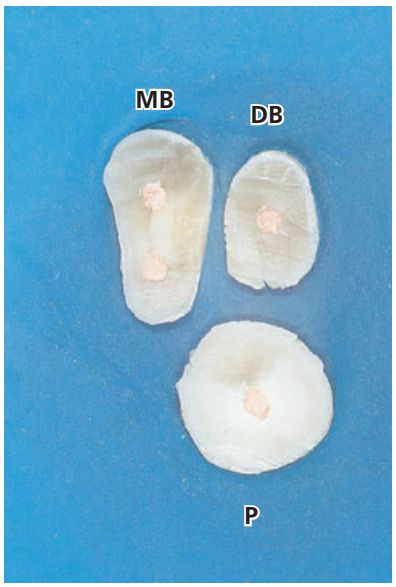

Fig. 39-5 Root-shape of a maxillary first molar in a horizontal cut at the level of the coronal third of the cones. Note the circular shape of the palatal root in comparison with the mesio-distally compressed shape of the mesio-buccal root, which also exhibits a concavity in the distal aspect.

Maxillary premolars

In about 40% of cases the maxillary first premolars have two root cones, one buccal and one palatal, and hence have a mesiodistal furcation. A concavity (about 0.5 mm deep) is often present in the furcation aspect of the buccal root. In many cases the furcation is located in the middle or in the apical third of the root complex (Fig. 39-6). The mean distance between CEJ and the furcation entrance is about 8 mm. The width of the furcation entrance is about 0.7 mm.

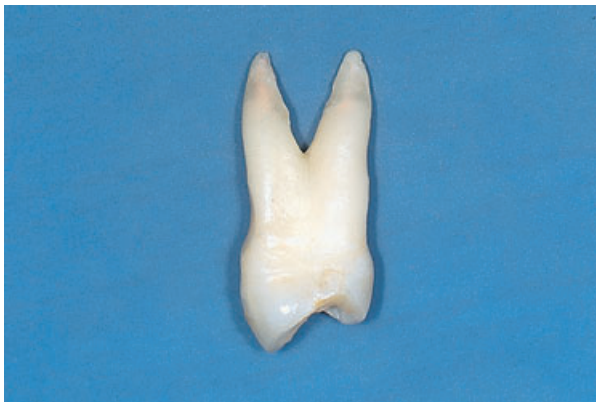

Fig. 39-6 A maxillary first premolar with the furcation located in the apical third of the root complex.

Mandibular molars

The mandibular first molar is larger than the second molar, which in turn is larger than the third molar. In the first and second molars the root complex almost always includes two root cones, one mesial and one distal. The mesial root is larger than the distal. The mesial root has a position which is mainly vertical while the distal root projects distally. The mesial root is wider in the bucco-lingual direction and has a larger cross-sectional area than the distal root. The cross section of the distal root is circular while the mesial root has an "hour-glass" shape. In addition, furrows and concavities often occur on the distal surface of the mesial root (Fig. 39-7). The distal concavity of the mesial root is more pronounced than that of the distal root (Bower 1979a,b; Svärdström & Wennström 1988).

The root trunk of the first molar is often shorter than the trunk of the second molar. The furcation entrances of the mandibular first molar, similar to

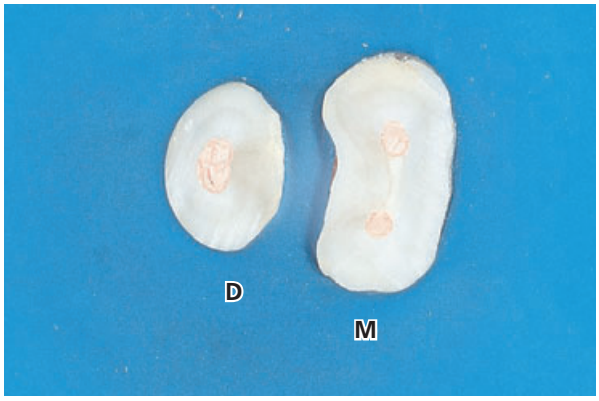

Fig. 39-7 "Hour-glass" shape of the mesial root – with a concavity in the distal aspect – and the circular shape of the distal root (horizontal section at the level of the coronal third of the cones).

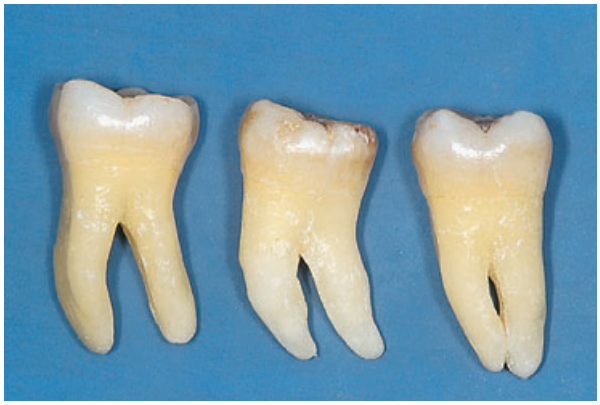

Fig. 39-8 From left to right, differences in degree of separation and in divergence between the root cones from the first to the mandibular third molar.

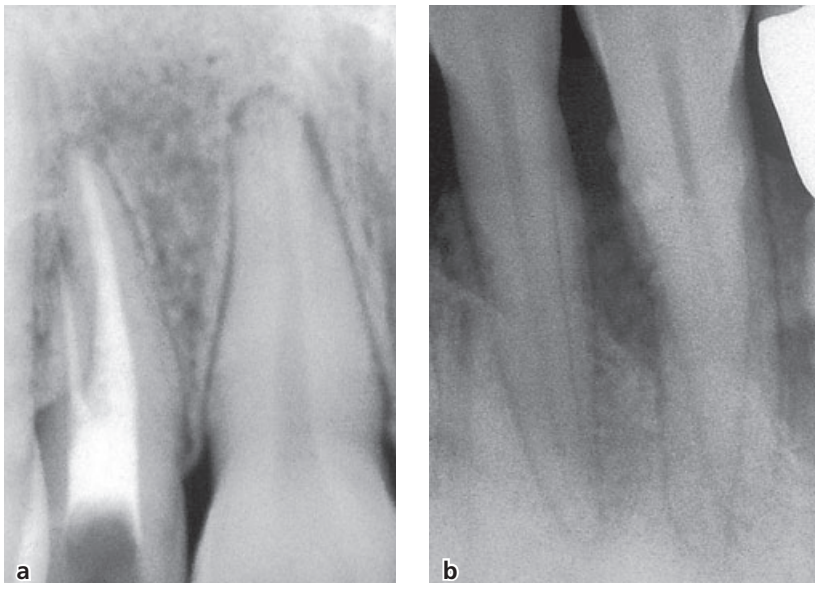

Fig. 39-9 Radiographs illustrating morphologic variations represented by two-rooted (a) maxillary lateral incisor and (b) mandibular canine.

those of the maxillary first molar, are located at different distances from the CEJ. Thus, the lingual entrance is frequently found more apical to the CEJ (>4 mm) than the buccal entrance (>3 mm). Thus, the furcation fornix is inclined in the bucco-lingual direction. The buccal furcation entrance is often <0.75 mm wide while the lingual entrance is >0.75 mm in most cases (Bower 1979a,b). The degree of separation and divergence between the roots decreases from the first to the third molar (Fig. 39-8).

It should also be observed that the buccal bone plate is thinner outside the roots of the first than of the second molar. Bone fenestrations and dehiscences are, as a consequence, more frequent in the first than in the second molar region.

Other teeth

Furcations may be present also in teeth which normally have only one root. In fact, two-rooted incisors (Fig. 39-9a), canines (Fig. 39-9b), and mandibular premolars may exist. Occasionally three-rooted maxillary premolars (Fig. 39-10a) and three-rooted mandibular molars can be found (Fig. 39-10b).

Diagnosis

The presence of furcation-involved teeth in a periodontal patient will influence the treatment plan (see Chapter 31). The selection of procedures to be used in the treatment of periodontal disease at multirooted teeth can first be made when the presence and depth of furcation lesions have been assessed. In this examination traditional measures of periodontal disease are used (see Chapter 26) but special attention is paid to findings from clinical *probing* and analysis of *radiographs* from the premolar–molar regions.

The classification description of the involved furcation is based on the amount of periodontal tissue destruction that has occurred in the inter-radicular area, i.e. degree of "horizontal root exposure" or

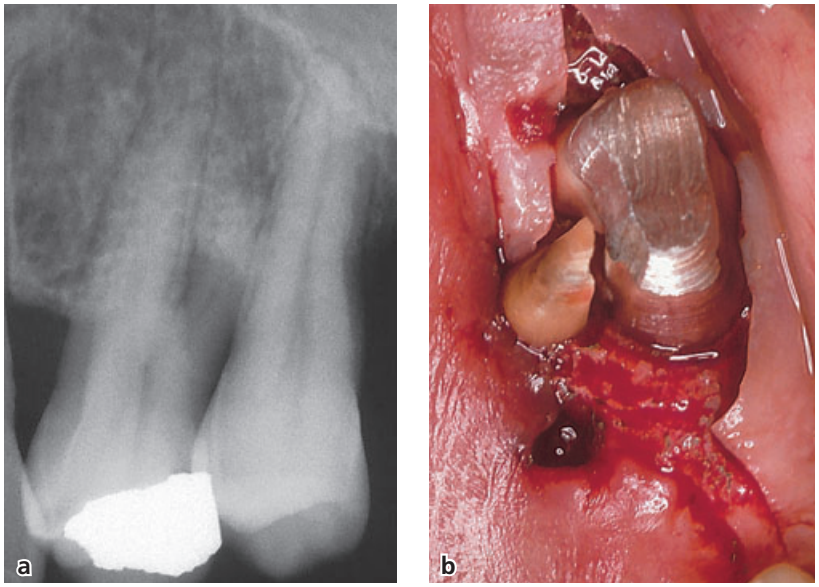

Fig. 39-10 (a) Anatomic variation represented in a radiograph of a three-rooted mandibular first premolar. (b) Clinical photograph illustrating, during surgery, the separation – before extraction – of an "abnormal" second mesial root of a mandibular molar.

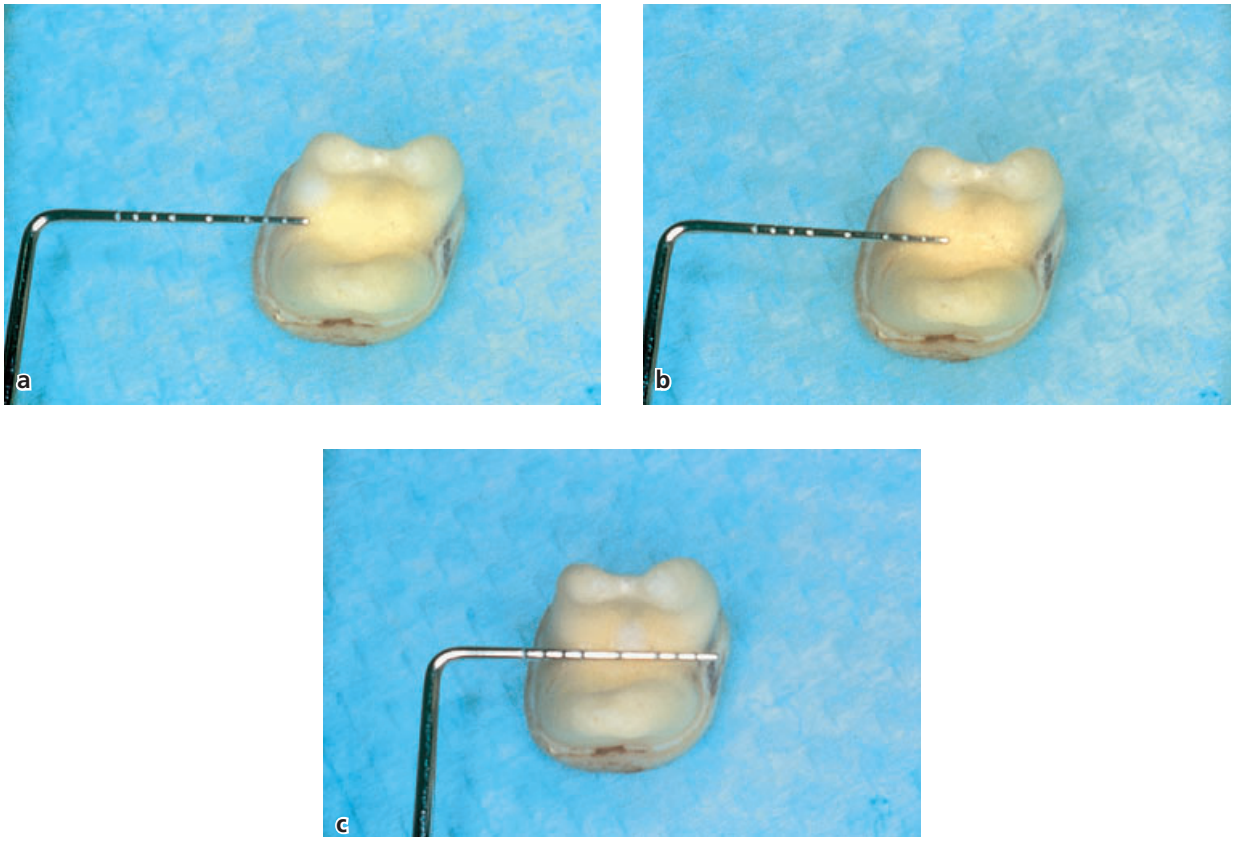

Fig. 39-11 Different degrees of furcation involvement in relation to the probe (penetration/superimposition) in the interradicular space of a mandibular molar. (a) Degree I. (b) Degree II. (c) Degree III.

attachment loss that exists within the root complex. Hamp *et al*. (1975) has suggested the following classification of the involved furcation:

- Degree I: horizontal loss of periodontal support not exceeding one third of the width of the tooth (Fig. 39-11a).
- Degree II: horizontal loss of periodontal support exceeding one third of the width of the tooth, but not encompassing the total width of the furcation area (Fig. 39-11b).
- Degree III: horizontal "through-and-through" destruction of the periodontal tissues in the furcation area (Fig. 39-11c).

It is important to understand that each furcation entrance must be examined and each entrance must be classified according to the above criteria.

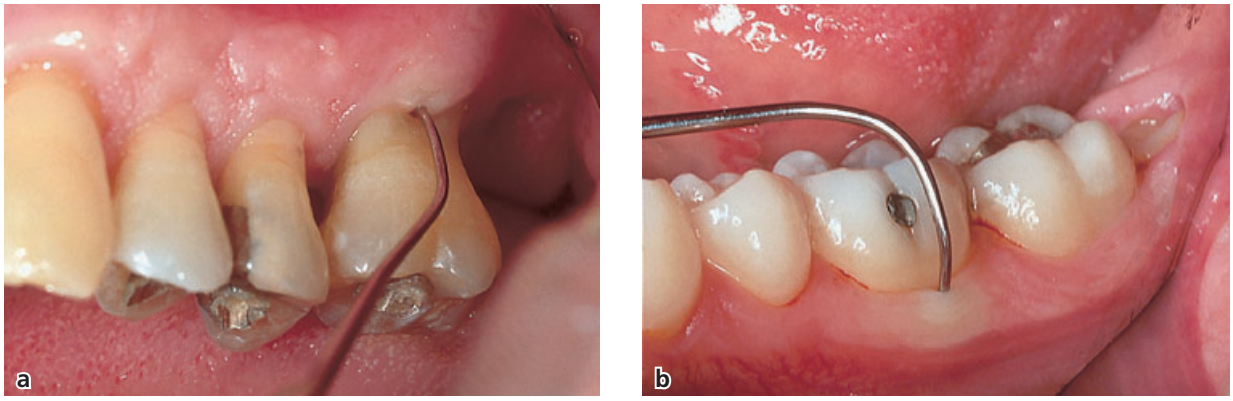

Fig. 39-12 Easily accessible vestibular furcation entrances for probing of a (a) maxillary molar and (b) mandibular molar.

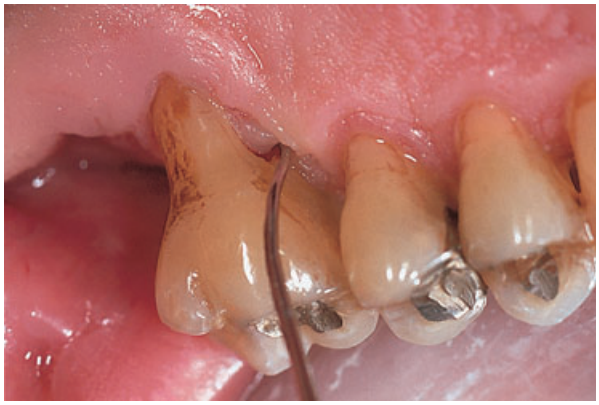

Fig. 39-13 Common access for probing of a mesial furcation entrance of a maxillary molar. The mesial furcation entrance is generally located at the palatal aspect of the tooth, while the distal entrance is located midway between the buccal and the palatal surface.

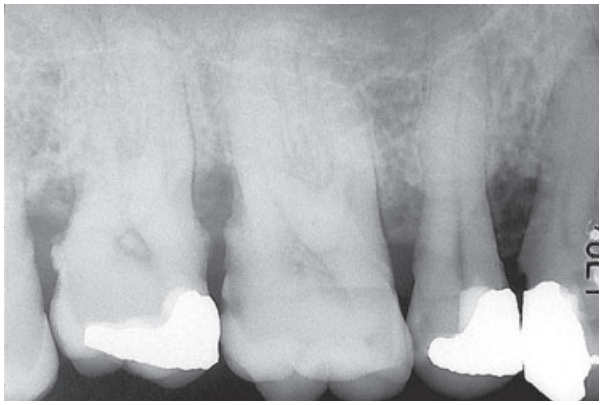

Fig. 39-14 Radiograph showing the location of the interdental bone level in relation to the furcation entrances of the maxillary first and second molar.

Probing

The buccal furcation entrance of the *maxillary molars* and the buccal and lingual furcation entrances of the *mandibular molars* are normally accessible for examination using a curved graduated periodontal probe (Fig. 39-12), an explorer or a small curette. The examination of approximal furcations is more difficult, in particular when neighboring teeth are present. Large contact areas between the teeth further impair access to approximal furcation entrances.

In maxillary molars the mesial furcation entrance is located much closer to the palatal than to the buccal tooth surface. Thus, the mesial furcation should be probed from the palatal aspect of the tooth (Fig. 39-13). The distal furcation entrance of a *maxillary molar* is generally located midway between the buccal and palatal surfaces and, as a consequence, this furcation could be probed from either the buccal or the palatal aspect of the tooth.

In *maxillary premolars* the root anatomy often varies considerably. The roots may also harbor irregularities such as longitudinal furrows, invaginations or true furcations, which may open at varying distances from the CEJ. Due to the above variations and limited access, the clinical assessment of a furcation involvement in maxillary premolars is often difficult. In some patients, a furcation involvement may, in such teeth, first be identified after the elevation of a soft tissue flap.

Radiographs

Radiographs must always be obtained to confirm findings made during probing of a furcation-involved tooth. The radiographic examination should include both paralleling "periapical" and vertical "bite-wing" radiographs. In the radiographs the location of the interdental bone as well as the bone level within the root complex should be examined (Fig. 39-14). Situations may occur when findings from clinical probing and from the radiographs are inconsistent. Thus, the localized but extensive attachment loss which may be detected within the root complex of a maxillary molar with the use of a probe, will not always appear in the radiograph. This may be due to the superimposition in the radiograph of the palatal root and of remaining bone structures (Fig. 39-15a). In such a case, additional radiographs with different angles of orientation of the central beam should be used to identify bone loss within the root complex (Fig. 39-15b).

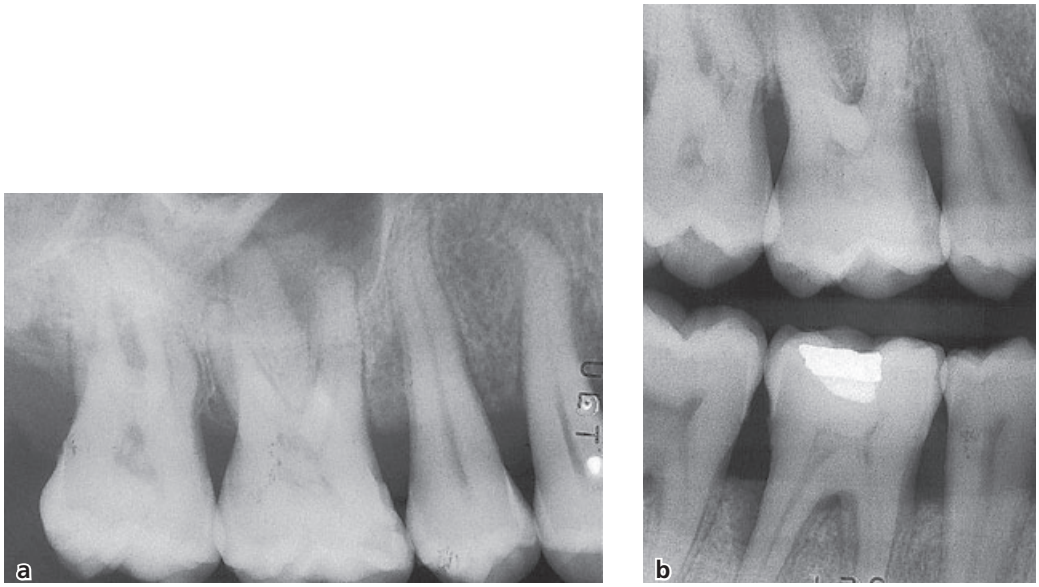

Fig. 39-15 (a) Radiographs of the right maxillary molar region where, with a normal bisecting projection, the furcation defect of the first molar is not evident. (b) It is, however, easily identified in a bitewing radiograph.

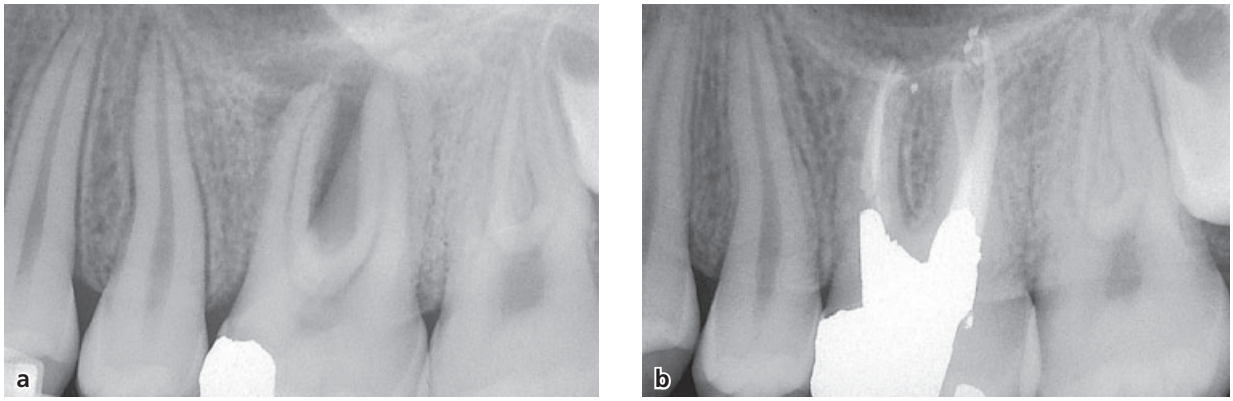

Fig. 39-16 (a) Radiograph demonstrating a destruction of inter-radicular bone and the presence of periapical defects at the mesial and distal roots of a maxillary first molar. (b) Radiographic appearance of complete healing of the inter-radicular and periapical lesions after endodontic treatment.

Differential diagnosis

A lesion in the inter-radicular space of a multi-rooted tooth may be associated with problems originating from the root canal or be the result of occlusal overload. The treatment of a furcation-involved tooth, therefore, should not be initiated until a proper differential diagnosis of the lesion has been made.

Pulpal pathosis may sometimes cause a lesion in the periodontal tissues of the furcation (see Chapter 23). The radiographic appearance of such a defect may have some features in common with a plaque-associated furcation lesion. In order to differentiate between the two lesions the vitality of the affected tooth must *always* be tested. If the tooth is vital, a plaque-associated lesion should be suspected. If the tooth is non-vital, the furcation involvement may have an endodontic origin. In such a case, proper endodontic treatment must *always* precede periodontal therapy. In fact, endodontic therapy may resolve the inflammatory lesion, soft and hard tissue healing may occur and the furcation defect will disappear (Fig. 39-16). If signs of healing of a furcation defect fail to appear within 2 months of endodontic treatment, the furcation involvement is probably associated with marginal periodontitis.

Trauma from occlusion

Forces elicited by occlusal interferences, e.g. bruxers and clenchers (see Chapters 14 and 51), may cause inflammation and tissue destruction or adaptation within the inter-radicular area of a multi-rooted tooth. In such a tooth a radiolucency may be seen in the radiograph of the root complex. The tooth may exhibit increased mobility. Probing, however, fails to detect an involvement of the furcation. In this particular situation, occlusal adjustment must always precede periodontal therapy. If the defects seen

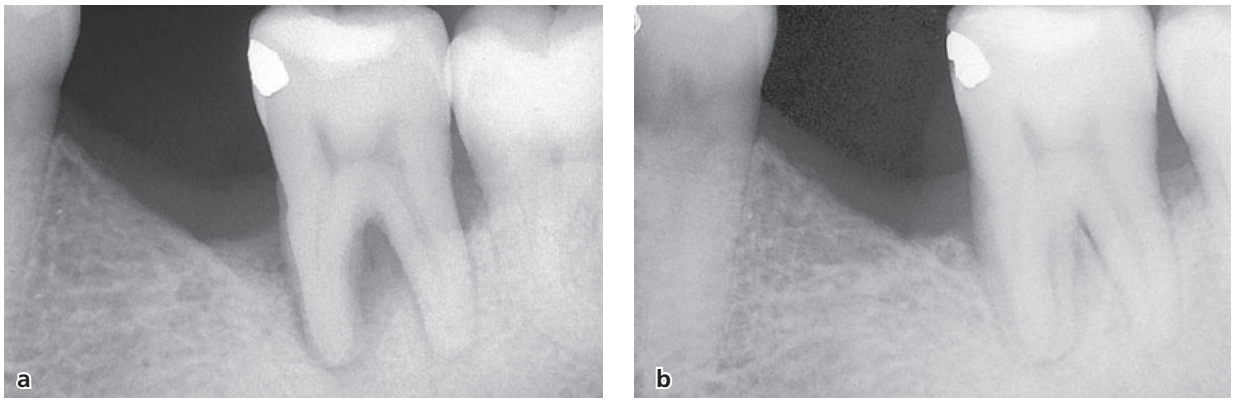

Fig. 39-17 (a) Radiographic appearance of a defect in the furcation area caused by occlusal overload. After occlusal adjustment the interradicular defect spontaneously healed, as documented 6 months after therapy in a radiograph (b). (Courtesy of M. Cattabriga.)

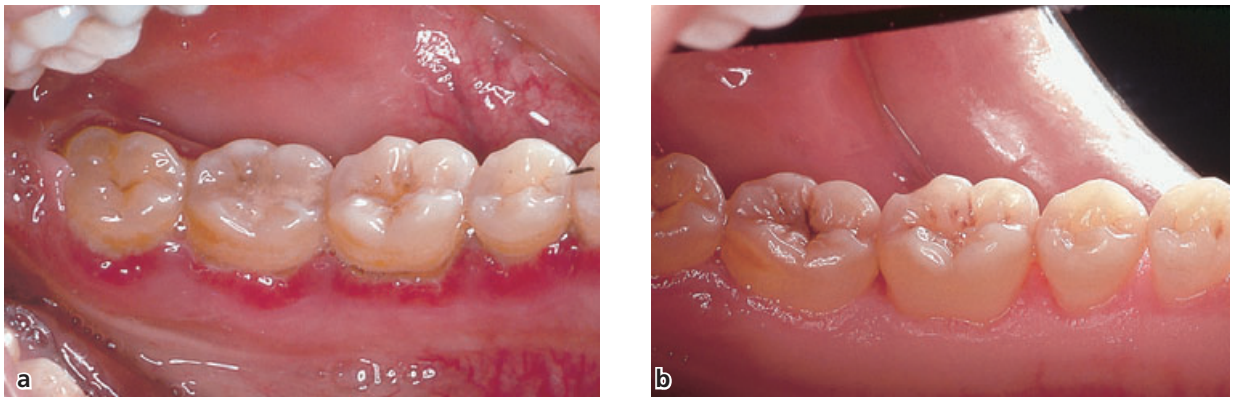

Fig. 39-18 Resolution of inflammatory lesions in the gingiva achieved by scaling, root planing and the re-establishment of a correct tissue morphology in the inter-radicular area of degree I furcation-involved mandibular molars. (a) Before therapy. (b) 6 months after therapy.

within the root complex are of "occlusal" origin, the tooth will become stabilized and the defects disappear within weeks following correction of the occlusal overload (Fig. 39-17).

Therapy

Treatment of a defect in the furcation region of a multi-rooted tooth is intended to meet two objectives:

1. The elimination of the microbial plaque from the exposed surfaces of the root complex.
2. The establishment of an anatomy of the affected surfaces that facilitates proper self-performed plaque control.

Different methods of therapy are recommended:

- Degree I furcation involvement. Recommended therapy: scaling and root planing; furcation plasty.
- Degree II furcation involvement. Recommended therapy: furcation plasty; tunnel preparation; root resection; tooth extraction; guided tissue regeneration at mandibular molars.
- Degree III furcation involvement. Recommended therapy: tunnel preparation; root resection; tooth extraction.

Scaling and root planing

Scaling and planing of the root surfaces in the furcation entrance of a degree I involvement in most situations result in the resolution of the inflammatory lesion in the gingiva. Healing will re-establish a normal gingival anatomy with the soft tissue properly adapted to the hard tissue walls of the furcation entrance (Fig. 39-18).

Furcation plasty

Furcation plasty (Fig 39-19) is a resective treatment modality which should lead to the elimination of the inter-radicular defect. Tooth substance is removed (odontoplasty) and the alveolar bone crest is remodeled (osteoplasty) at the level of the furcation entrance.

Furcation plasty is used mainly at buccal and lingual furcations. At approximal surfaces access is

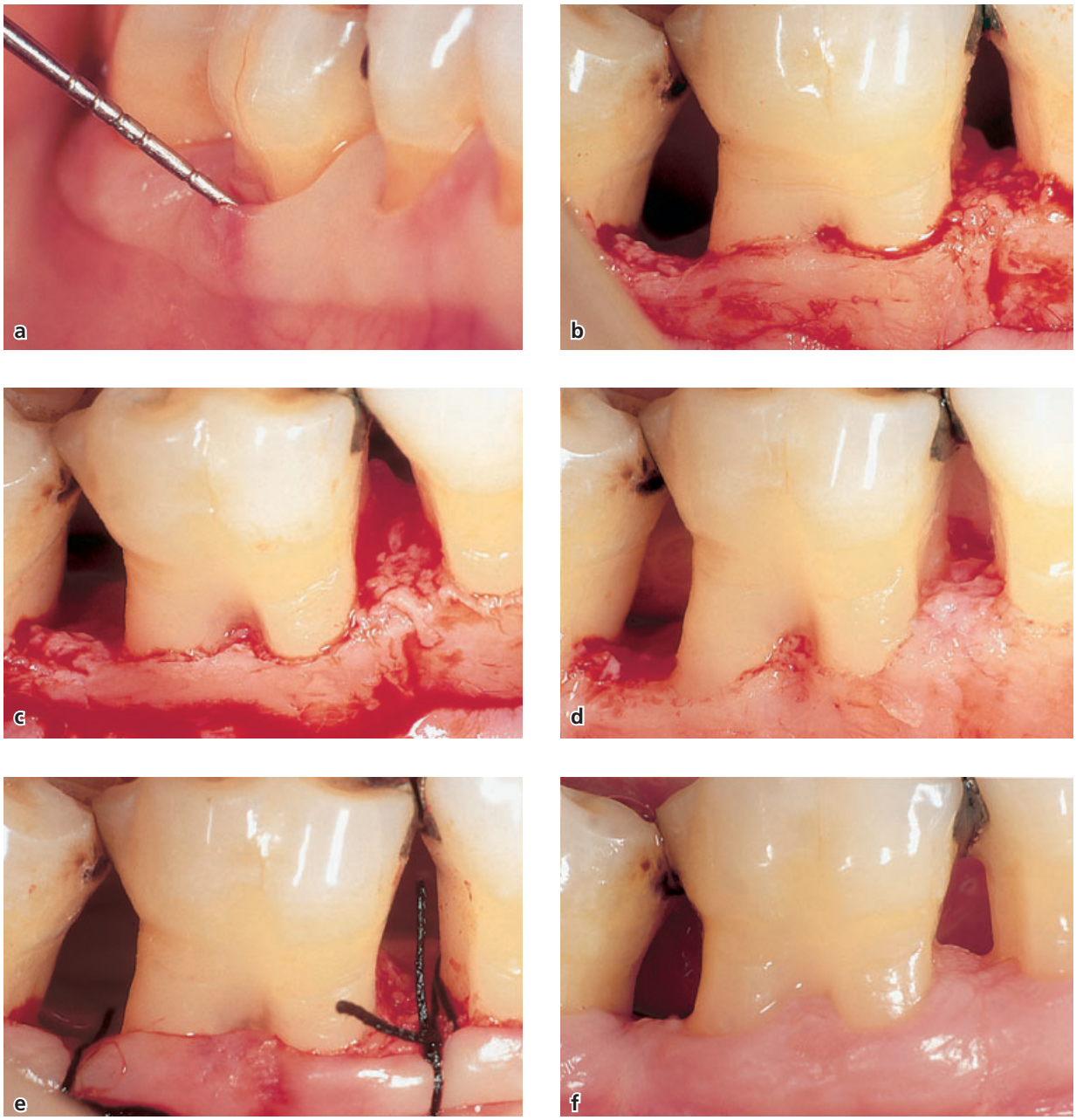

Fig. 39-19 Furcation plasty performed at the buccal aspect of a mandibular molar. (a) Initial degree II furcation involvement. (b) After flap elevation, removal of the granulation tissue and scaling of the exposed root surfaces. (c) After odontoplasty. (d) After osteoplasty. (e) Apical position of the flap managed by periosteal sutures. (f) Healing resulting in the elimination of the furcation defect and in the establishment of a proper soft tissue morphology.

often too limited for this treatment. Furcation plasty involves the following procedures:

- The dissection and reflection of a soft tissue flap to obtain access to the inter-radicular area and the surrounding bone structures.
- The removal of the inflammatory soft tissue from the furcation area followed by careful scaling and root planing of the exposed root surfaces.
- The removal of crown and root substance in the furcation area (odontoplasty) to eliminate or reduce the horizontal component of the defect and to widen the furcation entrance.
- The recontouring of the alveolar bone crest in order to reduce the buccal–lingual dimension of a bone defect in the furcation area.
- The positioning and the suturing of the mucosal flaps at the level of the alveolar crest in order to cover the furcation entrance with soft tissue. Following healing a "papilla-like" tissue should close the entrance of the furcation.

Care must be exercised when odontoplasty is performed on vital teeth. Excessive removal of tooth structure will enhance the risk for increased root sensitivity.

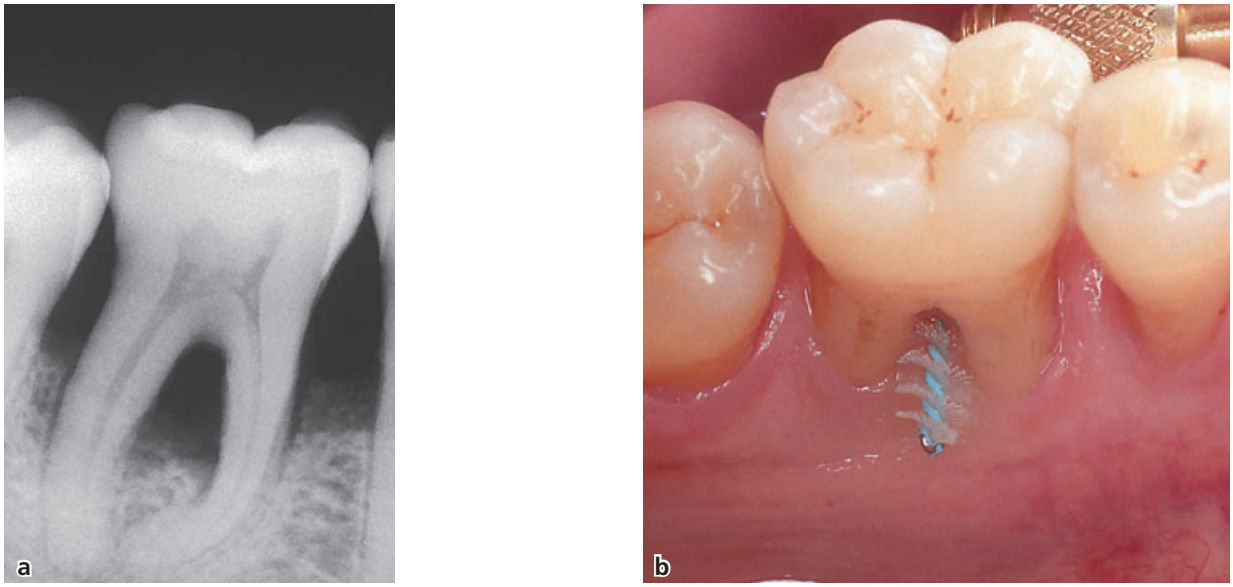

Fig. 39-20 Tunnel preparation of a degree III-involved mandibular molar. Radiograph (a) and photograph (b) showing a wide inter-radicular space where self-performed plaque control can be obtained by the use of an interproximal brush.

Tunnel preparation

Tunnel preparation is a technique used to treat deep degree II and degree III furcation defects in mandibular molars. This type of resective therapy can be offered at mandibular molars which have a short root trunk, a wide separation angle, and long divergence between the mesial and distal root. The procedure includes the surgical exposure and management of the entire furcation area of the affected molar.

Following the reflection of buccal and lingual mucosal flaps, the granulation tissue in the defect is removed and the root surfaces are scaled and planed. The furcation area is widened by the removal of some of the inter-radicular bone. The alveolar bone crest is recontoured; some of the interdental bone, mesial and distal to the tooth in the region, is also removed to obtain a flat outline of the bone. Following hard tissue resection enough space has been established in the furcation region to allow access for cleaning devices to be used during self-performed plaque-control measures (Fig. 39-20). The flaps are apically positioned to the surgically established inter-radicular and interproximal bone level.

During maintenance the exposed root surfaces should be treated by topical application of chlorhexidine digluconate and fluoride varnish. This surgical procedure should be used with caution, because there is a pronounced risk for root sensitivity and for carious lesions developing on the denuded root surfaces within artificially prepared tunnels (Hamp *et al*. 1975).

Root separation and resection (RSR)

Root separation involves the sectioning of the root complex and the maintenance of all roots. *Root resection* involves the sectioning and the removal of one or two roots of a multi-rooted tooth. RSR is frequently used in cases of deep degree II and degree III furcation-involved molars.

Before RSR is performed the following factors must be considered:

- *The length of the root trunk*. In a patient with progressive periodontal disease a tooth with a *short* root trunk may have an early involvement of the furcation (Larato 1975; Gher & Vernino 1980). A tooth with a short root trunk is a good candidate for RSR; the amount of remaining periodontal tissue support following separation and resection is often sufficient to ensure the stability of the remaining root cone. If the root trunk is *long*, the furcation involvement occurs later in the disease process, but, once established, the amount of periodontal tissue support left apical to the furcation may be insufficient to allow RSR.
- *The divergence between the root cones.* The distance between the root cones must be considered. Roots with a short divergence are technically more difficult to separate than roots which are wide apart. In addition, the smaller the divergence is, the smaller also is the inter-radicular (furcation) space. In cases where the divergence between two roots is small, the possibility of increasing the inter-radicular distance with an orthodontic root movement may be considered (Fig. 39-21). The furcation space may also be increased by odontoplasty performed during surgery. Figure 39-22 illustrates that *odontoplasty* was performed on (1) the distal part of the mesial root and (2) the mesial part of the distal root and deep finishing lines prepared for the subsequent restoration (Di Febo *et al*. 1985).
- *The length and the shape of the root cones*. Following separation, short and small root cones (Fig. 39-23)

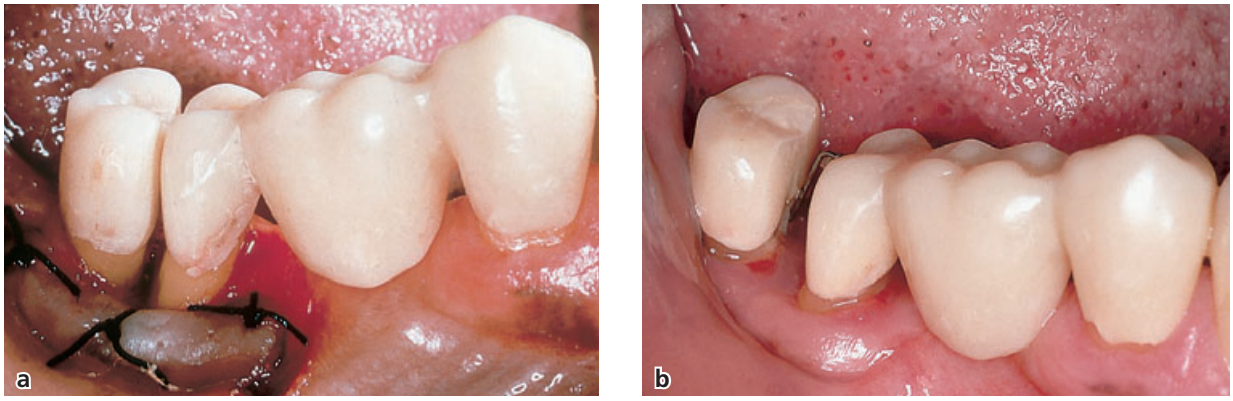

Fig. 39-21 Effect of orthodontic treatment of a separated mandibular molar with a small root divergence. (a) After root separation. (b) 3 months after completion of orthodontic therapy.

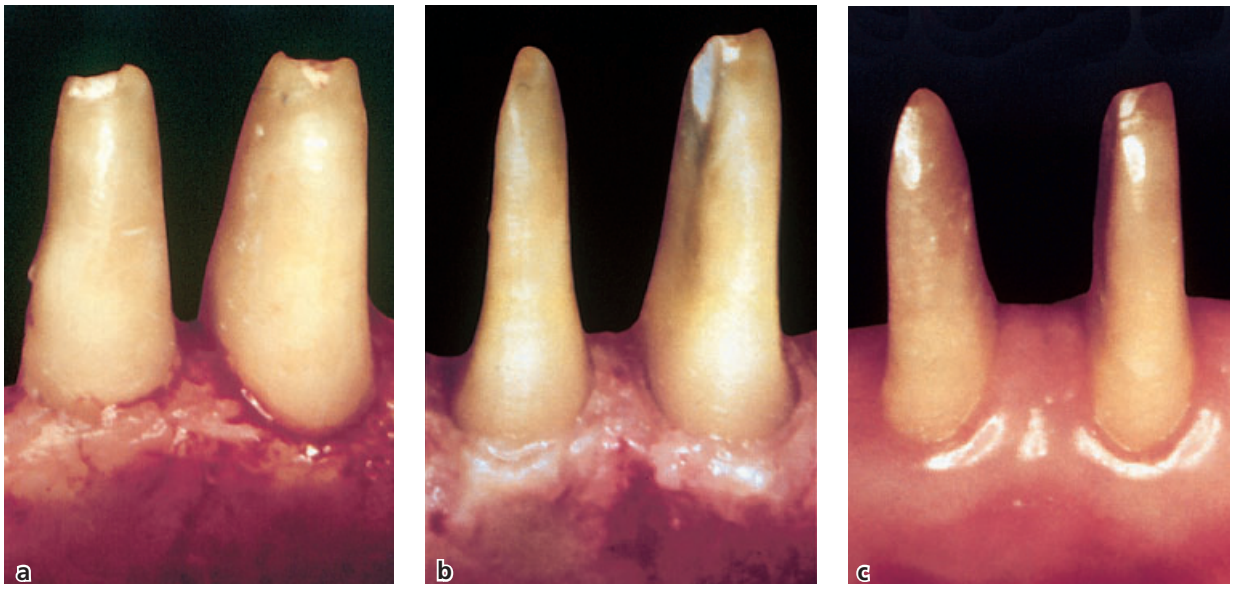

Fig. 39-22 Odontoplasty of a separated mandibular molar performed during surgery to increase the furcation space. After flap elevation and exposure of the alveolar bone, it is evident that the distance between the two roots is small (a). By preparing the inter-radicular surfaces during surgery (b) the furcation space is increased and is sufficient for self-performed plaque control measures (c).

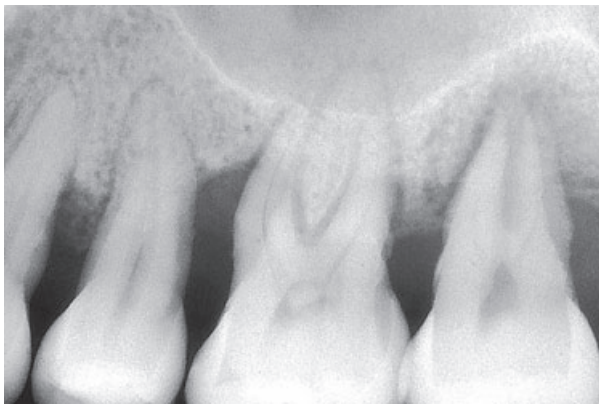

Fig. 39-23 Radiograph showing maxillary molars with thin, short, and conical roots.

tend to exhibit an increased mobility. Such roots, in addition, have narrow root canals which are difficult to ream. Short and small roots consequently should be regarded as poor abutments for prosthetic restorations.

- *Fusion between root cones*. When a decision has been made to perform RSR, it is important that the clinician first determines that the cones within the root complex are not fused. This is generally an uncomplicated diagnostic problem for mandibular molars or for the buccal furcation of maxillary molars (Fig. 39-24). At such teeth the separation area between the roots can easily be identified both with the probe and in a radiograph. It is more difficult to identify a separation line between mesio-buccal (or disto-buccal) and palatal roots of a maxillary molar or maxillary first premolar with a narrow root complex. In such situations, a soft tissue flap must often be raised to allow the operator to get proper

access to the approximal tooth surfaces. The mesial (or distal) entrance of the furcation must be probed to a depth of 3–5 mm to ascertain that a fusion does *not* exist between the roots scheduled for RSR.

- *Amount of remaining support around individual roots.* This should be determined by probing the entire circumference of the separated roots. It should be observed that a localized deep attachment loss at one surface of one particular root (e.g. on the buccal surface of the palatal root, or the distal surface of the mesio-buccal root of a maxillary molar) may compromise the long-term prognosis for an otherwise ideal root.
- *Stability of individual roots*. This must be examined following root separation. Rule of thumb: the more mobile the root cone is, the less periodontal tissue support remains.
- *Access for oral hygiene devices*. After completion of therapy the site must have an anatomy which facilitates proper self-performed tooth cleaning.

Maxillary molars

General example

Several decisions must be made when RSR is planned for a furcation-involved maxillary molar. Since such teeth have three root cones, one or two cones may be retained after separation. Different treatment alternatives exist. They are listed in Table 39-1.

Prior to RSR, the morphology of the individual roots as well as the surface area of each root must be carefully analyzed.

The *disto-buccal root* of a maxillary molar (1) is the shortest of the three roots; (2) the root trunk is comparatively long. Thus, the distal root has a small quantity of bone support and once separated, the cone may exhibit increased mobility. The disto-buccal root is, therefore, often removed as part of RSR (Rosenberg 1978; Ross & Thompson 1980).

The *mesio-buccal root* has (1) a wide buccopalatal dimension, (2) an hour-glass cross section, and therefore a large root surface area. In fact, the mesio-buccal cone often has a total root surface area that is equal to or greater than that of the palatal root cone. The mesio-buccal root (1) is located centrally in the alveolar process, (2) is properly aligned with the maxillary premolars and is in an ideal position to function as a separate unit (Fig. 39-25). For these reasons, the mesio-buccal root may be preferred for retention when the clinician is selecting between the mesio-buccal or palatal root. It should be remembered, however, that the root canals of the mesio-buccal root are narrow and more difficult to treat than the single and wide canal of the palatal root.

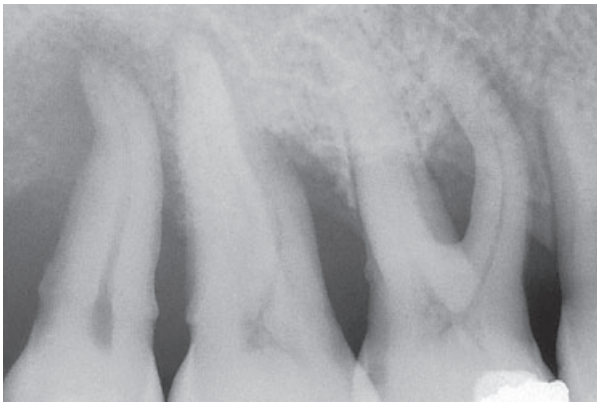

Fig. 39-24 Radiograph indicating the presence of a degree III involvement of the buccal furcation of the maxillary first molar. This tooth is a candidate for root resection.

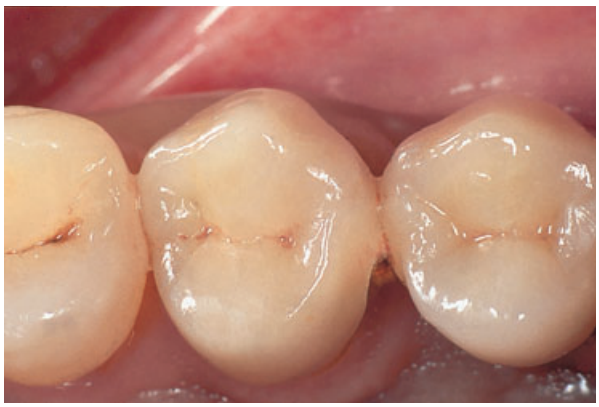

Fig. 39-25 Occlusal view of a restoration using the mesial root of a maxillary first molar as abutment. Note the alignment of the mesial root and the adjacent premolars.

Table 39-1 Root resective treatment possibilities in molars with furcation involvement

Furcation involvement	Root resection	Root resection plus separation of the remaining roots
1 Buccal	Mesio-buccal, disto-buccal	
Mesial	Mesio-buccal, palatal	
Distal	Disto-buccal, palatal	
2 Buccal & distal	Disto-buccal, mesio-buccal & palatal	Palatal
Buccal & mesial	Mesio-buccal, disto-buccal & palatal	Palatal, disto-buccal
Mesial & distal	Palatal, mesial & disto-buccal	Distobuccal
3 Buccal, distal & mesial	Disto-buccal & palatal, mesio-buccal & palatal, mesio- & disto-buccal	Palatal, disto-buccal

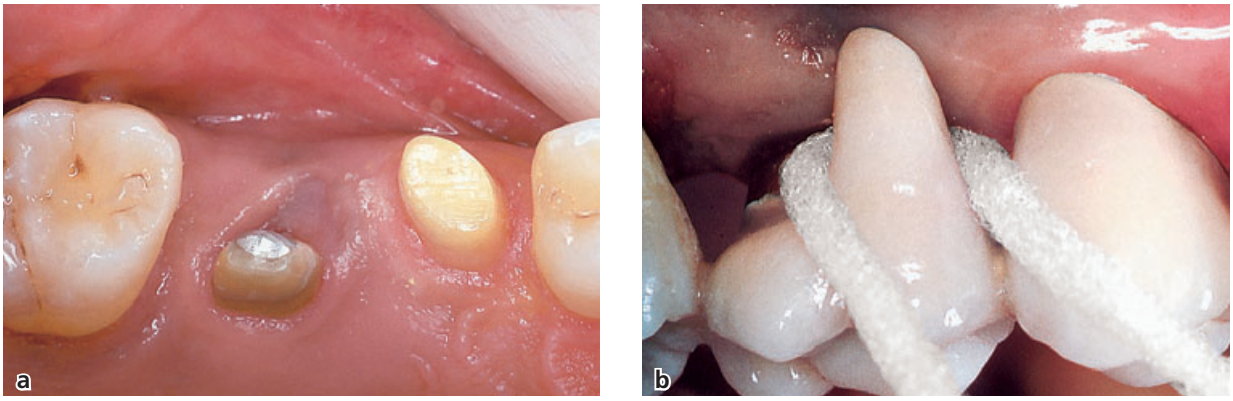

Fig. 39-26 (a) Palatal root of a root-resected maxillary molar serving as a single abutment for a crown restoration. (b) A mesio-buccal root was included in the restoration for esthetic reasons.

The tissue destruction in the furcation area often causes deep attachment and bone loss at the distal palatal surface of the mesio-buccal root. In such situations the palatal root remains as the only candidate for retention (Fig. 39-26).

The series of illustrations presented in Fig. 39-27 demonstrates two left maxillary molars (teeth 26 and 27) with degree III involvement of all six furcation entrances. Both teeth were, following a detailed examination and diagnosis, scheduled for treatment with RSR. Note that in this case the second premolar was missing. In cases of advanced periodontal disease at maxillary molars, it is often necessary to separate all three roots of the individual tooth to obtain access to the inter-radicular area for assessment of the height of the remaining bone at (1) the buccal surface of the palatal root and (2) the palatal surfaces of the buccal roots. Figure 39-27b illustrates the two maxillary molars with all six roots separated. Because of anatomic considerations and increased mobility, the distobuccal roots of 26 and 27 were extracted (Fig. 39-27c). The palatal root of the first molar had a deep area of localized attachment loss on its buccal surface, was considered to be a poor candidate for a bridge abutment, and was extracted. The mesio-buccal root of the first molar as well as the mesio-buccal and palatal roots of the second molar (27) were stable and exhibited moderate probing depth. It was anticipated that at all three roots the anatomy would allow proper plaque control following healing after treatment. The three roots were maintained (Fig. 39-27d). Figure 39-27e shows the area after 3 months' healing and Fig. 39-27f illustrates the segment properly restored. Since in this segment one premolar was missing, the mesio-buccal root of the first molar was used as second premolar in the prosthetic reconstruction and the two roots of the second molar served as abutments for a crown restoration in the position of a molar.

Maxillary premolars

Root resection of maxillary first premolars is possible only in rare instances due to the anatomy of the root complex (Joseph *et al*. 1996) (Fig. 39-28). The furcation of this premolar is often located at such an apical level that the maintenance of one root serves no meaningful purpose. In most cases, therefore, the presence of a deep furcation involvement of degree II or degree III in a maxillary first premolar calls for tooth extraction.

Mandibular molars

If RSR must be applied in a furcation-involved mandibular molar, three treatment alternatives exist:

1. Separate the two roots, but maintain both roots (premolarization)
2. Separate and extract the mesial root
3. Separate and extract the distal root.

In some situations, both roots may be maintained following separation. If one root is to be removed, the following facts must be considered:

- The *mesial* root has a significantly greater root surface area than the distal root. The mesial root, however, has an hour-glass-shaped cross section which may be difficult to manage (1) in the self-performed plaque control and (2) in the restorative procedure. In addition, the mesial root frequently has two narrow root canals. The root canals are often close to the external root surface. This may complicate root preparation during the subsequent restorative treatment.
- The *distal* root has an oval cross section and, as a rule, only one, wide root canal. The distal root is: (1) comparatively large, providing a greater mass of dentin to resist root fracture (Langer *et al*. 1981); and (2) a good candidate for pin or post placement. Further, when the resected mandibular molar is a terminal abutment for a bridge, the retention of the distal root will result in a longer dental arch than would be the case had the mesial root been retained (Fig. 39-29).

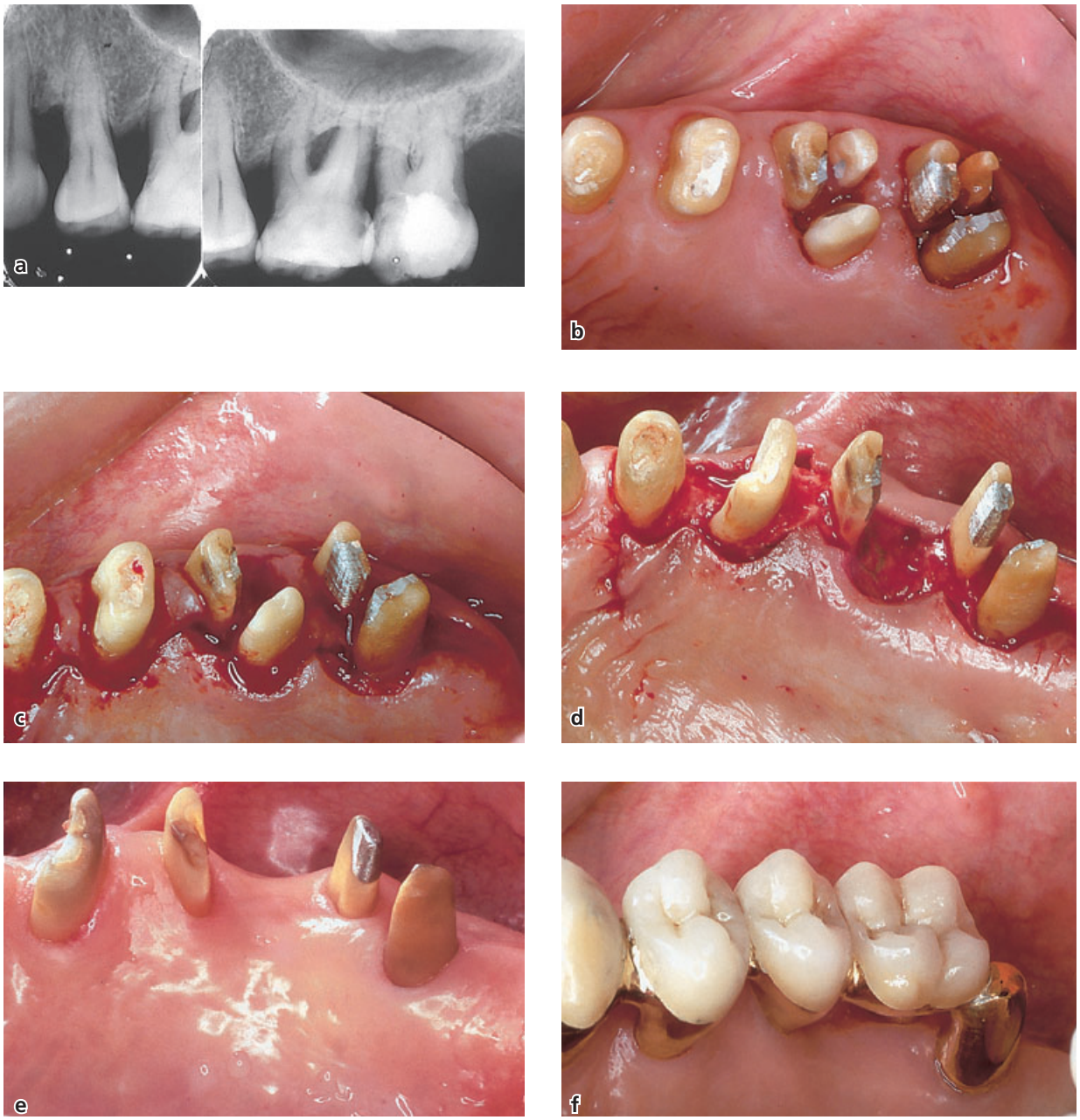

Fig. 39-27 The sequential stages of root resection of two maxillary molars with degree III involvement. (a) Radiograph showing the pre-RSR situation. (b)The roots were separated before flap elevation. (c,d) The distal roots of both molars and the palatal root of the first molar were extracted and the teeth prepared. (e) After 3 months of healing. (f) The final prosthetic restoration of the site.

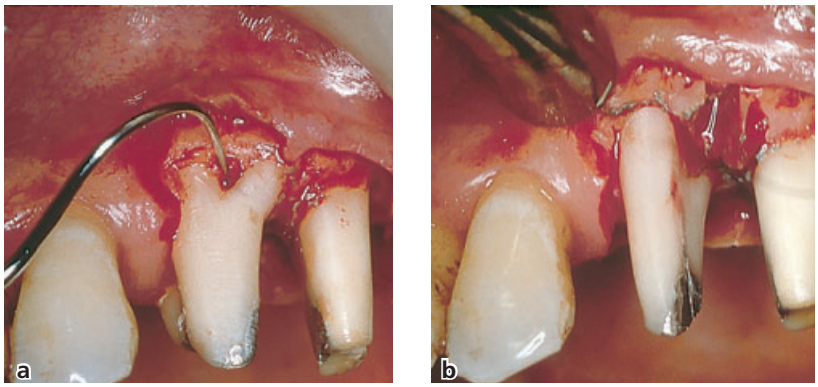

Fig. 39-28 Resection of the disto-buccal root of a three-rooted maxillary first premolar.

Sequence of treatment at RSR

Once anatomic and pathologic characteristics of the root complex(es) of multi-rooted teeth have been documented, treatment should follow a logical plan (see also Chapter 31).

Endodontic treatment

If the tooth to be resected is vital or if an improper root canal filling was placed in a non-vital tooth, RSR starts with endodontic therapy. Rubber dam can be placed, and optimal conditions thus be established for the important management (cleaning and shaping) of the root canal. The structural integrity of the root must be maintained and minimal amounts of root dentin should be removed (Fig. 39-30a,b). Direct filling with amalgam or chemically cured composite of the endodontically treated tooth should be performed before RSR (Fig. 39-30c). Each root should have individual retention for a restoration which should not break or detach during RSR, removal and relining of the provisional restorations, impressions, and prosthetic try-in. Endocanal posts or endodontic screws are used only if natural retention needs improvement.

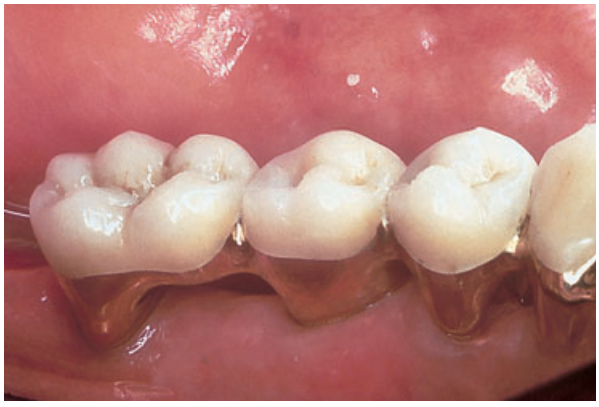

Fig. 39-29 Results of the root resection of a mandibular first molar of which the distal root was retained.

Occasionally, a furcation involvement may first be identified during periodontal surgery. In this emergency situation RSR may be completed but the root canal entrance(s) of the remaining root(s) must be properly sealed. Definitive root canal therapy must be completed within 2 weeks (Smukler & Tagger 1976).

Provisional restoration

Alginate impressions of the area to be treated are taken and sent to the laboratory together with a wax record of the intercuspal position. A provisional restoration is prepared.

Root separation and resection

Root separation and root resection may be performed as part of the preparation of the segment for prosthetic rehabilitation ("prosthetic preparation"), i.e. prior to periodontal surgery (Carnevale *et al*. 1981). During the prosthetic preparation it is important to *avoid*

- Exposing the interradicular bone to undue mechanical trauma (Fig. 39-31)
- Leaving behind parts of the furcation fornix (Fig. 39-32)
- Perforating the root canals
- Preparing the vertical surfaces of the remaining roots with sharp angles (Fig. 39-33).

Situation 1: *mandibular molar*. Following separation, both roots are maintained. The distal surface of the distal root and the mesial surface of the mesial root must be prepared parallel to each other to increase the retention for a subsequent restoration. The mesial surface of the distal root and the distal surface of the mesial root should be prepared with diverging angles to increase the space available between the separated roots (Fig. 39-34).

Situation 2: *maxillary molar*. Following separation, the disto-buccal root was extracted. The distal surface of the crown is prepared with a bevel cut and in such

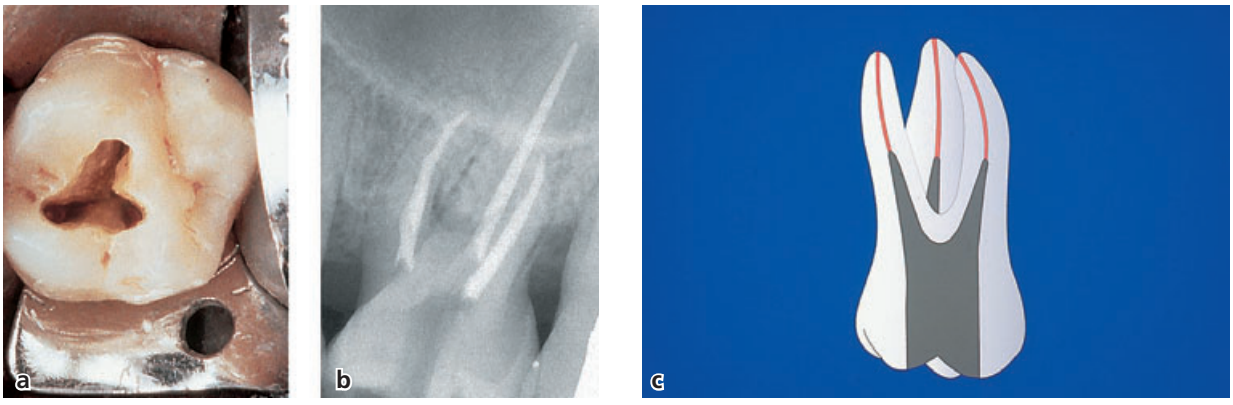

Fig. 39-30 Combined photograph and radiograph showing the "conservative" approach both regarding the access to the pulp chamber (a) and the shaping and filling of the root canal system (b). (c) Schematic illustration showing the temporary restoration of the endodontically treated tooth.

a way that the concave curvature (in apicocoronal direction) is eliminated (Fig. 39-35). If the mesio-buccal and the palatal roots of this molar must be separated but maintained, it is important that the buccal surface of the mesio-buccal root and the palatal surface of the palatal root are prepared parallel to each other. This will enhance the retention of the subsequent restoration. The palatal surface of the mesio-buccal root and the buccal surface of the palatal root must be prepared at diverging angles to increase the space available between the separated roots (Fig. 39-36). At this stage the provisional restoration is relined with cold cured acrylic and cemented after RSR.

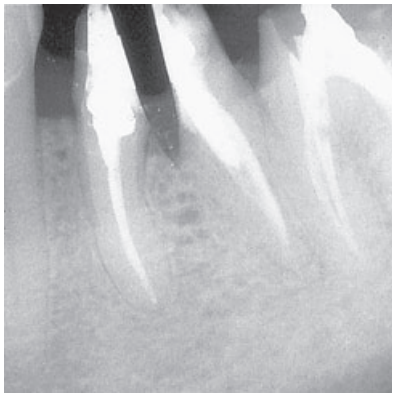

Fig. 39-31 Radiograph illustrating the damage which occurred to the inter-radicular septum during root separation.

Periodontal surgery

Following flap elevation, osseous resective techniques are used to eliminate angular bone defects that may exist around the maintained roots. Bone resection may also be performed to reduce the buccolingual dimension of the alveolar process of the extraction site. The remaining root(s) may be prepared with a bevel cut to the level of the supporting bone (Levine 1972; Ramfjord & Nissle 1974; Carnevale *et al*. 1983). This additional preparation may serve the purpose of (1) eliminating residual soft and hard deposits and (2) eliminating existing undercuts to facilitate the final impression (Fig. 39-37). The provisional restoration is relined. The margins of the provisional restoration must end ≥3 mm coronal of the bone crest. The soft tissue flaps are secured with sutures at the level of the bone crest. The relined provisional restoration is cemented and a periodontal dressing is applied to cover the surgical area. The dressing and the sutures are removed 1 week later. The roots are debrided and a new dressing applied. After another week, the dressing is finally removed

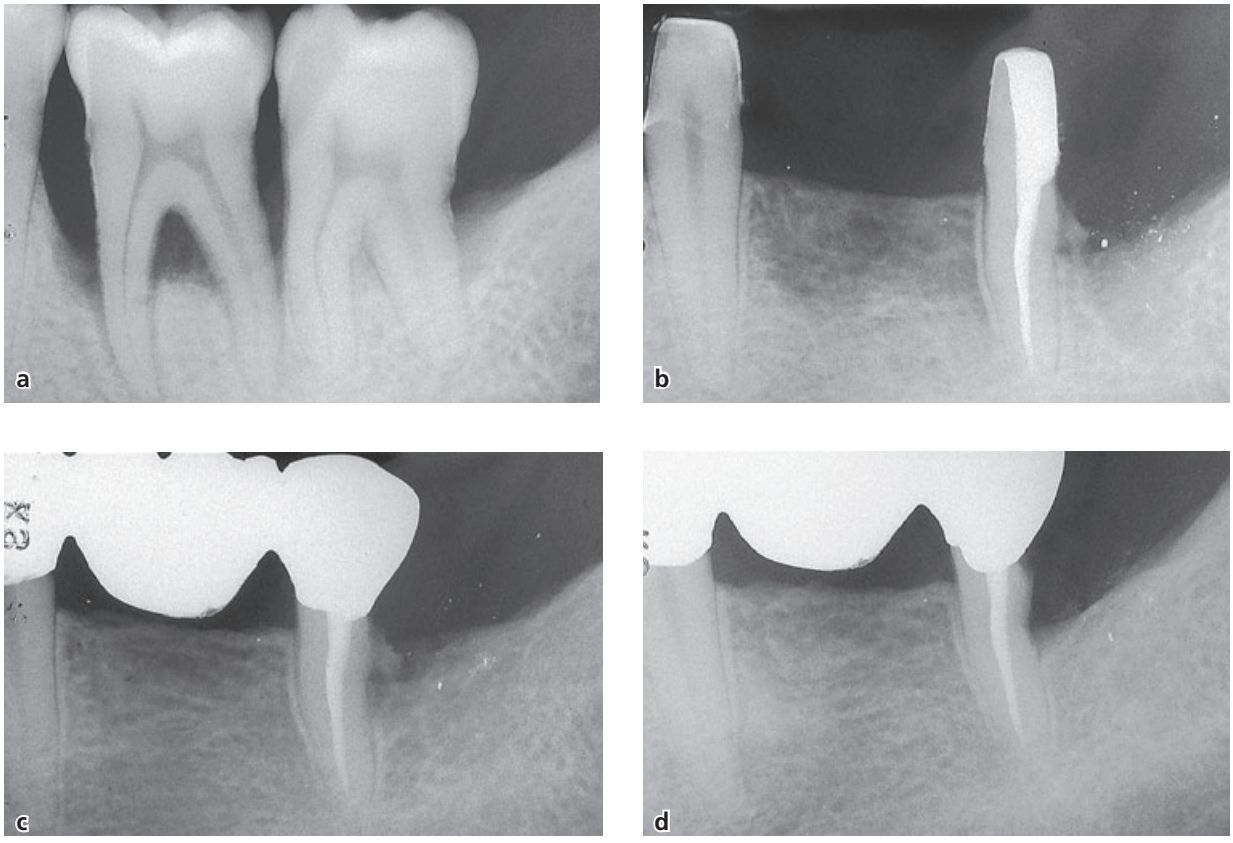

Fig. 39-32 (a) Radiographs of a mandibular first molar to be extracted and of a second molar to be root resected. (b) During hemisection an overhang is left behind as a result of an oblique sectioning of the tooth distal to the furcation. (c) In a radiograph obtained 2 years later, the presence of an angular bony defect can be seen adjacent to the "overhang". The lesion was resolved and the angular defect disappeared following removal of the "overhang". (d) Radiograph after 2 years.

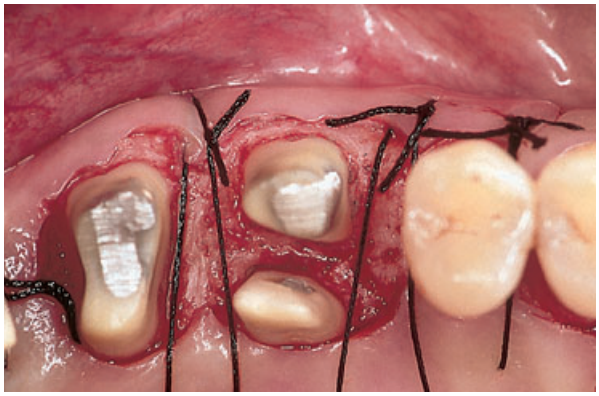

Fig. 39-33 Maintenance of the two fused buccal roots of a maxillary first molar. The buccal roots were separated from the palatal root. Note the rounded line angles and the wide space created between the separated roots.

Fig. 39-34 Mandibular molar after root separation. Note the diverging angle of preparation performed to increase the inter-radicular space between the mesial and distal roots and the parallel approximal surfaces.

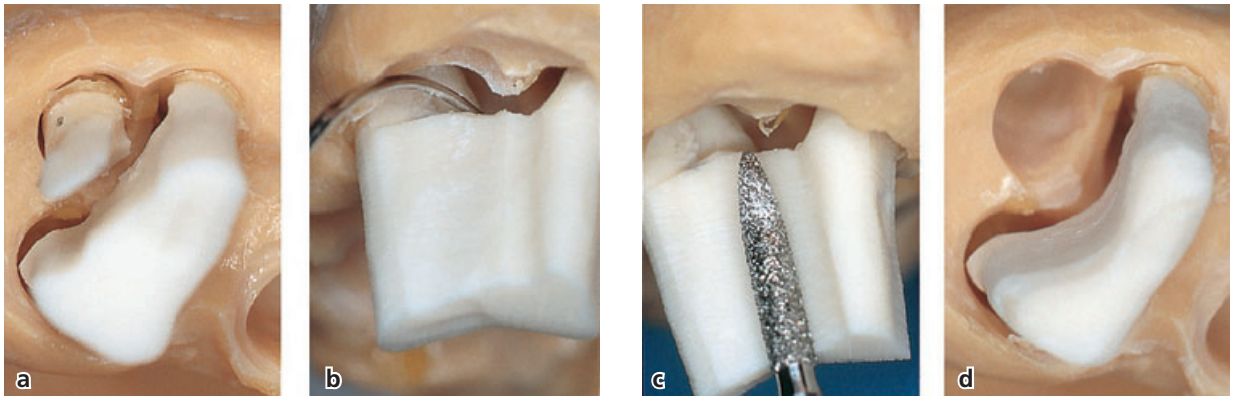

Fig. 39-35 (a,b) The sequential stages of root resection and extraction of the distal root of a maxillary molar. In order to minimize the concave outline of the cut surfaces, the sectioning should be performed with a straight line cut. (c, d) After extraction of the distal root, the furcation area of the remaining roots must be re-prepared to eliminate undercuts.

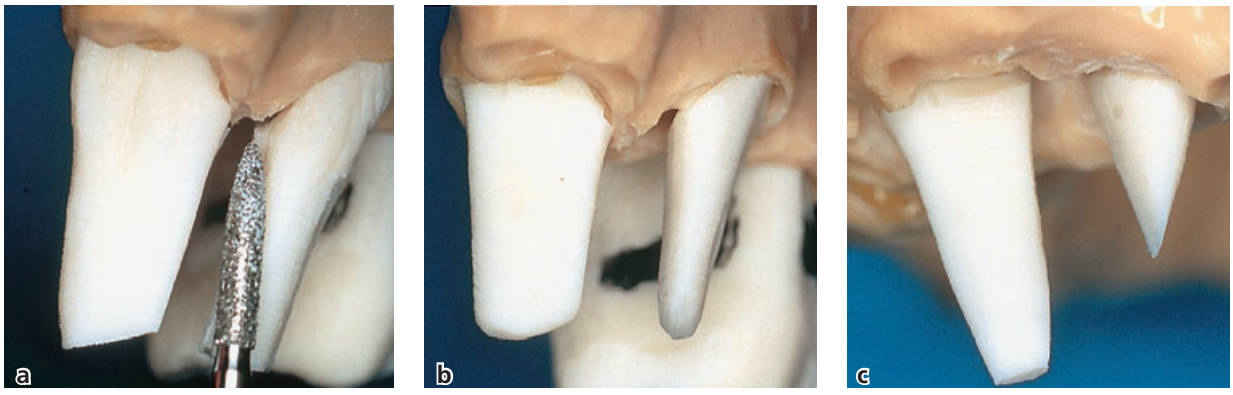

Fig. 39-36 (a,b) Preparation, during separation, of the mesio-buccal and palatal roots after the disto-buccal root of a maxillary molar had been extracted. The internal (furcation) surfaces of the two roots should be prepared with diverging angles to increase the inter-radicular space, while the external surfaces of the two roots should be prepared parallel to each other to increase the subsequent retention of the restoration. (c) When the palatal surface of the palatal root is not prepared parallel to the buccal surface, the palatal abutment will become shortened and not self-retentive.

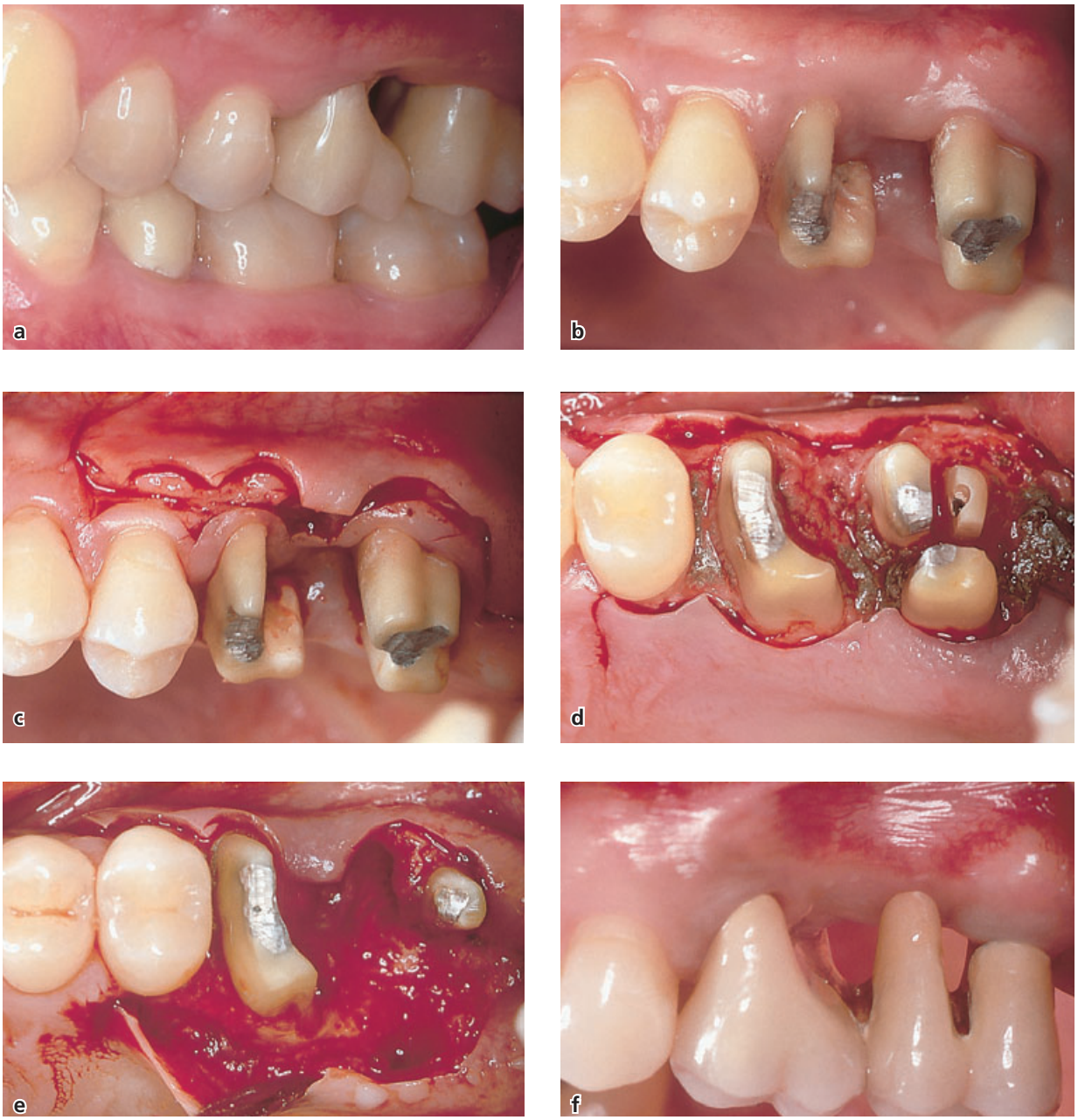

Fig. 39-37 (a,b) Sequential stages of root resection at maxillary first and second molars. The extraction of the distal root of the first molar was performed during tooth preparation and prior to the insertion of the provisional restoration. (c,d,e) During the surgical procedure, after flap elevation, the furcation-involved second molar was separated, the mesial and palatal roots were extracted and the osseous defects were eliminated. (f) Healing with the definitive prosthetic restoration in place.

and the patient instructed in proper plaque-control techniques.

Final prosthetic restoration

Since the prosthetic preparation of the roots was completed during surgery, the clinician concerns him-/herself only with minor adjustments. The preparation margins are located supragingivally, which improves the precision of the definitive crown restoration. The framework of the restoration must be rigid to compensate for the compromised abutments (roots) with a compromised periodontal tissue support. The occlusion should be designed to minimize the infliction of lateral deflective forces (see Chapter 51) (Fig. 39-38).

Regeneration of furcation defects

The possibility of regenerating and closing a furcation defect has been investigated (see Chapter 43). Following an early case report publication (Gottlow *et al*. 1986), where histologic documentation of new attachment formation in human furcation defects (Fig. 39-39) treated by "guided tissue regeneration" (GTR) therapy was provided, the results of several investigations on this form of treatment in furcation-

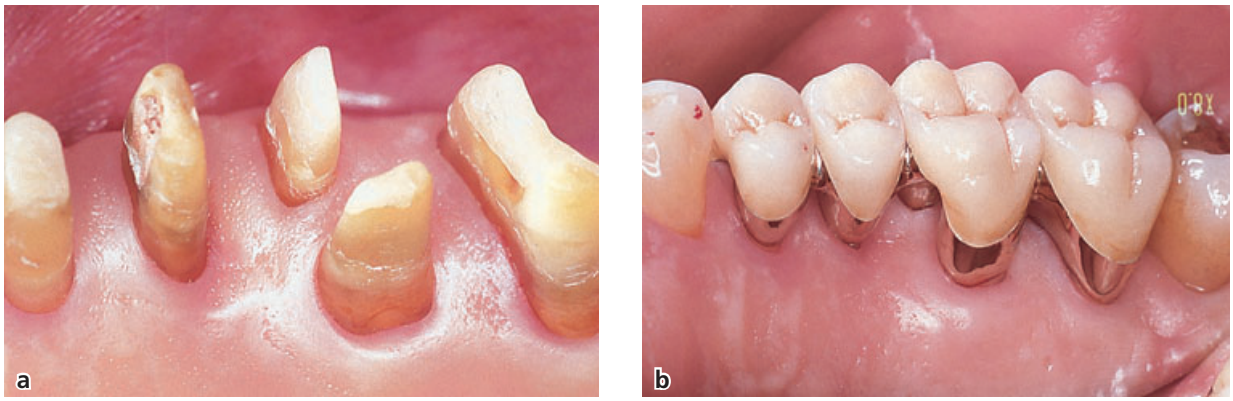

Fig. 39-38 (a) Soft tissue healing at a separated maxillary first molar and at a root-resected second molar. (b) The final prosthetic restoration in place with the occlusion designed to minimize the lateral stresses on the roots left as abutments.

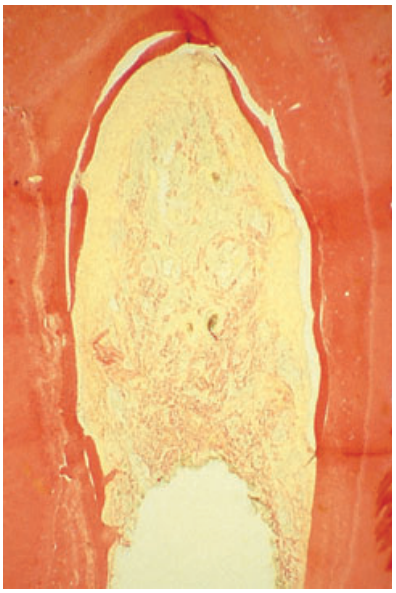

Fig. 39-39 Histologic mesiodistal section of a previous degree II furcation involvement of a human mandibular molar, treated with GTR. The section demonstrates that the newly formed cementum covers the entire circumference of the furcation defect.

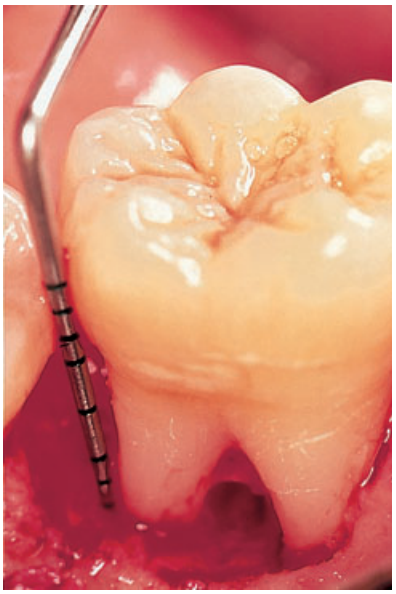

Fig. 39-40 Position of the furcation fornix in relation to the level of the supporting bone and attachment apparatus in a lingual degree II furcation-involved mandibular molar.

involved teeth have been presented. In these reports, a reasonably predictable outcome of GTR therapy was demonstrated only in degree II furcation-involved mandibular molars, where a clinical soft tissue closure or a decreased probing depth of the furcation defect was recorded (Pontoriero *et al*. 1988; Lekovic *et al*. 1989; Caffesse *et al*. 1990).

Less favorable results have been reported when GTR therapy was used in other types of furcation defects such as degree III furcation-involved mandibular and maxillary molars (Pontoriero *et al*. 1989; Pontoriero & Lindhe 1995a) and degree II furcations in maxillary molars (Metzeler *et al*. 1991; Pontoriero & Lindhe 1995b).

The reason for the limited predictability of GTR therapy in furcation-involved teeth may be related to several factors:

- The morphology of the periodontal defect, which in the root complex often has the character of a "horizontal lesion". New attachment formation is hence dependent on coronal upgrowth of periodontal ligament tissue (Fig. 39-40).
- The anatomy of the furcation, with its complex internal morphology, may prevent proper instrumentation and debridement of the exposed root surface (Fig. 39-41).
- The varying and changing location of the soft tissue margins during the early phase of healing with a possible recession of the flap margin and early exposure of both the membrane material and the fornix of the furcation (Fig. 39-42).

GTR treatment could be considered in dentitions with isolated degree II furcation defects in mandibular molars. The predictability of this treatment outcome improves following GTR therapy if:

- The *interproximal* bone is located at a level which is close to the CEJ of the approximal surface. This "key-hole" type of degree II involvement allows for an effective retention of the membrane material and retention also of the position of the coronally placed flap margins (Fig. 39-43).
- The debridement of the exposed root surfaces in the furcation area is comprehensive. Since the width of the furcation entrance and the internal morphology of the inter-radicular area may limit the access of curettes for proper debridement, the removal of hard and soft bacterial deposits from the root surfaces must frequently be made with ultrasonic instruments, rotating, flame-shaped fine diamond burs, and endodontic files (Fig. 39-44).
- The membrane material is properly placed and a "space" between the tooth and the material

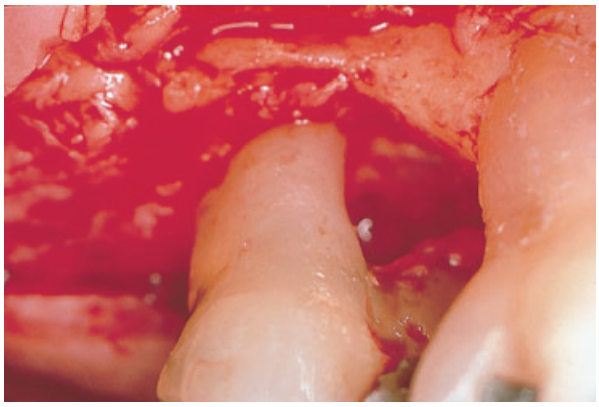

Fig. 39-41 Internal morphology of the furcation of a maxillary molar. Note the invagination of the palatal root.

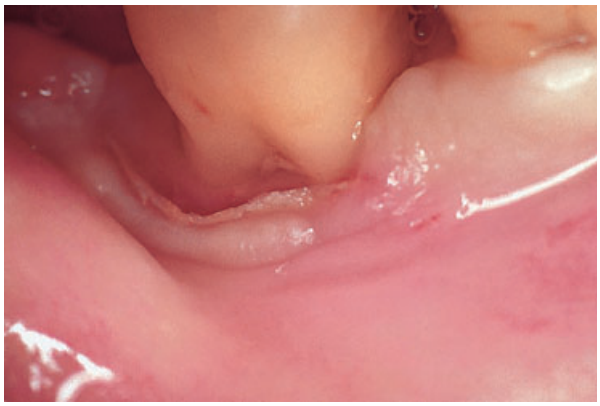

Fig. 39-42 Exposure of the membrane and of the furcation entrance as a consequence of recession of the flap margin. The photograph is taken at 3 weeks of healing after GTR treatment of a degree II buccal furcation of a mandibular molar.

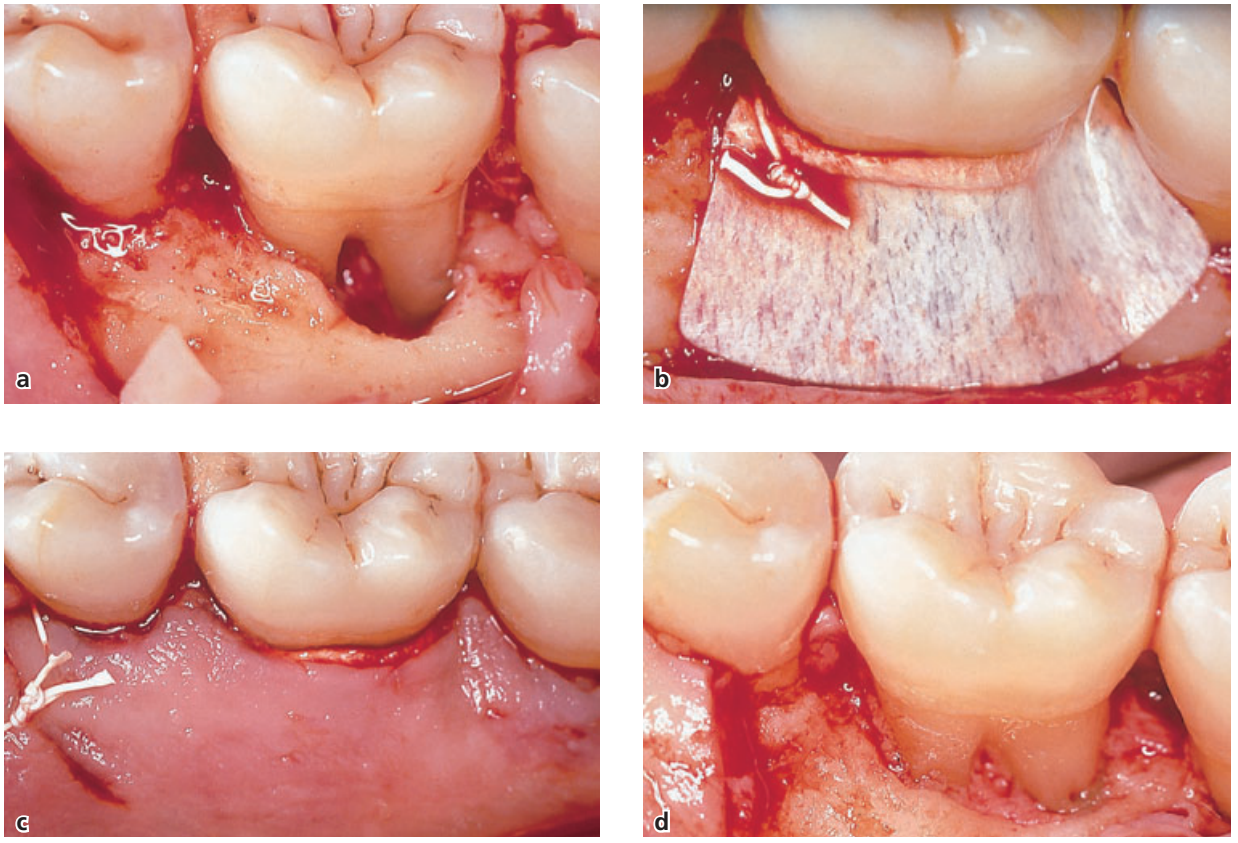

Fig. 39-43 Aspect of a lingual degree II furcation involvement in a mandibular first molar. (a) Note the infrabony component of the defect and the level of the approximal supporting bone in relation to the furcation fornix. (b) The Teflon membrane sutured in position and supported by the interproximal alveolar bone. (c) The flap positioned and sutured over the membrane. (d) At re-entry, after 6 months of healing, the previously exposed furcation defect was closed and filled with bone tissue.

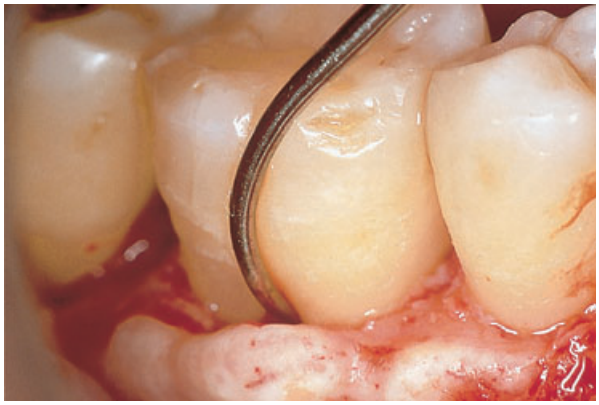

Fig. 39-44 Phase of debridment of a buccal degree II furcation defect by the use of an "extra-fine" ultrasonic tip.

established. A "primary" wound closure is thereby obtained, blood clot protection will occur, and recession of the soft tissue margin during the early phase of healing will be minimized (Fig. 39-45).

- A plaque-control program is put in place. This should include daily rinsing with a chlorhexidine solution and professional tooth cleaning once a week for the first month, and once every 2–3 weeks for at least another 6 months of healing following the surgical procedure.

Enamel matrix proteins included in a commercially available product (Emdogain®; Straumann, Basel, Switzerland) were used in the treatment of furcation defects in experimental studies in animals (Araùjo & Lindhe 1998) and in clinical trials in humans (Jepsen *et al*. 2004; Meyle *et al*. 2004). The ability of Emdogain® (EMD), applied to the root surfaces in the furcation area, to stimulate periodontal regeneration in surgically created degree III furcation defects in dogs was documented histologically by Araùjo and Lindhe (1998). In a multicenter randomized controlled clinical trial, including 45 subjects with 45 paired mandibular molars with buccal degree II furcation involvements, Jepsen *et al*. (2004) compared the EMD with GTR therapy. After 14 months of healing, the subjects were re-examined. The authors reported a mean reduction in the open horizontal furcation depth of 2.8 mm for EMD-treated sites and of 1.8 mm for GTR-treated defects. In addition the frequency of complete closed furcation defects was higher for EMD sites (8/45) than for GTR sites (3/45). It was concluded that both treatment modalities resulted in significant clinical improvements although the EMD method provided (1) greater reduction of the furcation depths, (2) a smaller incidence of post-operative pain/swelling, and (3) less gingival recession (Meyle *et al*. 2004) as compared to GTR therapy.

The outcome of the regenerative procedures at furcation-involved molars should result in the complete elimination of the defect within the interradicular space in order to establish anatomic conditions which facilitate optimal self-performed plaque-control measures. In fact, partial gain of clinical attachment levels within the furcation defect, although statistically significant, will not necessarily improve the site's accessibility for plaque-control measures.

Extraction

The extraction of a furcation-involved tooth must be considered when the attachment loss is so extensive that no root can be maintained or when the treatment will not result in a tooth/gingival anatomy which allows proper self-performed plaque-control measures. Moreover, extraction can be considered as an alternative form of therapy when the maintenance of the affected tooth will not improve the overall treatment plan or when, due to endodontic or caries-related lesions, the preservation of the tooth will represent a risk factor for the long-term prognosis of the overall treatment.

The possibility of substituting a furcation-involved tooth with an osseointegrated implant should be considered with extreme caution and only if implant therapy will improve the prognosis of the overall treatment (see Chapter 32). In fact, the implant alternative has obvious anatomic limitations in the maxillary and mandibular molar regions.

Prognosis

Several studies have evaluated the long-term prognosis of multi-rooted teeth with furcation involvement that were treated in accordance with the principles described in this chapter (Table 39-2). In a 5-year study, Hamp *et al*. (1975) observed the outcome of treatment of 175 teeth with various degrees of furcation involvement in 100 patients. Of the 175 teeth, 32 (18%) were treated by scaling and root planing alone, 49 (28%) were subjected, in addition to scaling and root planing, to furcation plasty which included odonto- and/or osteoplasty. In 87 teeth (50%) root resection had been carried out and in seven teeth (4%) a tunnel had been prepared. At the completion of the active phase of therapy the patients were enrolled in a maintenance program which included a recall visit every 3–6 months. The plaque and gingivitis scores assessed immediately after treatment and once a year during maintenance indicated that the patients' oral hygiene was of high quality. None of the teeth treated was lost during the 5 years of study. Only 16 furcation sites exhibited probing depths exceeding 3 mm. During the observation period carious lesions were detected in 12 surfaces of the 32 teeth which had been treated by scaling and root planing, in three surfaces of the 49 teeth subjected to furcation plasty, in five surfaces of the

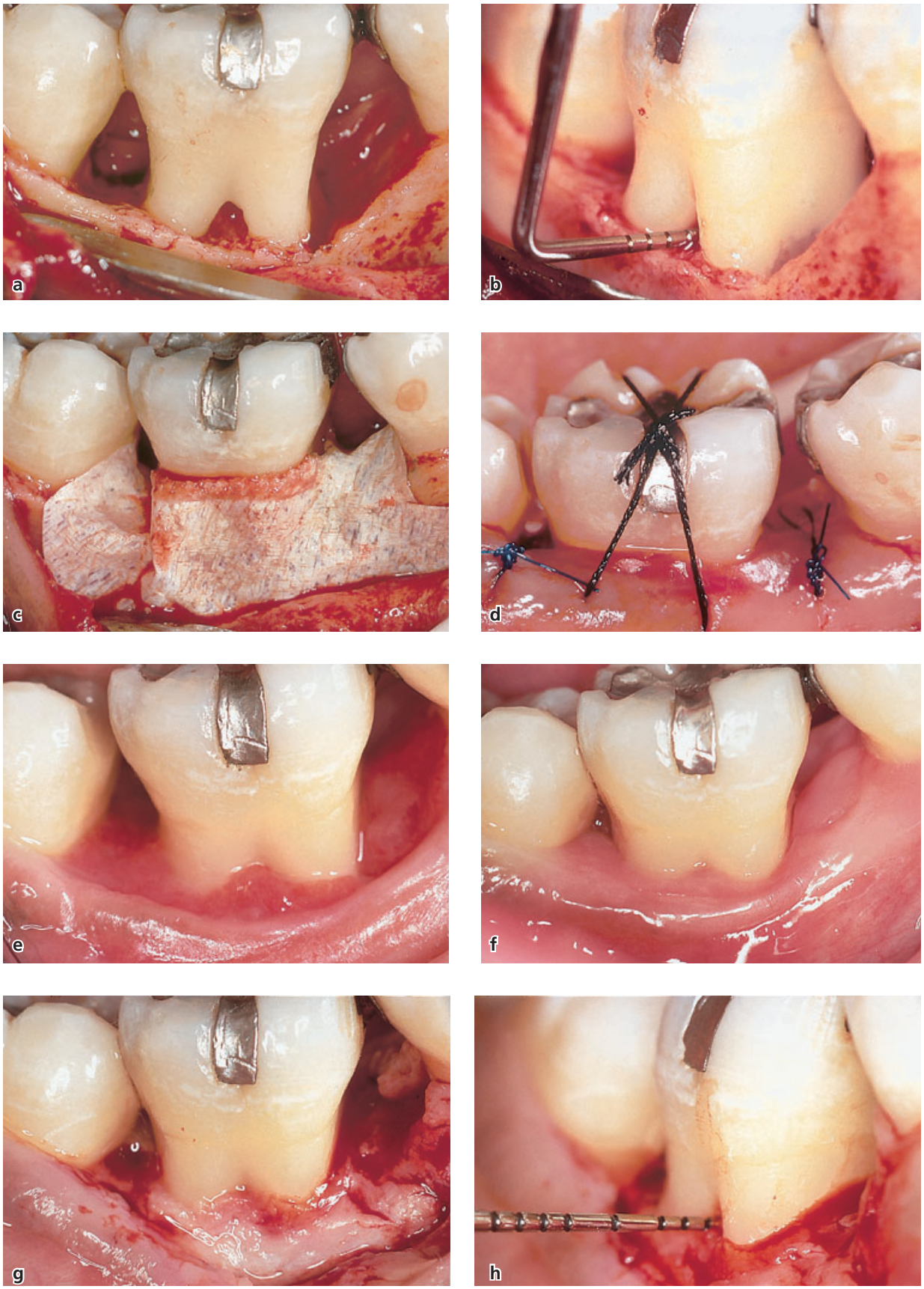

Fig. 39-45 The sequential stages of GTR treatment of a buccal degree II furcation-involved mandibular first molar. (a,b) The clinical appearance and the horizontal probing of the defect. (c,d) Membrane placement and retention. (e) The clinical aspect of the soft tissue at 4 weeks after membrane removal. (f) The clinical aspect after 6 months of healing. During the re-entry procedure the furcation defect appeared completely closed (g) and was not probeable (h).

Table 39-2 Long-term clinical studies on root resection therapy in molars with furcation involvement

Author	Observation period	No. of teeth examined	Causes of tooth loss					
			% teeth lost	% root/ tooth fracture	% periodontal	% endodontic	% caries or decementation	% strategic
Bergenholtz (1972)	21 teeth/2–5 yrs 17 teeth/5–10 yrs	45	6		4	2		
Klavan (1975)	3 yrs	34	3		3			
Hamp *et al.* (1975)	5 yrs	87	0					
Langer *et al.* (1981)	10 yrs	100	38	18	10	7	3	
Erpenstein (1983)	4–7 yrs	34	9		3	6		
Bühler (1988)	10 yrs	28	32	3.6	7.1	17.7	3.6	
Carnevale *et al.* (1991)	303 teeth/3–6 yrs 185 teeth/7–11 yrs	488	4	1.8	0.4	0.9	0.9	
Basten *et al.* (1996)	2–23 yrs	49	8			2	4	2
Carnevale *et al.* (1998)	10 yrs	175	7	1.1	1.8	2.3	1.8	

78 root-resected teeth, and in four surfaces of the seven teeth where a tunnel was prepared.

The results of this study were basically confirmed in a more recent investigation (Hamp *et al*. 1992). In this 7-year study, the authors followed 100 patients with 182 furcation-involved teeth. Out of the 182 furcation-involved teeth, 57 had been treated by scaling and root planing only, 101 were treated by furcation plasty, and 24 were subjected to root resection or hemisection. No tunnel preparation was performed. After the active phase of therapy, the patients were enrolled in a meticulous maintenance care program including recall appointments once every 3–6 months. During the course of the study, more than 85% of the furcations treated with scaling root planing alone, or in conjunction with furcation plasty, maintained stable conditions or showed signs of improvement. Only one tooth and one mesial root of a mandibular molar were extracted among the root-resected or hemisected teeth.

Carnevale *et al*. (1998), in a 10-year prospective controlled clinical trial, demonstrated a 93% survival rate of root resected furcation-involved teeth and a 99% survival rate of non-furcation-involved teeth.

More recently, Svärdström (2001) presented the results of a retrospective analysis on factors influencing the decision-making process regarding the treatment for 1313 molars with furcation involvement in 222 patients and the outcome of the treatment decisions after 8–12 years (mean 9.5 years) of regular maintenance care. The treatment options included were: tooth extraction, root separation/resection, and maintenance of the tooth with non-surgically/surgically performed scaling and root planing with or without furcation plasty. Of the 1313 furcation-involved molars, 366 (28%) were extracted during the active phase of therapy. The decision for tooth extraction was primarily influenced by factors such as tooth mobility, tooth position, absence of occlusal antagonism, the degree of furcation involvement, probing depth, and the amount of remaining periodontal support. Out of the 685 molars with furcation involvement and the 160 patients that were available for the follow-up examination 8–12 years after treatment, 47 teeth were root separated/resected and 638 teeth were considered to be maintainable after a non-surgical or conservative surgical therapy.

The factor found to have the strongest influence for the decision to perform root separation/resection was the degree of furcation involvement (degree II and III). Tooth position, probing depth, and tooth mobility were also factors of statistical significance. The author explained that other factors such as endodontic conditions, root anatomy, and overall treatment strategy may also have influenced the choice of treatment. The long-term outcome of the treatment decisions made for furcation-involved molars showed a favorable survival rate for both root resective (89%)

Table 39-3 Factors to consider in treatment of furcation-involved molars

Tooth-related factors
Degree of furcation involvement
Amount of remaining periodontal support
Probing depth
Tooth mobility
Endodontic conditions and root/root-canal anatomy
Available sound tooth substance
Tooth position and occlusal antagonisms
Patient-related factors
Strategic value of the tooth in relation to the overall plan
Patient's functional and esthetic demands
Patient's age and health conditions
Oral hygiene capacity

and non-resective (96%) therapy options in patients included in a proper maintenance care program. Of the 47 root separated/resected teeth, only five (11%) were lost during the 9.5 years of follow-up. Of the 638 molars initially considered to be maintainable by a non-resective treatment, 21 teeth (3.5%) were extracted and three teeth were root resected.

Conclusion

In treatment decisions for furcation-involved molars, it must be realized that there is no scientific evidence that a given treatment modality is superior to the others (Table 39-3).

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Chapter 40

Endodontics and Periodontics

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Introduction

Inflammatory lesions of the attachment apparatus of teeth involve a variety of etiologies other than plaque accumulations in the dentogingival region; these require attention in diagnosis and treatment planning processes. In fact, signs and symptoms, seen as typical of periodontitis, such as pocket probing depths, loss of attachment, increased tooth mobility, pain, swellings and suppurations, may reflect several tooth-associated infections including infections of endodontic origin (here termed endodontic lesion), infections initiated and maintained by iatrogenic root perforations, vertical root fractures, and external root resorption.

Differentiating between inflammatory disease conditions of the periodontium is not normally a thorny exercise. This is because symptoms of periodontitis usually affect several teeth in the dentition and are confined to the marginal periodontium. Other tooth-associated infections, by contrast, are usually isolated to a single tooth and display rather typical clinical and radiographic signs. These conditions can nevertheless produce confusing clinical expressions and lead to misinterpretation of their cause, especially when affecting teeth in dentitions diseased by periodontitis. Diagnostic difficulties particularly arise when lesions appear deep down the lateral aspects of roots in what can be designated a marginal–apical communication. These so-called "endo–perio lesions" present the clinician with exceptional challenges in that the origin and thus the proper course of treatment are not readily revealed. An "endo–perio lesion", as the term implies, involves a condition where both the pulp and the periodontium are diseased simultaneously in what appears to be a single periodontal lesion. However, a complicating factor is that the process may be of periodontal origin in its entirety and may have caused the death of the pulp in the process or the lesion may just be a representation of a root canal infection alone. Hence, determination of causality is crucial in these cases not only to avoid unnecessary and possibly detrimental treatment, but also to assess whether the disease condition stands a reasonable chance of being successfully treated.

To guide clinical decision making on diagnosis and treatment of inflammatory lesions in the periodontium, the focus of this chapter is on various tooth-associated disorders that display similar signs and symptoms to periodontitis. Specifically addressed are the clinical presentations and the means by which endodontic infections and infections associated with root perforations, root fractures, and root resorptions can be identified and distinguished from manifestations of periodontitis. Management principles will be given where appropriate. Non-infectious processes *viz.* developmental cysts and tumors, which also can interfere with the supporting tissues, will not be discussed in this chapter.

Infectious processes in the periodontium of endodontic origin

General features

Disease conditions of the dental pulp are for the most part infectious in nature and involve inflammatory processes. Caries, restorative procedures, and traumatic injuries are common etiologies (see Chapter 23). In fact, any loss of hard tissue integrity of teeth, exposing dentin or the pulp directly to the oral environment, may allow bacteria and bacterial elements to adversely affect the normally healthy condition of the pulp. The resulting inflammatory lesion will then be directed towards the source of irritation and be confined for as long as the inflammatory defense does not collapse and convert into a major destructive breakdown of the pulpal tissue. Consequently, inflammatory alterations in the vital pulp will not normally produce lesions in the adjoining periodontium that can be detected by clinical means. Yet, disruption of the apical lamina dura or widening of the periodontal ligament space can occasionally be observed radiographically (Fig. 40-1a). Teeth, particularly in young individuals with large pulp chambers, may also display minor radiolucent areas either apically or laterally along the root surface at exits of accessory canals and apical foramina or both, in spite of the fact that vital pulp functions prevail (Langeland 1987; Gesi *et al*. 2006). In such cases, typical clinical signs of pulpitis, including spontaneous pain, thermal sensitivity or tenderness to percussion, may or may not be present.

Overt lesions in the periodontium, on the other hand, are common in teeth where the pulp has lost its vitality. In these cases the process is associated either with a non-treated necrotic pulp or a tooth that has been the subject of endodontic treatment. In the latter case, the cause of the lesion is usually to be found in an existing, although not successfully managed, root canal infection (Fig. 40-1b). Extrusion of toxic medicaments and root-filling materials into the periodontium in conjunction with endodontic treatments may also cause periodontal lesions. While severe damage of the periodontal tissue support formerly was a rather common complication following the use of arsenic- or formaldehyde-based preparations to devitalize pulps, medicate, and fill root canals (Fig. 40-2), modern day medicaments for canal irrigation and disinfection as well as materials for root canal filling are comparatively well tolerated (Geurtsen & Leyhausen 1997). However, acute toxic and allergic reactions may be encountered from the use of highly concentrated sodium hypochlorite (Pashley *et al*. 1985) and adverse components of root-filling material (Hensten-Pettersen *et al*. 1985).

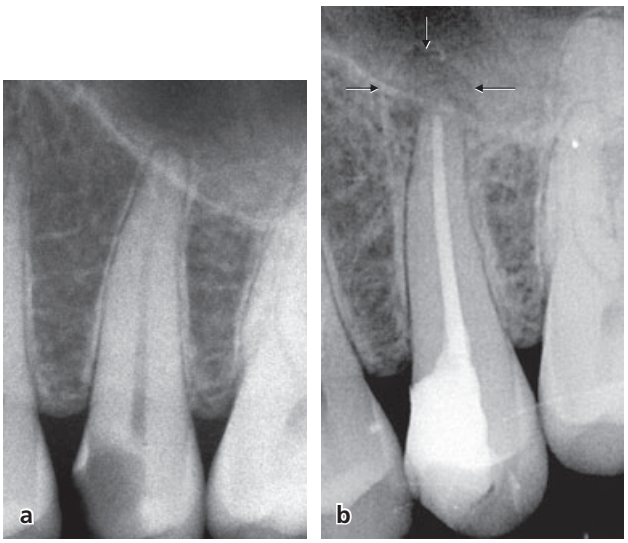

Fig. 40-1 (a) Radiograph of an upper second premolar with caries extending to the vicinity of the pulp. There is loss of lamina dura at the root tip. (b) The 3-year recall radiograph after pulpectomy of the vital pulp and root filling shows a periapical radiolucency suggesting existence of a persistent root canal infection in this case.

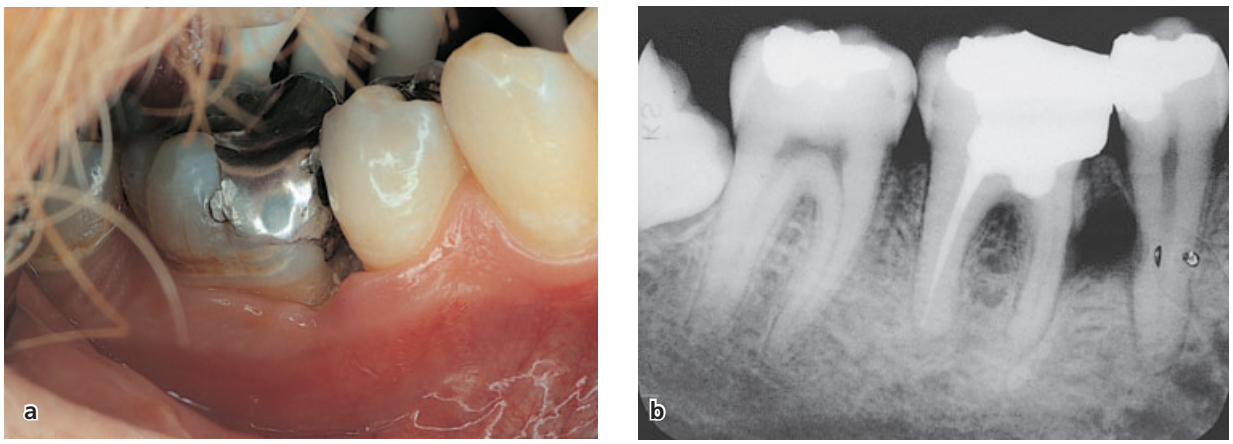

Fig. 40-2 (a) Clinical photograph showing a periodontal defect at the mesial aspect of tooth #46. The pulp had been subjected to devitalization by the use of a paraformaldehyde-containing paste. (b) Leakage of the agent along the temporary filling margins obviously occurred as suggested by the subsequent loss of proximal bone and the emergence of a bone sequestrum.

Conclusion

It is important to realize that as long as the pulp maintains vital functions, although inflamed or scarred, it is unlikely to produce irritants that cause overt periodontal tissue lesions. For clinically significant lesions to occur the pulp must have lost its vitality. Consequently no benefit will normally be gained from extirpation of vital pulps (pulpectomy) as an adjunct or alternative to the treatment of teeth for periodontal disease.

Clinical presentations

Inflammatory lesions in the periodontal tissues, induced and maintained by root canal infection, typically expand around the apex of teeth, where the root canal space interconnects with the periodontium along apical foramina. Lesions develop more seldom in a juxtaposition that is at the lateral aspects of roots (Fig. 40-3) and in furcations of multi-rooted teeth (Fig. 40-4). An important reason is that accessory canals that can mediate the release of bacterial elements from the pulpal chamber are relatively uncommon in cervical and mid-root portions (see Chapter 23). Another important factor is that an intact layer of root cementum blocks potential dissemination of bacteria and their products along the dentinal tubules.

The clinical presentation varies. Lesions can either be in a silent, non-symptomatic state or appear with more or less salient signs of acute infection. In the former case a balanced host–parasite interrelationship has usually been established. The only means to diagnose the condition is then by radiography (Fig. 40-1b). Unless transformed to a cyst, the extension of such non-symptomatic lesions may remain limited and stable over many years. This applies in particular to lesions associated with root-filled teeth, where the persisting root canal infection has assumed a relatively low grade of metabolic activity (see Chapter 23).

Lesions associated with untreated infections of a necrotic pulp or with inadequately treated root canals may any time, either soon after pulp tissue breakdown or after a period of silence, turn into an exacerbating, acute inflammatory process. Exacerbating lesions may also be induced in conjunction with endodontic treatment from over-instrumentation along with extrusion of bacterial organisms and tissue-irritating medicaments. Exudation and pus production dictate the clinical course. Typical symptoms

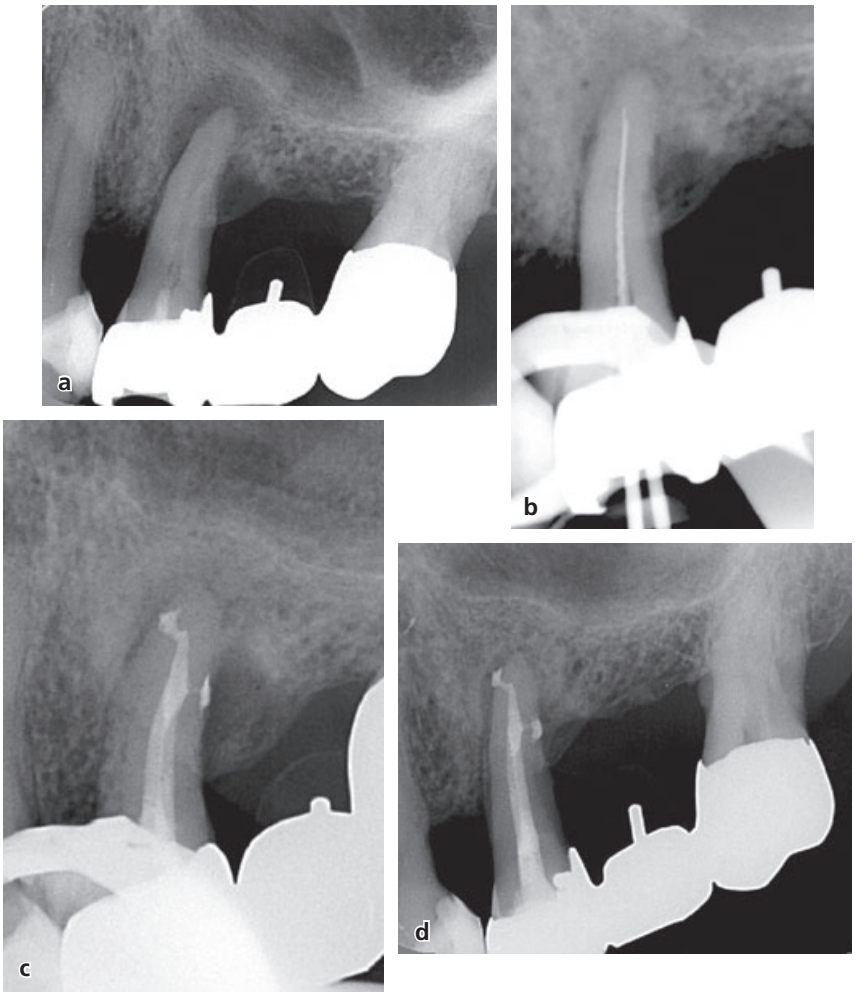

Fig. 40-3 Series of radiographs showing endodontic treatment of an upper premolar included as an abutment in a three-unit bridge. The patient, a 78-year-old male, had been treated and maintained for periodontal disease. (a) There are bone lesions both at the apical and at the distal aspect of the tooth. Following endodontic treatment of the necrotic pulp (b) and root filling (c), an accessory canal communicating with the lateral lesion became evident. (d) The 6-month recall radiograph shows substantial reduction of both bone lesions. Case kindly provided by Dr. Peter Jonasson.

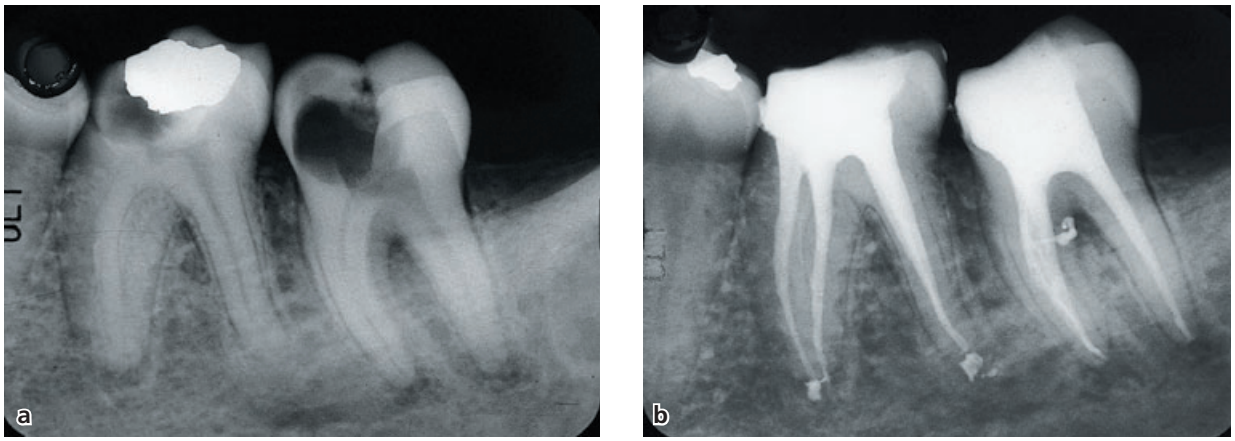

Fig. 40-4 (a) Bone loss of the furcal region in a second left molar in addition to apical bone lesions at both the mesial and the distal roots. (b) Upon endodontic treatment an accessory canal became filled, suggesting that the furcal lesion was of endodontic origin. Case kindly provided by Dr. Pierre Machtou.

include throbbing pain, pain on percussion, tenderness to palpation, increased tooth mobility, and apical as well as marginal swellings. The severity of these symptoms may have escalated successively over a period of time, although a single sign may be the only presenting symptom. It should be noted that the very same symptoms occur with some forms of aggressive periodontitis, iatrogenic root perforation, root fracture, and external root resorption (see below).

The pressure the exudative process exerts results in tissue destruction as a path for drainage is sought. This expansion of the lesion may take a variety of directions. Significant in the context of differential diagnosis to periodontitis are those lesions that drain at or near the gingival margin. The character of the accompanying bone lesion may add to the risk of misdiagnosis, as it may look similar to that of aggressive periodontitis (Fig. 40-5).

Several routes of drainage from an acute endodontic lesion should be recognized (Fig. 40-6):

1. The suppurative process may drain off along the periodontal ligament space and exit at the bottom of the sulcus (Fig. 40-6a). This usually results in only a narrow opening of the fistula into the gingival sulcus/pocket and may not be detected unless careful probing of the sulcus is carried out at multiple sites. Such a sinus tract may readily be probed down to the apex of the tooth, where no increased probing depth otherwise may exist around the tooth. In multi-rooted teeth a sinus tract along the periodontal ligament can drain into the furcation area as it exits along the root surface. The resulting bone lesion may then resemble a "through-and-through" furcation defect from periodontal disease (Figs. 40-7 and 40-8).
2. A periapical abscess can also perforate the cortical bone close to the apex. In this acute stage the soft tissue including the periosteum may be elevated from the bone surface to the extent that a wide opening for drainage of pus is created in the gingival sulcus/pocket area (extraosseous drainage; Fig. 40-6b). Later this route of drainage may develop into in a chronic sinus tract that may remain in or near the sulcus, often at the buccal aspect of the involved tooth. Such a fistula may also emerge following a less aggressive process. It is important to note that this type of drainage is not associated with loss of bone tissue at the inner walls of the alveolus, and that a periodontal probe cannot penetrate into the periodontal ligament space.

Conclusion

Endodontic lesions either do not have overt clinical signs or may present with various acute manifestations of root canal infection. The asymptomatic lesions usually assume a limited extension around the apex, while rapid and extensive destruction that may extend marginally along the attachment apparatus may follow acute exacerbations. Exudation and pus formed in the process may drain off in different directions; pathways along the periodontal ligament space or following penetration of the alveolar bone at the apical region with drainage in or near the gingival sulcus/pocket warrant particular attention from a differential diagnostic point of view. In addition to deep pocket probing depths, the accompanying bone lesion may mimic that of periodontitis.

Distinguishing lesions of endodontic origin from periodontitis

Pulp vitality testing

Differential diagnosis is important because at times endodontic lesions may produce clinical signs and symptoms similar to those of periodontitis. Tools to distinguish the two disease conditions from each

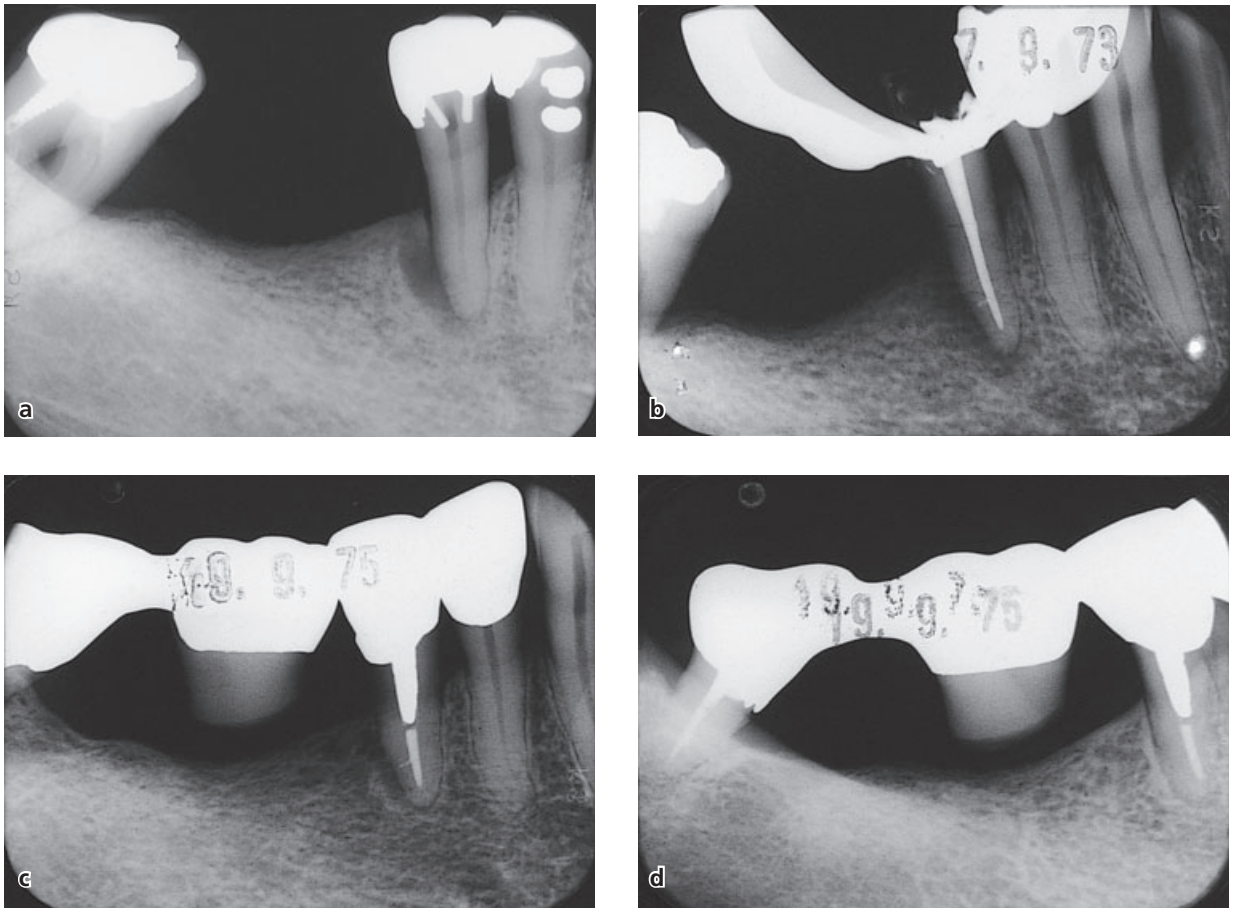

Fig. 40-5 (a) A radiolucent area along the distal root surface of tooth #45 is combined with horizontal loss of marginal bone. (b) As the pulp was non-vital it was subjected to endodontic treatment. After prosthodontic treatment (c) the 2-year recall radiograph (d) shows bone fill in the previous angular defect. Careful examination of the radiographs in (b) and (c) reveals a filled accessory canal communicating with the lateral bone defect.

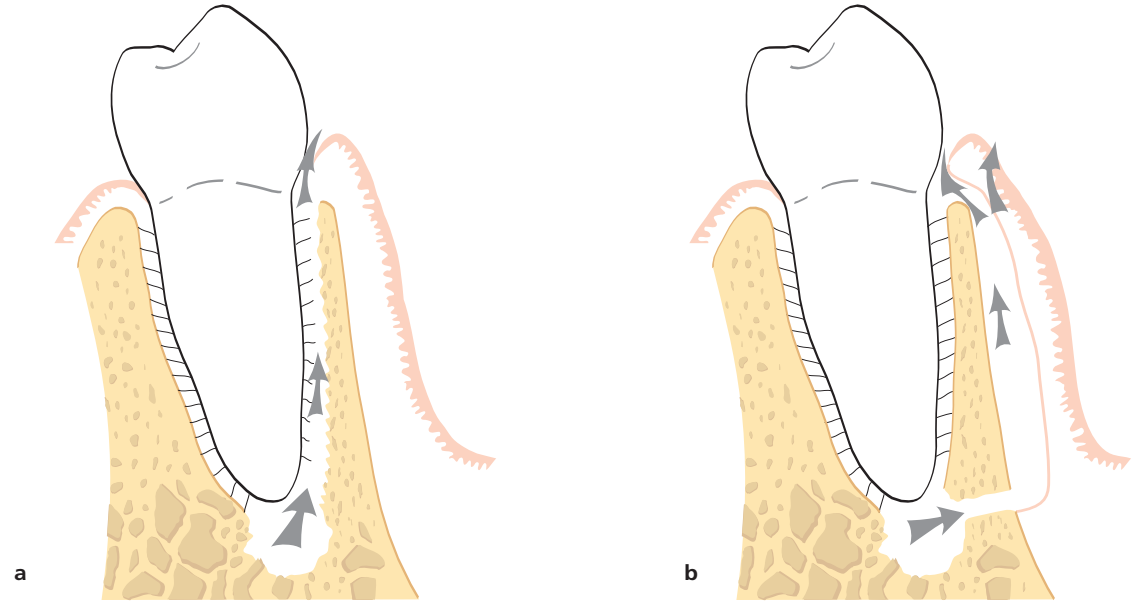

Fig. 40-6 Schematic illustrations demonstrating possible pathways for drainage of a periapical abscess. (a) Drainage along the periodontal ligament with an exit in the sulcus. (b) Extraosseous drainage with exits either in or near the sulcus.

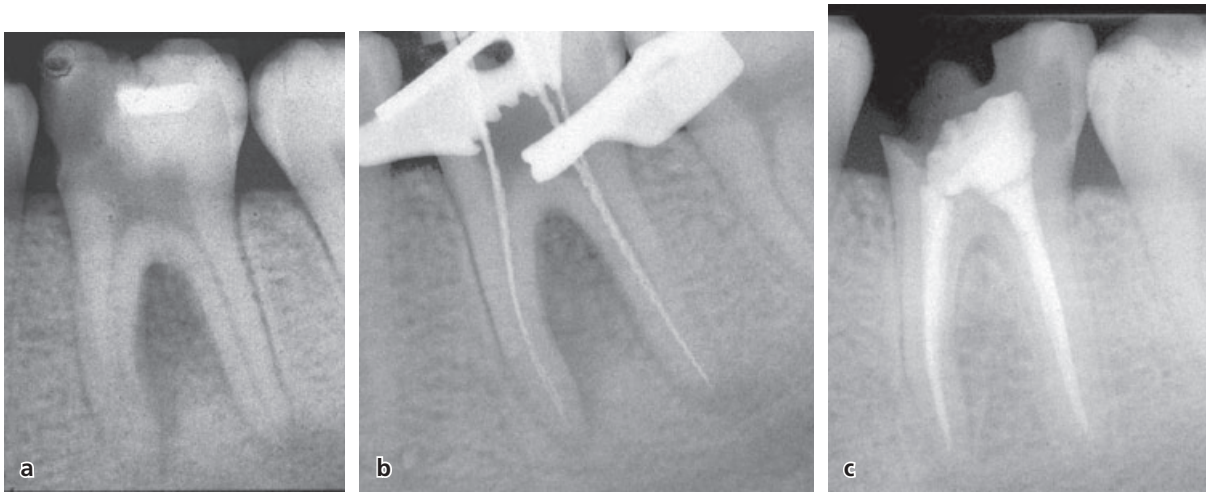

Fig. 40-7 (a) A large radiolucent area is present in the furcal region of a lower left first molar mimicking a furcation involvement caused by periodontal disease. In this case the lesion was of endodontic origin as indicated by the large caries lesion and necrosis of the pulp. (b) Endodontic treatment resulted in complete resolution of the bone lesion as demonstrated by the 18-month follow-up radiograph (c). Case kindly provided by Dr. Kevin Martin.

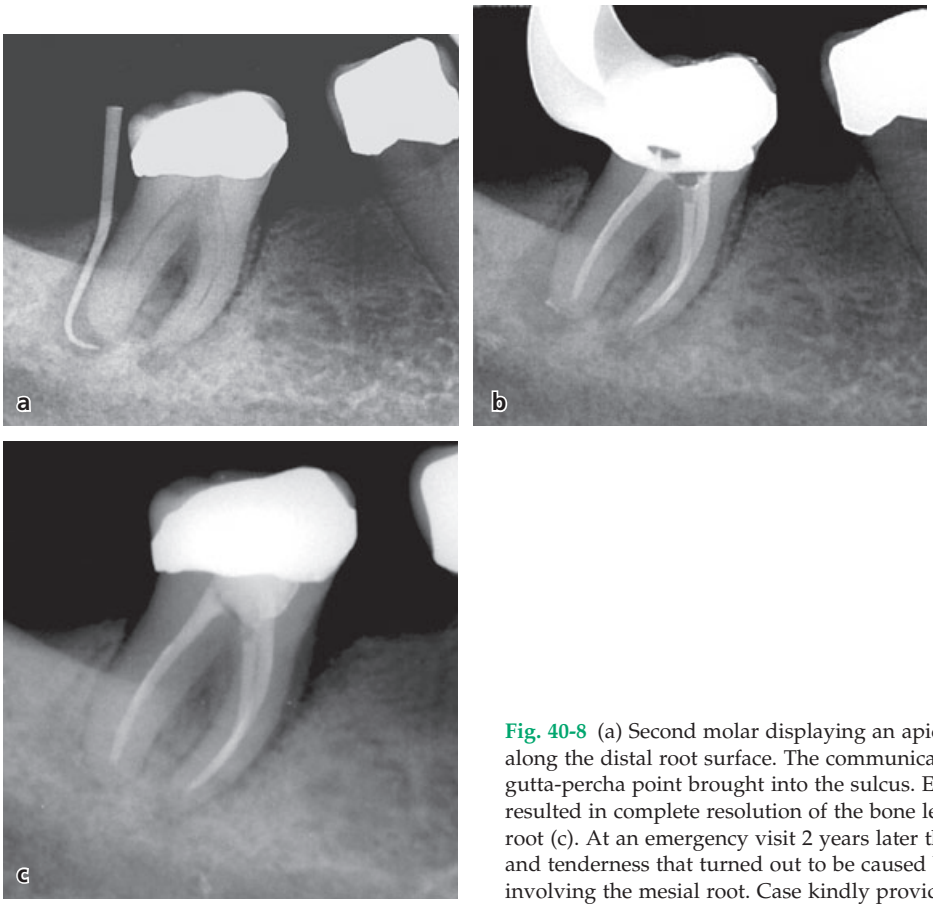

Fig. 40-8 (a) Second molar displaying an apical–marginal communication along the distal root surface. The communication was made visible by a gutta-percha point brought into the sulcus. Endodontic treatment (b) resulted in complete resolution of the bone lesions associated with the distal root (c). At an emergency visit 2 years later the patient complained of pain and tenderness that turned out to be caused by a longitudinal root fracture involving the mesial root. Case kindly provided by Dr. Peter Jonasson.

other, however, are limited as neither the patient's disease history, the clinical presentation nor the character of the radiographic signs invariably are clear-cut. As an endodontic lesion of clinical significance in this context cannot emerge unless the tissue has turned necrotic and become infected, determination of pulp vitality is a most important measure in cases where an endodontic etiology is suspected. Endodontic lesions associated with root-filled teeth are discussed separately, below.

Pulp vitality implies that the tissue has an intact neurovascular supply to support cell and tissue functions. Although a vital pulp may be inflamed or display a variety of degenerative changes, the vasculature is still functioning in a vital pulp. Most methods of determining pulp vitality act by stimulating the

pulp's sensory nerve function and presume that the provocation of a sharp pain sensation indicates a vital pulp. This means that in reality the *sensibility* of the pulp is tested rather than the *vitality* of it. However, there is ample documentation to support the concept that a tooth which responds to sensory stimuli has vital pulp functions. Conversely, if a tooth does not respond, the pulp may be non-vital (Petersson *et al*. 1999; Peters *et al*. 1994; Pitt Ford & Patel 2004). Means to detect blood flow within the pulp by non-invasive methods, for example by laser light scattering, have been developed and tested, but have so far gained limited clinical application (see review by Pitt Ford & Patel 2004).

Caution should be exercised in interpreting sensibility tests as findings can reflect both false-positive and false-negative readings (Mumford 1964; Petersson *et al*. 1989; Peters *et al*. 1994; Pitt Ford & Patel 2004). A combination of different test methods should be employed to ensure correct diagnosis, especially in doubtful cases. Also the equipment and the results should be tested for reliability by comparing results from tests of neighboring and contralateral teeth. No test has so far been advanced, which can identify the disease status of the pulp in other terms than vital or non-vital.

Testing non-restored or minimally restored teeth in dentitions affected by periodontitis can usually be successfully conducted by mechanical, thermal, and electric stimulation. Common methods utilize hydrodynamic forces to stimulate nociceptive mechanoreceptors at the pulp–dentin border, primarily the fast conducting A-delta fibers. Useful techniques include direction of a jet of compressed air against an exposed root surface, scratching such surfaces, use of a rubber wheel to generate frictional heat, and various cold tests; all intended to elicit movement of dentinal fluid. Highly effective and reliable are carbon dioxide snow (Fulling & Andreasen 1976) and dichlorodifluoro-methane sprayed on a cotton pledge. Boiling points of these two agents are at –72°C and –50°C, respectively. For this reason patients should be cautioned prior to application that an intense pain response might be elicited. Clues can also be obtained with less potent means such as ice sticks and ethyl chloride as well as heated gutta-percha sticks (for review see Pitt Ford & Patel 2004).

In dubious cases, mechanical and thermal provocation should be supplemented with electric pulp testing. Units are available which provide a read-out value of the voltage or micro-current being applied to generate the pain response. This function is important so that the test result can be repeated and compared for assessment of patient reliability. Electric pulp testing is technique sensitive and therefore warrants extra precaution to avoid leakage of current to the gingiva and neighboring teeth. To avoid this problem, the test should only be carried out on cleaned and dry teeth isolated from saliva and adjacent teeth with pieces of rubber dam placed in the tooth contacts (Fig. 40-9). The test further requires that the tooth electrode be provided with proper conducting medium and applied directly on to enamel or dentin.

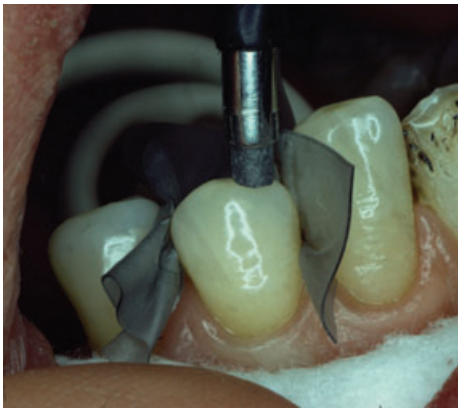

Fig. 40-9 Demonstration of proper tooth isolation to avoid leakage of current during pulp sensibility testing with an electric pulp tester.

Cases with extensive restorations and crowned teeth present special challenges as none of the normal test procedures are useful. Unless tooth substance can be reached underneath the restoration with a good margin to the gingiva, the restoration must be pierced to the extent that the test procedure can be conducted in a so-called test cavity. Even then a false-negative response can be obtained as extensive hard tissue repair may have developed in the pulp from previous disease and cutting traumas thus attenuating the stimulus.

Three cases are described below to illustrate the significance of pulp vitality testing in the process of distinguishing endodontic lesion from periodontitis. The cases demonstrate, in addition, that diagnostic entities such as location, form, and extension of radiolucencies, clinical symptoms of pain or swelling, and increased probing depths may not serve as precise diagnostic signs.

The clinical photograph in Fig. 40-10a shows swelling of the marginal gingiva on the buccal aspect of tooth #11. The swelling had been preceded by severe throbbing pain for a few days. Radiographic examination (Fig. 40-10b) disclosed the presence of an angular bone defect that involved the apical portions of the tooth. In this case the pulp clearly responded sensible on testing, indicating that the pathologic condition was not of endodontic origin. Pocket debridement was combined with irrigation with 0.2% chlorhexidine digluconate solution and systemic administration of an antibiotic. The lesion healed rapidly. Seven months following treatment new bone had formed around the apex and in the defect along the mesial root surface (Fig. 40-10c). In this case, therefore, the periodontal lesion was a manifestation of periodontal disease.

In Fig. 40-11a the radiograph taken of the lower front teeth demonstrates bone loss associated with

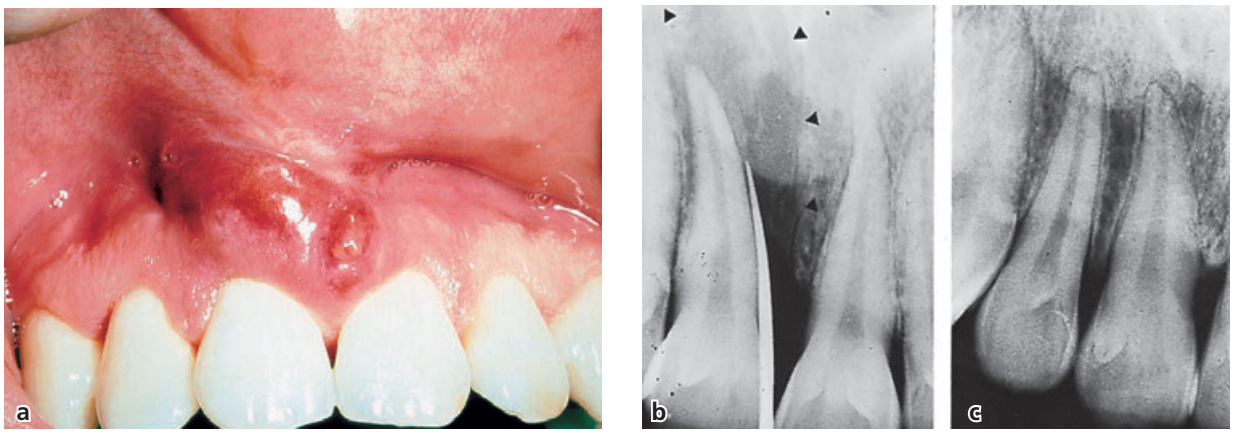

Fig. 40-10 (a) Gingival swelling at the buccal aspect of tooth #11. (b) There is advanced destruction of alveolar bone along the mesial aspect of the root (arrowheads). Following periodontal treatment bone lesion resolved. Case kindly provided by Dr. Harald Rylander.

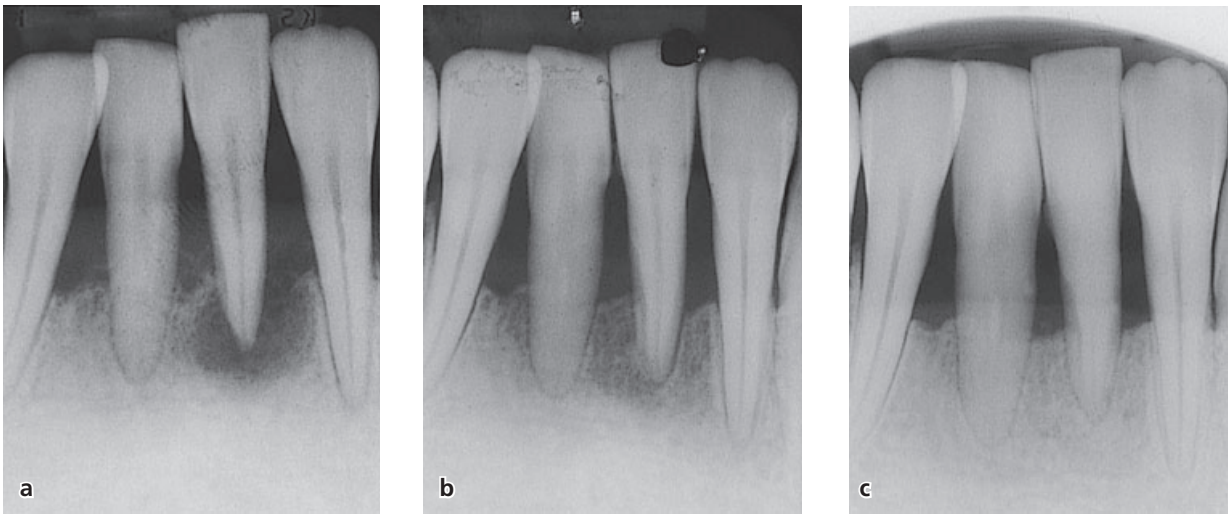

Fig. 40-11 Advanced bone destruction of alveolar bone including an angular bone defect simulating an endodontic periapical lesion around the root tip of tooth #31. The pulp responded vital on testing and the tooth was therefore not subjected to endodontic therapy but to periodontal treatment only. For further case history see the text. Case kindly provided by Dr. Ingvar Magnusson.

the apex of tooth #31 in addition to a generalized horizontal loss of alveolar bone in this young individual. The form and extension of the apical radiolucency around tooth #31 suggests an endodontic lesion. Clinically, a deep periodontal pocket could be probed along the disto-buccal aspect of the root. The patient had been on a recall program after treatment for periodontal disease and had previously shown excellent gingival conditions. Sensibility tests by cold and electricity indicated vital pulp. Therefore, endodontic treatment was not performed. On elevating a mucoperiosteal flap an angular bone defect was found at the buccal aspect of the root without involvement of the root tip. The wound area was debrided along with scaling of the root surface. Rapid bone fill followed surgery without undertaking any adjunctive measures to support tissue regeneration (Fig. 40-11b). The pulp maintained its vitality, although later the root canal became obliterated by hard tissue, most likely as a consequence of the surgical trauma (Fig. 40-11c). The apically positioned radiolucency in Fig. 40-11a is explained by superimposition of the buccal loss of alveolar bone on the root tip of tooth #31, which went beyond its most apical level (Fig. 40-12) without interfering with the neurovascular supply of the pulp.

Figure 40-13 demonstrates a clinical case where pulp vitality testing was difficult to carry out and which gave inconclusive findings even upon the preparation of a test cavity. A swelling had appeared at the buccal aspect of tooth #46 (Fig. 40-13a) after the patient had experienced pain and tenderness in the area for approximately 1 week. Periodontal probing disclosed a deep facial pocket along the mesial root (Fig. 40-13b). Radiographic examination indicated a lesion that seemed to circumscribe the mesial root with a marginal extension into the furcation (Fig. 40-13c). Frictional heat by drilling, as well as cold and

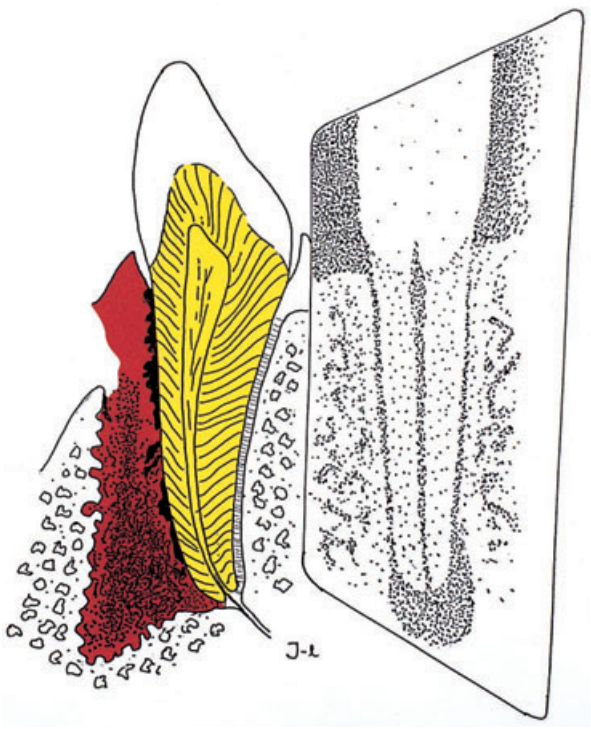

Fig. 40-12 Drawing depicting a potential mechanism for the radiographic lesion in tooth #31, Fig. 40-11. While there was substantial breakdown of alveolar bone there was no interference of the inflammatory lesion with the neurovascular supply of the pulp. The fact that the bone lesion appeared as an apical radiolucency is explained by the superimposition of the bone loss on the root tip. Courtesy of Dr. Mats Joatell.

electric tests, failed to give a positive response even in a test cavity preparation. After finding a sensitive and bleeding pulp in the distal root, a necrotic pulp with pus drainage was detected in the mesial root canals confirming an endodontic cause of the lesion. Endodontic treatment with a temporary intracanal dressing with calcium hydroxide over 3 months resulted in an obvious reduction of the bone lesion (Fig. 40-13d). The gingival lesion resolved with no abnormal pocket-probing depth (Fig. 40-13e), although a small bone defect remained in the furcation area (Fig. 40-13d). Treatment was then completed with root canal fillings. The 12-month recall radiograph demonstrates complete resolution of the bone defect (Fig. 40-13f).

Other indications of endodontic lesion

Except for a negative pulp test response, single-tooth lesions in a dentition otherwise free from periodontal disease strongly suggest an endodontic cause, provided other tooth-associated disorders such as external root resorption and root fracture can be excluded. An endodontic etiology should be explored particularly in cases with extensive restoration or a crowned tooth (Figs. 40-8 and 40-13), bridge abutment (Fig. 40-3), caries (Fig. 40-7), a root-filled tooth, and in patients with a history of a previous dental trauma. The character of the pocket probing depth should also be taken into consideration. Endodontic lesions, when extending marginally, usually do not follow more than one root surface and then exit in a rather narrow area of the sulcus. Pocket probing depth may also be in an area uncharacteristic of periodontitis, for example at the buccal aspect, when all other sites display normal probing depths.

Conclusion

The clinical presentation and the character of radiographic findings may lead to erroneous diagnosis in cases, where an endodontic lesion emerges in a patient with periodontal disease. The recognition of pulp vitality is crucial because clinically significant lesions of endodontic origin rarely develop in teeth with vital but inflamed pulps. The clinician should always be watchful for false leads and consider features which normally are associated with diseased pulps, such as extensive restoration, previous pulp capping, history of dental trauma, and endodontic treatment.

Endo–perio lesions – diagnosis and treatment aspects

The potential for an infected, necrotic pulp to cause breakdown of the attachment apparatus with extension into the marginal periodontium has been addressed above, along with the measures to establish the diagnosis. Once confirmed, the mode of treatment in this type of case is simple and should involve only conservative root canal therapy. Following adequate treatment, directed to elimination of the root canal infection, the lesion should be expected to heal without a persistent periodontal defect (Figs. 40-3, 40-5, 40-8, and 40-13). Adjunctive periodontal therapy would have no treatment effect and would be inappropriate.

A more complex situation arises when a periodontal lesion is sustained by both plaque infection and a root canal infection concurrently. This kind of lesion is associated with a deep pocket probing depth and a lateral bone defect that extends to the apex (Fig. 40-8). The problem here is that it is not normally possible to determine how much of the lesion is sustained by one or the other infection. In fact there are three scenarios. Firstly, the entire lesion may be a manifestation of a root canal infection alone. Secondly, the entire lesion may be the result of plaque infection. Thirdly, there are, in fact, two disease processes, one marginal associated with a plaque infection and one apical associated with a root canal infection. It is just that the two soft tissue lesions have merged and there is no longer a clear demarcation zone between the two as a probe can penetrate both soft tissue lesions. This latter condition has been termed a “true endo–perio lesion”.

Pulp vitality testing only partly settles the diagnostic quandary in this kind of case. Yet, if distinctly

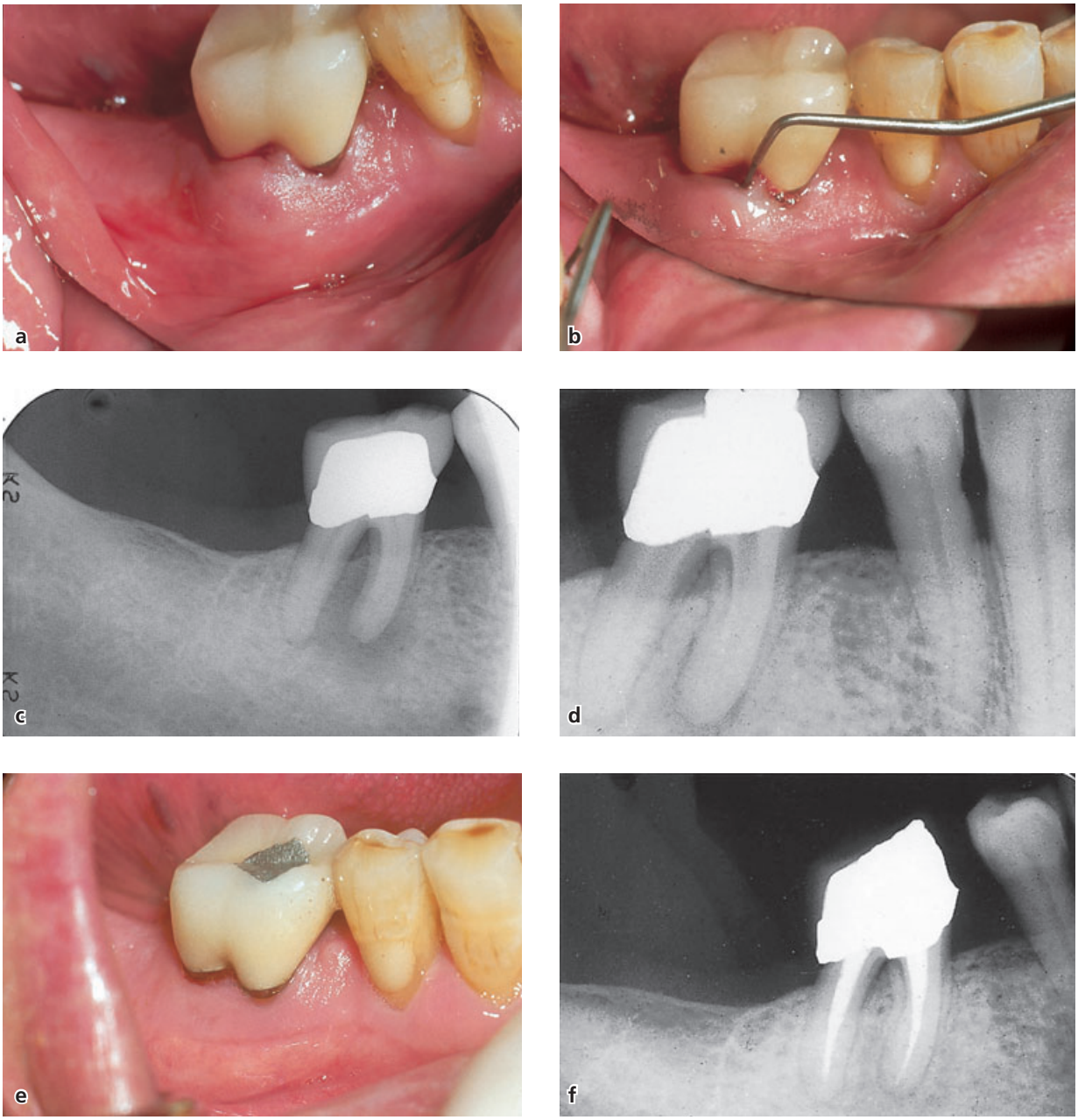

Fig. 40-13 Case with an initial unclear etiology of a facial swelling and deep pocket probing depth that turned out to have an endodontic etiology. The case history is given in the text. Diagnosis and treatment of this case was carried out by one of the authors (G.B.) in collaboration with Dr. David Simpson.

positive, one can exclude contribution of an endodontic infection and the process should be subject to periodontal therapy. Taking the pulp out and replacing it with a root filling is then a meaningless and unnecessary treatment effort. In the case of a negative pulp test, death of the pulp may have occurred as a direct result of the periodontal disease process or it may have developed independently as a separate condition. In the former case, prognosis for any other treatment than extraction must be regarded as bleak. A major reason is that not only may a substantial portion of the attachment apparatus be lost, but the root surface may be bacterially infected close to the root tip as well. In addition, the infection may have entered the root canal after necrosis of the pulp (see Chapter 23). Accessing this kind of infection for treatment is therefore a very challenging task with a questionable outcome.

If a portion of the lesion is sustained by a root canal infection independent of periodontal disease, the potential for periodontal tissue regeneration is much increased. Because it is not possible to know beforehand how far the endodontic lesion has extended along the root, root canal treatment should be attempted first and periodontal treatment postponed until the result of the endodontic treatment can be evaluated. The part of the lesion sustained by root canal infection can usually be expected to heal rapidly (Fig. 40-3). Periodontal attachment along with bone healing can then be expected within a few

Table 40-1 Outline of treatment strategies

Cause	Condition of the pulp	Treatment
Endodontic	Non-vital	Endodontic
Periodontal	Vital	Periodontal
Endodontic/periodontal	Non-vital	Endodontic – first observe the result of this therapy and institute periodontal therapy later if necessary

months. The part of the lesion caused by plaque infection may also heal following adequate periodontal therapy. Yet little or no regeneration of the attachment apparatus should be anticipated. Table 40-1 outlines the strategy to be taken for treatment of "endo–perio lesions".

Conclusion

Deep pocket probing depths associated with angular bone defects may reflect a combined endodontic and periodontal lesion. Yet, the extent to which an endodontic infection has contributed to the attachment loss cannot normally be determined upon a negative sensibility test, as the entire loss might be caused by plaque infection. Therefore, a treatment strategy should be applied which includes endodontics in the first place, but only in cases where an endodontic etiology is reasonably plausible, that is in teeth with large restorations, full-coverage crowns or history of dental trauma. If the tooth is completely intact without major restoration, caries or history of trauma, the potential of an endodontic etiology of the process is remote.

Endodontic treatments and periodontal lesions

Periodontal lesions, as already stated, may be maintained by infectious elements released from endodontically treated teeth. The lesion may have never resolved or may have developed after the completion of treatment. Several routes for dissemination of bacterial products are possible. Except for apical foramina and accessory canals, another possible pathway is inadvertently produced communication by root perforation (see below). The clinical presentation is no different to the one described above and consequently may involve acute exacerbations with quite extensive breakdowns of the attachment apparatus as well as localized, non-symptomatic lesions, only apparent in radiographs.

A persistent infection in root-filled teeth may also impact on the periodontium along dentinal tubules in areas where cementum has been damaged or lost (Hammarström *et al*. 1986; Blomlöf *et al*. 1988). The potential significance of such an avenue has been highlighted in clinical studies. Comparing teeth with healthy pulps, endodontically treated teeth with periapical pathology, indicating presence of persistent root canal infection, showed increased pocket probing depths (Jansson *et al*. 1993a), more marginal bone loss (Jansson *et al*. 1993b), and retarded or impaired periodontal tissue healing subsequent to periodontal therapy (Ehnevid *et al*. 1993a, b). Although the differences in probing depths and attachment losses in these studies were rather small, the observations suggest that endodontic re-treatment should be considered as an adjunct to periodontal therapy when a root canal filling is defective and/or displays signs of periapical inflammation. In individuals with no or minor evidence of periodontal disease, the root canal condition, whether root filled or not or infected or not, did not seem to affect the periodontal status in a controlled study (Miyashita *et al*. 1998).

Conclusion

Unfilled spaces in endodontically treated root canals can sustain bacterial growth, and infectious products from these may reach the periodontium along the very same pathways as in an untreated tooth with infected pulp. Endodontic re-treatment may be considered as an adjunct to periodontal therapy when a root canal filling is of poor quality and/or displays signs of periapical inflammation because of the potential that bacterial elements may become disseminated to the periodontium along dentinal tubules exposed by periodontal instrumentation.

Iatrogenic root perforations

During endodontic treatment, and in conjunction with preparation of root canals for insertion of posts, instrumentation can accidentally result in perforation of the root and wounding of the periodontal ligament (Sinai 1977; Kvinnsland *et al*. 1989; Eleftheriadis & Lambrianidis 2005). Perforations can be made through the lateral walls of the root or through the pulpal floor in multi-rooted teeth. The clinical course from then on depends largely on the extent the wound site becomes infected (Beavers *et al*. 1986). If made in the crestal bone area, a typical feature is epithelial proliferation and periodontal pocket formation (Lantz & Persson 1967; Petersson *et al*. 1985). If the perforation is more apical along the root, a wound site infection process may first lead to an acute pain condition, including abscess formation and drainage of pus, followed by further loss of fibrous attachment and periodontal pocketing (Fig. 40-14).

Early detection is critical for a successful outcome of treatment as long-standing perforations with a manifest infection have poor potential for repair.

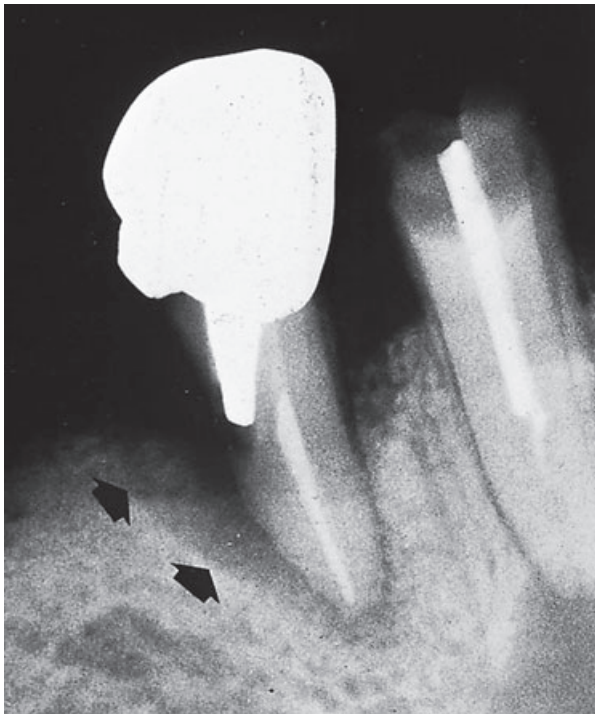

Fig. 40-14 Angular bone defect at the distal root surface of a mandibular molar (arrows). The root is perforated as indicated by the misaligned post. Clinical symptoms included drainage of pus from the pocket and increased tooth mobility. The tooth was extracted.

Successful treatments have, however, been attained in such cases (Tsesis & Fuss 2006).

Diagnosis is based on the occurrence of sudden pain and bleeding during preparation of root canals coronal to the working length. Such signs are likely to be less distinct, however, if the perforation occurs during a procedure conducted under local anesthesia. A perforation may also go undetected as bleeding may not invariably be provoked. For example, when post preparations are carried out by means of a machine-driven instrument, a smear layer is formed that may clog up the blood vessels. Thus, in many instances no bleeding will be noticed until the following visit, when granulation tissue has proliferated into the root canal space along the perforation defect. Granulation tissue usually bleeds profusely on attempts to remove it. Electronic apex locators are helpful in the confirmation of a root perforation, when readings obtained are substantially shorter than the root canal length (Fuss *et al*. 1996).

Over the years many therapeutic agents and methods have been proposed for the management of root perforations (reviewed by Tsesis & Fuss 2006). Materials proposed for sealing from the inside of the root canal space include amalgam, zinc oxide and eugenol cements, both chemically cured and light-cured calcium hydroxide-containing pastes, and plaster of Paris. More recently, mineral trioxide aggregate (MTA) based on Portland cement has shown great promise by its ability to permit cementum repair (Arens & Torabinejad 1996; Schwartz *et al*. 1999).

Regardless of the material used, healing of the lesion in the periodontium depends on whether bacterial infection can be excluded from the wound site by a tight seal of the perforation (Beavers *et al*. 1986) (Fig. 40-15). This may be difficult to achieve, particularly if the perforation is made deep into the root canal at an oblique angle giving it an oval-shaped orifice into the periodontium. Nevertheless, for mid-root and cervical perforations, non-surgical approaches, including placement of an internal seal, are preferable to a surgical approach, as the latter often results in persistent pocket formation and furcation involvement. Furthermore, surgical treatment is not always feasible because of the inherent difficulty of accessing many perforation sites. As a last resort, extraction followed by repair and reimplantation of the tooth may be attempted (Tsesis & Fuss 2006). In multi-rooted teeth, hemisection and extraction of one or two roots may be a treatment of choice.

Conclusion

Inflammatory lesions in the marginal periodontium, as manifested by increased probing depth, suppuration, increased tooth mobility, and loss of fibrous attachment, may result from an undetected or unsuccessfully treated root perforation. If an iatrogenic root perforation occurs during instrumentation of root canals, filling of the artificial canal to the periodontium should be carried out without delay to prevent granulation tissue formation and wound site infection. Outcome of treatment depends on how well the wound site can be sealed. The closer the perforation is to the bone margin, the greater the likelihood is for proliferation of epithelium at the perforation site with a deep, potentially suppurating pocket as a result.

Vertical root fractures

Clinical symptoms that are typical of tooth-associated infections such as endondontic lesions and plaque-induced periodontitis may also appear at teeth with vertical root fractures. A vertical root fracture is defined as a fracture of a root that is longitudinally oriented at a more or less oblique angle relative to the long axis of the tooth (Fig. 40-16). It can traverse the root in different directions mesially/distally or facially/lingually; it may, but does not always, engage the root canal space. A vertical root fracture can extend the entire length of a root and then involve the gingival sulcus/pocket area. It may also be incomplete and confined to either coronal or apical ends. It should be noted that vertical root fractures although expanding in opposite directions may extend to one root surface only.

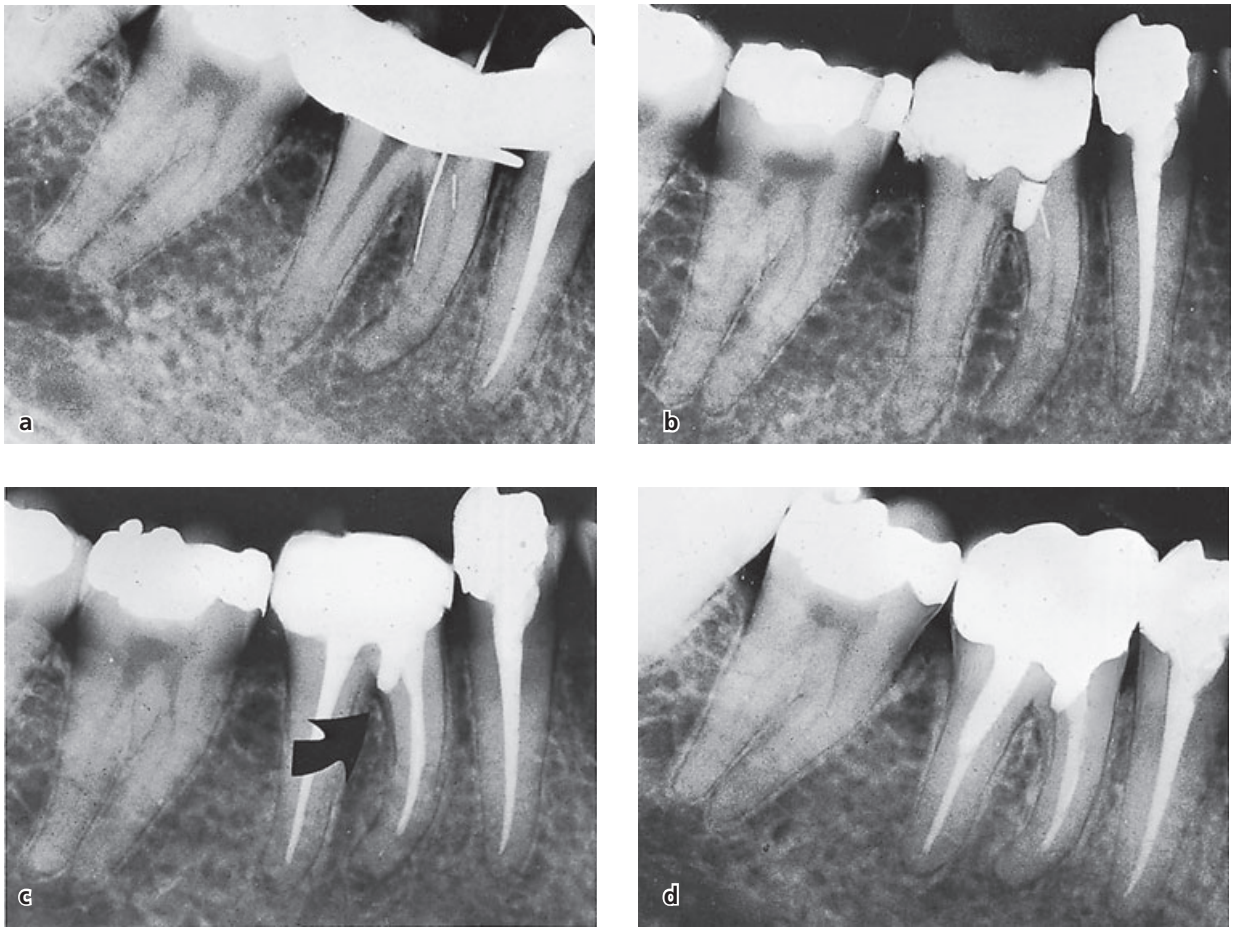

Fig. 40-15 (a) Perforation of the pulpal floor of the mandibular first molar occurred in conjunction with a search for root canal openings. There is also a file fragment in one of the mesial canals. (b) The perforation was immediately sealed with gutta-percha. (c) In a radiograph taken 1 month after treatment a slight radiolucency is seen at the site of the perforation (arrow). (d) Follow-up after 2 years showed normal periodontal conditions both clinically and radiographically. Case kindly provided by Dr. Gunnar Heden.

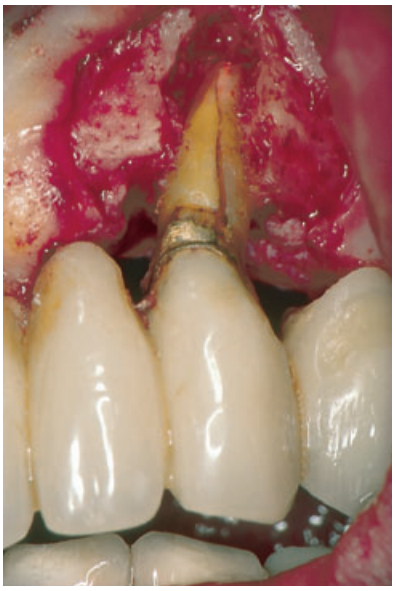

Fig. 40-16 Vertical root fracture of a root-filled upper canine included as an abutment in a prosthetic reconstruction. Due to inflammatory breakdown of the buccal plate a typical bone dehiscence is seen.

Mechanisms

Endodontically treated teeth appear over-represented among teeth with vertical root fracture in comparison to teeth with vital pulps (Meister *et al*. 1980; Gher *et al*. 1987; Patel *et al*. 1995). Generally the increased fracture propensity of root-filled teeth has been attributed to loss of tooth structure as a result of endodontic instrumentation and subsequent restorative procedures (Reeh *et al*. 1989; Sedgley & Messer 1992). Loss of fracture resistance increases especially after overzealous root canal preparation leaving thin dentin walls to the periodontium (Tjan & Whang 1985). Notches, ledges, and cracks induced by root canal preparation, root canal filling procedures, and seating of threaded pins and posts also contribute to sites of stress concentration during mastication that eventually may lead to fracture (Kishen 2006). Decrease of moisture content following root canal treatment is another claimed cause of increased fracture susceptibility of root-filled teeth; insignificant moisture differences were found, however, when dentin of teeth with vital pulps and dentin of root-filled teeth were compared (Papa *et al*. 1994). More recent observations have nevertheless demonstrated

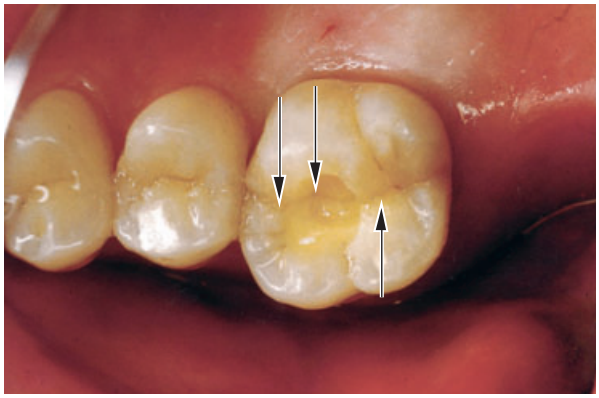

Fig. 40-17 Crack in an unrestored maxillay molar causing symptoms of pulpitis. The patient, a 47-year-old male, had thought the pain problem originated from the temporomandibular joint. Following the preparation of a test cavity, a clear split line was observed at the bottom of the cavity (arrows), confirming the cause of the pain condition. Case kindly provided by Dr. Hideaki Suda.

that biomechanical effects occur in dehydrated dentin that may render endodontically treated teeth prone to fracture (Kishen 2006). Dehydrated dentin *in vitro* was observed to assume increased stiffness as well as a decrease in toughness (e.g. the total energy a material can absorb before fracturing) in comparison to hydrated dentin (Jameson *et al*. 1994; Kahler *et al*. 2003; Kishen & Asundi 2005). Hence, fluid-filled dentinal tubules as well as a water-rich pulp tissue may give normal teeth better resistance to occlusal loading forces than root-filled teeth. It has also been speculated that, along with loss of vital pulp tissue, mechanoreceptive functions are lost concomitantly, allowing larger loads to be placed during mastication than the patient normally would feel tolerable (Löwenstein & Rathkamp 1955; Randow & Glantz 1986).

Vertical root fracture may also occur in clinically intact teeth with no or minor restoration (Fig. 40-17). As posterior teeth are exposed to more heavy occlusal forces, mandibular molars appear to be especially at risk for fracture (Yang *et al*. 1995; Chan *et al*. 1999). Subsequent to fracture of teeth with vital pulps, typical pulpitis symptoms may be initiated, together with pain on percussion and mastication.

Incidence

Data on the incidence of vertical root fractures are scarce in the literature. While it appears to be low, vertical root fractures probably occur more often than clinicians are able to diagnose (Tamse *et al*. 1999b). Molars and premolars appear more often affected than incisors and canines (Meister *et al*. 1980; Testori *et al*. 1993). In longitudinal clinical follow-up studies of patients treated with fixed prostheses, vertical root fractures were frequent in root-filled teeth with posts and especially so in teeth serving as terminal abutments in cantilever bridges (Randow *et al*. 1986).

It is important to recognize that root fracture of endodontically treated teeth may occur several years after the completion of endodontic therapy and final restoration of the tooth (Fig. 40-18). In a study comprising 32 vertical root fractures, the average time between the completion of endodontic treatment and diagnosis of fracture was 3.25 years, with a range varying between 3 days and 14 years (Meister *et al*. 1980). In another study comprising 36 teeth, symptoms of root fracture developed on average more than 10 years after completion of treatment (Testori *et al*. 1993).

Clinical expressions

Clinical signs and symptoms associated with vertical root fractures vary hugely. Occasionally, there may be pronounced pain symptoms and abscess formation because of active bacterial growth in the fracture space (Fig. 40-18). In other instances clinical symptoms may be limited to tenderness on mastication, mild pain, and dull discomfort. Sinus tracts may emerge near the gingival margin (Fig. 40-19). A strong indication of a vertical root fracture is sinus tracts occurring at both buccal and lingual/palatal sites (Tamse 2006). In other instances, a narrow, local deepening of a periodontal pocket in an area not typical for periodontal disease may be the only clinical finding (Fig. 40-20).

The osseous defect emanating from the periodontal tissue lesion may take different shapes depending on how the fracture extends. If there is a buccal extension, the thin alveolar bone plate readily resorbs and a typical bone cleft can be seen upon raising a mucoperiosteal flap (Fig. 40-16). At palatal or lingual extensions, the lesion may not resorb the entire bone wall. Therefore, the osseous defect may take a U-form shape with the height of the bone margin preserved. On fractures that are limited to the apical portion of the root, the bone defect may center on the root apex, similar to that of a periapical lesion associated with an infected root canal.

In conventional intraoral periapical radiographs these bone lesions may not be readily visible, depending on the location, character, and shape of the bone destruction (Fig. 40-20). Absence of lesion, even when taken at different angles, can also be explained by superimposition of roots and bone structures over the bone dehiscence. In yet other cases radiographic signs may be limited to widening of the periodontal ligament space. Lateral radiolucency along one or both of the lateral root surfaces may be discerned with more pronounced bone lesions. A thin halo-like apical radiolucency is another example of a radiographic lesion suggestive of a vertical root fracture (Pitts & Natkin 1983; Testori *et al*. 1993; Tamse *et al*. 1999a). Recent developments of tomographic techniques have brought valuable new diagnostic tools as they can remove interfering anatomic structures and thereby help to visualize presence, location, and

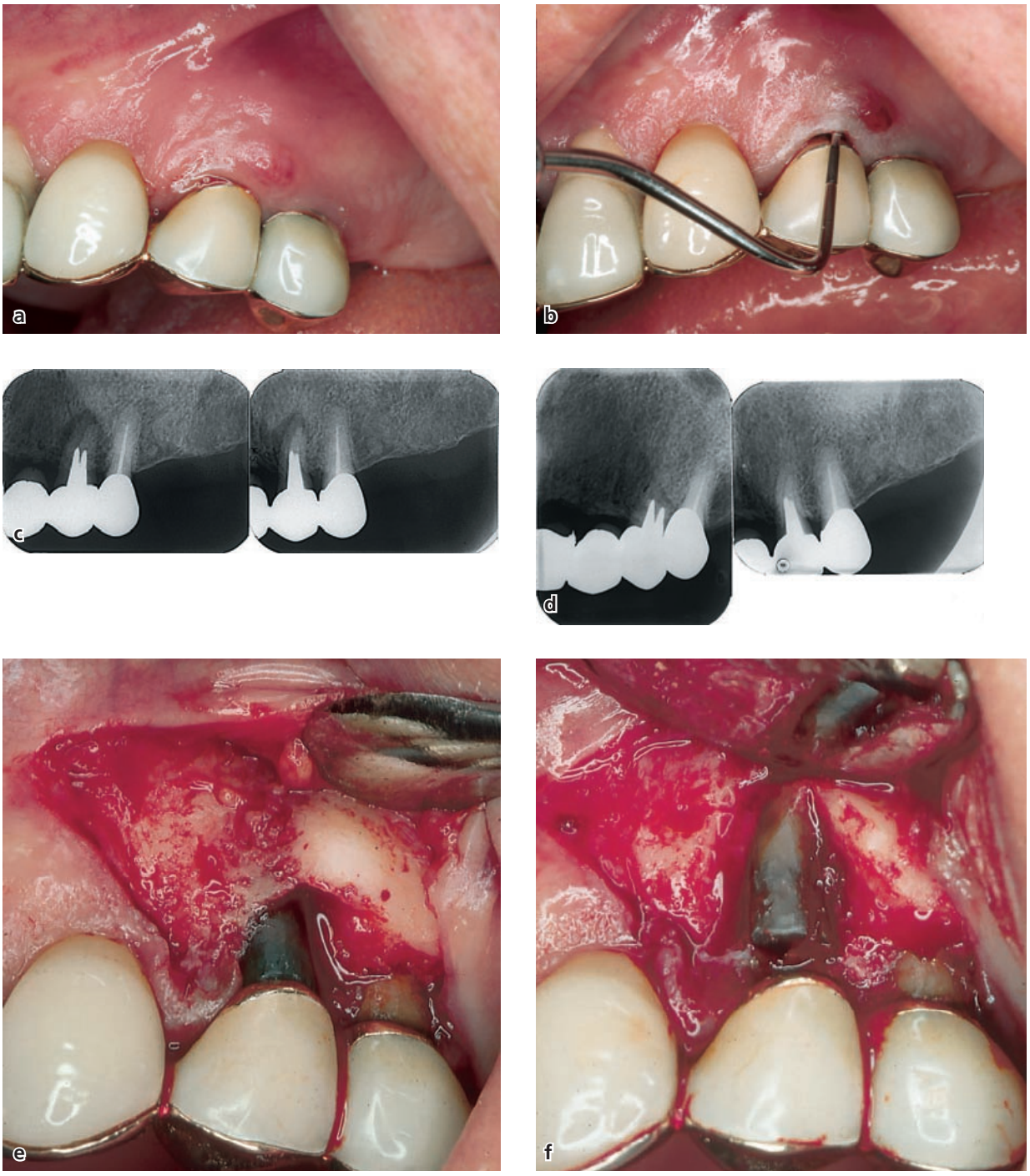

Fig. 40-18 A typical case of a root fracture. (a) The first maxillary premolar had been asymptomatic for 20 years after completion of endodontic treatment and bridge-work. Patient sought treatment because of suddenly appearing pain, tenderness and facial swelling. (b) A deep periodontal pocket could be probed at the buccal aspect of the tooth, while all other sites displayed normal pocket probing depths. (c) Radiographs revealed a radiolucent area along the mesial aspect of the root system. (d) A set of radiographs taken 6 months earlier showed no such lesion. (e) Elevation of a mucoperiosteal flap revealed substantial loss of marginal bone at the buccal aspect of the root. A fracture going in a mesio-distal direction was subsequently confirmed. (f) Following removal of bone tissue, the roots were separated from the crown and extracted.

extension of bone lesions (Gröndahl & Hummonen 2004) (Fig. 40-20e,f).

Diagnosis

The diagnosis of a vertical root fracture is often difficult to ascertain because the fracture is usually not readily detectable by clinical inspection unless there is a clear separation of the root fragments. To give a radiographic appearance of the fracture in the absence of separation, the central X-ray beam has to be parallel to the fracture plane (Fig. 40-21). This is rarely achieved. The suspicion of a vertical root fracture is often inferred from a pocket probing depth in an

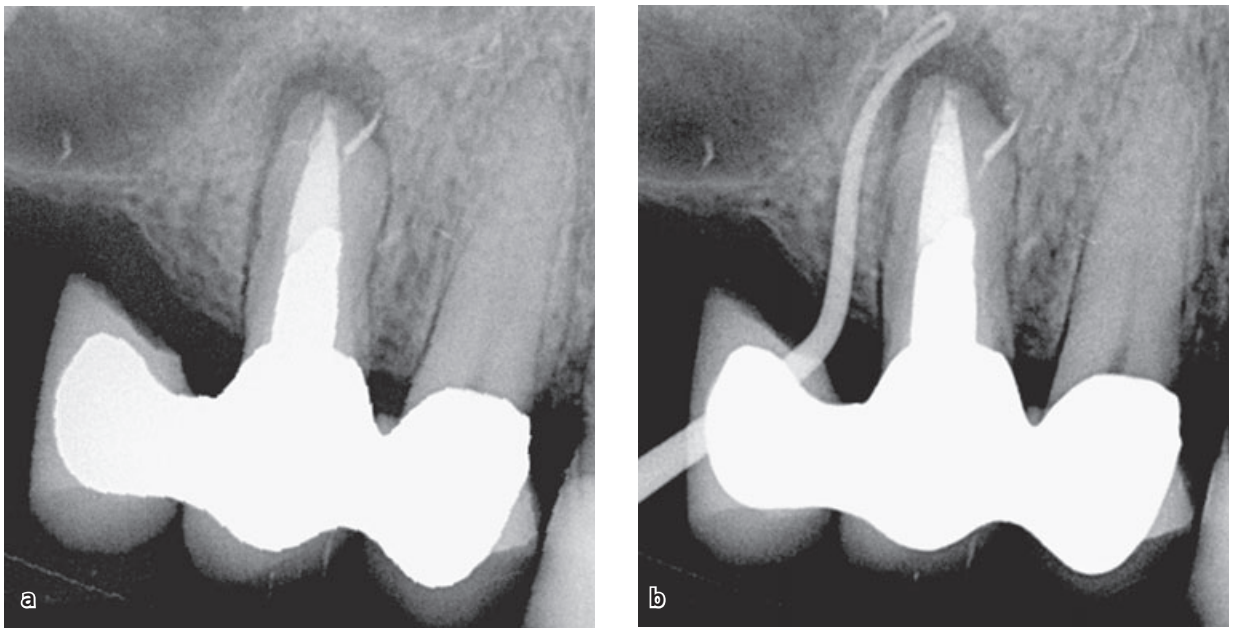

Fig. 40-19 (a) Periapical radiolucency associated with an upper second premolar that turned out to be caused by a vertical root fracture. There was a buccal, deep pocket-probing depth and a sinus tract near the gingival margin. (b) A gutta-percha point inserted in the fistulous tract points to the root apex but provided no additional clue in this case. The widely prepared root canal and the use of the tooth as an abutment in a cantilever bridge provided likely contributors to the fracture in this case kindly provided by Dr. Thomas Kvist.

aberrant position, for example at a buccal or lingual aspect of a tooth, in a dentition which otherwise is free from symptoms of periodontal disease. Another strong indication is the sudden appearance of clinical symptoms and/or radiographic lesion on a root-filled tooth that has remained asymptomatic and without lesion for years (Fig. 40-18).

A number of diagnostic procedures can be undertaken to confirm the diagnosis. Application of various dye solutions, e.g. methylene blue or iodine tincture, on to the crown and the root surface can sometimes be indicative. As the dye enters the fracture space, it will show up as a distinct line against the surrounding tooth substance. Indirect illumination of the root, using fiber-optic light, can also be of value. The fiber-optic probe should then be placed at various positions on the crown or the root, whereby the fracture line may clearly present itself. A surgical microscope or an endoscope, providing both enlargement and directed light, are other valuable tools to disclose vertical root fractures.

In premolars and molars the diagnosis may be supported from observation of varying pain sensations elicited by loading facial and lingual cusps. The procedure includes asking the patient to bite down on a rubber wheel or a specially designed plastic stick (FracFinder). Separate loading of either buccal or lingual cusps eliciting pain sensation from one, but not the other loaded cusp indicates the potential of a fracture. Often the diagnosis of a vertical root fracture has to be confirmed by surgical exposure of the root for direct visual examination (Walton *et al*. 1984) at which one may also discover a typical bone dehiscence (Fig. 40-16).

Treatment considerations

Vertical root fractures that involve the gingival sulcus/pocket area usually have a hopeless prognosis due to continuous bacterial invasion of the fracture space from the oral environment. While there are reports of successful management of fractured teeth by re-attaching the fragments with bonding resin or laser fusing after extraction followed by re-implantation, fractured teeth are normally candidates for extraction. In multi-rooted teeth a treatment alternative is hemisection and extraction of the fractured root.

Conclusion

Symptoms and signs associated with vertical root fractures vary and may be difficult to distinguish from those prevalent with other tooth-associated infections. A variety of diagnostic procedures should therefore be considered. Except for the leads obtained from anamnestic findings and pocket probing depths in buccal or lingual positions or both, clinical examination should include measures to make fracture lines visible *viz.* application of disclosing solutions, the use of fiber-optic light, inspection by a surgical microscope or endoscope, or by raising a surgical flap. Pain on selective loading of cusps may indicate root fracture. A vertical root fracture should be anticipated in root-filled teeth, which, after a long history of being asymptomatic and without signs of infection, suddenly present with tenderness, pain, and radiographic bone lesion (Fig. 40-18). Roots with vertical root fracture usually have a hopeless prognosis and are clear candidates for extraction.

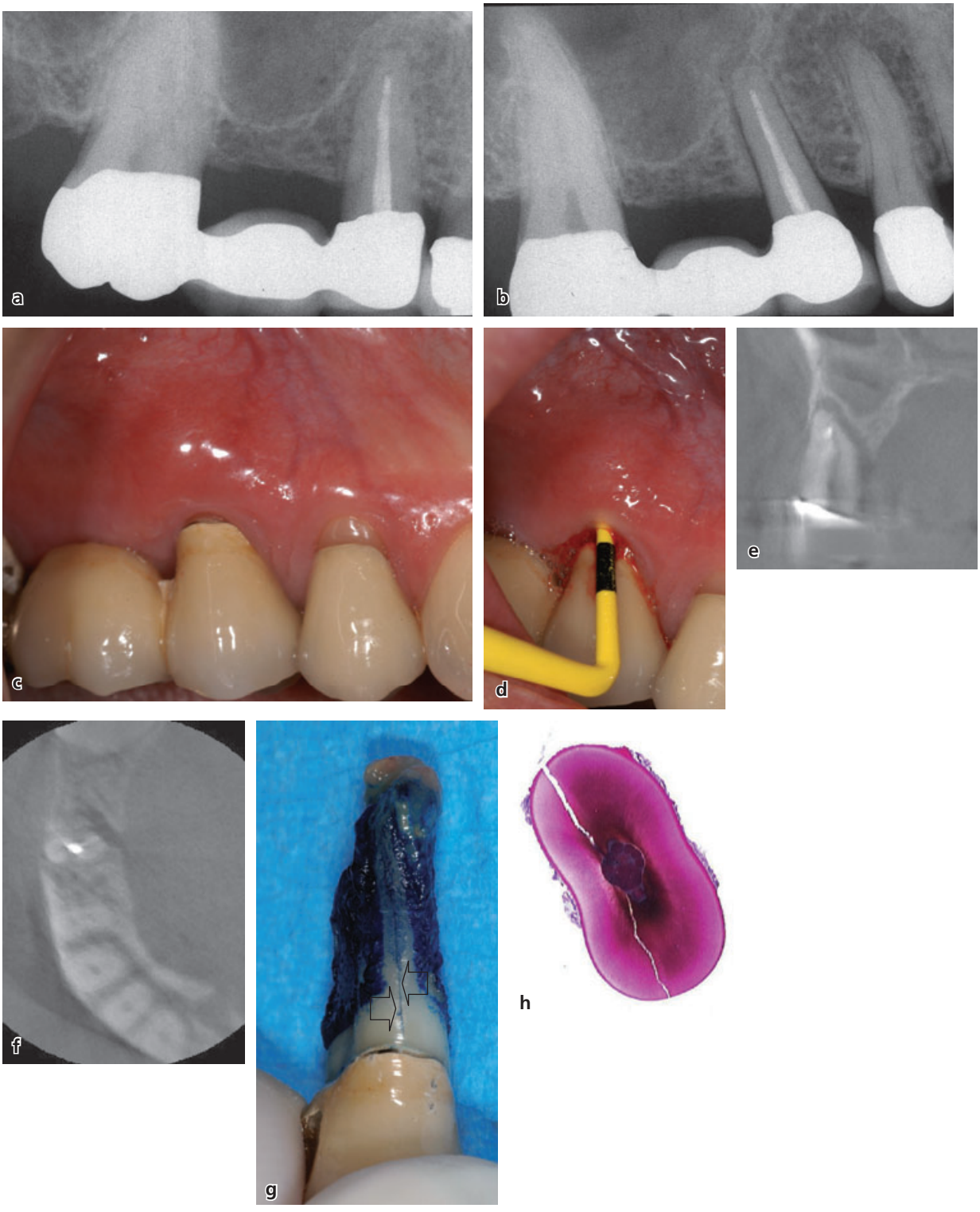

Fig. 40-20 Case of vertical root fracture, where ordinary intraoral radiographs failed to provide evidence of the associated bone lesion. (a) Radiograph shows normal periodontal contours. (b) A second radiograph indicates a widened periodontal ligament space. (c) The patient had complained of recurrent pain on occlusal load for several weeks and presented at the clinic with a light swelling on the buccal aspect that had appeared several weeks before. (d) Clinically there was an isolated 9 mm pocket probing depth mid-buccally, suggesting root fracture. (e,f) Limited cone beam computed tomography was helpful to reveal a bone lesion in this case along the palatal aspect of the tooth. (g) After extraction methylene blue staining visualized the fracture line (arrows) that turned out to extend to both the lingual and the buccal root surface (h). Case kindly provided by Dr. Thomas von Arx.

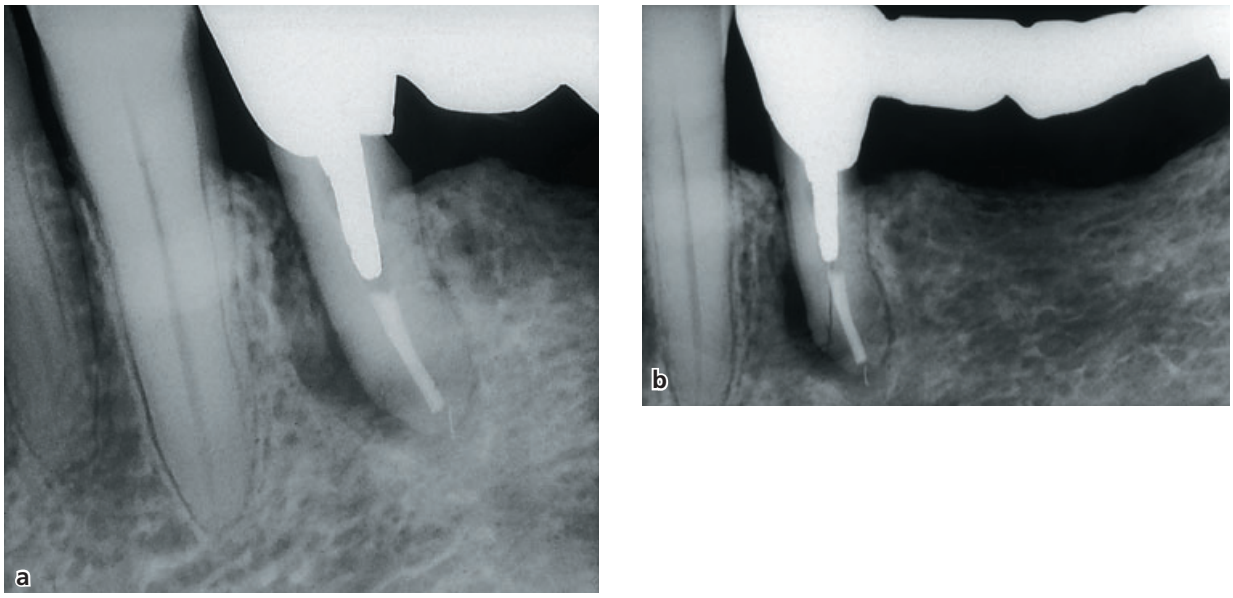

Fig. 40-21 (a) Mandibular premolar included in a four-unit bridge showing a bone lesion at the mesial aspect of the root. In this projection there is no sign of fracture, while in a radiograph (b) taken with a slight shift of angle, a fracture line is clearly visible. Case kindly provided by Dr. K-G. Olsson.

External root resorptions

Root surface resorptions, here termed external root resorptions, usually progress without producing clinical symptoms and may therefore go undetected unless observed radiographically. However, in advanced stages, the surface defect may interfere with the gingival sulcus and thereby initiate an infectious process. As such lesions can be associated with increased pocket probing depths as well as drainage of pus upon probing, this section of the chapter addresses various forms of external root resorptions, their mechanism, clinical features, and management.

Mechanisms of hard tissue resorption in general

The hard tissues of the body consist of two major components, mineral and matrix. While the ratio of these two components varies between bone, cementum, and dentin, the same tools – acids and enzymes – are used by nature to perform the degradation of these tissues. Bone is normally remodeled to adapt to functional changes. Resorption of dental hard tissues of permanent teeth, on the other hand, should be seen as an expression of a pathological process. Clast cells carry out resorption of bone as well as cementum, dentin, and enamel (Hammarström & Lindskog 1992; Suda *et al*. 1996). These cells are large, multinucleated, motile cells emanating from hematopoietic precursor cells in the bone marrow (Marks 1983; Vaes 1988; Pierce *et al*. 1991; Suda *et al*. 1996) and termed osteoclasts when involved in bone remodeling processes. Phenotypically the very same kind of clast cells conduct resorption of the hard tissues of the tooth. Mononucleated cells are also involved in the later phase of the resorption process by eliminating the organic matrix that became released following dissolution of the mineral components (Wedenberg & Lindskog 1985; Lindskog *et al*. 1987; Brudvik & Rygh 1993; Lerner 2006).

Under normal, physiologic conditions, hard tissues are protected from resorption by their respective surface layers of blast cells; in the case of cementum by cementoblasts. As long as these blast cell layers remain intact with the unmineralized layer of osteoid or cementoid at the surface of the mineralized tissue, resorption will not occur. It is known that bone resorption is under hormonal regulation and is mediated by osteoblasts (Lerner 2006). Stimulation by parathyroid hormone makes the osteoblasts first degrade the osteoid and then contract to expose the bone surface for osteoclastic demineralization (Jones & Boyde 1976; Rodan & Martin 1981; Lerner 2006). However, parathyroid hormone exerts no influence on cementoblasts (Lindskog *et al*. 1987), which may explain why bone, but not teeth, is remodeled to adapt to functional changes. However, dental trauma, excessive orthodontic forces and aggressive scaling and root planing during periodontal therapy are examples of injuries that can initiate root resorption (Andreasen 1981; Rygh 1977). Subsequent to the injury, the denuded hard tissue surface, without its blast cell layer and cementoid, attracts motile clast cells (Chambers 1981), which seal themselves to the hard tissue surface and excrete acids for demineralization. Concomitantly an acid environment is created that is essential for the degradation of tissue matrix by lysosomal enzymes at low pH optima (Vaes 1988; Kremer *et al*. 1995; Pascoe & Oursler 2001; Czupalla *et al*. 2006; Henriksen *et al*. 2006).

Consequently, a trigger mechanism is required to set off root resorption. For the resorption process to continue, a lasting osteoclast stimulus is required, for example an infection or a continuous mechanical force such as the one elicited by orthodontic

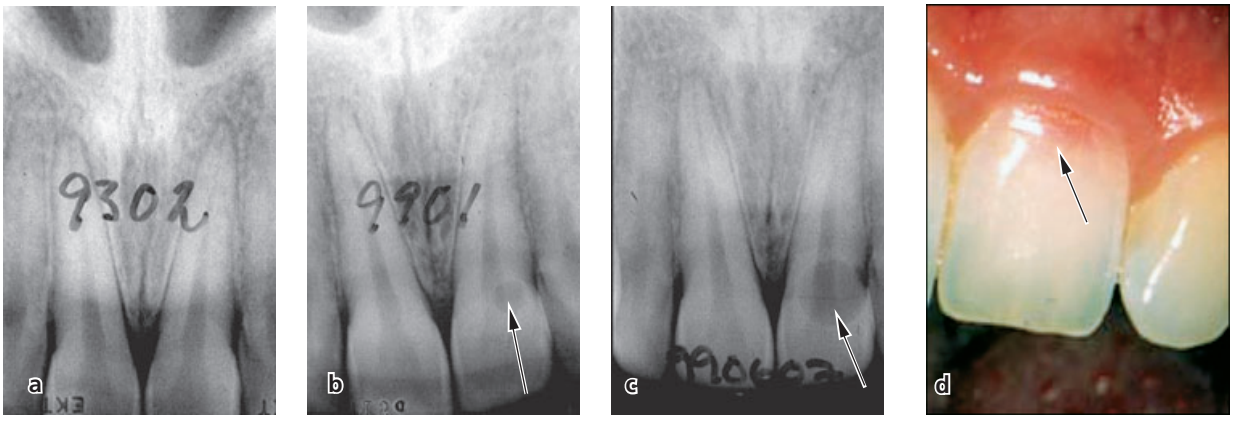

Fig. 40-22 Series of radiographs taken at different time intervals showing the appearance of an external root resorption in a young adult patient. (a) At the age of 15 years there is no sign of resorption. (b) Six years later a small radiolucency is seen (arrow). (c) In just 6 months the lesion expanded considerably (arrow). (d) The lesion appeared clinically as a pink spot in the cervical area of the tooth (arrow). Case kindly provided by Dr. Anders Molander.

treatment. In both instances the resorptive process may be halted if the cause for prolongation can be curbed; in the case of orthodontic tooth movement, by releasing the forces, and in the case of a root canal infection, by root canal therapy.

Conclusion

Two mechanisms are involved in resorption of a hard tissue: (1) a trigger mechanism and (2) a reason for the resorption to continue. Thus, treatment of active root resorption should be directed to eliminate the cause for its continuance.

Clinical presentations and identification

Root resorptions *per se* do not cause painful symptoms. Unless a resorptive process is located coronally and is undermining the enamel, giving it a pinkish appearance (Fig. 40-22), the only way to detect and diagnose dental resorption is by means of radiography (Fig. 40-22b,c). Only in very late stages, as the resorptive process engages the gingival sulcus, may an infectious process emerge with typical features of a periodontal abscess (Fig. 40-23).

A single radiograph is usually not sufficient to define a radiolucent area within the confines of a root as an external resorption. A radiolucency may portray a variety of conditions including a resorptive process inside the root canal (internal root resorption), or a resorptive defect located buccally or lingually as the image of the root is superimposed. It may also be an artifact and reflect a radiolucent bone area superimposed on the root. Therefore, one should always take more than one radiograph and use different angulations to observe whether the radiolucent area belongs to the root or not (Fig. 40-23). New tomographic techniques can be of great benefit to distinguish external from internal root resorptions.

The initial stage of a resorptive process usually passes undetected as radiographs can only present a resorptive cavity after a certain size has been reached (Andreasen *et al*. 1987) (Fig. 40-23). The location of the lesion is also important for detection. A facial or lingual root resorption defect is more difficult to visualize radiographically than a proximal cavity, unless tomography is used. Be aware that in the cervical region it may be difficult to differentiate radiographically between cavities caused by caries and those caused by resorption. To distinguish caries from resorption it is useful to recognize that bacterial acids that demineralize dentin leave a soft cavity surface. By contrast, clastic resorption removes both the mineral and the organic phases of the hard tissues resulting in a cavity floor that is hard to probing.

Different forms

There are different forms of external root resorption. The underlying mechanism is understood only for some of them. A genetic link can be seen in certain cases as external root resorptions run in families. There are also instances when only the enamel of an unerupted tooth is resorbed. Furthermore, external resorptions can be caused by precipitation of oxalate crystals in the hard tissues of patients as a result of increased concentration of oxalates in the blood due to kidney failure (Moskow 1989). Malignant tumors close to a tooth can also cause root resorption (Fig. 40-24).

Andreasen (1981) has published a classification of those external root resorptions that have a known etiology:

- Surface resorption
- Replacement resorption associated with ankylosis
- Inflammatory resorption associated with persistent inflammation in the periodontium adjacent to the resorption site.

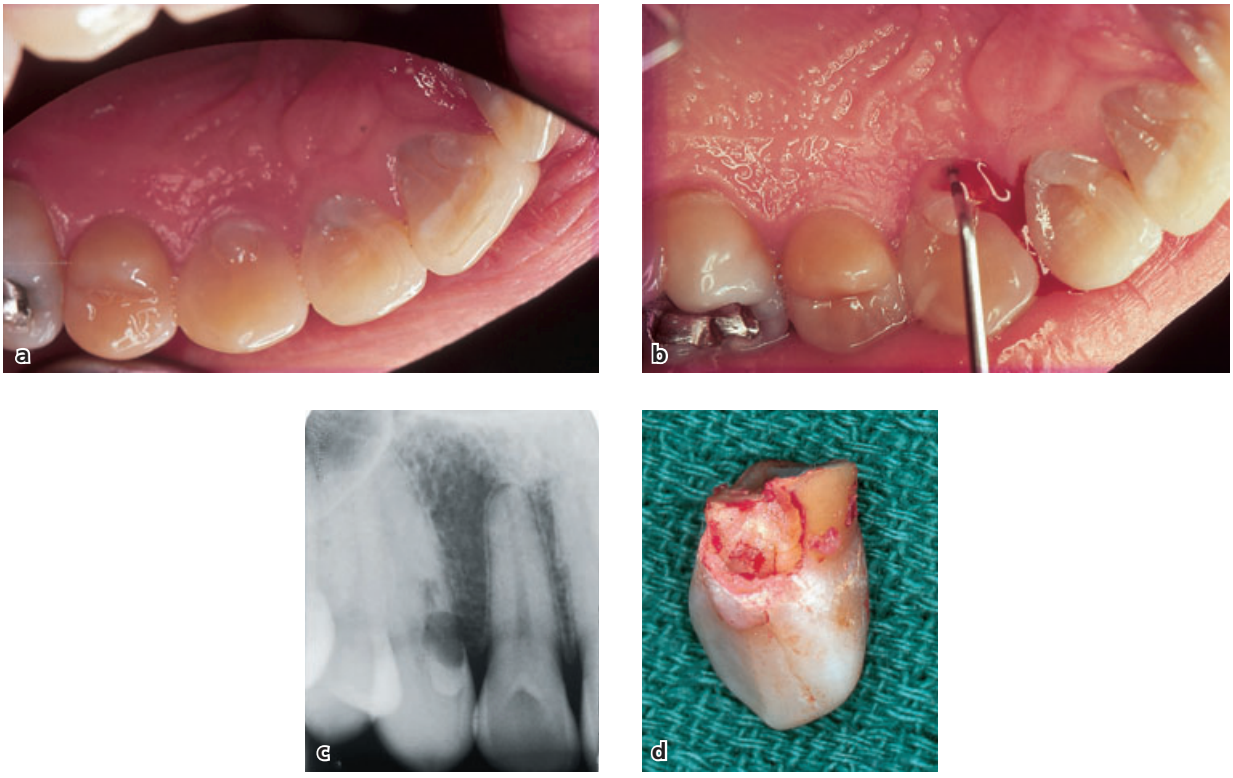

Fig. 40-23 Case of peripheral inflammatory root resorption (PIRR). Pain and tenderness of the right maxilla for several weeks prompted the 30-year-old male patient to seek treatment. (a) Clinical inspection revealed no obvious pathology. (b) Periodontal probing, however, released pus drainage from the lingual aspect of tooth #13. Pulp-vitality test of the tooth as well as neighboring teeth gave clear positive responses. (c) An angulated radiograph disclosed the presence of a resorptive defect. (d) The tooth was extracted as successful treatment was deemed unlikely. An extensive resorptive defect had undermined the clinical crown.

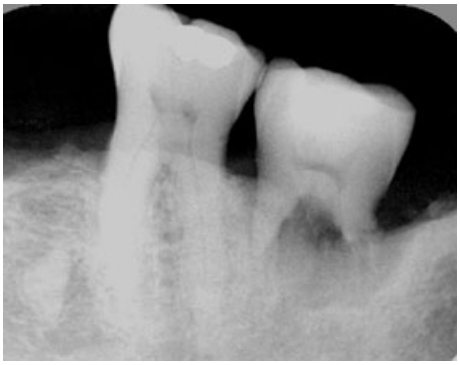

Fig. 40-24 External root resorption of a lower second molar caused by breast cancer metastasis. Case kindly provided by Dr. John Kuo-Hung Yu.

Subforms are:

- Peripheral inflammatory root resorption (PIRR)
- External inflammatory root resorption (EIRR).

Surface resorption

This type of resorption is common, self-limiting, and reversible (Harding 1878; Andreasen 1981). In a histologic study of human teeth from individuals varying in age from 16–58 years, only 10% of the teeth showed absence of active resorption or signs of healed resorptions (Henry & Weinman 1951). Resorptions were noted twice as often in older than in young subjects. Another study demonstrated up to 88% of teeth with active or, in most instances, healed resorptions (Hötz 1967).

The mechanisms behind surface resorptions are only partly understood. These resorptions are normally initiated in conjunction with a localized injury to the cementoblast cell layer, for example by external trauma (Andreasen 1981) or by trauma from occlusion. As clast cells are attracted to the denuded root surface, hard tissue is resorbed for as long as the activating factors are released at the site of injury (Hammarström & Lindskog 1992). The resorptive process then stops within a few days following the disappearance of clast cells along with the defect becoming populated with hard tissue repairing cells leading to cementum repair (Lindskog *et al*. 1983, 1987). The regulating factors governing this process are virtually unknown.

Surface resorption may also result from orthodontic forces. Light forces produce insignificant cemental cratering (root resorption) with rapid tooth movement. On the other hand, intermediate and heavy forces produce substantial cemental cratering and slower tooth movement (Rygh 1977). Following

application of an orthodontic force three main stages for the tooth movement can be identified:

1. *Initial minor movement due to the compression of pliable tissues*. During the initial stage of tooth movement, osteoclasts, macrophages, fibroblasts, and resorption lacunae in bone increase on the pressure side (Kurihara 1977; Brudvik & Rygh 1993, 1995).
2. *Delay period with no movement*. The induced tissue damage to the periodontal ligament is resolved by macrophages and osteoclasts during a delay period (Rygh 1977; Brudvik & Rygh 1993, 1995). If excessive forces are placed on teeth, there is increased damage to the surrounding tissues, which prolongs the delay period (Storey 1973). In this phase, the tissues show signs of hyalinization, i.e. development of a cell-free, structureless zone (Sandstedt 1904; Reitan 1951; Kvam 1967; Brudvik & Rygh 1993) as compressed collagen fibers gradually unite to a more or less cell-free mass (Rygh 1972, 1977).
3. *Rapid tooth movement and extensive bone remodeling*. Elimination of the hyalinized tissue leads to removal of the mature collagen and cementoid layer leaving a raw root surface lacking a protective blast cell barrier. The denuded root surface subsequently attracts clast cells and root resorption continues for as long as the force is present (Storey 1973; Rygh 1977; Brudvik & Rygh 1993, 1995). Major loss of dental hard tissue may follow this kind of iatrogenic injury.

Conclusion

Signs of active or healed surface resorptions or both are common in the large majority of teeth of the adult dentition. It is conceivable that minor traumata caused by unintentional biting on hard objects, bruxism, high fillings, etc., cause localized damage to the periodontal ligament and trigger the initiation of this type of resorption. The process is self-limiting and self-healing and no active treatment is required. During orthodontic treatment caution should be exercised and the forces moderated so that the risk of root foreshortening is minimized. When heavy forces are used the involved teeth should be monitored radiographically.

Replacement resorption

This type of resorptive process involves replacement of the dental hard tissues by bone, hence the name (Andreasen 1981). When a surface resorption stops, cells from the periodontal ligament will proliferate and populate the resorbed area (Lindskog *et al*. 1983, 1987). If the surface resorption defect is large, it will take some time before periodontal ligament cells have covered the entire surface. In the interim period osteoblasts from the nearby bone tissue may then arrive first and establish themselves at the resorbed surface (Andreasen & Kristerson 1981; Gottlow *et al*. 1986). Bone is thus being formed directly upon the dental hard tissue. This results in a fusion between the bone and the tooth substance, which is known as ankylosis. Note that replacement resorption and ankylosis are often erroneously used as synonyms. While replacement resorption describes the active process during which the tooth is resorbed and replaced by bone tissue, ankylosis is the Greek word for immobile. Thus, it describes the situation of a tooth lacking normal mobility due to the fusion between tooth and bone.

The fusion can be permanent or transient and appears to depend on the size of the resorbed area. If the ankylotic area is small, the bone on the tooth surface can resorb and be replaced with reparative cementum (Andreasen & Skougaard 1972; Andreasen & Kristerson 1981; Andersson *et al*. 1985; Hammarström *et al*. 1986). If the ankylotic area is large, a sufficient amount of bone will be formed on the root surface to make the fusion between bone and tooth permanent (Andreasen 1981; Andreasen & Kristersson 1981; Hammarström *et al*. 1986). It has been shown that long-term rigid splinting following external trauma results in a higher incidence of dento-alveolar ankylosis than with a short-term, less rigid fixation (Andreasen 1975).

Clinically, ankylosis is diagnosed by absence of tooth mobility and by a percussion tone that is higher than in a normal tooth (Andreasen 1975; Andersson *et al*. 1985). Radiographically, a local disappearance of the periodontal ligament contour may show an initial stage of fusion. However, even in non-ankylosed teeth it is not always possible to observe the entire contour of the periodontal ligament. Percussion and tooth mobility testing are therefore more sensitive diagnostic tools than radiography in the early stages of replacement resorption (Andersson *et al*. 1985). When dento-alveolar ankylosis occurs at a young age, the tooth will not erupt resulting in infra-occlusion (Andreasen & Hjörting-Hansen 1966; Malmgren *et al*. 1984; Kürol 1984).

The formation of bone on a dentin surface is not a pathologic process, but one to be regarded as a form of repair. The bone has accepted the dental hard tissue as a part of itself and the tooth becomes involved in the normal skeletal turnover (Löe & Waerhaug 1961; Hammarström *et al*. 1986). The turnover phase is fast in a growing child, but slower in an adult. Hence, the rate of bone replacement follows the pattern of bone remodeling. The detailed mechanism directing the resorptive process is not understood.

Conclusion

Ankylosis caused by apposition of bone to a root surface is a prerequisite for replacement resorption. The condition may be seen as a form of repair of root surface resorptions, albeit not desirable from a

clinical standpoint as the root structure will become successively destroyed. No treatment is available for this condition.

External inflammatory resorption

The term external inflammatory resorption describes the presence of an inflammatory lesion in the periodontal tissues adjacent to a resorptive process (Andreasen 1985). There are two main forms – peripheral inflammatory root resorption (PIRR) and external inflammatory root resorption (EIRR). Both forms are triggered by destruction of cementoblasts and the cementoid. In PIRR the factor maintaining osteoclast activation is thought to be provided by an inflammatory lesion in the adjacent periodontal tissue (Andreasen 1985; Gold & Hasselgren 1992). EIRR, on the other hand, receives its stimulus from an infected necrotic pulp (Andreasen 1985; Andreasen & Andreasen 1992).

Peripheral inflammatory root resorption

The major feature of this type of resorption is its location close to the gingival margin and its invasive nature. In teeth with a normal height of bone crest it usually becomes localized cervically, whereas in cases where the periodontal tissue has receded it can develop more apically. Different names have been proposed, including subosseous resorption (Antrim *et al*. 1982) and (the complete opposite) supraosseous extra-canal invasive resorption (Frank & Bakland 1987) reflecting the confusion that has surrounded the cause of this type of resorptive lesion. As it extends into the peripheral dentin towards the pulp, and as clast-activating factors seem to emanate from an inflammatory lesion in the periodontium, the term peripheral inflammatory root resorption (PIRR) was proposed to reflect the potential etiology of this phenomenon (Gold & Hasselgren 1992).

The clinical features of PIRR include a granulation tissue that bleeds freely on probing. Occasionally, a periodontal abscess may develop due to marginal infection, which may mimic a periodontal or endodontic condition (Fig. 40-23). When the lesion is located more apically or proximally, probing is usually difficult. Radiographically, the lesion may only be seen after a certain size has been reached (Fig. 40-22c). Sometimes the appearance is mottled due to the proliferation of bone tissue into the resorptive defect (Seward 1963) (Fig. 40-25). The outline of the root canal can often be seen within the radiolucent area (Figs. 40-22, 40-25 and 40-26) and this is a diagnostic feature for external root resorption in general. The presence of profuse bleeding upon probing and

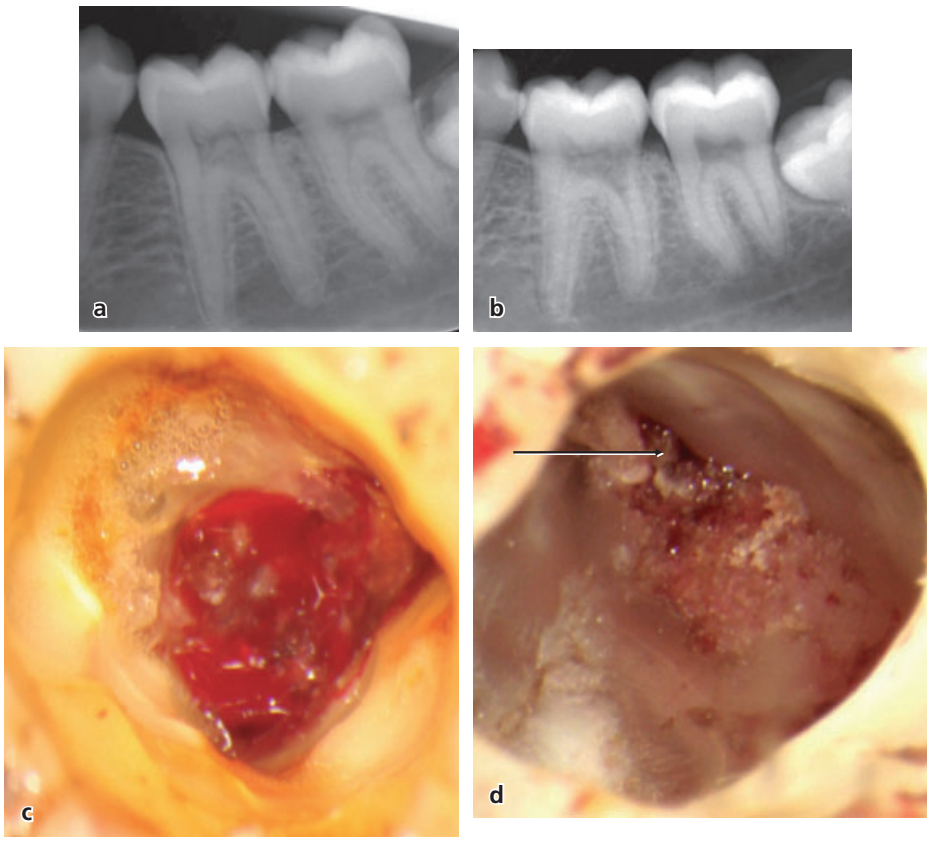

Fig. 40-25 (a,b) Peripheral inflammatory root resorption in a first lower molar showing a mottled appearance. There are pulp stones within the pulp tissue and bone tissue formation within the resorptive defect superimposed on the pulpal space. Following accessing both the pulp and the resorptive process (c) and removing the bleeding tissue, bone tissue appeared at the lingual wall of the cavity, where the resorptive process had entered the tooth (d). Arrow in (d) indicates the orifice of the root canal in the distal root. Case kindly provided by Dr. Magnus Fridjon Ragnarsson.

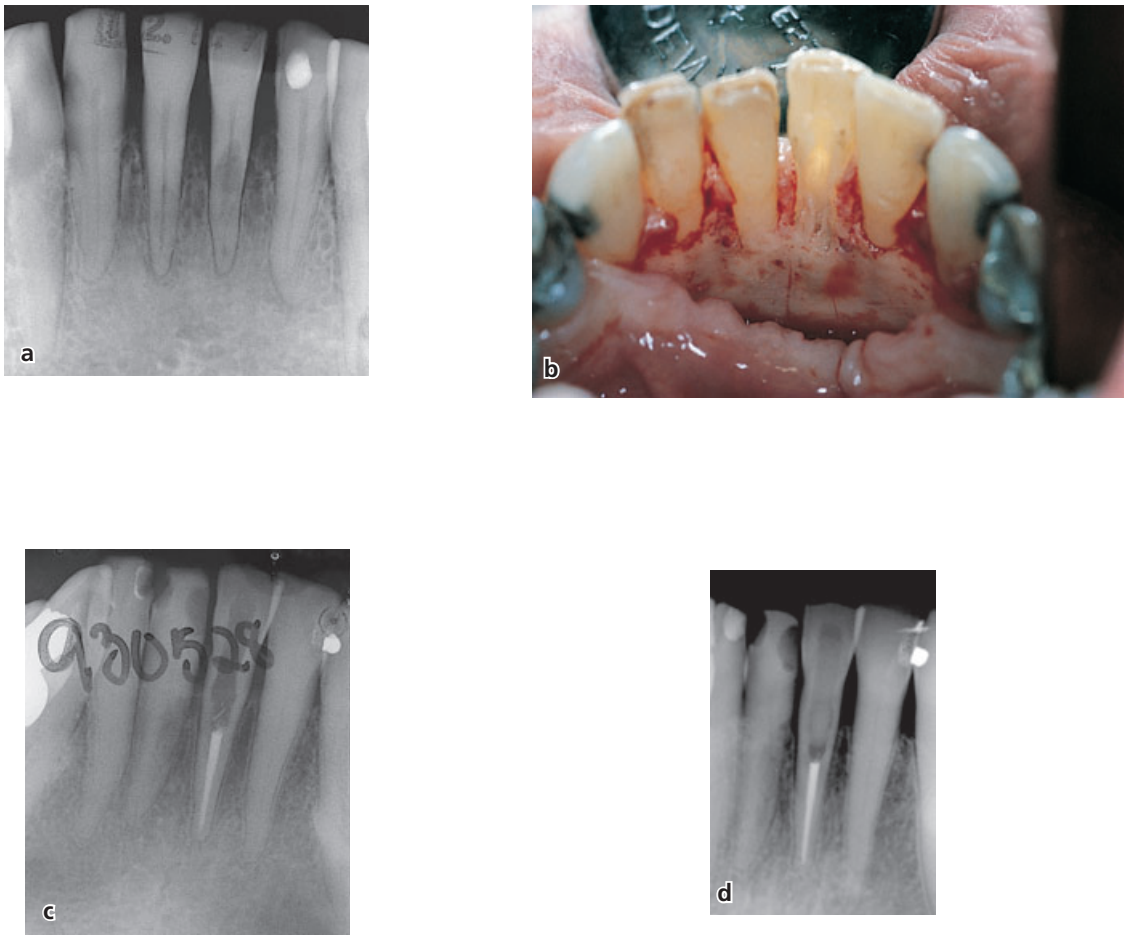

Fig. 40-26 Case with external root resorption on the lingual aspect of both central incisors. (a) The patient, a 78-year-old lady, had presented herself to the clinic after an episode of severe pain and development of a lingual periodontal abscess. The medical history was unremarkable. The patient was initially managed by antibiotic treatment. (b) Later, upon flap elevation and accessing the resorbing area and removal of the granulation tissue, exposure to a necrotic pulp of tooth #31 was noted. (c) Endodontic treatment was carried out during the surgery procedure. Tooth #41 was left without any further treatment and the case was followed clinically and radiographically. No recurrence of resorption occurred on either tooth and the patient remained comfortable. (d) Radiograph of the last follow-up is 8 years after treatment. Note that there is no progression of the resorptive process associated with tooth #41.

granulation tissue formation, in combination with a hard cavity bottom confirm the diagnosis of PIRR. Electric pulp test and cold tests are usually positive, but will not distinguish this condition from caries or internal resorption, the two major differential diagnostic options (Frank & Bakland 1987).

The mechanism for this form of resorption is far from completely understood. Predisposing factors seem to be orthodontic treatment, trauma, and intracoronal bleaching, while periodontal therapy had a low incidence among 222 analyzed cases (Heithersay 1999). The reason for the low incidence following periodontal treatment could be that, even upon excessive scaling and root planing, the damaged area of the root surface usually becomes covered by junctional epithelium. If a resorptive process is triggered it seems that its continuance has an infectious cause (Brosjö *et al*. 1990; Gold & Hasselgren 1992).

Unmineralized, newly formed tissue in cementum (Gottlieb 1942) and in predentin (Stenvik & Mjör 1970) appears resistant to resorption and explains why PIRR expands laterally without invading the pulp. Yet, this peripheral extension can markedly undermine the tooth structure (Fig. 40-23). If there is a non-vital pulp and thus no resorption inhibition in the form of odontoblast-supported predentin, PIRR may extend to the pulpal space. In root-filled teeth, which have been subjected to intracoronal bleaching, tissue toxic bleaching agents such as hydrogen peroxide have been found to be capable of penetrating through dentin and cementum (Fuss *et al*. 1989). If this occurs during the bleaching process, periodontal tissue injury will be inflicted and a resorptive processs may be initiated (Harrington & Natkin 1979; Montgomery 1984). The ensuing progression is thought to be a function of persisting inflammation as bacteria have colonized the chemically emptied dentinal tubules (Cvek & Lindvall 1985).

Obviously there are also different forms of this kind of resorption, some of which may be associated with a broad opening to the periodontium, as in the

cases initiated by bleaching agents. Others may have smaller openings through the cementum layer along which the resorptive process continues inside the tooth structure without causing major peripheral breakdown. The two patterns dictate the choice of treatment attempt. Surgical exposure of the area including removal of the granulation tissue is the only reasonable option in the former case; a dental filling, e.g. a resin composite, is placed in the defect followed by resuturing the flap. Other treatment options include repositioning of the flap apical to the restoration or orthodontic extrusion of the tooth (Gold & Hasselgren 1992). Guided tissue regeneration has also been advocated after surgical removal of the granulation tissue, to promote ingrowth of periodontal ligament cells into the resorbed area (Rankow & Krasner 1996)

External inflammatory root resorption

This type of resorption usually occurs as a complication to luxation injuries in conjunction with dental traumata. It begins as a surface resorption due to damage of the periodontal ligament and the cementum layer. There is good support for the view that the stimulus for continuance is infectious in nature and that the source is an infected pulp that succumbed as a result of the traumatic injury (Bergenholtz 1974; Andreasen 1985; Andreasen & Andreasen 1992). Following the initial surface resorption the often rapid progression is then due to the release of bacterial elements into the periodontal tissue by way of the exposed dentinal tubules. While the inflammatory process is maintained, the resorptive process, aimed at eliminating the irritants in the dentin tubules, moves in the direction of the infected pulp. As dentin is further resorbed, more infectious products are released thus perpetuating the inflammatory reaction with acceleration of the resorptive process as a result (Andreasen 1985).

The earliest stages are not radiographically visible due to the small size of the resorptive cavity and the first radiographic signs following trauma cannot usually be seen for several weeks (Andreasen *et al*. 1987). Treatment is directed towards the cause of the resorption, that is, the root canal infection (Cvek 1993), and the procedure to be carried out is no different to the one applied in normal cases. While a successful halt of the resorption can be anticipated (Cvek 1973) there is always risk of ankylosis after the initial healing phase. The greater the resorbed area, the greater is the risk for this complication (Andreasen & Kristerson 1981; Andersson *et al*. 1985; Gottlow *et al*. 1986).

Conclusion

Peripheral inflammatory root resorption (PIRR) and external inflammatory root resorption (EIRR) are two forms of progressive external root resorption associated with persistent inflammation in the periodontal tissues. While the direct cause for progression is not well understood, infectious elements maintaining periodontal inflammation close to a root surface that is not covered by periodontal ligament or epithelium appear to drive PIRR. To remedy the condition it is necessary to remove all resorbing granulation tissue surgically and fill the resorption cavity. In certain cases it may be possible to carry out the treatment from the pulpal side (Fig. 40-25). Regardless of approach, periodontal tissue complications may ensue, including deep pockets and suppuration from such pockets. Treated cases should therefore be monitored by regular clinical/radiographic follow-ups to

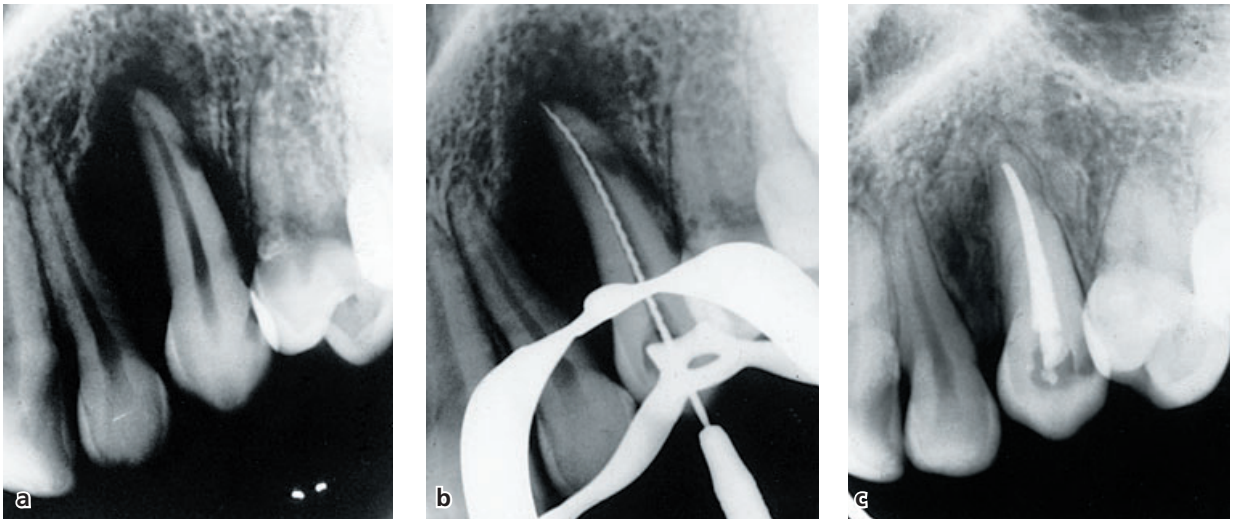

Fig. 40-27 Radiographs from a 27-year-old woman showing the emergence of external inflammatory root resorptions on the left maxillary canine, which had been autotransplanted into a surgically prepared socket 2 months earlier (a). Endodontic treatment of the necrotic pulp (b) halted the resorptive process. (c) Radiograph following root filling shows that the external resorption cavity is rounded. A normal contour of the periodontal ligament space can be seen between the root and bone, which has filled the prepared socket.

observe any signs of recurrence and how the periodontal tissue copes. In advanced cases extraction is the only reasonable treatment option. EIRR is usually seen as a complication to luxation injuries in conjunction with dental traumata. The primary impetus for its progression is an infected pulp that releases bacterial elements to the resorbing area along exposed dentinal tubules by which an inflammatory lesion is also maintained in the periodontium. EIRR can usually be stopped by focusing the treatment on the endodontic infection (Fig. 40-27) although ankylosis and replacement resorption may appear as complications that may not be detected until years later.

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Chapter 41

Treatment of Peri-implant Lesions

Tord Berglundh, Niklaus P. Lang, and Jan Lindhe

Introduction

Inflammatory lesions occurring in the peri-implant tissues were described in Chapter 24. Such processes are the result of opportunistic infections (see Chapter 10) and may, if left untreated, progress deep into the supporting bone and lead to implant loss. It is, therefore, imperative that the tissues around implants be monitored at regular intervals to discover arising biologic complications and to interfere with the disease process at an early stage. The appropriate therapy instituted following diagnosis must be aimed towards the reduction of the submucosal biofilm and the alteration of the ecologic conditions for the bacterial habitat.

The diagnostic process

The examination of the tissues around implants has many features in common with the periodontal examination and must include parameters relevant to the pathogenic process of the peri-implant lesion. It should be understood that, while advanced peri-implant lesions are easily recognized on radiographs, early alterations in the mucosa are often discrete (see also Chapter 24). Hence, a systematic examination for their detection is required that should include assessments of:

- Bleeding on probing (BoP)
- Suppuration
- Probing depth (PPD)
- Radiographic bone loss
- Implant mobility.

Assessments of BoP, suppuration, and PPD must be made at four surfaces (mesial, buccal, distal, and lingual) of each implant, while radiographic evaluation is limited to mesial and distal aspects.

Treatment strategies

The decision on treatment strategies is based on the diagnosis and the severity of the peri-implant lesion. Peri-implant mucositis and incipient forms of peri-implantitis require less extensive measures than advanced peri-implantitis lesions with severe bone loss. In all situations of peri-implant disease, however, the treatment strategies must include mechanical cleaning (infection control) procedures. Thus, information and instruction on the use of oral hygiene measures must be provided to the patient in combination with professional mechanical cleaning, including removal of plaque and calculus on implant surfaces. In this context it is important that the design of the implant-supported prosthesis allows access for oral hygiene. Thus, in cases where access for implant cleaning is obstructed, the prosthesis has to be modified to promote self-performed and professional mechanical infection control.

Two cases that illustrate the outcome of self-performed and professional mechanical cleaning are presented in Figs. 41-1 and 41-2. While plaque, calculus, and signs of inflammation are evident at implants in the initial examination, the follow-up visit at 3 months of infection control demonstrates improved oral hygiene and soft tissue conditions.

There are obvious similarities between teeth and implants regarding the strategies in treatment of

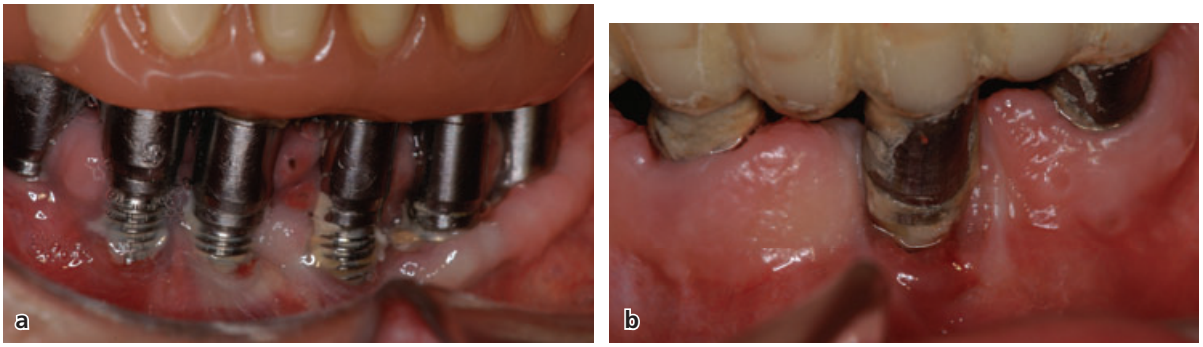

Fig. 41-1 Clinical photograph from implant sites in the mandible of a 75-year-old male (a) and a 62-year-old woman (b). Note the large amounts of plaque and calculus and the overt signs of inflammation in the peri-implant mucosa (a).

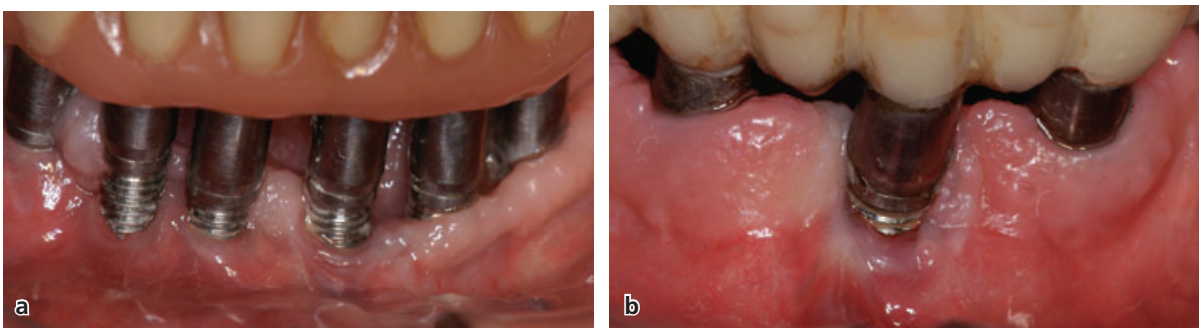

Fig. 41-2 Implant sites in Fig. 41-1 after 3 months of self-performed mechanical infection control combined with professional cleaning. Improved oral hygiene and soft tissue conditions.

periodontal and peri-implant infections. One important difference, however, relates to difficulties with instrumentation of the implant surface below the margin of the mucosa. Thus, subgingival scaling and root planing are well known procedures in the treatment of periodontitis, while in peri-implantitis the geometry of the implant with threads of different designs may impede the ability of the clinician to detect and remove calculus located below the mucosal margin. During such "blind" instrumentation at implants there is also a risk that deposits may be dislodged and become displaced into the mucosa. It is thus recommended that non-surgical debridement of implant surfaces, i.e. procedures that aim to remove calculus and plaque, should be restricted the portion of the implant located coronal to or at the level of the mucosal margin. While calculus may be chipped off using carbon fiber (Fig. 41-3) or plastic curettes, plaque is removed by polishing the implant surface with rubber cups and a polishing paste. Carbon fiber curettes do not damage the implant surface. They may be sharpened and are strong enough to remove most accumulations of calculus. Conventional steel curettes or ultrasonic instruments with metal tips should not be used because they may cause severe damage to the implant surface (Matarasso *et al.* 1996).

Peri-implant mucositis and incipient peri-implantitis lesions may be resolved using the cause-related measures described above. A re-examination

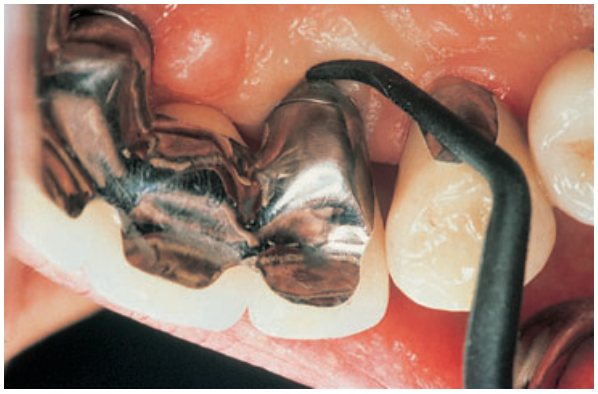

Fig. 41-3 Calculus deposits may be chipped off using carbon fiber curettes with the aim of not scratching the implant surface.

of peri-implant tissues following initial therapy that reveals absence of BoP and pocket closure indicates resolution of peri-implant lesions. On the other hand, if signs of pathology, i.e. BoP/suppuration in combination with deep pockets remain at the re-examination, additional therapy is required. Surgical procedures are one treatment option which provides access to the implant surfaces harboring biofilms. A prerequisite for surgical therapy in treatment of peri-implantitis is appropriate standards of self-performed infection control.

Surgical therapy of peri-implantitis lesions is illustrated in Figs. 41-4, 41-5, and 41-6. Clinical signs

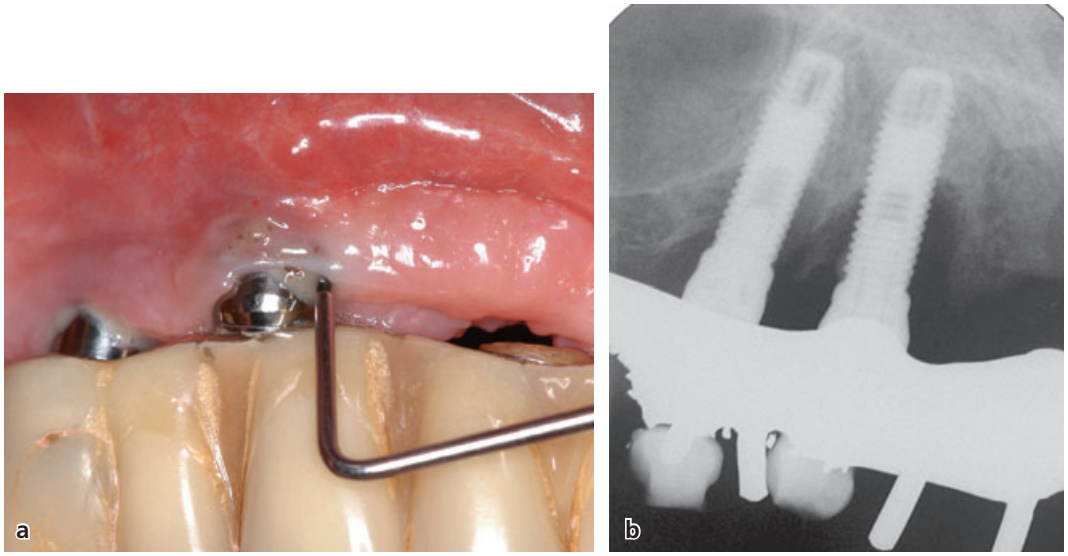

Fig. 41-4 Clinical photograph from implant sites with peri-implantitis. Note the PPD of 10 mm and suppuration (a) and the crater-formed defects in the radiograph (b).

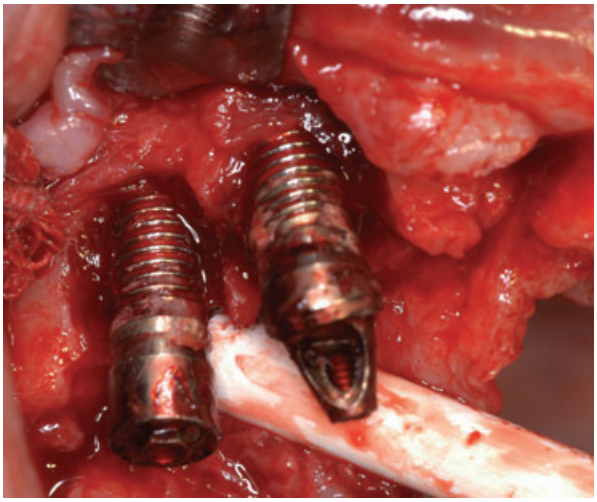

Fig. 41-5 Implant sites in Fig. 41-3 after flap elevation and removal of granulation tissue. Note the absence of buccal bone walls of the osseous defects. The implant surfaces are accessible for mechanical debridement.

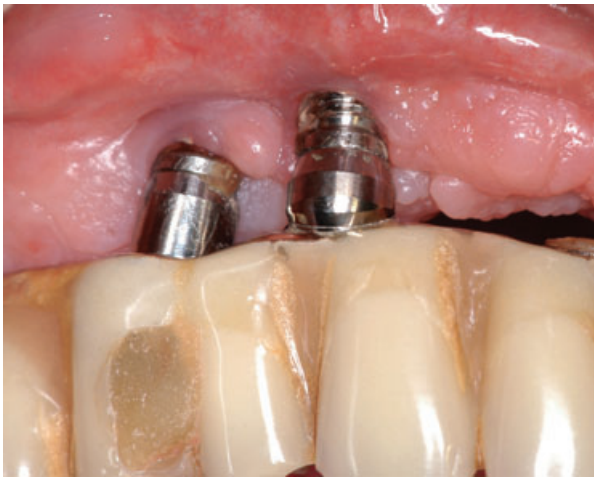

Fig. 41-6 Implant sites in Fig. 41-3 at 6 months after surgical therapy. Maintenance therapy with supervised infection control is provided. Note the soft tissue recession following the pocket elimination procedure.

of inflammation, PPD of about 10 mm in combination with BoP and suppuration were detected at the initial examination (Fig. 41-4). The radiograph revealed crater-formed defects around the two implants. Flap elevation allowed access to the area and granulation tissue in the defects was removed using steel curettes (Fig. 41-5). Mechanical debridement of the implant surface was performed using carbon fiber curettes and small pieces of gauze or pellets soaked in saline. The peri-implantitis associated bone defect may be treated using either resective or regenerative procedures (see also Chapter 46). In this case the morphology of the osseous defect was not suitable for regenerative techniques and, hence, resective procedures were performed to adjust the morphology of the interproximal bone walls. At the 6-month follow-up after surgery, PPD was reduced and clinical signs of inflammation were absent (Fig. 41-6).

Recent reviews on treatment of peri-implant mucositis and peri-implantitis indicated that most articles in the literature consist mainly of case reports (Klinge *et al*. 2002; Roos-Jansåker *et al*. 2003). In addition to mechanical debridement a vast number of different treatment procedures have been suggested including antiseptic agents and local and/or systemic antibiotics. Klinge *et al*. (2002) concluded that there is insufficient evidence to support a specific treatment protocol.

Resolution of peri-implantitis lesions

In dog experiments by Ericsson *et al*. (1996) and Persson *et al*. (1996, 1999), peri-implantitis lesions

were first produced according to the technique previously described (Lindhe *et al*. 1992). The peri-implantitis lesions were subsequently exposed to therapy. Antibiotics (amoxicillin and metronidazole) were administered to the animals via the systemic route but local treatment was provided to only some of the diseased implant sites. Following several months of healing, it was observed that in implant sites also given local therapy, i.e. submarginal debridement, the inflammatory lesions were resolved. In implant sites not exposed to local debridement, however, the inflammatory infiltrate persisted in the mucosa as well as in locations immediately adjacent to the bone tissue.

These observations clearly demonstrate that a treatment regimen that is restricted to systemic administration of antibiotics is not effective in the management of peri-implantitis, but must always be combined with meticulous removal of the biofilm from the contaminated implant surface. In this context it must be remembered that in the treatment of chronic periodontitis administration of systemic antibiotics without local therapy (i.e. scaling and root planing) will not resolve the inflammatory lesion in the gingiva and will also fail to arrest further progression of tissue breakdown (Lindhe *et al*. 1983a,b; Berglundh *et al*. 1998).

Cumulative Interceptive Supportive Therapy (CIST)

Preventive and therapeutic strategies

Depending on the clinical, and eventually the radiographic, diagnosis, protocols for preventive and therapeutic measures were designed to intercept the development of peri-implant lesions. This system of supportive therapy is cumulative in nature and includes four steps, which should not be used as single procedures, but rather as a sequence of therapeutic procedures with increasing anti-infective potential depending on the severity and extent of the lesion. Diagnosis, therefore, represents a key feature of this supportive therapy program (Lang *et al*. 2004).

The major clinical parameters to be used have been discussed above and include:

- Presence of a biofilm
- Presence or absence of BoP
- Presence or absence of suppuration
- Increased peri-implant probing depth
- Evidence and extent of radiographic alveolar bone loss.

Oral implants without plaque and calculus and surrounded by healthy peri-implant tissues, as evidenced by (1) absence of BoP, (2) absence of suppuration, and (3) probing depth usually not exceeding 3 mm, should be considered clinically stable. Such sites should not be exposed to therapeutic measures (Fig. 41-7).

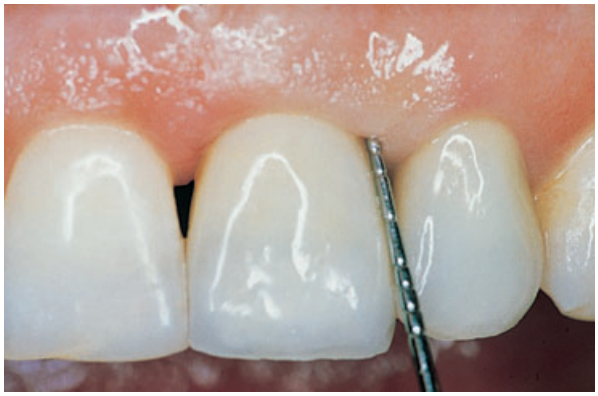

Fig. 41-7 Clinically stable implant with VMK crown (region 21) characterized by absence of bleeding on probing, suppuration, and a peri-implant probing depth not exceeding 3 mm.

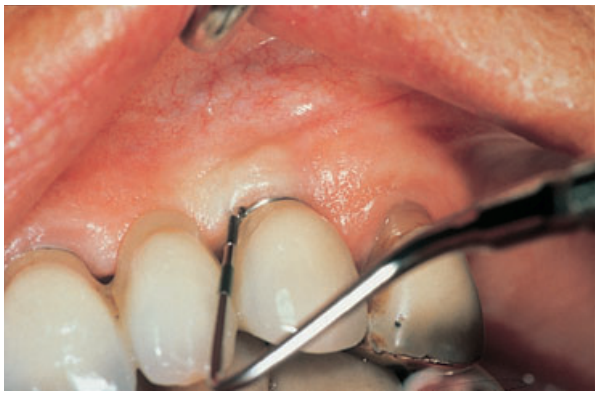

Fig. 41-8 Peri-implant mucositis characterized by presence of bleeding on probing, absence of suppuration, and a peri-implant probing depth of 4 mm.

Mechanical debridement; CIST protocol A

Implants with plaque and calculus deposits and surrounded by a mucosa that is BoP positive but suppuration negative and with a PPD ≤4 mm are to be subjected to mechanical debridement as described above (Fig. 41-8).

Antiseptic therapy; CIST protocol A+B

At implant sites which are BoP positive, exhibit an increased probing depth (4–5 mm) and may or may not demonstrate suppuration, antiseptic therapy is delivered in addition to mechanical debridement. A 0.2% solution of chlorhexidine digluconate is prescribed for daily rinsing, or a 0.2% gel of the same antiseptic is recommended for application to the affected site (Fig. 41-9). Generally, 3–4 weeks of antiseptic therapy are necessary to achieve positive treatment results.

Antibiotic therapy; CIST protocol A+B+C

At BoP-positive implant sites with deep pockets (PPD ≥6 mm) (suppuration may or may not be present), there are frequently also radiographic signs of bone loss. Such pockets represent an ecologic habitat which is conducive for the colonization of Gram-negative and anaerobic putative periodontal pathogens (Mombelli *et al*. 1987). Anti-infective treatment must include the use of antibiotics to eliminate or reduce the pathogens in this habitat. This, in turn, will allow soft tissue healing as demonstrated in a clinical study by Mombelli and Lang (1992). Prior to administering antibiotics the mechanical (CIST A) and the antiseptic (CIST B) protocols have to be applied. During the last 10 days of the antiseptic treatment regimen, an antibiotic directed against anaerobic bacteria (e.g. metronidazole or ornidazole) is used. Thus for instance, 350 mg tid of Flagyl® (Rhone-Poulenc) or 500 mg bid of Tiberal® (Roche) is administered via the systemic route. A site treated according to the above protocol is depicted in Fig. 41-10. A fistula can be seen in the buccal aspect of implant site 45 (Fig. 41-10a). The site exhibited BoP and had a probing depth of 7 mm. After therapy the inflammation is resolved (Fig. 41-10b) and some recession of the mucosal margin has occurred. In Fig. 41-10c the bone fill that took place in the angular defect is illustrated in a subtraction radiography image using contrast enhancing. Figure 41-10d presents the site 8 years after active therapy.

An alternative to systemic administration is the controlled, local delivery of antibiotics. It must be realized, however, that only devices with proper release kinetics must be used to assure successful

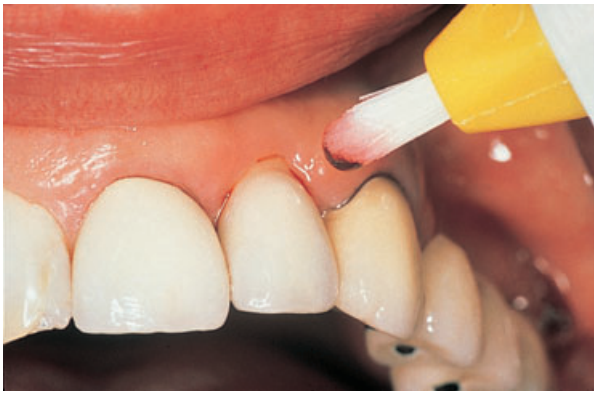

Fig. 41-9 Mechanical and antiseptic cleansing. Application of chlorhexidine gel (Plakout®, 0.2%) to a site with peri-implant mucositis.

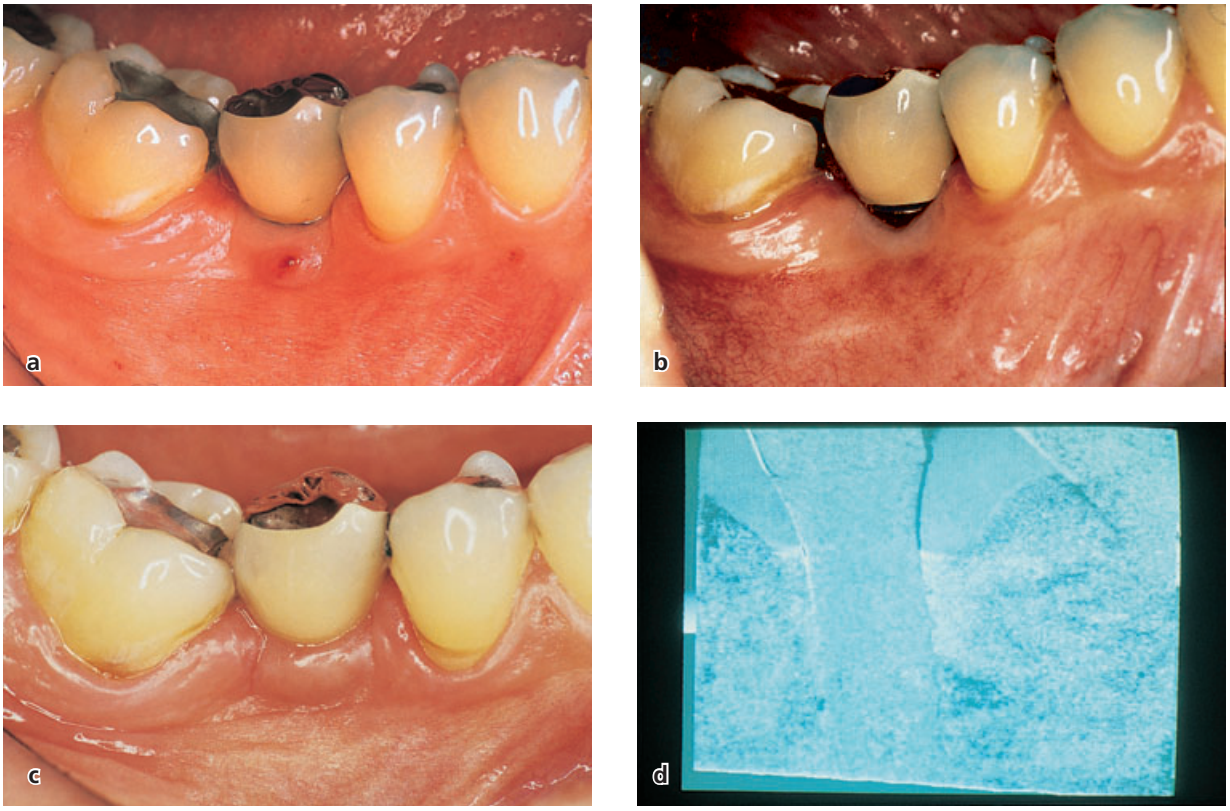

Fig. 41-10 Treatment of peri-implantitis according to the protocol of CIST (cumulative interceptive supportive therapy). (a) Clinical diagnosis of peri-implantitis: presence of bleeding on probing, suppuration, development of a fistula, loss of alveolar bone. Peri-implant probing depth 7 mm. (b) Clinical resolution of the peri-implant infection 1 year after mechanical and antiseptic cleansing, followed by the systemic application of antibiotics (500 mg Tiberal® bid for 10 days). Some recession is visible. (c) Absence of mucositis, reduced peri-implant probing depth to 3 mm, and bone fill of the lesion. (d) Documentation of the healed peri-implant infection by contrast-enhanced subtraction radiography. The intrabony crater has been completely filled 1 year after therapy.

clinical results. The antibiotic must thus remain at the site of action for at least 7–10 days and in a concentration high enough to penetrate the submucosal biofilm (Mombelli *et al*. 2001). An example of such a controlled-release device is the tetracycline-containing periodontal fiber (Actisite®; Alza). The therapeutic effect of this controlled-release device appears to be identical to the effect obtained by the systemic use of antibiotics (Mombelli *et al*. 2001).

In a more recent development, minocycline microspheres (1 mg Arestin®; Orapharma, Johnson & Johnson) have been used as a controlled-release device in a similar manner to the application of tetracycline fibers (Mombelli *et al*. 2001). These microspheres are easily applied into the peri-implant pocket by means of a syringe. The antibiotic is contained in very small beads that stick to the lateral walls of the pocket and to the implant surface providing enough substantivity (high enough concentration for up to 14 days) to penetrate the biofilm. The principle has been tested in a randomized controlled clinical trial with a 1% chlorhexidine gel as a control (Renvert *et al*. 2006) and a prospective cohort study in patients with peri-implantitis (Persson *et al*. 2006; Salvi *et al*. 2007). Both studies demonstrated reduction in bleeding on probing, pocket depth reduction, and slight recession. Significantly lower bacterial loads were seen after 10 days and up to 180 days for some presumptive pathogens (Persson *et al*. 2006). This indicates that the application of minocycline microspheres adjunctive to the CIST protocols A+B represents a valuable alternative to the administration of systemic antibiotics for the treatment of incipient peri-implant infections.

Regenerative or resective therapy; CIST protocol A+B+C+D

It is imperative to understand that regenerative or resective therapy is not instituted until the peri-implant infection is under control. Thus, before surgical intervention is planned, the previously diseased site should have become BoP negative, exhibit no suppuration, and have a reduced probing depth. Depending on the extent and severity of the local bone loss, a decision is made whether regenerative or resective measures are to be applied. In this context it must be realized that the goal of regenerative therapy, including the use of barrier membranes, is new bone formation in the crater-like defect around the implant, although *de novo* osseointegration may occur to a limited extent (Persson *et al*. 1999; Wetzel *et al*. 1999).

Conclusions

An implant patient must always be enrolled in a supportive therapy program that involves recall visits at regular intervals. Each recall visit must start with an examination to assess whether the implant sites are healthy or exhibit signs of inflammation. Cumulative Interceptive Supportive Therapy (CIST) includes a series of four protocols to be used when the examination and the diagnostic process are completed.

Figure 41-11 outlines (1) the decision process to be used for the peri-implant tissue diagnosis (Lang *et al*. 2004) and (2) the different therapeutic measures that are available to treat and/or prevent peri-implant infections.

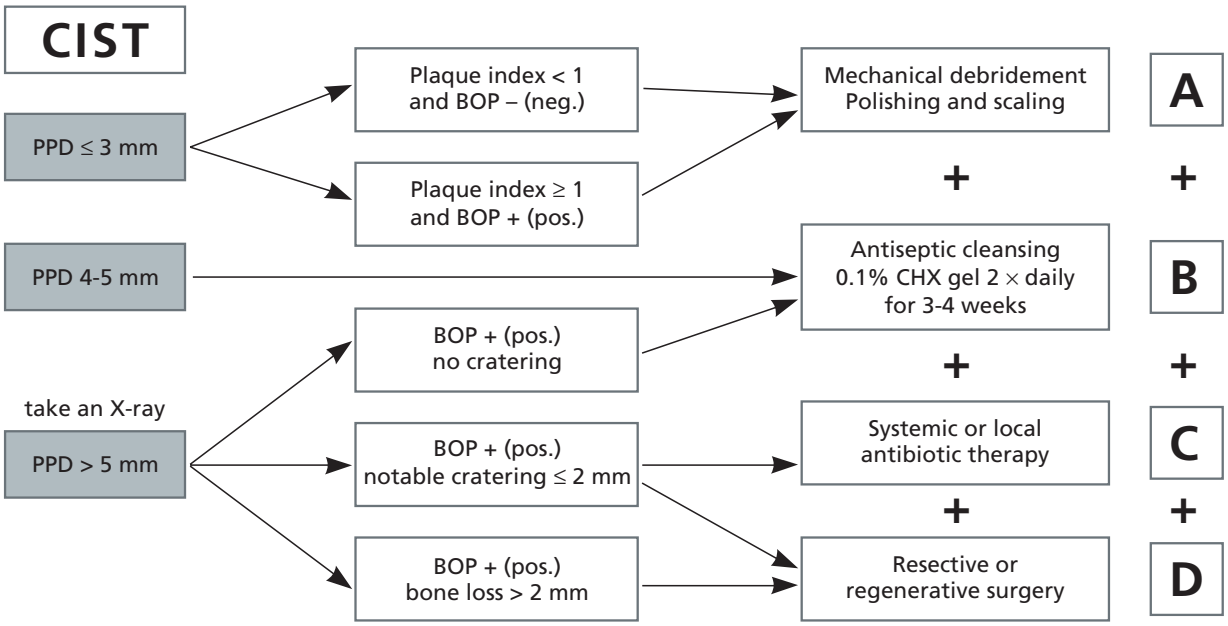

Fig. 41-11 Decision tree for cumulative interceptive supportive therapy (CIST). Depending on the mucosal condition and probing depth, either regime A or regime A+B, regime A+B+C or regime A+B+C+D are performed. A = Mechanical debridement; B = Antiseptic cleansing; C = Antibiotic therapy; D = Resective or regenerative surgery.

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Chapter 42

Antibiotics in Periodontal Therapy

Andrea Mombelli

Principles of antibiotic therapy

Antibiotics are drugs that can kill or stop the multiplication of bacterial cells, at concentrations that are relatively harmless to host tissues, and therefore can be used to treat infections caused by bacteria. The capacity of the drug to reach the infected site, and the ability of targeted bacteria to resist or inactivate the agent determine the effectiveness of therapy. Based on their effect at concentrations tolerated by the host, antibiotics can be categorized as "bactericidal" or "bacteriostatic", and, depending on the range of susceptible bacteria, "narrow-spectrum" or "wide-spectrum". Antibiotics are just one group of antimicrobial agents, which also comprise antiviral, antifungal, and antiparasitic chemicals. The term was originally applied to substances extracted from fungus or other living organisms, but today also includes synthetic products.

As antibiotics can kill or suppress bacteria, the recognition of periodontitis as an infection – caused or sustained by certain bacteria living and multiplying in diseased sites – is a fundamental issue for any antimicrobial treatment concept. Antibiotics do not remove calculus and bacterial residues, and this is traditionally perceived to be an essential part of periodontal therapy.

The limitations of mechanical therapy: can antimicrobial agents help?

The continued presence of large masses of bacteria on hard oral surfaces induces inflammation in adjacent soft tissues such as gingiva or mucosa, and the importance of removing bacterial plaque for resolution of gingivitis or mucositis is undisputed. The propensity of sites to undergo further periodontal destruction is felt to be more specific in nature, since not all sites with gingivitis invariably progress to periodontitis, and since increased proportions and detection frequencies of suspected oral pathogens are found in periodontitis lesions. Nevertheless, thorough mechanical cleaning of the root surfaces has also proven to be beneficial in the case of periodontitis, of whatever class, and under whatever clinical circumstances. Furthermore, it has been shown that the ability of the patient to prevent the re-formation of structured bacterial deposits by toothbrushing is crucial for long-term stability (for review see Chapter 59). However, this way of dealing with periodontal disease is time consuming, requires high levels of motivation and manual skills – of both the clinician and the patient – and has unwanted effects. It would be irrational to believe that mechanical instruments are able to completely remove periodontal pathogens from all infected sites (Mombelli *et al*. 2000). Bacteria may be inaccessible to mechanical instruments in concavities, lacunae, and dentin tubules, not to mention invaded soft tissues. Substantial hard tissue trauma may arise from repeated attempts at instrumentation in locally unresponsive sites, or sites with recurrent disease (Fig. 42-1). In addition, successfully treated sites may be recolonized by pathogens persisting in non-dental areas. Although we know that mechanical therapy can be clinically successful in many patients even if all putative pathogens are not completely eradicated, persistence or regrowth of certain microorganisms in treated sites should be

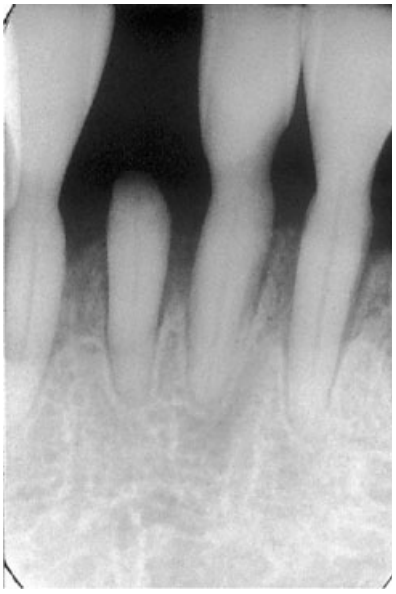

Fig. 42-1 Conventional periodontal therapy and maintenance imply repeated treatment of sites with localized unresponsive or recurrent disease, resulting in sometimes substantial hard tissue trauma.

considered as a cause of unsatisfactory treatment outcomes.

A closer look at the composition of the subgingival microbiota reveals that mechanical treatment is targeted at a variable mixture of different bacteria. The number of different species and subspecies occasionally identified in samples from human plaque by far exceeds 100, but only relatively few show a distinctive pattern of association with disease. While most frequently identified organisms are thought to harm tissues significantly only if present in high numbers over prolonged periods of time, in susceptible individuals certain species may have a negative effect even at relatively low numbers. On the basis of their pathogenicity, demonstrated in animal experiments, and the identification of virulence factors, a few organisms have been suggested to be specific periodontal pathogens (for review see Chapter 9). *Aggregatibacter actinomycetemcomitans* (formerly known as *Actinobacillus actinomycetemcomitans*) (Norskov-Lauritsen & Kilian 2006) and *Porphyromonas gingivalis* have attracted particular attention because longitudinal and retrospective studies have indicated an increased risk for periodontal breakdown in positive sites and because results of treatment have been better if the organisms could no longer be detected at follow-up (Bragd *et al*. 1987; Wennström *et al*. 1987; Carlos *et al*. 1988; Haffajee *et al*. 1991; Grossi *et al*. 1994; Haffajee & Socransky 1994; Dahlén *et al*. 1996; Rams *et al*. 1996; Chaves *et al*. 2000). If periodontal disease is in fact caused by a limited number of bacterial species, then non-specific continuous plaque removal is not the only possibility for prevention and therapy. Specific suppression of pathogenic bacteria becomes a valid alternative, and antibiotic approaches to regain and maintain periodontal health may have a better efficiency ratio.

In the late 1930s and early 1940s, the appearance of powerful agents selectively active against bacteria – sulfonamides, penicillin, and streptomycin – revolutionized the treatment of bacterial infections. The phenomenal success of these agents in the treatment of formerly life-threatening diseases led many to believe that bacterial infections would never again be a major medical concern. More than six decades of experience with these, and hundreds of additionally developed antimicrobial drugs have shown that, despite all the success, this view was too optimistic. Emerging problems, resulting from the widespread use of antibiotics have modified the general perception of the capabilities of antimicrobial agents. Over the years, many bacteria have developed a remarkable ability to withstand or repel antibiotic agents and are increasingly resistant to formerly potent agents. It has been noted that the use of antibiotics may disturb the delicate ecologic equilibrium of the body, allowing the proliferation of resistant bacteria or non-bacterial organisms. Sometimes this may initiate new infections that are worse than the ones originally treated. In addition, no antibacterial drug is absolutely non-toxic and the use of any antimicrobial agent carries with it accompanying risks. Thus, before we can start to administer antibiotics routinely to our periodontal patients we need to be sure about the specific benefit in comparison to standard treatment approaches. To limit the development of microbial antibiotic resistance in general, and to avoid the risk of unwanted systemic effects of antibiotics for the treated individual, a precautionary, restrictive attitude towards using antibiotics is recommended.

Specific characteristics of the periodontal infection

The term infection refers to the presence and multiplication of microorganisms in or on body tissues. The uniqueness of plaque-associated dental diseases as infections relates to the lack of massive bacterial invasion of tissues. Although there is evidence for bacterial penetration in severely diseased periodontal tissues, notably in periodontal abscesses and in acute necrotizing ulcerative lesions (Listgarten 1965; Saglie *et al*. 1982a,b; Allenspach-Petrzilka & Guggenheim 1983; Carranza *et al*. 1983), it has not been generally accepted that true bacterial invasion (including multiplication of bacteria within tissues) is crucial for periodontal disease progression. Bacteria in the subgingival plaque obviously interact with host tissues even without direct tissue penetration. Thus, to have an effect, any antimicrobial agent used in periodontal therapy needs to be available at a sufficiently high concentration not only within the periodontal tissues, but also in the environment of the periodontal pocket (Fig. 42-2). Antibiotic resistance always occurs first in sites where penetration of the agent is restricted, and

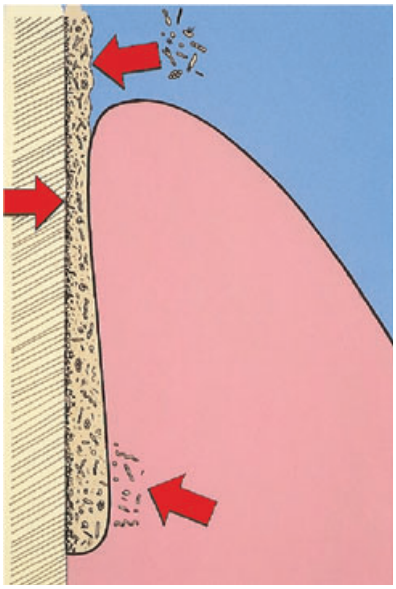

Fig. 42-2 Specific conditions for the use of antimicrobial agents in periodontal therapy. The periodontal pocket as an open site is subject to recolonization after therapy (top arrow). The subgingival bacteria are protected from antimicrobial agents in a biofilm (middle arrow). The agent must be available at a sufficiently high concentration not only within, but also in the subgingival environment, outside the periodontal tissues (bottom arrow).

therapeutic concentrations are difficult to achieve. A periodontal pocket may contain very large amounts of bacteria, and the antimicrobial agent may be inhibited, inactivated or degraded by non-target microorganisms.

The subgingival microbiota accumulate on the root surface to form an adherent layer of plaque. Accumulation of bacteria on solid surfaces can be observed on virtually all surfaces immersed in natural aqueous environments and is called "biofilm" formation. Extensive bacterial growth, accompanied by excretion of copious amounts of extracellular polymers, is a typical phenomenon in biofilms. Biofilms effectively protect bacteria from antimicrobial agents (Anwar *et al*. 1990, 1992). Bacteria involved in adhesion-mediated infections that develop on permanently or temporarily implanted materials, such as intravascular catheters, vascular prostheses or heart valves, are notoriously resistant to systemic antimicrobial therapy and tend to persist until the device is removed (Gristina 1987; Marshall 1992). Several mechanisms leading to this increased resistance of bacteria in biofilms have been proposed. Due to limited diffusion, antimicrobial agents may simply not reach deeper parts of a biofilm at sufficiently high levels during a given time of exposure. Within biofilms an unequal distribution of electrical charge may develop. Intrusion may thus be further complicated in certain areas of the biofilm depending on the charge of the penetrating molecule. Because of a limited availability of nutrients within the biofilm, bacteria may also reduce their metabolism, rendering them less susceptible to killing by agents interfering with protein, DNA or cell wall synthesis. *In vitro* experiments indicate that the attachment of bacteria to surfaces can trigger genes, which activate specific resistance mechanisms. Since these mechanisms are switched on upon contact, they may occur already in newly forming, very thin biofilms (Costerton *et al*. 1995).

Recognizing the above described problems there is currently a general consensus that mechanical instrumentation must always precede antimicrobial therapy. First, we should quantitatively reduce the large mass of bacteria, which otherwise may inhibit or degrade the antimicrobial agent. Second, we should mechanically disrupt the structured bacterial aggregates that can protect the bacteria from the agent.

Since the periodontal flora never consists of one single species, synergistic, but also antagonistic, relationships between microorganisms could occur. Based on the concept that the presence of beneficial bacterial species may suppress the activity of pathogens, one can speculate that it may be advantageous specifically to eliminate target bacteria only and to allow the growth of potentially beneficial microorganisms. Such contemplations have been used as an argument to propagate narrow-spectrum antibiotics for periodontal therapy.

Drug delivery routes

Oral antibiotics (*per os*, by mouth, abbreviated "p.o.") are the most common approach for treating bacterial infections. Administration by means other than through the alimentary tract (as by intramuscular or intravenous injection) is usually reserved for serious medical conditions if the oral route is proven ineffective. Some local infections can be treated with topically administered antibiotics, as with eyedrops or ointments. In the therapy of periodontal diseases antibiotics may be delivered via the systemic route or by direct placement into the periodontal pocket. Each method of delivery has specific advantages and disadvantages (Table 42-1). Local therapy may allow the application of antimicrobial agents at levels that cannot be reached by the systemic route and may be suitable for agents, i.e. antiseptics, that are too toxic to be delivered by the systemic route. This form of application seems to be particularly promising if the presence of target organisms is confined to the clinically visible lesions. Systemic administration of antibiotics may be better if the targeted bacteria are distributed wider. Studies have shown that periodontal bacteria may in fact be distributed throughout the whole mouth in some patients (Mombelli *et al*. 1991a, 1994), including non-dental sites, such as the dorsum of the tongue or tonsillary crypts (Zambon *et al*. 1981; van Winkelhoff *et al*. 1988; Müller *et al*. 1993, 1995; Pavicic *et al*. 1994). Disadvantages of systemic antibiotic therapy relate to the fact that the

Table 42-1 Comparison of local and systemic antimicrobial therapy

Issue	Systemic administration	Local administration
Drug distribution	Wide distribution	Narrow effective range
Drug concentration	Variable levels in different body compartments	High dose at treated site, low levels elsewhere
Therapeutic potential	May reach widely distributed microorganisms better	May act locally on biofilm associated bacteria better
Problems	Systemic side effects	Re-infection from non-treated sites
Clinical limitations	Requires good patient compliance	Infection limited to the treated site
Diagnostic problems	Identification of pathogens, choice of drug	Distribution pattern of lesions and pathogens, identification of sites to be treated

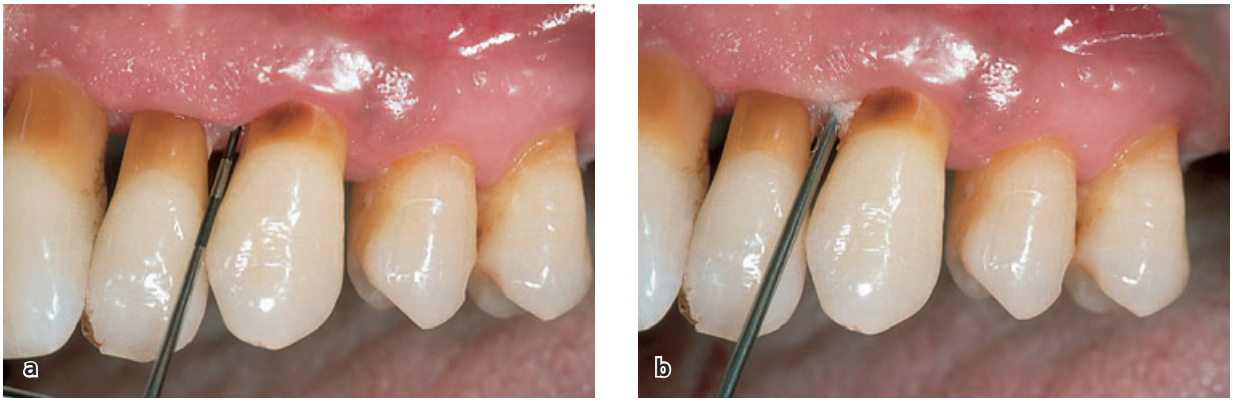

Fig. 42-3 (a) An antimicrobial gel is applied with a syringe inserted into a residual pocket. (b) For retention of the agent in the site, the viscosity of the carrier should change immediately. A large portion of the product may otherwise be expelled from the pocket quickly.

drug is dissolved by dispersal over the whole body, and only a small portion of the total dose actually reaches the subgingival microflora in the periodontal pocket. Adverse drug reactions are a greater concern and more likely to occur if drugs are distributed via the systemic route. Even mild forms of unwanted effects may severely decrease patient compliance (Loesche *et al*. 1993). Local delivery is independent of patient compliance.

Local drug delivery systems are means of drug application to confined areas. For the treatment of periodontal disease, local delivery of antimicrobial drugs ranges from simple pocket irrigation, over the placement of drug-containing ointments and gels, to sophisticated devices for sustained release of antibacterial agents. In order to be effective, the drug should not only reach the entire area affected by the disease, including especially the base of the pocket, but should also be maintained there at a sufficiently high local concentration for some time. With a mouth rinse or supragingival irrigation it is not possible to deliver an agent predictably to the deeper parts of a periodontal defect (Eakle *et al*. 1986; Pitcher *et al*. 1980). The crevicular fluid rapidly washes out agents brought into periodontal pockets by subgingival irrigation. Based on an assumed pocket volume of 0.5 ml and a crevicular fluid flow rate of 20 µl/hr, Goodson (1989) estimated that the half-time of a non-binding drug placed into a pocket is about 1 minute. Even a highly concentrated, highly potent agent would thus be diluted below a minimal inhibitory concentration (MIC) for oral microorganisms within minutes. If an agent can bind to surfaces and be released in active form, a prolonged time of antibacterial activity could be expected. Such an effect has in fact been noted for salivary concentrations of chlorhexidine after use of chlorhexidine mouth rinse (Bonesvoll & Gjermo 1978). Although there are indications that this may also occur to a certain extent within the periodontal pocket, for instance after prolonged subgingival irrigation with tetracycline (Tonetti *et al*. 1990), the potential to create a drug reservoir of significant size on the small surface area available in a periodontal pocket is limited. To maintain a high concentration over a prolonged period, the flushing action of the crevicular fluid flow has to be counteracted by a steady release of the drug from a larger reservoir. Considering the small volume of a periodontal pocket and the pressure exerted by the tonus of the periodontal tissues on anything inserted, it appears unlikely that this task can be completed by a carrier that does not maintain its physical stability for some time and that cannot be secured against premature loss. Gels, for instance, rapidly disappear after instillation into periodontal pockets (Fig. 42-3), unless they change their viscosity immediately after

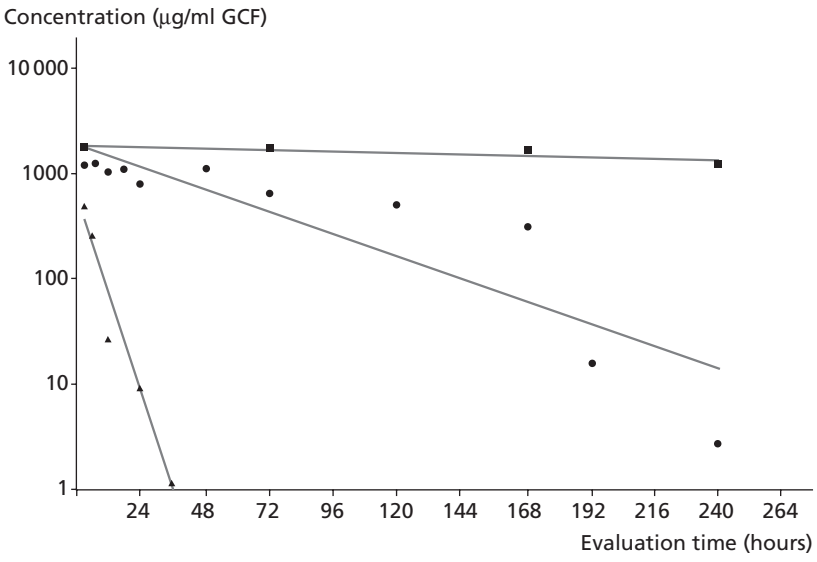

Fig. 42-4 Mean concentration of tetracycline (■) in gingival crevicular fluid (GCF) during tetracycline fiber treatment (Tonetti *et al*. 1990), of doxycycline hyclate (•) after application in a biodegradable polymer (Stoller *et al*. 1998), and of metronidazole (▲) after application of 25% metronidazole dental gel (Stoltze 1992).

placement (Oostervaal *et al*. 1990; Stoltze 1995). Viscous and/or biodegradable devices show an exponential decrease of their concentration in gingival fluid. In order to have sustained control over drug release it is necessary to have a matrix that lasts longer than the drug load. Controlled delivery of an antimicrobial agent over several days has been shown for tetracycline released from non-degradable monolithic ethylene vinyl acetate fibers (Fig. 42-4).

Evaluation of antibiotics for periodontal therapy

In the large range of antimicrobial agents, a limited number have been tested thoroughly for use in periodontal therapy. The drugs more extensively investigated for systemic use include tetracycline, minocycline and doxycycline, erythromycin, clindamycin, ampicillin, amoxicillin, and the nitroimidazole compounds metronidazole and ornidazole. The drugs investigated for local application include tetracycline, minocycline, doxycycline, metronidazole, and chlorhexidine.

The first antibiotics used in periodontal therapy were mainly systemically administered penicillins. The choice was initially based exclusively on empiric evidence. Penicillins and cephalosporins act by inhibition of cell wall synthesis. They are narrow-spectrum and bactericidal. Among the penicillins, amoxicillin has been favored for treatment of periodontal disease because of its considerable activity against several periodontal pathogens at levels available in gingival fluid. The molecular structure of penicillins includes a β-lactam ring that may be cleaved by bacterial enzymes. Some bacterial β-lactamases have a high affinity for clavulanic acid, a β-lactam molecule without antimicrobial activity. To inhibit bacterial β-lactamase activity, clavulanic acid has been added successfully to amoxicillin. This combination (Augmentin®) has been tested for periodontal therapy in clinical studies.

Tetracycline-HCl became popular in the 1970s due to its broad-spectrum antimicrobial activity and low toxicity. The tetracyclines, clindamycin, and erythromycin are inhibitors of protein synthesis. They have a broad spectrum of activity and are bacteriostatic. In addition to their antimicrobial effect, tetracyclines are capable of inhibiting collagenase (Golub *et al*. 1985). This inhibition may interfere with tissue breakdown in periodontal disease. Furthermore they bind to tooth surfaces, from where they may be released slowly over time (Stabholz *et al*. 1993).

The nitro-imidazoles were introduced into the periodontal field in 1962 when *The Lancet* published the report of a female patient, who after a week of treatment for trichomonal vaginitis with metronidazole (200 mg tid) declared she had undergone "a double cure". The vaginitis was cured and the "acute marginal gingivitis" she was also suffering from was relieved (Shinn 1962). The nitro-imidazoles (metronidazole and ornidazole) and the quinolone antibiotics (e.g. ciprofloxacin) act by inhibiting DNA synthesis. Metronidazole is known to convert into several short-lived intermediates after diffusion into an anaerobic organism. These products react with the DNA and other bacterial macromolecules, resulting in cell death. The process involves reductive pathways characteristic of strictly anaerobic bacteria and protozoa, but not aerobic or microaerophilic organisms. Thus, metronidazole affects specifically the obligately anaerobic part of the oral flora, including *P. gingivalis* and other black-pigmenting Gram-negative organisms, but not *A. actinomycetemcomitans*, a facultative anaerobe.

The concentrations following systemic administration of the most common antimicrobial agents used in the treatment of periodontal disease are listed in Table 42-2. The *in vitro* susceptibility of *A. actinomycetemcomitans* to selected antimicrobial agents is given in Table 42-3 and the susceptibility of *P. gingivalis* is listed in Table 42-4. The data given in these tables may serve as a base for the choice of an

Table 42-2 Characteristics of antimicrobial agents used in the treatment of periodontal disease (adapted from Lorian 1986; Slots & Rams 1990)

Antibiotic	Dose (mg)	c serum (μg/ml)	c crevicular fluid (μg/ml)	t_{max} serum (h)	Half-life (h)
Penicillin	500	3	ND	1	0.5
Amoxicillin	500	8	3–4	1.5–2	0.8–2
Doxycycline	200	2–3	2–8	2	12–22
Tetracycline	500	3–4	5–12	2–3	2–3
Clindamycin	150	2–3	1–2	1	2–4
Metronidazole	500	6–12	8–10	1–2	6–12
Ciprofloxacin	500	1.9–2.9	ND	1–2	3–6

c = concentration; t_{max} = hours to reach peak serum concentration; ND = not determined.

Table 42-3 Susceptibility of *A. actinomycetemcomitans* to selected antimicrobial agents. MIC90: minimal inhibitory concentration for 90% of the strains (adapted from Mombelli & van Winkelhoff 1997)

Antibiotic	MIC90 (μg/ml)	Reference
Penicillin	4.0	Pajukanta *et al*. (1993b)
	1.0	Walker *et al*. (1985)
	6.25	Höffler *et al*. (1980)
Amoxicillin	1.0	Pajukanta *et al*. (1993b)
	2.0	Walker *et al*. (1985)
	1.6	Höffler *et al*. (1980)
Tetracycline	0.5	Pajukanta *et al*. (1993b)
	8.0	Walker (1992), Walker *et al*. (1985)
Doxycycline	1.0	Pajukanta *et al*. (1993b)
	3.1	Höffler *et al*. (1980)
Metronidazole	32	Pajukanta *et al*. (1993b)
	32	Jousimies-Somer *et al*. (1988)
	12.5	Höffler (1980)

Table 42-4 Susceptibility of *P. gingivalis* to selected antimicrobial agents (adapted from Mombelli & van Winkelhoff 1997)

Antibiotic	MIC90 (μg/ml)	Reference
Penicillin	0.016	Pajukanta *et al*. (1993a)
	0.29	Baker *et al*. (1983)
Amoxicillin	0.023	Pajukanta *et al*. (1993a)
	<1.0	Walker (1992)
Doxycycline	0.047	Pajukanta *et al*. (1993a)
Metronidazole	0.023	Pajukanta *et al*. (1993a)
	2.1	Baker *et al*. (1983)
	2.0	Walker (1992)
Clindamycin	0.016	Pajukanta *et al*. (1993a)
	<1.0	Walker (1992)

appropriate agent. However, it is important to remember that *in vitro* tests do not reflect the true conditions found in periodontal pockets. In particular, they do not account for the biofilm effect. One should add that MIC values depend on technical details that may vary between laboratories. As a consequence, demonstration of *in vitro* susceptibility is no proof that an agent will work in treatment of periodontal disease.

Since the subgingival microbiota in periodontitis often harbors several putative periodontopathic species with different antimicrobial susceptibility, combination drug therapy may be useful. A combination of antimicrobial drugs may have a wider spectrum of activity than a single agent. Overlaps of the antimicrobial spectrum may reduce the possible development of bacterial resistance. For some combinations of drugs there may be synergy in action against target organisms, allowing a lower dose of the single agents. A synergistic effect against *A. actinomycetemcomitans* has been noted *in vitro* between metronidazole and its hydroxy metabolite (Jousimies-Somer *et al*. 1988; Pavicic *et al*. 1991) and between these two compounds and amoxicillin (Pavicic *et al*. 1992). With some drug combinations there may, however, also be antagonistic drug interaction. For instance, bacteriostatic agents such as tetracyclines, which suppress cell division, may decrease the antimicrobial effect of bactericidal antibiotics such as β-lactam drugs or metronidazole, which act during bacterial cell division. Combination drug therapy may also lead to increased adverse reactions.

Table 42-5 lists common adverse reactions to systemic antibiotic therapy (for a detailed overview the reader is referred to Walker 1996). The penicillins are among the least toxic antibiotics. Hypersensitivity reactions are by far the most important and most common adverse effects of these drugs. Most reactions are mild and limited to a rash or skin lesion in the head or neck region. More severe reactions may induce swelling and tenderness of joints. In highly sensitized patients a life-threatening anaphylactic reaction may develop. The systemic use of tetracyclines may lead to epigastric pain, vomiting or

Table 42-5 Adverse effects of antibiotics used in the treatment of periodontal diseases

Antibiotic	Frequent effects	Infrequent effects
Penicillins	Hypersensitivity (mainly rashes), nausea, diarrhea	Hematologic toxicity, encephalopathy, pseudomembranous colitis (ampicillin)
Tetracyclines	Gastrointestinal intolerance, candidiasis, dental staining and hypoplasia in childhood, nausea, diarrhea, interaction with oral contraceptives	Photosensitivity, nephrotoxicity, intracranial hypertension
Metronidazole	Gastrointestinal intolerance, nausea, antabus effect, diarrhea, unpleasant metallic taste	Peripheral neuropathy, furred tongue
Clindamycin	Rashes, nausea, diarrhea	Pseudomembranous colitis, hepatitis

diarrhea. Tetracyclines can induce changes in the intestinal flora, and superinfections with non-bacterial microorganisms (i.e. *Candida albicans*) may emerge. Tetracyclines are deposited in calcifying areas of teeth and bones where they cause yellow discoloration. Systemic administration of clindamycin may be accompanied by gastrointestinal disturbances, leading to diarrhea or cramps, and may cause mild skin rashes. The suppression of the normal intestinal flora increases the risk for colonization of *Clostridium difficile*, which may cause a severe colon infection (antibiotic-associated colitis). Although not related to *C. difficile*, gastrointestinal problems are also the most frequent adverse event of systemic metronidazole therapy. Nausea, headache, anorexia, and vomiting may be experienced. Symptoms may be more pronounced with alcohol consumption, because imidazoles affect the activity of liver enzymes. Because some cases have developed permanent peripheral neuropathies (numbness or paresthesia), patients should be advised to stop therapy immediately if such symptoms occur.

Systemic antimicrobial therapy in clinical trials

Although clinical efficacy is not an absolute proof for bacteriologic efficacy (Marchant *et al*. 1992), the ultimate evidence to advocate the use of systemic antibiotics must come from clinical trials in humans with periodontitis. A large number of reports suggesting beneficial effects in various clinical situations have been published. However, many of them score low when evaluated by established study quality criteria, e.g. those proposed by the Oxford Centre for Evidence-based Medicine (http://www.cebm.net/levels_of_evidence.asp). Studies may be difficult to interpret due to an unclear status of patients at baseline (treatment history, disease activity, composition of subgingival microbiota), insufficient or non-standardized maintenance after therapy, short observation periods, or lack of randomization and controls. Comparisons may be possible because studies not only vary with regard to the treatment provided, but also in the selection of subjects, sample size, range of study parameters, outcome variables, the duration of the study, and the control to which the test procedure is compared. In most trials, systemic antibiotics have been used as an adjunct to scaling and root planing. Typically, the effect of mechanical therapy plus the antimicrobial agent has been compared to mechanical treatment alone. In studies evaluating the effect of antimicrobial therapy in patients with refractory periodontitis or with recurrent abscess formation, placebo control is often lacking for ethical reasons.

In recent years systematic reviews have become the preferred method of analyzing the medical literature. They use explicit procedures to perform a thorough literature search, critically appraise individual reports, and try to combine valid studies by applying appropriate statistical techniques. Two systematic reviews have been conducted to determine whether systemically administered antibiotics improve the clinical outcome of periodontal therapy (Herrera *et al*. 2002; Haffajee *et al*. 2003). Both have been prepared in the context of structured consensus conferences, where the findings have been translated into consensus statements on periodontal therapy.

Herrera *et al*. (2002) sought studies of at least 6 months' duration, designed as controlled clinical trials, in which systemically healthy subjects with either chronic or aggressive periodontitis had been treated with scaling and root planing, with or without systemic antibiotics. Main outcome variables were changes in clinical attachment level and pocket probing depth. Twenty-five papers were eligible for inclusion, but due to difficulties encountered when pooling the data, only limited meta-analyses could be performed. Overall, antibiotic groups showed better results than control groups. A specific benefit in change of attachment level was found in deep pockets for the combination of metronidazole plus amoxicillin.

Haffajee *et al*. (2003) sought clinical trials in periodontitis patients of more than 1 month duration, comparing systemic antibiotic therapy with non-antibiotic therapy, and using mean attachment level change as primary outcome. A meta-analysis included the data from 27 eligible studies. The authors noted that by and large therapeutic procedures were diverse, although metronidazole, alone or in combination with amoxicillin, was the most frequently

used drug. In all studies the antibiotic groups showed significantly better mean attachment level changes than the control groups, and this benefit averaged 0.45 mm. Although tests of heterogeneity were not significant, indicating that the outcomes were consistent, differences in the magnitude of the effect were noted in some patient populations: aggressive periodontitis groups had a larger adjunctive benefit than patients with chronic periodontitis. Results varied more between trials in which antibiotics had been used adjunctively to surgery than in trials where antibiotics had been tested adjunctively to scaling and root planing. Where it was possible to discriminate, sites with deep pockets seemed to show the greatest improvements. The reviews were unable to clarify which agents should be used for which infection, and what the optimal dosage and duration of antibiotic therapy should be. Furthermore it remained open how long the benefit would persist, and to what extent the antibiotics induced resistance or other changes in the oral microbiota. The low level of evidence with regards to the dosing regimen is very regrettable since the amount of drug administered is known to be a critical determinant of antimicrobial efficacy (Craig 1998).

In many trials the antibiotic has not been chosen based on a microbiologic analysis. This approach does not consider the possibility that some pathogens may be resistant to the tested drugs. We have mentioned *A. actinomycetemcomitans*, which is not susceptible to metronidazole when used as a monotherapy. Therefore, clinical studies including patients for an antibiotic therapy irrespective of their microbiologic status may underestimate the potential of the tested drug. Some studies have in fact indicated that systemic antibiotics were only effective in patients with a specific microbial profile (Flemmig *et al*. 1998; Winkel *et al*. 2001). Others, however, have demonstrated considerable adjunctive benefits to mechanical treatment even in the absence of specific target organisms (e.g. Rooney *et al*. 2002), and one could argue that nobody has ever shown certain patients to be better off, if treated *without* antibiotics.

In recent years the combination of metronidazole and amoxicillin has become the favorite treatment modality for many practitioners and clinical researchers. Studies corroborating the benefit of this regime, for example in non-surgical treatment of generalized aggressive periodontitis (Guerrero *et al*. 2005), continue to be published. Its remarkable ability to suppress or even eliminate *A. actinomycetemcomitans* and other subgingival organisms from periodontitis lesions and other oral sites (Christersson *et al*. 1989; Kornman *et al*. 1989; van Winkelhoff *et al*. 1989, 1992; Goené *et al*. 1990; Pavicic *et al*. 1992, 1994) has made it the first choice especially for the treatment of advanced periodontitis associated with *A. actinomycetemcomitans*. Gastrointestinal disturbances (diarrhea, nausea, and vomiting) have been noted as the most frequent side effects.

Systemic antibiotics in clinical practice

Overall, it can be stated that systemic antibiotic therapy can improve the clinical conditions and microbiologic status of periodontal patients. There is evidence to support the use of systemic antibiotics in cases of aggressive forms of periodontitis associated with *P. gingivalis* and/or *A. actinomycetemcomitans*. Systemic antibiotics are also indicated in generalized refractory periodontitis patients with evidence of ongoing disease despite previous mechanical therapy. Although some studies have shown a certain benefit of antibiotics even when administered without thorough subgingival debridement (Berglundh *et al*. 1998; Lopez & Gamonal 1998; Lopez *et al*. 2000, 2006) there is a general consensus that whenever possible antibiotics should not be administered before completion of root surface debridement (Mombelli 2006). Patients with acute signs of disease such as periodontal abscesses, or acute necrotizing gingivitis, with fever and malaise, may be the exception. Systemic antibiotics, given after scaling and root planing, provide an additional treatment benefit especially in deep pockets, and can reduce the need for further, surgical therapy (Loesche *et al*. 1992). In most cases however, mechanical therapy is initially carried out without antibiotics and evaluated after an appropriate period of time. The original treatment plan is then adapted, to account for the degree of clinical improvement already obtained. Immediately before starting the antibiotic regime the subgingival area should be re-instrumented once more to reduce the bacterial mass as much as possible and to disrupt the subgingival biofilm. This may be accomplished during a surgical intervention but is indicated also if no further mechanical therapy seems necessary from a clinical point of view.

Table 42-6 lists adjunctive systemic antibiotic regimens currently recommended for the therapy of periodontal diseases. Metronidazole alone has proven to be effective against *P. gingivalis*, *Tannerella forsythia*, spirochetes, and other strictly anaerobic Gram-negative bacteria. Clindamycin and tetracyclines have also been shown to act on a broad range of periodontal bacteria. Monotherapy with one antibiotic as an adjunct to mechanical instrumentation can change the composition of the subgingival microbiota significantly, but certain periodontal organisms cannot be eliminated predictably. For maximal suppression of subgingival *A. actinomycetemcomitans* the combination of metronidazole and amoxicillin is recommended. For patients who cannot tolerate amoxicillin it has been suggested to combine metronidazole with cefuroximaxetil or ciprofloxacin (Rams *et al*. 1992; van Winkelhoff & Winkel 2005).

Microbiologic tests can help to choose the appropriate antibiotic regimen. A microbial analysis should be comprehensive and sensitive enough to quantitatively identify the most important periodontal organisms. From the discussion above it follows that data

Table 42-6 Adjunctive systemic antibiotic regimens currently recommended for the therapy of periodontal diseases (adapted from van Winkelhoff & Winkel 2005)

Antibiotic	Usual dosage	Microbiology
Metronidazole	250–500 mg, tid 7–10 days	*P. gingivalis* *T. forsythia* *Treponema* spp.
Clindamycin	300 mg, qid 7–8 days	Gram-negative anaerobes Absence of *A. actinomycetemcomitans*
Doxycycline	100–200 mg, sid 7–14 days	Non-specific infection
Metronidazole + Amoxicillin	250–500 mg, tid 375–500 mg, tid 7 days	*A. actinomycetemcomitans* or *P. gingivalis* with high numbers of Gram-positive pathogens
Metronidazole + Cefuroximaxetil	250–500 mg, tid 250–500 mg, bid 7 days	*A. actinomycetemcomitans* Hypersensitivity towards amoxicillin
Metronidazole + Ciprofloxacin	250–500 mg, tid 500 mg, bid 7 days	*A. actinomycetemcomitans* Hypersensitivity towards β-lactams or presence of susceptible enteric microorganisms

indicating the involvement of *A. actinomycetemcomitans* and *P. gingivalis* have the highest practical utility. Microbial samples from the deepest pocket in each quadrant can give a good picture of the presence and relative proportion of these pathogens in the oral flora (Mombelli *et al*. 1991b, 1994). Since the antimicrobial profiles of most putative periodontal pathogens are quite predictable, susceptibility testing is not routinely performed. One should keep in mind, however, that some important microorganisms might demonstrate resistance to tetracyclines, β-lactam drugs or metronidazole.

As mentioned already, suboptimal dosage of antibiotics, caused by either inadequate prescribing or poor patient compliance, favors the spread of antibiotic-resistant bacterial clones. The classical oral dosage for metronidazole, used in most studies, has been 250 mg, three times a day, for 7–10 days. This dosage might not be sufficient in subjects with a high body mass. In addition, it has been proposed to prolong medication in smokers (van Winkelhoff & Winkel 2005), because smoking decreases the gingival blood flow and the amount of crevicular fluid, and hereby the availability of the drug in the subgingival environment (Morozumi *et al*. 2004). The specific conditions of smokers have become the subject of clinical research in recent time. The utilization of azithromycin, a macrolide antibiotic derived from erythromycin, has been advocated specifically for smokers (Mascarenhas *et al*. 2005). More research is however needed to substantiate the specific benefit of particular regimes for distinct groups of patients.

After resolution of the periodontal infection, the patient should be placed on an individually tailored maintenance care program. Optimal plaque control by the patient is of paramount importance for a favorable clinical response (Kornman *et al*. 1994) and long-term stability. Systemic antibiotics should never be applied as a means to compensate for inadequate oral hygiene.

Local antimicrobial therapy in clinical trials

Various methods to deliver antimicrobial agents into periodontal pockets have been devised and subjected to numerous kinds of experiments. The shortcomings of rinsing, irrigating, and similar forms of drug placement – rapid clearance resulting in inadequate exposure of subgingival bacteria to the drug and lack of significant clinical effects – have already been discussed. This section will deal with clinically tested drug delivery systems that fulfill at least the basic pharmacokinetic requirements of sustained drug release. Much of what has been stated about difficulties in the interpretation of studies dealing with the systemic use of antibiotics applies to the studies conducted with local delivery devices. Again, comparisons are complicated because studies vary with regard to sample size, selection of subjects, range of parameters, controls, duration of the study, and the inclusion of only one form of local drug delivery. Most of the evidence for a therapeutic effect of local delivery devices comes from trials involving patients with previously untreated adult periodontitis. Only few studies have addressed the use of local drug delivery in recurrent or persistent periodontal lesions – the potentially most valuable area for their application. Some protocols compare local drug delivery to a negative control, such as the application of only the carrier without the drug. These studies may be able to show a net effect of the drug, but they are not able to demonstrate a benefit over the most obvious

alternative – scaling and root planing – and the question remains as to how much value the procedure has in addition to mechanical treatment. If a study is unable to demonstrate a significant difference between local drug delivery and scaling and root planing, this is not automatically a proof of equivalence of the two treatments (equivalence testing requires statistical testing of the power of the data, taking into account the size of the study sample).

The following paragraphs focus on minocycline ointment and microspheres, doxycycline hyclate in a biodegradable polymer, metronidazole gel, tetracycline in a non-resorbable plastic co-polymer, and chlorhexidine gluconate in a gelatin chip. These are the predominant commercial formulations adequately tested for local antimicrobial periodontal therapy. Unfortunately some of them are currently unavailable in certain regions of the world, or have disappeared completely, while other products without properly evaluated clinical efficacy continue to be introduced and utilized on an empiric basis.

Minocycline ointment and microspheres

The subgingival delivery of minocycline has been investigated in different forms. The efficacy of a 2% minocycline ointment (Dentomycin; Cyanamid, Lederle Division, Wayne, NJ, US) has been evaluated in a randomized, controlled trial of 103 adults with moderate to severe periodontitis (van Steenberghe *et al*. 1993). All patients were treated by conventional scaling and root planing. In addition, the patients received either the test or a control ointment in four consecutive sessions at baseline and weeks 2, 4, and 6. A significantly greater reduction of probing depths was noted in the test group at week 12. An additional study evaluating the repeated application of minocycline ointment as an adjunct to subgingival debridement in chronic periodontitis, demonstrated better clinical and microbiologic conditions over a 15-month period (van Steenberghe *et al*. 1999). One study assessed the effect of a weekly repeated local application of minocycline ointment for 8 weeks after placement of teflon membranes to guide regeneration of periodontal tissue. Although bacterial colonization of treated sites could not be prevented, the mean clinical attachment gain of the test group was significantly greater than that of the control group (Yoshinari *et al*. 2001).

Currently the major device for local minocycline application is a product with the physical properties of a powder, consisting of resorbable polymer microspheres (Arestin; OraPharma, Warminster, PA, US). The efficacy and safety of locally administered microencapsulated minocycline was shown in a multicenter trial including 748 patients with moderate to advanced periodontitis. Minocycline microspheres plus scaling and root planing provided substantially more probing depth reduction than either scaling and root planing alone or scaling and root planing plus vehicle. The difference reached statistical significance after the first month and was maintained throughout the 9 months of the trial (Williams *et al*. 2001; Paquette *et al*. 2004).

Doxycycline hyclate in a biodegradable polymer

A two-syringe mixing system for the controlled release of doxycycline (Atridox; Block Drug, Jersey City, NJ, US) has been evaluated in a number of investigations, and has been commercially available for a few years. One syringe contained the delivery vehicle, flowable bioabsorbable poly (DL-lactide) dissolved in *N*-methyl-2-pyrrolidone, and the other syringe contained doxycycline hyclate powder. The clinical efficacy and safety of Atridox was assessed in two multicenter studies. Each study entered 411 patients who demonstrated moderate to severe adult periodontitis. The treatment was statistically superior to placebo control and oral hygiene, and equally effective as scaling and root planing in reducing the clinical signs of adult periodontitis over a 9-month period (Garrett *et al*. 1999). In a group of patients undergoing supportive periodontal therapy, attachment level gains and probing depth reductions were similar at 9 months after local treatment with doxycycline or traditional scaling and root planing (Garrett *et al*. 2000).

The effect of Atridox, applied after no more than 45 minutes of debridement without analgesia in subjects with moderately advanced chronic periodontitis, was compared to 4 hours of thorough deep scaling and root planing in a study involving 105 patients at three centers. Interestingly, clinical parameters indicated a better result for the pharmacomechanical treatment approach after 3 months, although considerably less time had been invested than for conventional mechanical therapy (Wennström *et al*. 2001).

Metronidazole gel

Dialysis tubing, acrylic strips, and poly-OH-butyric acid strips have been tested as solid devices for delivery of metronidazole. The most extensively used device for metronidazole application is a gel consisting of a semi-solid suspension of 25% metronidazole benzoate in a mixture of glyceryl mono-oleate and sesame oil (Elyzol Dental Gel; Dumex, Copenhagen, Denmark). The gel is applied with a syringe into the pocket, and should increase its viscosity after placement. The clinical response to subgingival application of the metronidazole gel twice within 1 week was compared to the effect of subgingival scaling in several studies including subjects with untreated adult periodontitis (Ainamo *et al*. 1992; Pedrazzoli *et al*. 1992; Grossi *et al*. 1995). The results indicated no significant difference between metronidazole gel application and scaling and root planing. The fact that no significant difference between the two

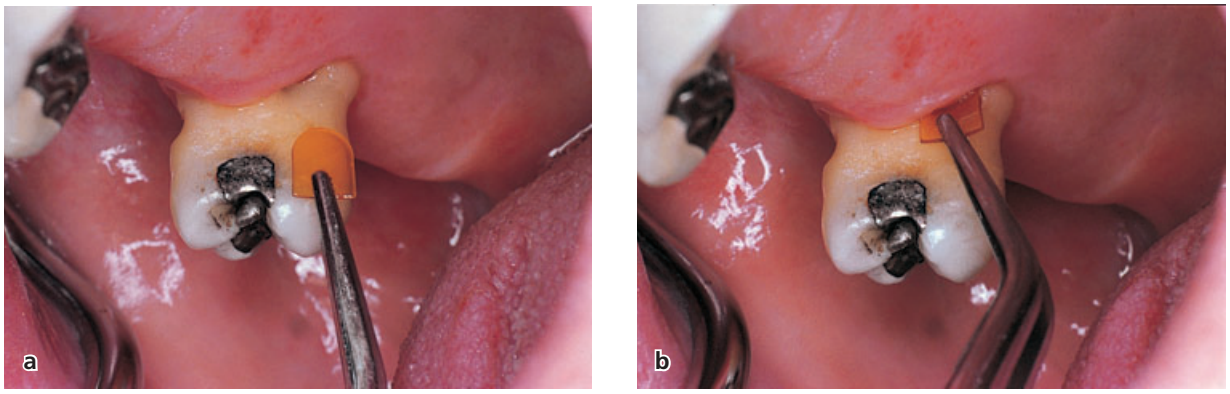

Fig. 42-5 Insertion of a chlorhexidine chip into a residual pocket mesial to an upper molar with a furcation involvement.

treatments was observed opened the question of equivalence between the two treatment modalities. Equivalence between scaling and root planing and metronidazole gel therapy has been evaluated using the lower bounds of confidence intervals in a parallel arm, multicenter, controlled clinical trial including 84 subjects (Pihlstrom *et al*. 1995). The estimates provided by this study indicated that metronidazole gel therapy is 82% as good as mechanical debridement at the 95% confidence level.

Tetracycline in a non-resorbable plastic co-polymer

Hollow devices, such as dialysis tubing, and solid devices, such as acrylic strips, collagen, or poly-OH-butyric acid strips, have been tested for tetracycline delivery in several experiments. Semi-solid viscous media include white petrolatum and poloxamer or carbopol gels. The most extensively tested tetracycline-releasing device is the Actisite periodontal fiber (ALZA, Palo Alto, CA, US). This currently unavailable product consists of a monolithic thread of a biologically inert, non-resorbable plastic co-polymer (ethylene and vinyl-acetate) containing 25% tetracycline hydrochloride powder. The fiber is packed into the periodontal pocket, secured with a thin layer of cyanoacrylate adhesive, and left in place for 7–12 days (Goodson *et al*. 1991a, 1983). By continuous delivery of tetracycline, a local concentration of the active drug in excess of 1000 mg/l can be maintained throughout that period (Fig. 42-4). Many clinical studies have been performed with Actisite, among them the following three large multicenter trials. The first showed better clinical results in deep pockets of 107 periodontitis patients 60 days after fiber therapy than control procedures (Goodson *et al*. 1991b). The second, conducted in periodontal maintenance patients needing treatment of localized recurrent periodontitis, demonstrated superiority after 6 months for scaling and root planing plus tetracycline fiber over scaling and root planing alone (Newman *et al*. 1994). The third indicated that the results obtained within 3 months after therapy were maintained over 1 year and that the combined treatment with fiber and scaling had a significantly lower incidence of disease recurrence than any of the other tested treatment modalities (Michalowicz *et al*. 1995).

Chlorhexidine gluconate in a gelatin chip

Several attempts have been made to develop local delivery devices for the subgingival application of antiseptic, rather than antibiotic agents. Acrylic strips and ethyl-cellulose compounds have been tested for this purpose. PerioChip (Perio Products, Jerusalem, Israel), a degradable gelatin chip containing 2.5 mg chlorhexidine, is the most extensively tested delivery device of this category (Fig. 42-5). Safety and efficacy of PerioChip were evaluated in a multicenter study of 118 patients with moderate periodontitis (Soskolne *et al*. 1997). The average pocket depth reduction in the treated sites with the chip was significantly greater than in the sites receiving mechanical treatment only. The efficacy of the chlorhexidine chip when used as an adjunct to scaling and root planing on reducing probing depth and improving clinical attachment level in adult periodontitis was evaluated in two double-blind, randomized, placebo-controlled multicenter clinical trials. At 9 months significant reductions from baseline were shown with the chlorhexidine chip compared with mechanical control treatments (Jeffcoat *et al*. 1998).

Comparison of treatment methods

Most studies have tested a single form of local drug delivery or systemic administration, instead of comparing various forms of therapy. Understandably, developers and distributors have the primary interest to register and promote their own product for the broadest possible usage, and not to differentiate specific benefits or shortcomings of various applications. The efficacy of three commercially available local delivery systems as adjuncts to scaling and root planing was tested in two trials including patients with persistent periodontal lesions: Actisite,

Dentomycin, Elyzol Dental Gel (Radvar *et al*. 1996; Kinane & Radvar 1999); Atridox, Elyzol Dental Gel, PerioChip (Salvi *et al*. 2002). One systematic review has tried to evaluate the combined literature-based evidence to determine the relative effect of local controlled release anti-infective drug therapy in patients with chronic periodontitis (Hanes & Purvis 2003). A meta-analysis including 19 studies, comparing scaling and root planing plus local sustained-release agents with scaling and root planing alone, confirmed the clinical advantages of minocycline gel, microencapsulated minocycline, doxycycline gel, and chlorhexidine chips over scaling and root planing alone. Due to the heterogeneity of the material the authors could not make any firm statements regarding the superiority of one system. A further systematic review looked at the relative adjunctive benefits of various locally applied agents (Bonito *et al*. 2005). Unfortunately data were combined from studies exploring various modes of local treatment, including irrigation, impregnated strips or pastes. Nonetheless, a statistically significant mean advantage resulted for four agents in terms of additional attachment gain, best for minocycline, followed by tetracycline, chlorhexidine, and metronidazole. One cannot exclude, however, that the differences noted between the drugs primarily reflect differences in modes of application and study populations, not the potency of the agent.

Few studies have addressed the problem of incorporating local or systemic antimicrobial therapy into an overall treatment strategy. As little direct evidence for a comparison of various methods of treatment is available so far, well founded decision algorithms to choose specific methods of intervention for distinct clinical situations are not yet available. A key issue requiring clarification refers to the selection of a local or a systemic delivery approach whenever the use of an antibiotic is indicated. One investigation addressed this question in patients with rapidly progressing periodontitis (Bernimoulin *et al*. 1995). Overall, no significant differences were noted between systemic administration of amoxicillin–clavulanic acid and tetracycline fibers as an adjunct to mechanical therapy. For patients with adult periodontitis, two studies reported better results of scaling and root planing supplemented with locally applied metronidazole than adjunctive systemic metronidazole (Paquette *et al*. 1994; Noyan *et al*. 1997).

As different oral distribution patterns can be recognized in periodontitis patients for microorganisms such as *P. gingivalis* (Mombelli *et al*. 1991a,b), local therapy may be less successful in patients where these organisms are widespread than in patients where the presence of pathogens is confined to isolated areas. This hypothesis was tested in a study comparing two extremes of local therapy. In one group of patients, a combination of measures including full mouth scaling and root planing, application of tetracycline fibers, and chlorhexidine rinse, was applied. In the other group, only two teeth were treated locally and no attempt was made to interfere with the overall conditions of the oral environment. Major clinical differences were found in the local healing response, depending on whether the rest of the dentition was left untreated or was also subjected to therapy (Mombelli *et al*. 1997). How can a clinician be sure that the areas he treats coincide with the sites harboring the pathogens? No diagnostic tool is available presently at a reasonable cost that could give the dentist a detailed distribution map of periodontal pathogens. Provided that such a tool would exist, could *P. gingivalis* and *A. actinomycetemcomitans* be eradicated from an infected dentition by microbiologically guided local antimicrobial therapy? A study evaluating the effect of local antibiotic therapy, given to every tooth with cultural evidence of *P. gingivalis* or *A. actinomycetemcomitans* after completion of conventional mechanical periodontal therapy demonstrated the limits of this approach (Mombelli *et al*. 2002). Even if a detailed microbiologic assessment provided information about the distribution pattern within the dentition, and all positive teeth were treated, the target organisms could be detected again after therapy in some sites in a considerable number of subjects.

Local antibiotics in clinical practice

To treat periodontal disease successfully, local delivery devices must provide therapeutic levels of antimicrobial agents in the subgingival area over several days. Clinical trials show the efficacy of local antibiotic therapy under these conditions. The current evidence suggests that local delivery may be most beneficial in the control of localized ongoing disease in otherwise stable patients. Maintenance patients with a few non-responding sites may therefore benefit most from local antimicrobial therapy. Local antibiotic therapy adds flexibility and improves efficacy of periodontal care by providing a non-surgical local treatment alternative with more powerful antibacterial effects than scaling and root planing. Potential uses for locally delivered antibiotics also include the treatment of peri-implant infections (Mombelli *et al*. 2001; Renvert *et al*. 2006). A comment made in the context of systemic antibiotics needs to be reiterated here with regards to local therapy: antibiotics are not a means to compensate for inadequate oral hygiene. For a maximal benefit, and a sustained local effect, patients should receive specific instructions on how to keep the treated sites plaque free with appropriate home care procedures.

Overall conclusion

Although mechanical periodontal treatment alone improves clinical conditions sufficiently in most cases, adjunctive antibiotics, delivered either

systemically or locally, can enhance the effect of therapy. Systemic antibiotics may be a useful adjunct to the mechanical treatment of aggressive forms of periodontitis and for cases with evidence of ongoing disease despite previous mechanical therapy. By providing an additional treatment benefit especially in deep pockets, systemic antibiotics can reduce the need for further, surgical therapy. Localized non-responding sites and localized recurrent disease may be treated with locally delivered antibiotics. Mechanical debridement before the application of antimicrobial agents, and mechanical plaque control after therapy, are essential for treatment success. To limit the development of microbial antibiotic resistance in general, and to avoid the risk of unwanted systemic effects of antibiotics for the treated individual, a precautionary, restrictive attitude towards using antibiotics is recommended.

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Part 13: Reconstructive Therapy

Chapter 43

Regenerative Periodontal Therapy

Pierpaolo Cortellini and Maurizio S. Tonetti

Introduction

The advances in the understanding of the biology of wound healing and periodontal regenerative technologies are applied to improve long-term clinical outcomes of teeth which are periodontally compromised by intrabony or inter-radicular defects. The treatment objective is to obtain shallow, maintainable pockets by reconstruction of the destroyed attachment apparatus and thereby also limiting recession of the gingival margin. In general periodontal regeneration is selected to obtain: (1) an increase in the periodontal attachment of a severely compromised tooth; (2) a decrease in deep pockets to a more maintainable range; (3) a reduction of the vertical and horizontal component of furcation defects. Current approaches, however, remain technique sensitive and clinical success requires application of meticulous diagnostic and treatment strategies.

Classification and diagnosis of periodontal osseous defects

Site-specific periodontal breakdown compromises the long-term prognosis of teeth by producing three types of defects: suprabony (or horizontal) defects, infrabony (or vertical) defects, and inter-radicular (or furcation) defects.

According to the classification by Goldman and Cohen (1958), suprabony defects are those where the base of the pocket is located coronal to the alveolar crest. Infrabony defects, on the other hand, are defined by the apical location of the base of the pocket with respect to the residual alveolar crest. This chapter does not deal with suprabony defects. With regard to infrabony defects, two types of defects can be recognized: intrabony defects and craters. Intrabony defects are bony defects whose infrabony component affects primarily one tooth, while in craters the defect affects two adjacent root surfaces to a similar extent. Intrabony defects (Fig. 43-1) have been classified according to their morphology in terms of residual bony walls, width of the defect (or radiographic angle), and in terms of their topographic extension around the tooth. Three-wall, two-wall, and one-wall defects have been defined on the basis of the number of residual alveolar bone walls. This represents the primary classification system. Frequently, intrabony defects present a complex anatomy consisting of a three-wall component in the most apical portion of the defect, and two- and/or one-wall components in the more superficial portions. Hemiseptal defects, that is, vertical defects in the presence of adjacent roots and where half of a septum remains on one tooth, represent a special case of one-wall defects. Several authors have also used

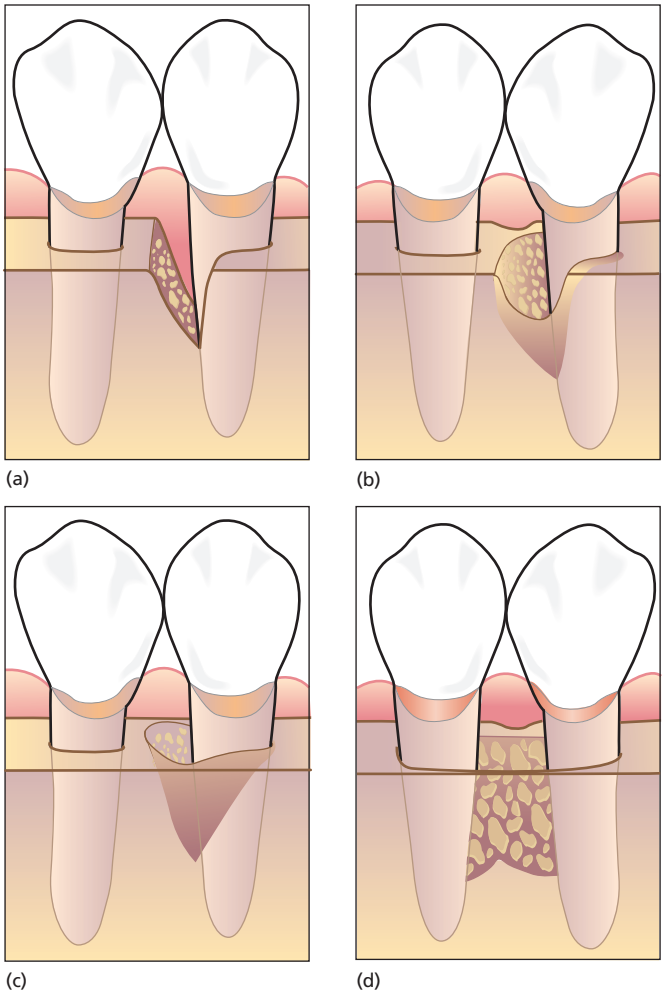


Fig. 43-1 Infrabony defects. (a) One-wall intrabony defect. (b) Two-wall intrabony defect. (c) Three-wall intrabony defect. (d) Interproximal crater. From Papapanou & Tonetti (2000).

descriptive terms to define special morphological characteristics: funnel-shaped defects, moat-like defects, trenches, etc. Of particular interest is a special morphology: the crater (Fig. 43-1). It is defined as a cup- or bowl-shaped defect in the interdental alveolar bone with bone loss nearly equal on the roots of two contiguous teeth and more coronal position of the buccal and lingual alveolar crest; the facial and lingual/palatal walls may be of unequal height. This defect can be considered as the result of the apical spread of periodontitis along two adjacent roots in a relatively narrow (mesiodistally) interproximal area. Notably, all the definitions above are not based on radiographic assessments but on the actual morphology of the defects after flap elevation. Conditions entailing pathologic resorption of bone within the furcation of a multi-rooted tooth, defined as furcation invasions, are also included in the group of periodontal bony defects; the reader however is referred to Chapter 39 for a discussion of the anatomy and classification of furcations.

The diagnosis of the presence and the morphology of periodontal osseous lesions represents a major clinical challenge. It is primarily performed combining clinical information derived from the evaluation of the attachment level with information derived from diagnostic-quality parallel-technique intraoral radiographs. A precise knowledge of root anatomy and its variations is also an important component for the diagnosis of periodontal osseous defects, and inter-radicular defects in particular. Diagnostic-quality radiographs provide additional information on the morphology of the alveolar bone resorption. In this context, interpretation of the radiographic image of the interdental septum is complicated, since the radiograph provides a two-dimensional illustration of a three-dimensional anatomy consisting of superimposed structures including alveolar bone, hard tooth substances, and soft tissue. This complexity of the visualized structures means that a certain amount of tissue destruction must occur before its radiographic detection becomes possible, often rendering incipient bone lesions obscure. Furthermore, even advanced lesions may be masked by the presence of superimposed structures. It is therefore generally stated that radiographic diagnosis has a high positive predictability (that is, the visualized lesions are indeed there) but a low negative predictability (that is, absence of radiographically detectable bone loss does not exclude the presence of an osseous lesion).

Clinical attachment level, on the other hand, is a highly sensitive diagnostic tool; its combination with radiographs, therefore, confers a higher degree of

accuracy to the diagnostic approach (Tonetti *et al.* 1993b). In particular, the site-specific comparison of radiographic bone loss with clinical attachment loss allows the clinician to make a qualified guess of the true osseous architecture, whose exact morphology, however, can only be established after flap elevation. Detection of the defect, its location and extension, along with its major morphologic features, should be performed before flap elevation. A further aid to this end is the use of transgingival probing or bone sounding.

Clinical indications

Periodontal treatment, either surgical or non-surgical, results in recession of the gingival margin after healing (Isidor *et al*. 1984). In advanced cases of periodontitis, this may lead to poor esthetics in the front areas of the dentition, in particular when applying surgical procedures, including bone contouring, for the eradication of bone defects. Treatment of such cases without bone contouring, on the other hand, may result in residual pockets inaccessible to proper cleaning during post-treatment maintenance. These problems can be avoided or reduced by applying regenerative surgical procedures by which the lost periodontal attachment in the bone defects can be restored. Thus, the indication of applying regenerative periodontal therapy is often based on esthetic considerations, besides the fact that the function or long-term prognosis of the treated teeth may be improved.

Another indication for regenerative periodontal therapy are furcation-involved teeth. The furcation area is often inaccessible to adequate instrumentation and frequently the roots present concavities and furrows that make proper cleaning of the area after resective surgery impossible. Considering the long-term results and complications reported following treatment of furcation involvements by traditional resective therapy (Hamp *et al*. 1975; Bühler 1988), the long-term prognosis of furcation-involved teeth can be improved considerably by successful regenerative periodontal therapy.

Case reports also exist demonstrating that "hopeless" teeth with deep vertical defects, increased tooth mobility or through-and-through furcations can be successfully treated with regenerative periodontal therapy (Gottlow *et al*. 1986). However, controlled clinical trials or serial case reports presenting a reasonable predictability of treating such advanced cases are not available.

Long-term effects and benefits of regeneration

A pertinent question with respect to regenerative treatment is whether the achieved attachment level gains can be maintained over an extended period of time. In a long-term follow-up study, Gottlow *et al*. (1992) assessed the stability of new attachment gained through guided tissue regeneration (GTR) procedures. Eighty sites in 39 patients, which 6 months after surgery exhibited a gain of clinical attachment of ≥2 mm (2–7 mm), were monitored during additional periods of 1–5 years. Of the 80 sites, 65 were monitored for 2 years, 40 for 3 years, 17 for 4 years, and 9 sites for 5 years. The results of this study and those of other trials indicate that attachment gain obtained following GTR treatment can be maintained on a long-term basis (Becker & Becker 1993; McClain & Schallhorn 1993).

An investigation on intrabony defects demonstrated that the stability of sites treated with GTR was dependent on participation of the patients in a recall program, and on the absence of bacterial plaque, bleeding on probing, and re-infection of the treated sites with periodontal pathogens (Cortellini *et al*. 1994). The susceptibility to disease recurrence at sites treated with non-bioabsorbable barrier membranes was assessed in a study comparing long-term changes in attachment levels at regenerated and non-regenerated sites in the same patient (Cortellini *et al*. 1996a). Results indicated that there was a high degree of concordance in the clinical outcomes (stability vs. recurrence of attachment loss) within the same patient suggesting that patient factors, rather than the site factors, including the specifics of the histologic type of expected wound healing, are associated with disease recurrence. Among patient factors, compliance with oral hygiene, smoking habits, and susceptibility to disease progression were the major determinants of stability of the treated sites, rather than the employed treatment modality.

Support for a limited impact of the histologic type of healing comes from an experimental study. In a study in monkeys (Kostopoulos & Karring 1994), periodontal breakdown was produced by the placement and retention of orthodontic elastics on experimental teeth until 50% bone loss was recorded. The experimental teeth were endodontically treated and subjected to a flap operation, and all granulation tissue was removed. The crowns of the teeth were resected at the level of the cemento-enamel junction and a barrier membrane was placed to cover the roots before they were submerged. Following 4 weeks of healing, the membranes were removed. At the same time the contralateral teeth that served as controls were endodontically treated and subjected to a sham operation during which the crowns were resected at the level of the cemento-enamel junction. Artificial composite crowns were then placed on both the experimental and the control roots. The sites were allowed to heal for 3 months during which period careful plaque control was performed. At the end of this period cotton-floss ligatures were placed on both experimental and control teeth to induce periodontal tissue breakdown. After another 6 months, the animals were sacrificed. With respect to attachment level, bone level, pocket depth, and gingival recession, similar results were recorded in histologic

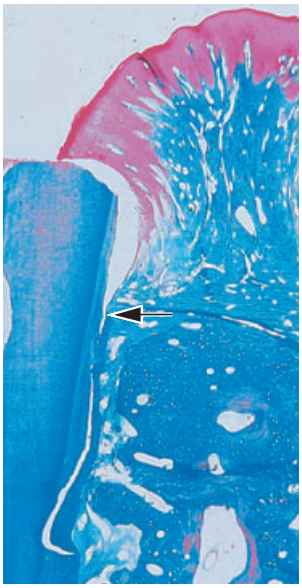


Fig. 43-2 Microphotograph of test specimen with a reformed connective tissue attachment. After 6 months of ligature-induced periodontitis, loss of attachment has occurred from the coronal cut root surface to the level indicated by the arrow.

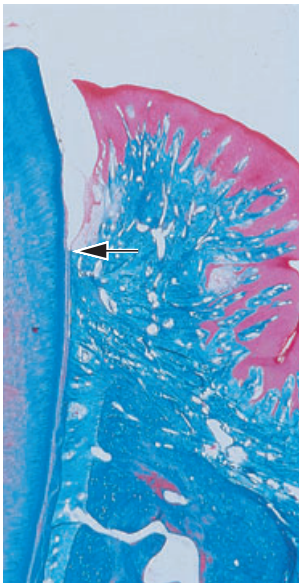


Fig. 43-3 Microphotograph of control specimen with a naturally existing periodontium. After 6 months of ligature-induced periodontitis, loss of attachment has occurred from the coronal cut tooth surface to the level indicated by the arrow.

specimens of experimental (Fig. 43-2) and control (Fig. 43-3) teeth. This indicates that the new connective tissue attachment formed with GTR is not more susceptible to periodontitis than the naturally existing periodontium.

A few studies have evaluated the long-term prognosis for furcation defects treated with regenerative therapy. Sixteen mandibular degree II furcation defects, following coronal flap positioning and citric acid root biomodification with and without implantation of demineralized freeze-dried bone allografts (DFDBA), were determined as completely resolved with bone fill assessed by re-entry surgery. They were re-evaluated after 4–5 years (Haney *et al*. 1997), when 12 of the 16 sites exhibited recurrent degree II furcations and all 16 sites demonstrated probable buccal furcation defects. The investigators concluded that these findings question the long-term stability of bone regeneration in furcations following coronally advanced flap procedures.

The long-term stability of mandibular furcation defects regenerated following GTR alone or in combination with root surface biomodification with citric acid and bone grafting, was also evaluated by McClain and Schallhorn (1993). Out of the 57% of the furcation defects that were assessed as completely filled at 6 and 12 months, only 29% were completely filled after 4–6 years. However, 74% of the furcations treated with GTR in combination with the placement of DFDBA were completely filled at both the short and long-term evaluation, suggesting that the results obtained with the combined procedure were more stable over time. Long-term results of GTR treatment of mandibular degree II furcations with e-PTFE membranes were also reported by Machtei *et al*. (1996). The teeth were followed up to 4 years and compared with non-furcated molars. Improvements assessed in vertical (V-CAL) and horizontal (H-CAL) clinical attachment levels after treatment were also maintained after 4 years, suggesting that changes obtained in degree II furcation defects by GTR are stable. Only 9% of the treated defects were unstable, which was similar to that observed for non-furcated molars. Good oral hygiene, as reflected in low plaque scores and elimination of periodontal pathogens, was closely related to the long-term stability. On the basis of these results, it was concluded that furcation defects treated with membrane barriers can be maintained in health for at least 4 years, provided good oral hygiene and frequent recall visits are established.

In summary, several clinical studies addressing the long-term effects of periodontal regeneration show that, if the patient participates in a professionally delivered supportive periodontal care program and maintains good oral hygiene, the regenerated attachment can be maintained long term (Gottlow *et al.* 1992; MacClain & Schallhorn 1993; Cortellini *et al.* 1994, 1996a; Machtei *et al.* 1996; Christgau *et al.* 1997; Eickholz *et al*. 1997; Sculean *et al.* 2006). Risk factors for attachment loss are those associated with disease recurrence: poor compliance with supportive periodontal care, poor oral hygiene, and cigarette smoking (Cortellini *et al.* 1996a; Cortellini & Tonetti 2004).

Few investigations have looked at the long-term effects of periodontal regeneration on tooth survival. Cortellini and Tonetti (2004) performed a Kaplan Mayer analysis of tooth survival following periodontal regenerative treatment in a sample of 175 patients followed up for 2–16 years (average 8 ± 3.4 years) in a specialist environment. In this study, 96% of teeth

Table 43-1 Survival analysis of regenerated periodontal attachment over a 16-year follow-up period in 175 subjects treated with periodontal regeneration. In this survival analysis, the event is represented by clinical attachment level (CAL) loss of 2 mm or more from the level of attachment obtained at completion of healing 1 year after regeneration. No substantial recurrence of periodontitis (CAL loss) was observed in 92% of treated cases who participated in a secondary prevention program. (From Cortellini & Tonetti (2004) with permission)

Time at risk (years)	N CAL loss ≥2 mm	Censored	Effective sample size	Conditional probability CAL loss (%)	Survival (%)
0–2	2	0	175	1.1	100
2–4	3	0	166	1.7	98.9
4–6	2	0	155	1.2	97.1
6–8	1	55	119	0.7	96
8–10	0	47	70.5	0	95.3
10–12	2	16	41	3.5	95.3
12–14	0	25	24.5	0	92
14–16	0	21	8	0	92
16	0	1	0.5	0	92

treated by periodontal regeneration survived. Of interest was the observation that tooth loss was observed only among the 32% of the population that were smokers (tooth survival was 89% among smokers and 100% among non-smokers). Clinical attachment levels were located at the same level or coronal to the pre-treatment levels in 92% of cases up to 15 years after treatment (Table 43-1, Fig. 43-4).

The potential clinical benefits of periodontal regeneration can be best illustrated in a consecutive case series of strategic abutments severely compromised by the presence of deep intrabony defects with associated deep pockets with up to 8 years' follow-up following regenerative treatment (Tonetti *et al*. 1996a; Cortellini *et al*. 1998). At baseline, the periodontal defect rendered these teeth unsuitable as abutments to be included in a reconstruction. In all cases, periodontal regeneration with barrier membranes was able to change the clinical prognosis by providing both a 30% increase in radiographic bone support and shallow, maintainable probing depths. These outcomes remained stable during the follow-up period (Fig. 43-5). A similar benefit has been recently reported following use of combination therapy (barrier membranes and demineralized freeze-dried bone allograft) in teeth compromised by class II furcation defects (Bowers *et al*. 2003): 92% of class II defects were either closed or transformed into class I and thus at lower risk of tooth loss 1 year after therapy (McGuire & Nunn 1996a,b).

The limitation of recession of the gingival margin observed in controlled clinical trials when comparing a regenerative treatment with a non-regenerative surgical procedure is also an important benefit.

Evidence for clinical efficacy and effectiveness

Questions of efficacy relate to the added benefit of a treatment modality under ideal experimental conditions (such as those of a highly controlled research center environment). Effectiveness, on the other hand, relates to the benefit that can be achieved in a regular clinical setting where the procedure is likely to be performed in relation to morbidity and adverse events. Besides efficiency considerations, both evidence for efficacy and effectiveness need to be available in order to provide support for adoption of a novel approach in clinical practice.

The clinical efficacy of periodontal regenerative procedures has been extensively evaluated in randomized controlled clinical trials that have compared the regenerative procedure with a standard approach.

To limit sample size and study duration, these trials have utilized surrogate outcomes – clinical attachment level changes, decrease in pocket depths, furcation closure or radiographic measurements – rather than changes in tooth survival. These surrogate outcomes, however, are considered to be adequate proxies of the true outcome represented by tooth survival: persistence of deep pockets or furcation involvement are associated with higher risk of periodontal breakdown and tooth extraction.

The majority of clinical trials were small single-center studies. The evidence of these studies has been recently summarized in meta-analyses performed on data retrieved by systematic reviews of the published literature. In 2002 and 2003, the European Workshop on Periodontology and the Workshop on Emerging Technologies in Periodontics provided much of the systematic assessment of the evidence for currently available technologies. These include the use of barrier membranes (guided tissue regeneration, GTR), the use of bone replacement grafts, and the use of biologically active regenerative materials. The clinical evidence must be interpreted in the context of the biologic mechanisms and evidence for regeneration discussed in Chapter 25.

The evidence of clinical efficacy of barrier membranes has been assessed in the systematic reviews and meta-analyses performed by Needleman *et al*.

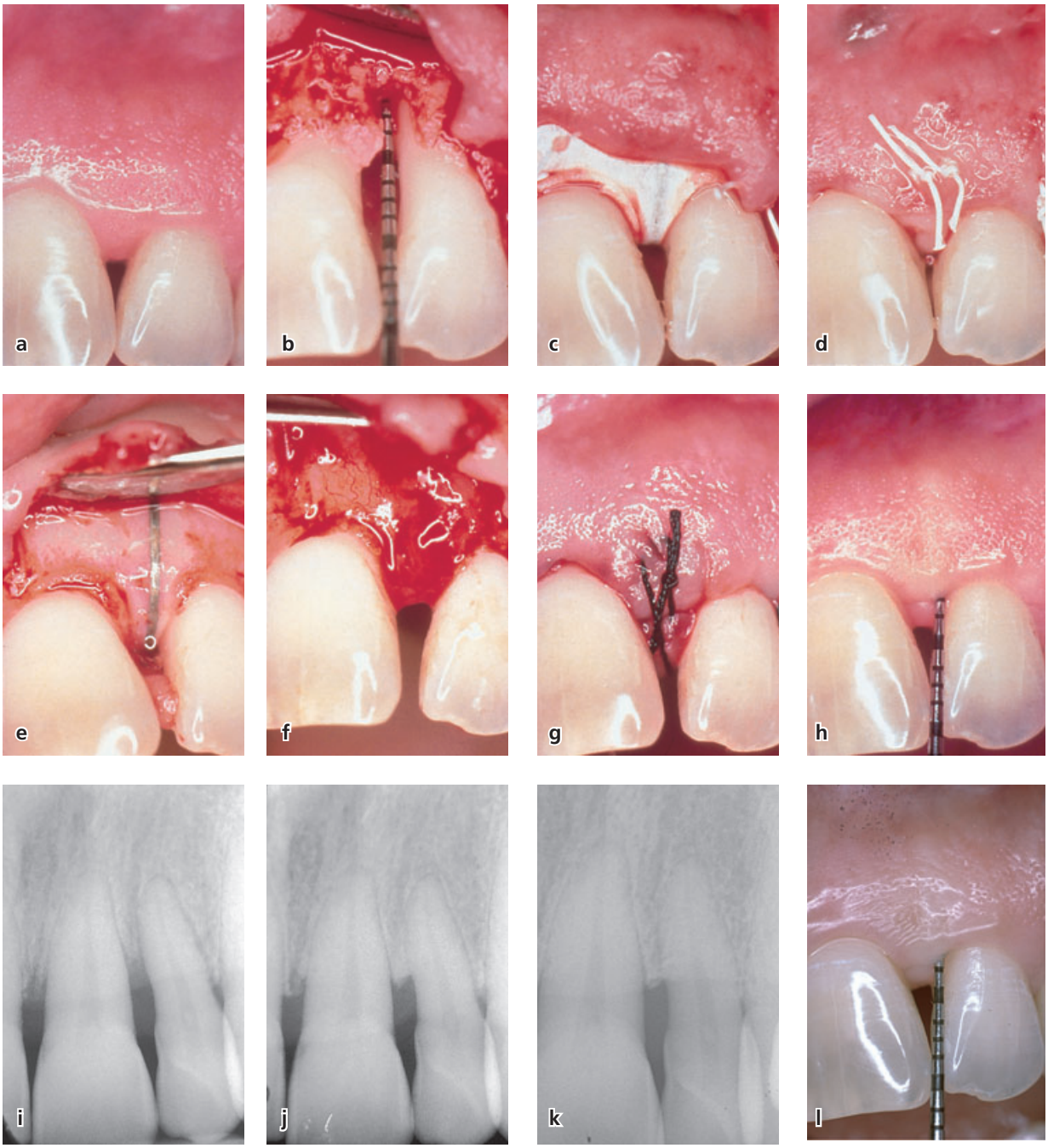


Fig. 43-4 (a,b) Left maxillary lateral incisor with a deep interproximal intrabony defect on the mesial surface. (c) Flaps are raised according to the modified papilla preservation technique, and a titanium-reinforced barrier membrane is placed over the defect. (d) By coronal displacement of the flap and preservation of the interdental papilla, the membrane is completely covered. (e,f) After 6 weeks of uneventful post-operative healing the membrane was removed, (g) and the newly formed tissue was completely covered. (h) At 1 year, residual probing pocket depth was 2 mm and no buccal or interdental recession had occurred. (i) The baseline radiograph shows radiolucency approaching the apex of the tooth, but after 1 year the intrabony defect is resolved and some supracrestal bone apposition seems to have occurred (j). The radiograph taken at 6 years confirms the supracrestal bone regeneration (k) and the clinical image shows the integrity of the interdental papilla with optimal preservation of the esthetic appearance (l).

(2002), Jepsen *et al*. (2002), and Murphy and Gunsolley (2003).

For intrabony defects, 26 controlled trials with 867 intrabony defects were included (Murphy & Gunsolley 2003). The application of barrier membranes resulted in an additional clinical attachment level gain of more than 1 mm compared to an access flap approach control (Fig. 43-6).

For class II furcation defects, 15 controlled trials with 376 involved teeth were included (Murphy & Gunsolley 2003). Membrane application resulted in additional vertical and horizontal (depth of the furcation involvement) clinical attachment level gains (Fig. 43-7).

These data alone, however, did not present conclusive evidence of efficacy as the possibility of bias

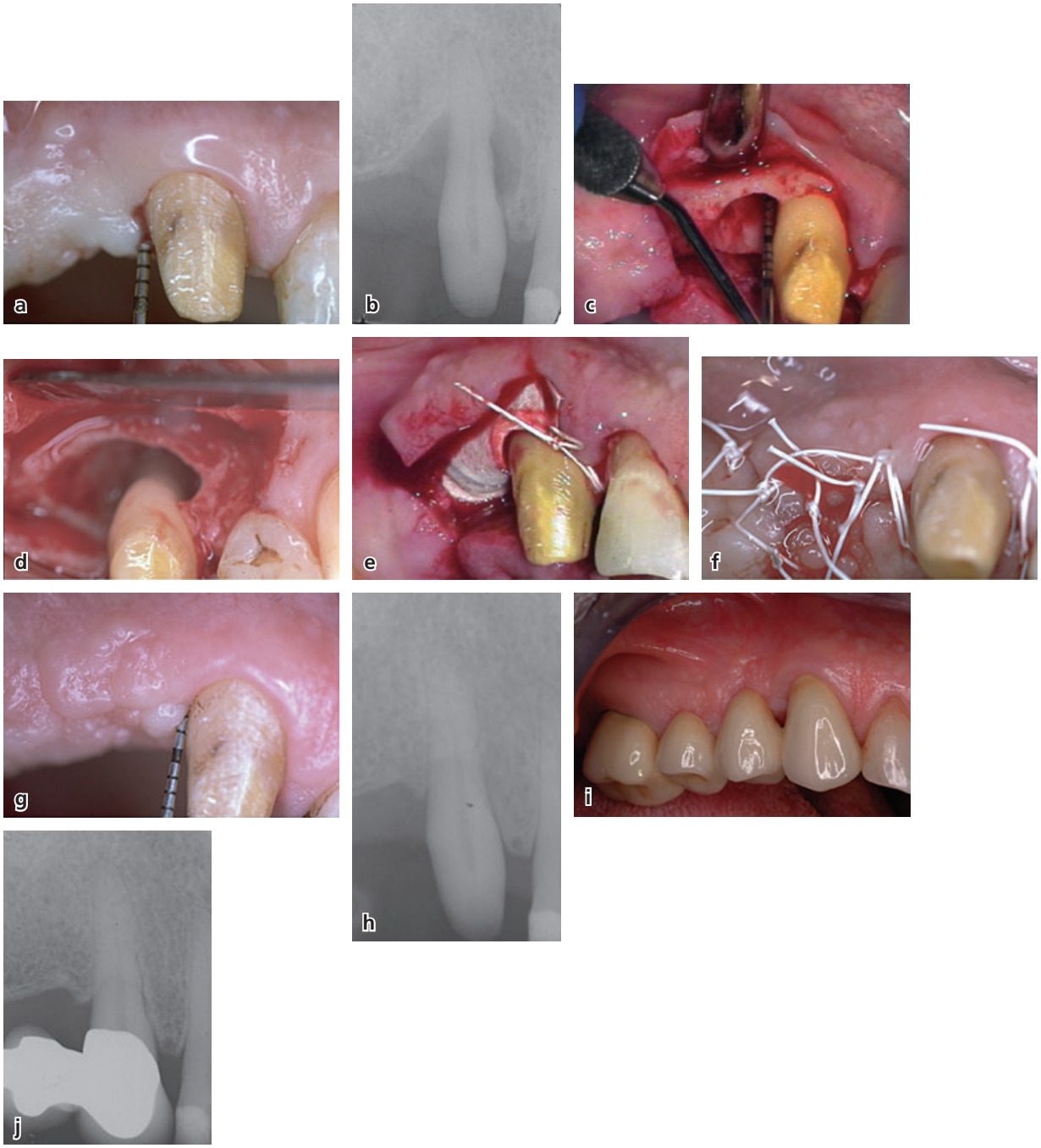


Fig. 43-5 Clinical benefits of periodontal regeneration. Patient presented with periodontally compromised mesial abutment of bridge: a 10-mm pocket was associated with a 10-mm intrabony defect extending on three of the four surfaces of the tooth (a–d). A barrier membrane was positioned and secured around the root of the tooth (e). Primary closure with internal mattress sutures was achieved (f) and maintained during the healing period. At 1 year, periodontal probing shows a shallow maintainable pocket (3 mm) (g) and the complete resolution of the defect (h). Clinical and radiographic stability of the outcome is illustrated 8 years following regenerative therapy (i,j): stability of the gingival margin, shallow pockets, good esthetics, and good periodontal support for the abutment are evident.

arising from a possible tendency to report studies with positive results could not be ruled out. Multicenter studies were designed to assess efficacy conclusively. These were performed in a private practice environment in order to assess also the generalizability of the benefit to this specific setting (effectiveness). The results of large prospective multi-center studies in private practice settings (Tonetti *et al*. 1998, 2004b; Cortellini *et al*. 2001) conclusively support the additional benefit of membranes in improving clinical attachment levels in intrabony defects and thus their efficacy and effectiveness. More limited evidence is also available for combination therapy (bone replacement grafts and barrier membranes) in furcation defects (Bowers *et al*. 2003).

The efficacy of bone replacement graft materials has been assessed in two systematic reviews (Trombelli *et al*. 2002; Reynolds *et al*. 2003). As these two

	Barrier	Reference	SD/SE date provided	Test barrier	N1	N2	Effect	N total	*P* value
	Collagen	Quteish 1992	N	Hum coll	16	16	0.703	32	0.050
	Collagen	Blumethal 1990	Y	Bov coll	10	10	0.706	20	0.117
	Collagen	Al-Arrayed 1995	N	Hum coll	11	11	0.743	22	0.085
Random	**Collagen (3)**				**37**	**37**	**0.716**	**74**	**0.004**
	e-PTFE	Nygaard-Østby 1996	Y	e-PTFE	15	13	0.121	28	0.744
	e-PTFE	Zybutz 2000	Y	e-PTFE	14	14	0.388	28	0.300
	e-PTFE	Pontoriero 1999	N	e-PTFE	10	10	0.691	20	0.124
	e-PTFE	Kilic 1997	Y	e-PTFE	18	18	0.796	36	0.020
	e-PTFE	Kim 1996	Y	e-PTFE	19	18	1.030	37	0.003
	e-PTFE	Cortellini 1995	Y	e-PTFE	15	15	1.153	30	0.003
	e-PTFE	Tonetti 1996	Y	e-PTFE	15	15	1.153	30	0.003
	e-PTFE	Cortellini 1995	Y	e-PTFE-TR	15	15	1.816	30	0.000
	e-PTFE	Cortellini 1996	Y	e-PTFE	12	12	2.545	24	0.000
Random	**e-PTFE (9)**				**133**	**130**	**1.014**	**263**	**0.000**
	Polymeric	Ratka-Kruger 2000	Y	PLA	16	16	–0.077	32	0.824
	Polymeric	Mayfield 1998	Y	PLA	22	22	0.109	44	0.714
	Polymeric	Cortellini 2001	Y	PGA	55	55	0.458	110	0.017
	Polymeric	Brathall 1998	Y	PLA/PGA	9	9	0.476	18	0.305
	Polymeric	Tonetti 1998	Y	PLA/PGA	69	69	0.552	138	0.001
	Polymeric	Zybutz 2000	Y	PLA	15	15	0.563	30	0.124
	Polymeric	Cortellini 1998	Y	PLA	23	23	0.786	46	0.009
	Polymeric	Pontoriero 1999	Y	PLA	10	10	0.879	20	0.055
	Polymeric	Pontoriero 1999	N	PLA/PGA	10	10	1.005	20	0.031
	Polymeric	Sculean 2001	N	PLA/PGA	14	14	1.046	28	0.008
	Polymeric	Joly 2002	Y	PLA/PGA	10	10	1.915	20	0.000
	Polymeric	Cortellini 1996	Y		12	12	2.221	24	0.000
Random	**Polymeric (12)**				**265**	**265**	**0.700**	**530**	**0.000**
Random	**combined (24)**				**435**	**432**	**0.811**	**867**	**0.000**

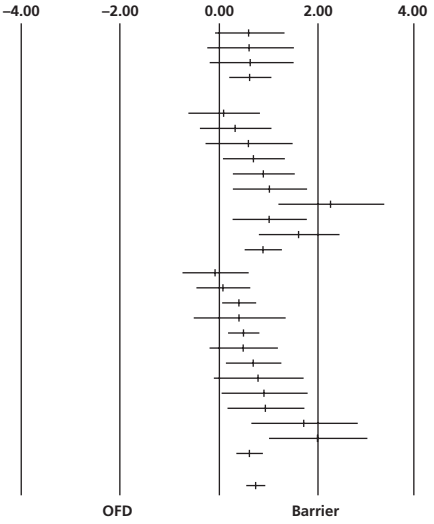


Fig. 43-6 Meta-analysis of intrabony defect studies examining open flap debridement versus GTR with barrier, using clinical attachment level (CAL) gain as an outcome variable. Bov coll = bovine collagen; e-PTFE = expanded polytetrafluoroethylene; Hum coll = human collagen; PLA = polylactic acid; PLA/PGA = polylactic/polyglycolic acid; TR = titanium-reinforced. From Murphy & Gunsolley (2003) with permission from the American Academy of Periodontology.

	Barrier	Reference	Location	SD/SE data provided	N1	N2	Effect	N total	*P* value
	Collagen	Wang 1994	Mand	Y	12	12	0.516	24	0.204
Random	**Collagen (1)**				**12**	**12**	**0.516**	**24**	**0.228**
	e-PTFE	Pontoriero 1995	Max	N	8	8	0.000	16	1.000
	e-PTFE	Lekovic 1989	Mand	Y	12	12	0.026	24	0.949
	e-PTFE	Pontoriero 1995	Max	N	10	10	0.190	20	0.663
	e-PTFE	Pontoriero 1995	Max	N	10	10	0.759	20	0.093
	e-PTFE	Metzler 1991	Max	Y	17	17	1.172	34	0.001
	e-PTFE	Pontoriero 1988	Mand	Y	21	21	1.450	42	0.000
	e-PTFE	Avera 1998	Max	Y	8	8	9.115	16	0.000
Random	**e-PTFE (7)**				**86**	**86**	**0.930**	**172**	**0.025**
	Por coll	Flanary 1991	Mixed	Y	19	19	0.857	38	0.011
	Peristeum	Lekovic 1991	Mand	Y	15	15	2.943	30	0.000
Random	**Other (2)**				**34**	**34**	**1.856**	**68**	**0.080**
Random	**Combined (10)**				**132**	**132**	**1.063**	**264**	**0.001**

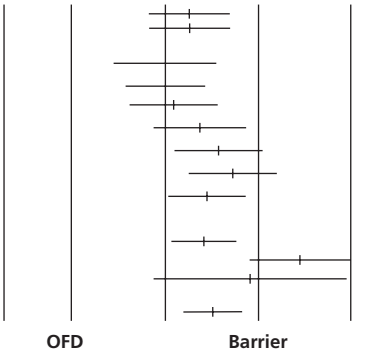


Fig. 43-7 Forest plot of furcation defect studies examining open flap debridement (OFD) versus GTR with barrier, using HOPA gain as an outcome variable. e-PTFE = expanded polytetrafluoroethylene; Mand = mandibula; Max = maxilla. From Murphy & Gunsolley (2003) with permission from the American Academy of Periodontology.

systematic reviews used significantly different criteria for study inclusion, results did not fully overlap. Trombelli *et al*. (2002), who included only controlled studies that reported changes in clinical attachment level as the primary outcome, concluded that there was insufficient evidence to support clinical use of bone replacement graft materials in intrabony defects, since: (1) there was significant heterogeneity among included studies; (2) the size of the adjunctive effect was small; and (3) there were differences that did not allow pooling of results obtained with different materials. In the other meta-analysis for intrabony defects, 27 controlled trials with 797 intrabony defects were included (Reynolds *et al*. 2003). The application of bone replacement grafts resulted in an additional clinical attachment level gain of 0.5 mm compared to an access flap approach control (Fig. 43-8). Greater additional benefits from the application of bone replacement grafts were observed whenever hard tissue measurements (bone fill or defect resolution) were utilized as outcome measures.

For furcation defects, the lack of consistent comparisons did not allow a meaningful assessment of the potential benefits of the use of bone replacement grafts alone (Reynolds *et al.* 2003). No large multicenter trials have provided definitive support for efficacy and/or effectiveness of the use of bone replacement grafts.

The evidence of clinical efficacy of biologically active regenerative materials has been summarized in meta-analyses only for enamel matrix derivative (Trombelli *et al*. 2002; Giannobile & Somerman 2003) and only for the application to intrabony defects. The outcomes of eight studies including 444 defects have indicated that enamel matrix derivative provides additional benefits of a magnitude of 0.75 mm in terms of clinical attachment level gains (Fig. 43-9). These data have been in accordance with those of a

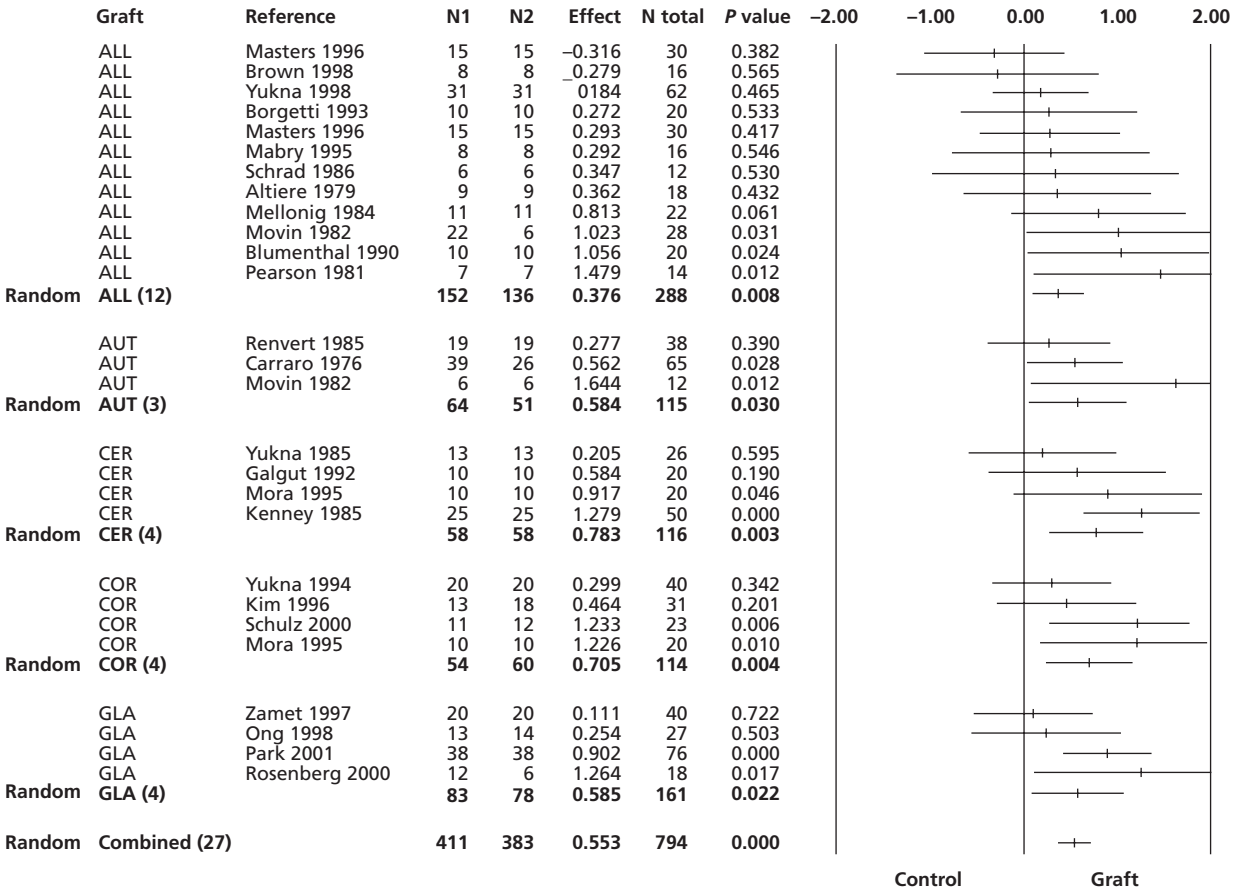


Fig. 43-8 Final meta-analysis of clinical attachment level in randomized controlled clinical studies comparing BRG to OFD in the treatment of intrabony defects. ALL = allograft; AUT = autograft; CER = calcium phosphate (hydroxyapatite) ceramic; COR = coralline calcium carbonate; GLA = bioactive glass. From Reynolds *et al*. (2003) with permission from the American Academy of Periodontology.

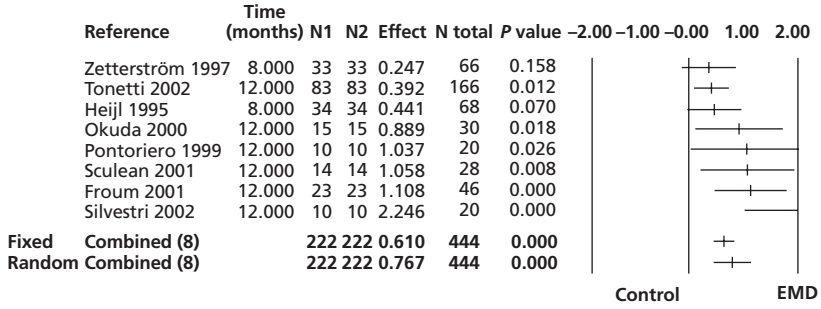


Fig. 43-9 Meta-analysis depicting the effectiveness of enamel matrix derivative (EMD) combined with surgery on clinical attachment level (CAL) gain as compared to control flap surgery alone. The use of EMD showed a significant improvement in CAL gain. Heterogeneity: Cohen's D, $P = 0.04$, Hedge's g, $P = 0.16$. From Giannobile & Somerman (2003) with permission from the American Academy of Periodontology.

large practice-based multi-center trial that demonstrated both efficacy and effectiveness of enamel matrix derivative in intrabony defects (Tonetti *et al*. 2002).

Patient and defect prognostic factors

The results reported in Table 43-2 indicate that clinical improvements beyond that of flap surgery can be obtained by treating intrabony defects with GTR, but they also suggest a great variability in clinical outcomes among the different studies. In addition, it is apparent from the results that the complete resolution of the intrabony component of the defect is observed in only a minority of sites. A series of prognostic factors associated with the clinical outcomes were identified using multi-variate approaches (Tonetti *et al*. 1993a, 1995, 1996a; Cortellini *et al*. 1994; Machtei *et al*. 1994; Falk *et al*. 1997). Attention has focused on some important patient and defect factors.

Table 43-2 Clinical outcomes of GTR treatment of deep intrabony defects

Authors	Membranes	N	Gains in CAL ± SD (mm)	Residual PPD ± SD (mm)
Becker *et al*. 1988	e-PTFE	9	4.5 ± 1.7	3.2 ± 1.0
Chung *et al*. 1990	Collagen	10	0.6 ± 0.6	
Handelsman *et al*. 1991	e-PTFE	9	4.0 ± 1.4	3.9 ± 1.4
Kersten *et al*. 1992	e-PTFE	13	1.0 ± 1.1	5.1 ± 0.9
Proestakis *et al*. 1992	e-PTFE	9	1.2 ± 1.3	3.5 ± 0.9
Quteish & Dolby 1992	Collagen	26	3.0 ± 1.5	2.2 ± 0.4
Selvig *et al*. 1992	e-PTFE	26	0.8 ± 1.3	5.4
Becker & Becker 1993	e-PTFE	32	4.5	3.9 ± 0.3
Cortellini *et al*. 1993b	e-PTFE	40	4.1 ± 2.5	2.0 ± 0.6
Falk *et al*. 1993	Polylactic acid	25	4.5 ± 1.6	3.0 ± 1.1
Cortellini & Pini-Prato 1994	Rubber dam	5	4.0 ± 0.7	2.4 ± 0.5
Laurell *et al*. 1994	Polylactic acid	47	4.9 ± 2.4	3.0 ± 1.4
Al-Arrayed *et al*. 1995	Collagen	19	3.9	2.5
Chen *et al*. 1995	Collagen	10	2.0 ± 0.4	4.2 ± 0.4
Cortellini *et al*. 1995c	e-PTFE	15	4.1 ± 1.9	2.7 ± 1.0
Cortellini *et al*. 1995c	e-PTFE+titanium	15	5.3 ± 2.2	2.1 ± 0.5
Cortellini *et al*. 1995°	e-PTFE+FGG	14	5.0 ± 2.1	2.6 ± 0.9
Cortellini *et al*. 1995°	e-PTFE	14	3.7 ± 2.1	3.2 ± 1.8
Cortellini *et al*. 1995b	e-PTFE+fibrin	11	4.5 ± 3.3	1.7
Cortellini *et al*. 1995b	e-PTFE	11	3.3 ± 1.9	1.9
Mattson *et al*. 1995	Collagen	13	2.5 ± 1.5	3.6 ± 0.6
Mattson *et al*. 1995	Collagen	9	2.4 ± 2.1	4.0 ± 1.1
Mellado *et al*. 1995	e-PTFE	11	2.0 ± 0.9	
Becker *et al*. 1996	Polylactic acid	30	2.9 ± 2.0	3.6 ± 1.3
Cortellini *et al*. 1996c	Polylactic acid	10	4.5 ± 0.9	3.1 ± 0.7
Cortellini *et al*. 1996b	e-PTFE	12	5.2 ± 1.4	2.9 ± 0.9
Cortellini *et al*. 1996b	Polylactic acid	12	4.6 ± 1.2	3.3 ± 0.9
Gouldin *et al*. 1996	e-PTFE	25	2.2 ± 1.4	3.5 ± 1.3
Kim *et al*. 1996	e-PTFE	19	4.0 ± 2.1	3.2 ± 1.1
Murphy 1996	e-PTFE+ITM	12	4.7 ± 1.4	2.9 ± 0.8
Tonetti *et al*. 1996b	e-PTFE	23	5.3 ± 1.7	2.7
Benqué *et al*. 1997	Collagen	52	3.6 ± 2.2	3.9 ± 1.7
Caffesse *et al*. 1997	Polylactic acid	6	2.3 ± 2.0	3.8 ± 1.2
Caffesse *et al*. 1997	e-PTFE	6	3.0 ± 1.2	3.7 ± 1.2
Christgau *et al*. 1997	e-PTFE	10	4.3 ± 1.2	3.6 ± 1.1
Christgau *et al*. 1997	Polyglactin	10	4.9 ± 1.0	3.9 ± 1.1
Falk *et al*. 1997	Polylactic acid	203	4.8 ± 1.5	3.4 ± 1.6
Kilic *et al*. 1997	e-PTFE	10	3.7 ± 2.0	3.1 ± 1.4
Cortellini *et al*. 1998	Polylactic acid	23	3.0 ± 1.7	3.0 ± 0.9
Eickholz *et al*. 1998	Polylactic acid	14	3.4 ± 1.6	3.2 ± 0.7
Smith MacDonald *et al*. 1998	e-PTFE	10	4.3 ± 2.1	3.7 ± 0.9
Smith MacDonald *et al*. 1998	Polylactic acid	10	4.6 ± 1.7	3.4 ± 1.2
Parashis *et al*. 1998	Polylactic acid	12	3.8 ± 1.8	3.5 ± 1.4
Tonetti *et al*. 1998	Polylactic acid	69	3.0 ± 1.6	4.3 ± 1.3
Cortellini *et al*. 1999	Polylactic acid	18	4.9 ± 1.8	3.6 ± 1.2
Pontoriero *et al*. 1999	Diff. barriers	30	3.1 ± 1.8	3.3 ± 1.3
Sculean *et al*. 1999a	Polylactic acid	52	3.4 ± 1.4	3.6 ± 1.3
Dorfer *et al*. 2000	Polylactic acid	15	4.0 ± 1.2	2.7 ± 0.7
Dorfer *et al*. 2000	Polidiossanon	15	3.4 ± 1.9	3.1 ± 1.1
Eickholz *et al*. 2000	Polylactic acid	30	3.9 ± 1.2	2.6 ± 1.0
Karapataki *et al*. 2000	Polylactic acid	10	4.7 ± 0.7	4.2 ± 1.4
Karapataki *et al*. 2000	e-PTFE	9	3.6 ± 1.7	4.6 ± 1.3
Ratka-Kruger *et al*. 2000	Polylactic acid	23	3.1 ± 2.3	4.7 ± 1.4
Zybutz *et al*. 2000	Polylactic acid	15	2.4 ± 1.9	
Zubutz *et al*. 2000	e-PTFE	14	2.4 ± 0.8	
Cortellini & Tonetti 2001	Diff. barriers	26	5.4 ± 1.2	3.3 ± 0.6
Cortellini *et al*. 2001	Polylactic acid	55	3.5 ± 2.1	3.8 ± 1.5
Weighted mean		**1283**	**3.8 ± 1.7**	**3.4 ± 1.2**

FGG = free gingival graft; ITM = interproximal tissue maintenance.

Patient factors

Periodontal infection

Periodontal regeneration does not treat periodontitis, but rather is an approach for regenerating defects that have developed as a result of periodontitis. Therefore, appropriate periodontal treatment should always be completed before periodontal regeneration is initiated. In this context – i.e. in patients who underwent a cycle of cause-related periodontal therapy to the satisfaction of the treating clinician – evidence suggests that the level of control of periodontitis, achieved before a periodontal regenerative procedure is initiated, is associated with outcomes: the persistence of poor plaque control, high levels of bleeding upon probing in the dentition, as well as the persistence of high loads of total bacteria or of specific microbial pathogens (or complexes of pathogens) have all been associated in a dose-dependent manner with poor clinical outcomes (Tonetti *et al*. 1993a, 1995; Cortellini *et al*. 1994; Machtei *et al*. 1994; Heitz-Mayfield *et al.* 2006).

The level of self-performed plaque control has a great and dose-dependent effect on the outcome of periodontal regeneration. Better clinical attachment level gains were observed in patients with optimal levels of plaque control as compared with those in patients with less ideal oral hygiene (Cortellini *et al*. 1994; Tonetti *et al*. 1995, 1996a). Patients with plaque on <10% of the tooth surfaces (full mouth plaque score, FMPS) had a gain of clinical attachment which was 1.89 mm greater than that observed in patients with FMPS >20% (Tonetti *et al*. 1995).

Although not formally tested for efficacy in randomized trials, achieving high levels of plaque control and suppression of the pathogenic microflora through behavioral intervention and intensive anti-infective periodontal therapy are generally advocated before proceeding with periodontal regeneration. Furthermore, some proof of principle investigations have assessed the adjunctive effect of using an antibiotic locally delivered within the wound area or in the regenerative material (Yukna & Sepe 1982; Sanders *et al*. 1983; Stavropoulos *et al*. 2003). Results showed consistently better outcomes in the groups that received the antibiotic. At present, however, no regenerative device with enhanced antimicrobial activity is commercially available.

Smoking

A retrospective study found that cigarette smokers displayed significantly impaired regenerative outcomes compared to non-smokers (Tonetti *et al*. 1995). Data showed that cigarette smoking was associated with reduced attachment level gains. The attachment gain in subjects smoking more than ten cigarettes/day was 2.1 ± 1.2 mm versus 5.2 ± 1.9 mm observed in non-smokers (Tonetti *et al*. 1995). Thereafter a series of investigations has confirmed that cigarette smoking displays a dose-dependent detrimental effect on clinical attachment level gains.

Although no formal evidence is available, it is generally suggested that smoking cessation counseling should be initiated in the context of cause-related periodontal therapy and that patients who have been unable to quit the habit should be informed of the possibility of reduced outcomes and of the need to abstain from smoking during the peri-operative and early healing period.

Other patient factors

It has been suggested that other patient factors, such as age, genetics, systemic conditions or stress levels, may be associated with sub-optimal regenerative outcomes. In the light of the lack of evidence, however, no action is required with the exception of considering the patient characteristics that represent a contraindication to surgery (e.g. uncontrolled diabetes or unstable, severe diseases).

Clinical relevance of patient factors

The data discussed above indicates that patient factors play an important role in regenerative periodontal therapy (Fig. 43-10). Some of these factors can be modified by appropriate interventions in some patients. These interventions should be performed before periodontal regenerative therapy. Whenever modification is not possible, reduced outcomes in terms of extent and predictability should be considered.

Defect factors

Type of defect

With the currently available periodontal regenerative technologies, there is no evidence that suprabony (horizontal) defects, supracrestal components of intrabony defects or class III furcation involvements can be predictably treated with regenerative approaches. This limitation is also true for interdental craters, thus limiting the type of defects that can be treated to intrabony defects and class II furcation defects.

Morphology of the defect

Defect morphology plays a major role in healing following periodontal regenerative treatment of intrabony defects. This was demonstrated in studies showing that the depth and width of the intrabony component of the defect influence the amount of clinical attachment and bone gained at 1 year. The deeper the defect, the greater was the amount of clinical improvements, while the wider the defect, the

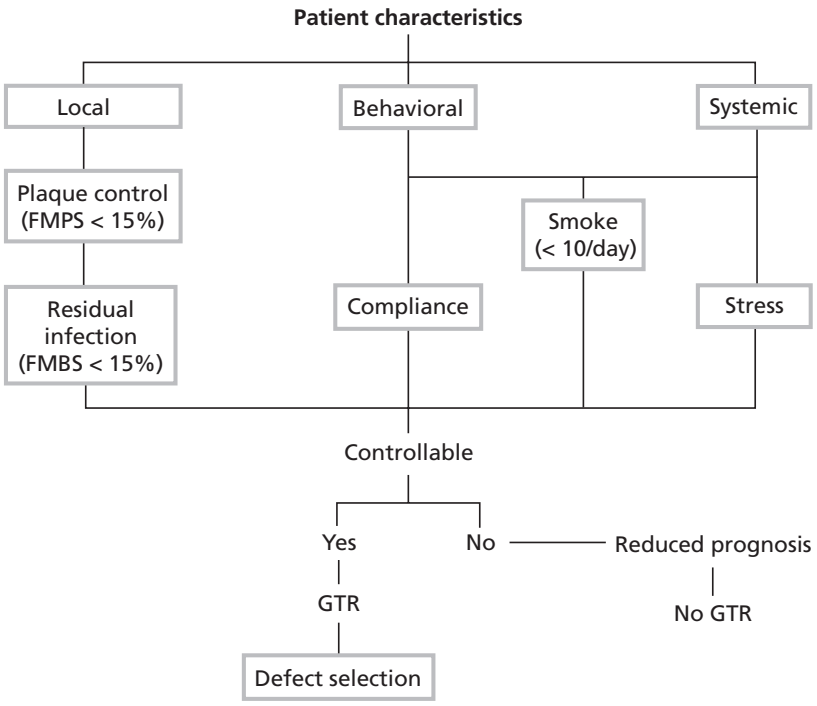


Fig. 43-10 Diagram illustrating patient selection criteria. It can be seen that control of local, behavioral, and systemic patient characteristics may improve the treatment outcomes. FMPS = full mouth plaque score; FMBS = full mouth bleeding score. Modified from Cortellini & Bowers (1995).

lower were the attachment and bone gains (Garrett *et al*. 1988; Tonetti *et al*. 1993a, 1996a).

In a controlled study, however, it was demonstrated that deep and shallow defects have the "same potential" for regeneration. In this study, deep defects (deeper than 3 mm) resulted in larger linear amounts of CAL gains than shallow defects (3.7 ± 1.7 mm versus 2.2 ± 1.3 mm), but the percentage of CAL gains as related to baseline defect depth was similar in deep (76.7 ± 27.7%) and in shallow (75.8 ± 45%) defects. The width of the intrabony component of the defects is measured as the angle that the bony wall of the defect forms with the long axis of the tooth. In a study on 242 intrabony defects treated with membranes, Cortellini and Tonetti (1999) demonstrated that defects with a radiographic angle of 25° or less gained consistently more attachment (1.6 mm on average) than defects of 37° or more.

Two recent follow-up studies have addressed the significance of the baseline radiographic angle of the intrabony defect following the use of either enamel matrix derivative (Tsitoura *et al*. 2004) or of a combination of bone replacement graft with a barrier membrane (Linares *et al*. 2006). The impact of the width of the baseline radiographic angle was confirmed for the non-space-making biological mediator but not for the more stable combination therapy. These data are consistent with the notion that choice of the regenerative technology may partially overcome negative morphologic characteristics of intrabony defects. An earlier secondary analysis of a controlled clinical trial using titanium-reinforced membranes (Tonetti *et al*. 1996a) indicated that the relevance of defect morphology parameters may be diminished with the use of supported membranes.

It was also shown that the number of residual bony walls was related to the outcomes of various regenerative approaches (Goldman & Cohen 1958; Schallhorn *et al*. 1970). This issue as related to GTR therapy was addressed in three investigations (Selvig *et al*. 1993; Tonetti *et al*. 1993a, 1996a). In one study, the reported 1-year mean clinical attachment level gain was 0.8 ± 1.3 mm. This gain corresponded to the depth of the three-wall intrabony component of the defect (Selvig *et al*. 1993). In the other two investigations, on the contrary, gains in attachment were not related to the defect configuration in terms of one-wall, two-wall, and three-wall subcomponents (Tonetti *et al*. 1993a, 1996a). A total of 70 defects were examined in these two latter studies, utilizing a multi-variate approach. The treatment resulted in mean attachment gains of 4.1 ± 2.5 mm and 5.3 ± 2.2 mm, and it was observed that the most coronal portion of the defects which is most susceptible to negative influences from the oral environment were often incompletely filled with bone, irrespective of whether these were one-wall, two-wall or three-wall defects. Thus, these studies questioned the impact of the number of residual bony walls of the defect on the clinical outcomes of periodontal regeneration with membranes and suggested that location of the one-wall subcomponent (the one most likely to be the most superficial one) may have acted as confounder in other studies and be an important predictor of the outcomes.

Tooth factors

The endodontic status of the tooth has been suggested as a potential relevant factor in periodontal

therapy. Emerging evidence (see Chapter 40) indicates that root canal treated teeth may respond differently to periodontal therapy. A clinical study on 208 consecutive patients with one intrabony defect each demonstrated that properly performed root canal treatment does not negatively affect the healing response and the long-term stability of results of deep intrabony defects treated with membranes (Cortellini & Tonetti 2000b).

Tooth mobility has long been considered an important factor for periodontal regeneration (Sanders *et al*. 1983). Recently, a multi-variate analysis of a multi-center controlled clinical trial demonstrated that tooth hypermobility was negatively and dose-dependently associated with the clinical outcomes of regeneration (Cortellini *et al*. 2001). Though significant, the size of the effect was small within the range of physiologic mobility. Another recent secondary analysis of three previously reported trials assessed the regenerative outcomes of hypermobile teeth (Trejo & Weltman 2004). This report indicated that teeth with baseline mobility amounting to less than 1 mm horizontally could be successfully treated by periodontal regeneration. Although no intervention trial has been performed to date, these results are generally considered supportive of an approach that does not set the prognosis of the tooth or the regenerative procedure based on tooth mobility but rather considers splinting hypermobile teeth before periodontal regenerative surgery.

Based on these results, it can be concluded that deep and narrow intrabony defects at either vital or endodontically treated teeth are the ones in which the most significant and predictable outcomes can be achieved by GTR treatment. Severe, uncontrolled dental hypermobility (Miller class II or higher) may impair the regenerative outcomes.

Factors affecting the clinical outcomes of GTR in furcations

Significant evidence has demonstrated that treatment of maxillary degree II furcations and maxillary and mandibular degree III furcation involvements with GTR is unpredictable, while clinical improvements can be expected treating mandibular degree II furcations. The great variability in clinical outcomes, following treatment of mandibular degree II furcations with GTR, is probably related to the factors discussed relative to intrabony defects.

Regarding defect factors, it was shown that first and second mandibular molars and buccal and lingual furcations respond equally well to GTR treatment (Pontoriero *et al*. 1988; Machtei *et al*. 1994). It was also demonstrated that the pre-operative horizontal pocket depth is directly correlated with the magnitude of attachment gain and bone formation in the furcation area (Machtei *et al*. 1993, 1994). The deeper the baseline horizontal pocket, the greater was the H-CAL and bone gain. The anatomy of the furcations in terms of height, width, depth, and volume, however, did not correlate with the clinical outcome (Machtei *et al*. 1994). Anderegg *et al*. (1995) demonstrated that sites with a gingival thickness of >1 mm exhibited less gingival recession post surgery than sites with a gingival thickness of <1 mm. The authors concluded that the thickness of the gingival tissue covering a barrier material must be considered if post-treatment recession is to be minimized or avoided.

The relevance of the surgical approach

At the beginning of the 1980s the need to modify standard periodontal surgical procedures to favor periodontal regeneration became apparent. In particular, the need to preserve soft tissues in order to attempt primary closure of the interdental space to contain grafts or coronally advanced flaps to cover furcation entrances led to the development of specific flap designs for periodontal regeneration (Takei *et al*. 1985; Gantes & Garret 1991).

In fact, graft exfoliation and membrane exposure with consequent bacterial contamination during healing represented the major complications of periodontal regenerative procedures at the time. Membrane exposure was reported to be a major complication with prevalence in the range of 50–100% (Becker *et al*. 1988; Cortellini *et al*. 1990, 1993b; Selvig *et al*. 1992, 1993; Murphy 1995a; DeSanctis *et al*. 1996a,b; Falk *et al*. 1997; Trombelli *et al*. 1997; Mayfield *et al*. 1998). Cortellini *et al*. (1995c,d) reported that the prevalence of membrane exposure could be greatly reduced with the use of access flaps, specifically designed to preserve the interdental tissues (modified papilla preservation technique) (Fig. 43-11).

Many studies have shown that the exposed membranes are contaminated with bacteria (Selvig *et al*. 1990, 1992; Grevstad & Leknes 1992; Machtei *et al*. 1993; Mombelli *et al*. 1993; Tempro & Nalbandian 1993; Nowzari & Slots 1994; Novaes *et al*. 1995; Nowzari *et al*. 1995; DeSanctis *et al*. 1996a,b). Contamination of exposed non-bioabsorbable as well as bioabsorbable membranes was associated with lower probing attachment level gains in intrabony defects (Selvig *et al*. 1992; Nowzari & Slots 1994; Nowzari *et al*. 1995; DeSanctis *et al*. 1996a,b). The impaired clinical results in some studies were associated with high counts of bacteria and with the presence of *P. gingivalis* and *A. actinomycetemcomitans* (Machtei *et al*. 1994; Nowzari & Slots 1994; Nowzari *et al*. 1995).

Bacterial contamination of the membrane may occur during surgery, but also during the post-operative healing phase. After placement, bacteria from the oral cavity may colonize the coronal part of the membrane. Frequently, this results in recession of the gingival tissues, which allows colonization of the membrane material further apically. In addition,

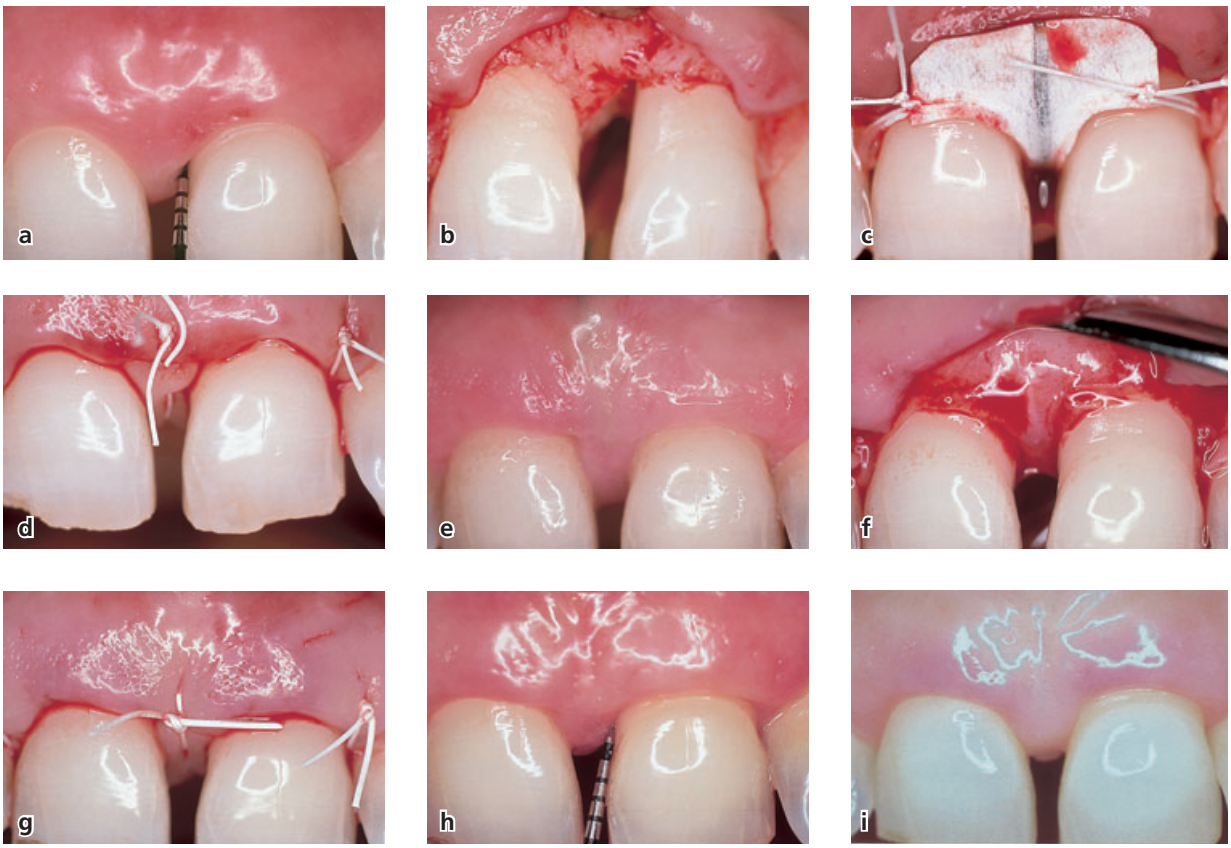


Fig. 43-11 (a) Left maxillary central incisor with a 10-mm pocket depth and 11 mm of clinical attachment loss on the mesial surface. A diastema is present between the two central incisors. (b) Full thickness buccal and palatal flaps have been raised and an intrabony defect can be seen. The interdental papilla has been incised on the buccal aspect and elevated with the palatal flap (modified papilla preservation technique). (c) A titanium-reinforced e-PTFE barrier membrane has been placed and fixed close to the level of the cemento-enamel junction. (d) The membrane is completely covered. This primary closure has been obtained by preserving the interdental papilla and by coronal displacement of the buccal tissue flap. (e) At 6 weeks, the membrane is completely covered with healthy tissue. (f) After membrane removal at 6 weeks, dense newly formed tissue is evident in the defect and in the supracrestal space maintained by the titanium-reinforced membrane. (g) The newly formed tissue is completely covered by the raised and well preserved tissue flaps. (h) The photograph after 1 year shows a 4 mm residual pocket depth. A gain of clinical attachment of 6 mm was recorded, and no recession has occurred compared to baseline. (i) Ten year photograph showing the optimal preservation of the interdental tissues.

"pocket" formation may occur on the outer surface of the membrane due to apical migration of the epithelium on the inner surface of the covering gingival tissue. This may allow bacteria from the oral cavity to colonize the subgingival area. The significance of bacterial contamination was addressed in an investigation in monkeys (Sander & Karring 1995). The findings of this study showed that new attachment and bone formation occurred consistently when bacteria were prevented from invading the membrane and the wound during healing.

In order to prevent wound infection, some investigators have administered systemic antibiotics to patients before and during the first weeks after membrane application (Demolon *et al*. 1993; Nowzari & Slots 1994). However, despite the application of systemic antibiotics, occurrence of post-operative wound infection related to implanted barrier membranes was noticed. This indicates that either the drug administered is not directed against the microorganisms responsible for the wound infection, or that the drug does not reach the infected site at a concentration sufficiently high to inhibit the target microorganisms. An improved effect on periodontal healing after GTR in association with local application of metronidazole was reported by Sander *et al*. (1994). Twelve patients with one pair of intrabony defects participated in the study. Metronidazole in a gel form was placed in the defects and on the membrane prior to wound closure, while the controls were treated with a membrane alone. Six months following membrane removal the medium gain in probing attachment level, presented as a percentage of the initial defect depth, was 92% for test defects versus 50% for the control defects. Other clinical parameters, like plaque index, bleeding on probing, pocket depth reduction or recession of the gingival margin, were similar in the test and control sites. Although the use of local or systemic antibiotics may reduce the bacterial load on exposed membranes, it seems ineffective in preventing the formation of a microbial biofilm (Frandsen *et al*. 1994; Nowzari *et al*. 1995). Apart from the erythema and swelling related to such infection of the wound, more severe post-operative complica-

tions such as suppuration, sloughing or perforation of the flap, membrane exfoliation, and post-operative pain have been reported (Murphy 1995a,b).

Another important issue associated with the clinical results is the coverage of the regenerated tissue after removal of a non-bioabsorbable membrane. Many authors have reported that the frequent occurrence of a gingival dehiscence over the membrane is likely to result in insufficient protection of the interdental regenerated tissue (Becker *et al*. 1988; Selvig *et al*. 1992; Cortellini *et al*. 1993b; Tonetti *et al*. 1993a). Exposure of the regenerated tissue to the oral environment entails the risks of mechanical and infectious insults that in turn may prevent complete maturation of the regenerated tissue into a new connective tissue attachment. In fact, incomplete coverage of the regenerated tissue was associated with reduced attachment and bone gain at 1 year (Tonetti *et al*. 1993a). Recently, the positioning of a saddle-shaped free gingival graft over the regenerated interdental tissue (Fig. 43-12) was suggested to offer better coverage and protection than a dehiscent gingival flap (Cortellini *et al*. 1995a). In this randomized controlled study, more gain of attachment was observed in the 14 sites where a free gingival graft was positioned after membrane removal (5.0 ± 2.1 mm), than in the 14 sites where conventional protection of the regenerated tissue was accomplished (3.7 ± 2.1 mm).

The systematic assessment of the relevant factors associated with variability of periodontal regenerative outcomes performed at the beginning of the 1990s (Tonetti *et al*. 1993a, 1995, 1996a; Machtei *et al*. 1994; Falk *et al*. 1997) provided further evidence that

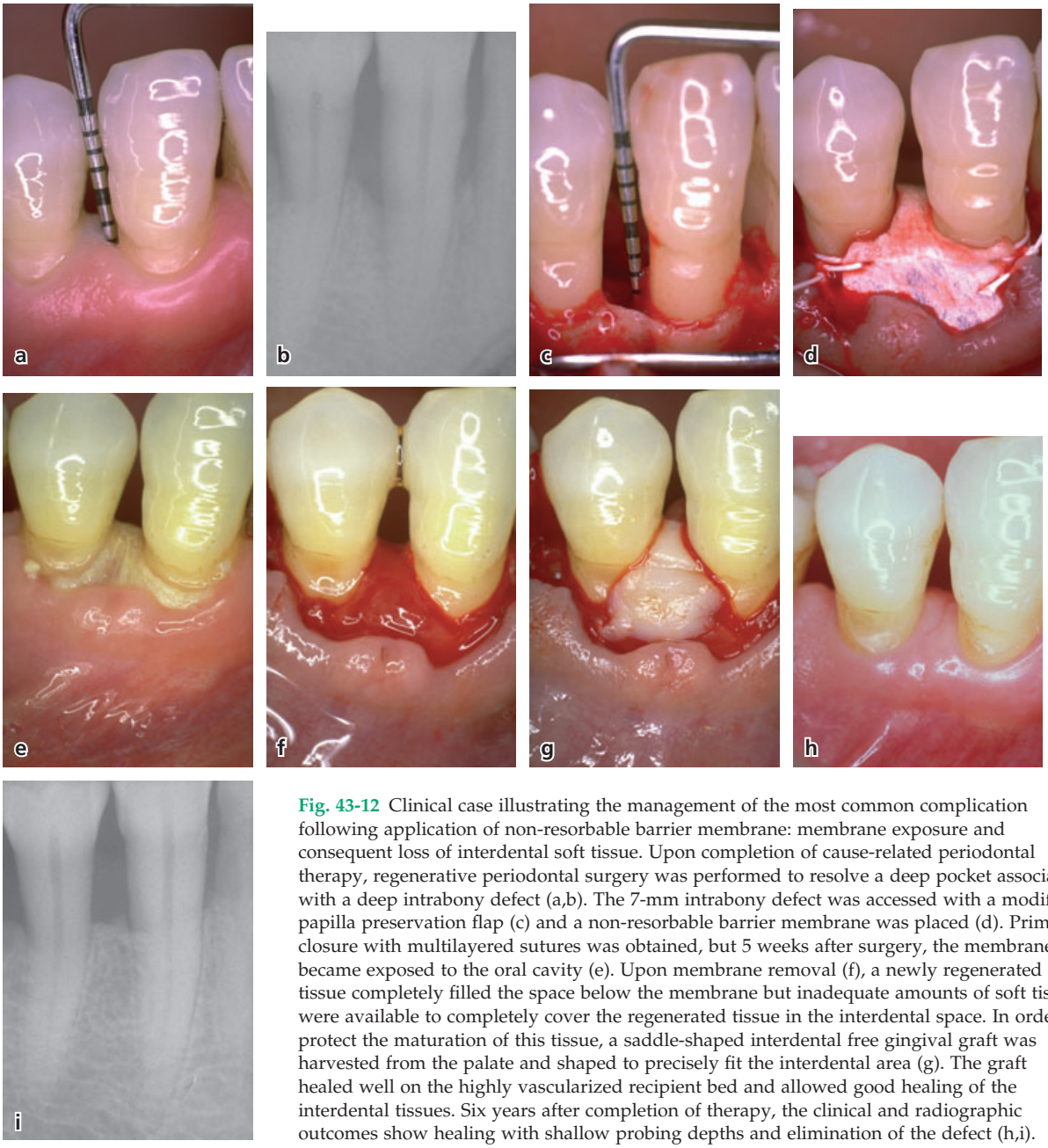
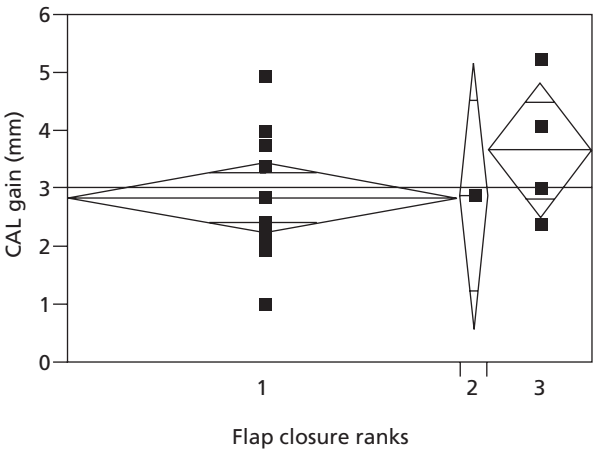


Fig. 43-12 Clinical case illustrating the management of the most common complication following application of non-resorbable barrier membrane: membrane exposure and consequent loss of interdental soft tissue. Upon completion of cause-related periodontal therapy, regenerative periodontal surgery was performed to resolve a deep pocket associated with a deep intrabony defect (a,b). The 7-mm intrabony defect was accessed with a modified papilla preservation flap (c) and a non-resorbable barrier membrane was placed (d). Primary closure with multilayered sutures was obtained, but 5 weeks after surgery, the membrane became exposed to the oral cavity (e). Upon membrane removal (f), a newly regenerated tissue completely filled the space below the membrane but inadequate amounts of soft tissue were available to completely cover the regenerated tissue in the interdental space. In order to protect the maturation of this tissue, a saddle-shaped interdental free gingival graft was harvested from the palate and shaped to precisely fit the interdental area (g). The graft healed well on the highly vascularized recipient bed and allowed good healing of the interdental tissues. Six years after completion of therapy, the clinical and radiographic outcomes show healing with shallow probing depths and elimination of the defect (h,i).

surgical factors had a great impact on regeneration and led the way to the development of procedures specifically designed for periodontal regeneration.

In general the development of new procedures was aimed at complete tissue preservation of the marginal tissue in order to achieve and maintain primary closure on top of the applied regenerative material during the critical stages of healing. Specifically, flap designs attempted to achieve passive primary closure of the flap combined with optimal wound stability.



Ranks	Number of studies	Mean (mm)
1	15	2.84
2	1	2.90
3	4	3.68

Fig. 43-13 Means of intrabony defect studies examining the relationship between flap closure technique ranking and the gain in clinical attachment level (CAL) (in mm) considering only e-PTFE barrier types. Groupings were not statistically different from one another. From Murphy & Gunsolley (2003) with permission from the American Academy of Periodontology.

Papilla preservation flaps

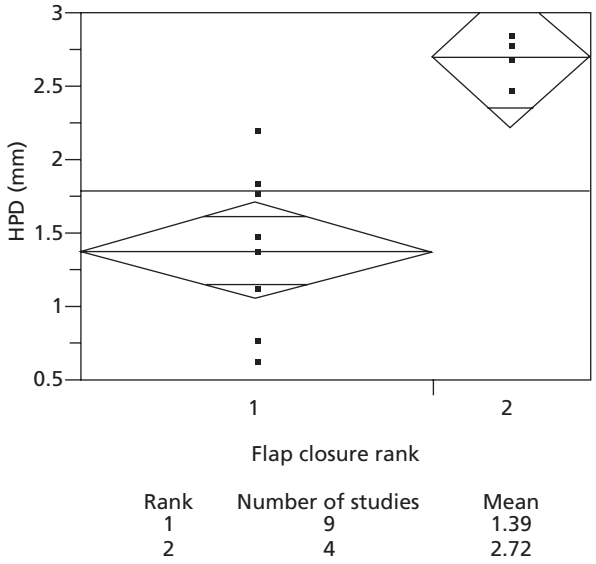
The modified papilla preservation technique (MPPT) was developed in order to increase the space for regeneration, and in order to achieve and maintain primary closure of the flap in the interdental area (Cortellini *et al*. 1995c,d). This approach combines special soft tissue management with use of a self-supporting titanium-reinforced membrane capable of maintaining a supra-alveolar space for regeneration. The MPPT allows primary closure of the interdental space, resulting in better protection of the membrane from the oral environment (Cortellini *et al*. 1995d). The technique involves the elevation of a full-thickness palatal flap which includes the entire interdental papilla. The buccal flap is mobilized with vertical and periosteal incisions, coronally positioned to cover the membrane, and sutured to the palatal flap through a horizontal internal crossed mattress suture over the membrane. A second internal mattress suture warrants primary closure between the flap and the interdental papilla. A representative case is shown in Figs. 43-4 and 43-11. In a randomized controlled clinical study on 45 patients (Cortellini *et al*. 1995c), significantly greater amounts of attachment gain were obtained with the MPPT (5.3 ± 2.2 mm), in comparison with either conventional GTR (4.1 ± 1.9 mm) or flap surgery (2.5 ± 0.8 mm), demonstrating that a modified surgical approach can result in improved clinical outcomes.

In this study 100% of the sites were closed on top of a titanium-reinforced membrane and 73% remained closed for up to 6 weeks, when the barrier membrane was removed. This study provided proof of principle of the benefit of specific flap designs for periodontal regeneration.

A recent meta-analysis (Murphy & Gunsolley 2003) showed the existence of a trend associating better clinical outcomes in studies using flap designs and closing techniques considered conducive to the achievement and maintenance of primary closure of the flap (Figs. 43-13, 43-14). The reported procedure can be successfully applied in sites where the interdental space width is at least 2 mm at the most coronal portion of the papilla.

When interdental sites are narrower, the reported technique is difficult to apply. In order to overcome this problem, a different papilla preservation procedure (the simplified papilla preservation flap) has been proposed for narrower interdental spaces (Cortellini *et al*. 1999). This approach includes an oblique incision across the defect-associated papilla, starting from the buccal angle of the defect-associated tooth to reach the mid-interdental part of the papilla at the adjacent tooth under the contact point. In this way, the papilla is cut into two equal parts of which the buccal is elevated with the buccal flap and the lingual with the lingual flap. In the cited study, 100% of the narrow interdental papillae could be closed on top of bioresorbable barriers, and 67% maintained primary closure over time, resulting in 4.9 ± 1.8 mm of clinical attachment level gains. This approach has been successfully applied in different multi-center randomized clinical trials designed to test the generalizability of the added benefits of using barrier membranes on deep intrabony defects (Tonetti *et al*. 1998; Cortellini *et al*. 2001).

In the cited studies, GTR therapy of deep intrabony defects performed by different clinicians on various patient populations resulted in both greater amounts and improved predictability of CAL gains than access flap alone. The issue of soft tissue manipulation to obtain stable protection of the regeneration site has been further explored, applying a microsurgical approach in the regenerative therapy of deep intrabony defects (Fig. 43-15). In a patient cohort study on 26 patients with 26 intrabony defects treated with papilla preservation techniques, primary closure on the barrier was obtained in 100% of the cases and maintained over time in 92.3% of the sites (Cortellini & Tonetti 2001). Treatment resulted in large amounts of CAL gains (5.4 ± 1.2 mm) and minimal gingival



	Difference	*t* test	DF	Prob > ltl
Estimate	–1.3319	–7.014	10.538	< 0.0001
Std error	0.1899			
Lower 95%	–1.9277			
Upper 95%	–0.7361			

Fig. 43-14 Regression analysis of furcation defect studies examining the relationship between flap closure technique ranking and the reduction (in mm) in horizontal probing depth (HPD). Groups 1 and 2 are statistically different from one another. From Murphy & Gunsolley (2003) with permission from the American Academy of Periodontology.

recession (0.4 ± 0.7 mm). Thus, the improved vision and better soft tissue handling improved the predictability of periodontal regeneration.

Today, the use of papilla preservation flap designs and closure techniques has become the standard approach for regenerative periodontal surgery.

Modified papilla preservation technique

The rationale for developing this technique was to achieve and maintain primary closure of the flap in the interdental space over the membrane (Cortellini *et al.* 1995d) (Figs. 43-16 to 43-18). Access to the interdental defect consists of a horizontal incision traced in the buccal keratinized gingiva at the base of the papilla, connected with mesio-distal buccal intrasulcular incisions. After elevation of a full-thickness buccal flap, the residual interdental tissues are dissected from the neighboring teeth and the underlying bone and elevated towards the palatal aspect. A full-thickness palatal flap, including the interdental papilla, is elevated and the interdental defect exposed. Following debridement of the defect, the buccal flap is mobilized with vertical and periosteal incisions, when needed.

This technique was originally designed for use in combination with self-supporting barrier membranes. In fact, the suturing technique requires a supportive (or supported) membrane to be effective (Figs. 43-16, 43-17). To obtain primary closure of the interdental space over the membrane, a first suture (horizontal internal crossed mattress suture) is placed beneath the mucoperiosteal flaps between the base of the palatal papilla and the buccal flap. The interdental portion of this suture hangs on top of the membrane allowing the coronal displacement of the buccal flap. This suture relieves all the tension of the flaps. To ensure primary passive closure of the interdental tissues over the membrane, a second suture (vertical internal mattress suture) is placed between the buccal aspect of the interdental papilla (i.e. the most coronal portion of the palatal flap which includes the interdental papilla) and the most coronal portion of the buccal flap. This suture is free of tension.

An alternative type of suture to close the interdental tissues has been proposed by Dr Lars Laurell. This modified internal mattress suture (see Fig. 38-56) starts from the external surface of the buccal flap, crosses the interdental area and gets through the lingual flap at the base of the papilla. The suture runs back through the external surface of the lingual flap and the internal surface of the buccal flap, about 3 mm apart from the first two bites. Finally, the suture is passed through the interdental area above the papillary tissues, passed through the loop of the suture on the lingual side, and brought back to the buccal side, where it is tied. This suture is very effective in ensuring stability and primary closure of the interdental tissues.

In a randomized controlled clinical study on 45 patients (Cortellini *et al.* 1995c), significantly greater amounts of PAL were gained with the MPPT (5.3 ± 2.2 mm), in comparison with either conventional GTR (4.1 ± 1.9 mm) or access flap surgery (2.5 ± 0.8 mm), demonstrating that a modified surgical approach can result in improved clinical outcomes. The sites accessed with the MPPT showed primary closure of the flap in all but one case, and no gingival dehiscence until membrane removal, in 73% of the cases.

This surgical approach has also been used in combination with non-supported bioresorbable barrier membranes (Cortellini *et al.* 1996c), with positive results. Clinical attachment level gains at 1 year were

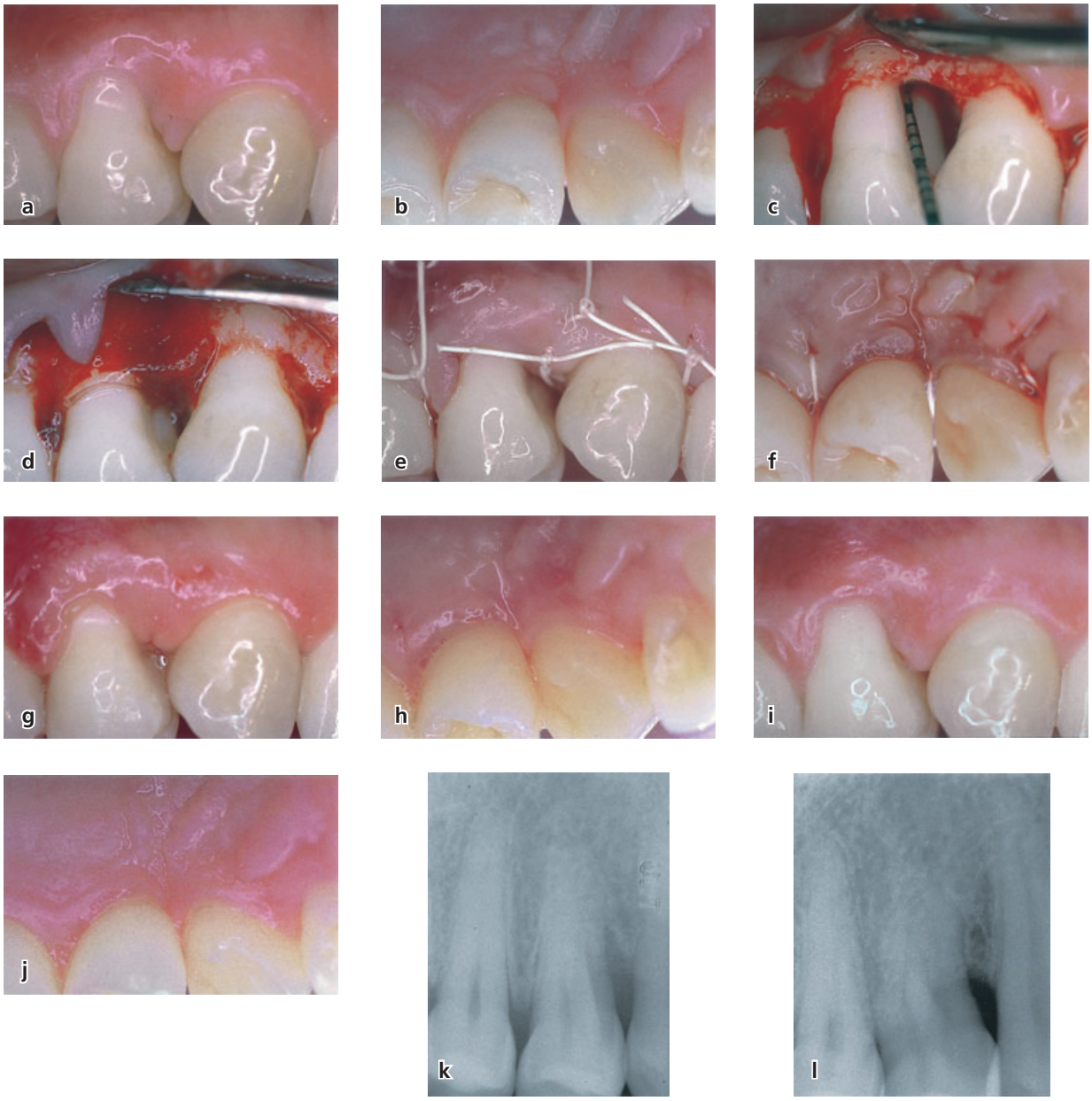


Fig. 43-15 (a) Right first maxillary premolar with a 7-mm pocket on the mesial surface. The interdental space (b) is very narrow (>2 mm), and is accessed with a simplified papilla preservation flap. The 5-mm deep intrabony defect (c) is covered with a bioresorbable barrier membrane (d). Primary closure of the flap over the membrane (e,f) is maintained over time (g,h). After 1 year, the interdental papilla is completely preserved and the residual pocket depth is 3 mm (i,j). The radiograph taken at baseline (k) compared with that taken 1 year after treatment (l) shows that the intrabony defect has healed completely.

4.5 ± 1.2 mm. In all the cases primary closure of the flap was achieved and about 80% of the sites maintained primary closure over time (Fig. 43-19). It should be underlined, however, that the horizontal internal crossed mattress suture most probably caused an apical displacement of the interdental portion of the membrane, thereby reducing the space for regeneration.

The MPPT can be successfully applied in conjunction with a variety of regenerative materials including biologically active materials such as enamel matrix derivative (EMD) (Tonetti *et al*. 2002) (Fig. 43-20) or growth factors and bone replacement grafts (Fig. 43-21) (Tonetti *et al*. 2004b; Cortellini & Tonetti 2005).

The surgical access of the interdental space with the MPPT is technically very demanding, but it has been reported to be very effective and applicable in wide interdental spaces (wider than 2 mm at interdental tissue level), especially in the anterior dentition. In properly selected cases, large amounts of attachment gain, and consistent reduction of pocket depths associated with no or minimal recession of the interdental papilla are consistently expected. It is, therefore, indicated in cases in which esthetics are particularly important.

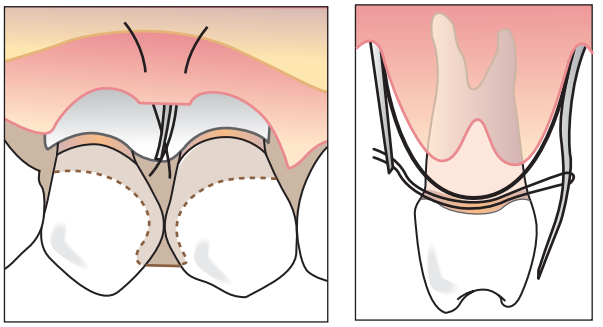


Fig. 43-16 Suture to obtain coronal positioning of the buccal flap: schematic illustration of the crossed horizontal internal mattress suture between the base of the palatal papilla and the buccal flap immediately coronal to the muco-gingival junction. Note that the suture crosses above the titanium reinforcement of the membrane. (a) Buccal view; (b) mesio-distal view. From Cortellini *et al.* (1995d) with permission from the American Academy of Periodontology.

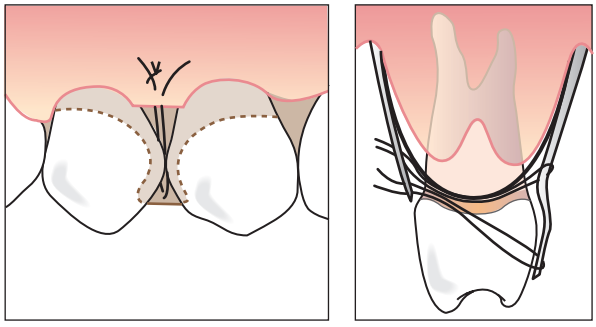


Fig. 43-17 Suture to obtain tension-free primary closure of the interdental space: schematic illustration of the vertical internal mattress suture between the most coronal portion of the palatal flap (which includes the interdental papilla) and the most coronal portion of the buccal flap. (a) Buccal view; (b) mesio-distal view. From Cortellini *et al.* (1995d) with permission from the American Academy of Periodontology.

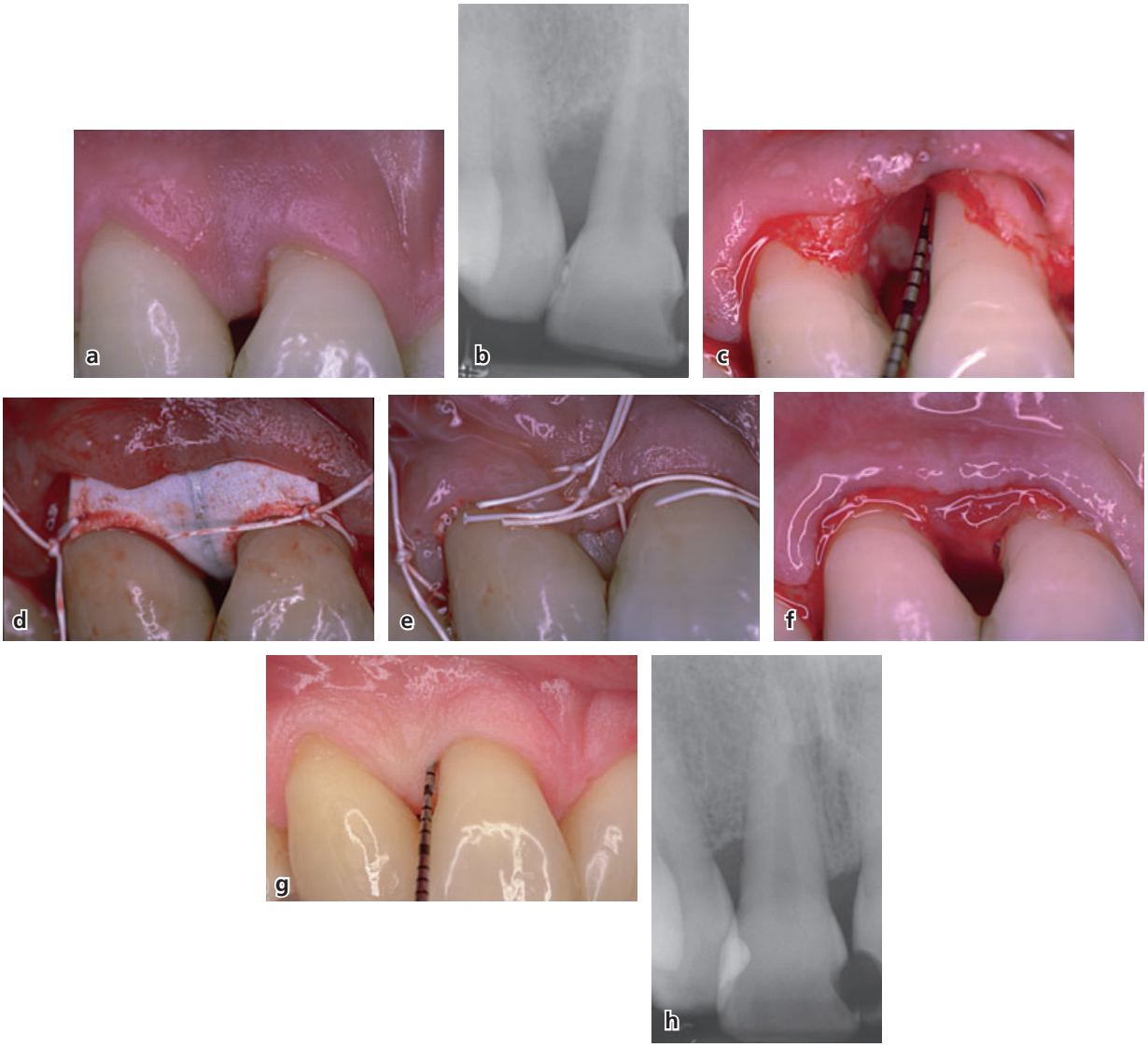


Fig. 43-18 Clinical case illustrating the operative procedure of the modified papilla preservation technique used to completely close the interdental space above a barrier membrane. Following completion of initial cause-related therapy, an 8-mm pocket associated with 2 mm of recession of the gingival margin was present on the distal of the central incisor (a). A wide intrabony defect was detectable on the radiograph (b). The defect was accessed with the modified papilla preservation technique keeping the whole interdental tissue connected with the palatal flap. A 7-mm intrabony defect was uncovered (c). Following root debridement, a titanium-reinforced barrier membrane was positioned (d). Primary closure of the interdental space was obtained by suturing back the papilla preservation flap using a multilayered suturing technique aimed at coronal advancement of the flap, complete relief of wound tension, and good flap stability (e). Six weeks thereafter, the same flap was elevated in order to remove the membrane that had remained completely submerged for the whole time. New tissue formed below the membrane was obtained with a shape that filled the space maintained under the membrane (f). Following completion of healing (1 year) a 3-mm probing depth and fill of the intrabony defect were observed. The results were maintained over time as indicated by the clinical and radiographic appearance 6 years after regeneration (g,h).

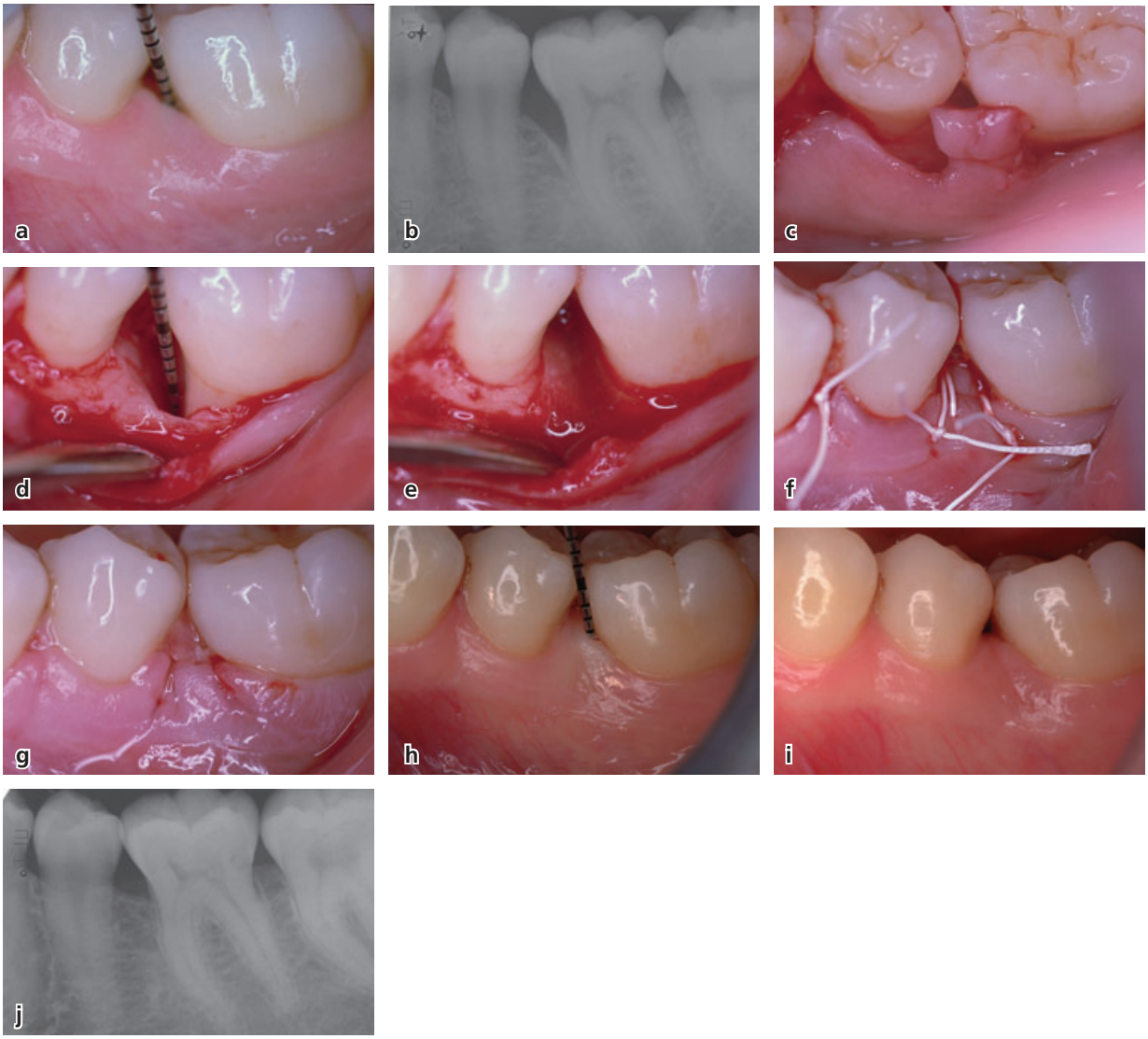


Fig. 43-19 Clinical case illustrating the application of the modified papilla preservation technique to a case treated with a resorbable barrier membrane. An 8-mm pocket associated with an intrabony defect persisted on the mesial aspect of the lower first molar following completion of initial cause-related therapy (a,b). The defect was accessed with the modified papilla preservation flap. Please note the papilla preserved attached to the lingual flap (c) as well as the presence of a 7-mm intrabony defect (d). Following root debridement, a bioresorbable barrier membrane was positioned and secured around the root of the tooth with bioresorbable sutures (e). Primary closure of the interdental space was obtained with multilayered sutures (f) and was fully maintained at the 1-week suture removal appointment (g). At 6 years, probing depths were 2–3 mm, the soft tissue profile was conducive to optimal self-performed oral hygiene measures and the radiograph showed elimination of the defect (h–j).

Simplified papilla preservation flap

To overcome some of the technical problems encountered with the MPPT (difficult application in narrow interdental spaces and in posterior areas, suturing technique not appropriate for use with non-supportive barriers) a different approach (simplified papilla preservation flap, SPPF) (Figs. 43-15, 43-22) was subsequently developed (Cortellini *et al*. 1999).

This different and simplified approach to the interdental papilla includes a first incision across the defect-associated papilla, starting from the gingival margin at the buccal-line angle of the involved tooth to reach the mid-interdental portion of the papilla under the contact point of the adjacent tooth. This oblique incision is carried out keeping the blade parallel to the long axis of the teeth in order to avoid excessive thinning of the remaining interdental tissues. The first oblique interdental incision is continued intrasulcularly in the buccal aspect of the teeth neighboring the defect. After elevation of a full-thickness buccal flap, the remaining tissues of the papilla are carefully dissected from the neighboring teeth and the underlying bone crest. The interdental papillary tissues at the defect site are gently elevated along with the lingual/palatal flap to fully expose the interdental defect. Following defect debridement and root planing, vertical releasing incisions and/or periosteal incisions are performed, when needed, to improve the mobility of the buccal flap. After

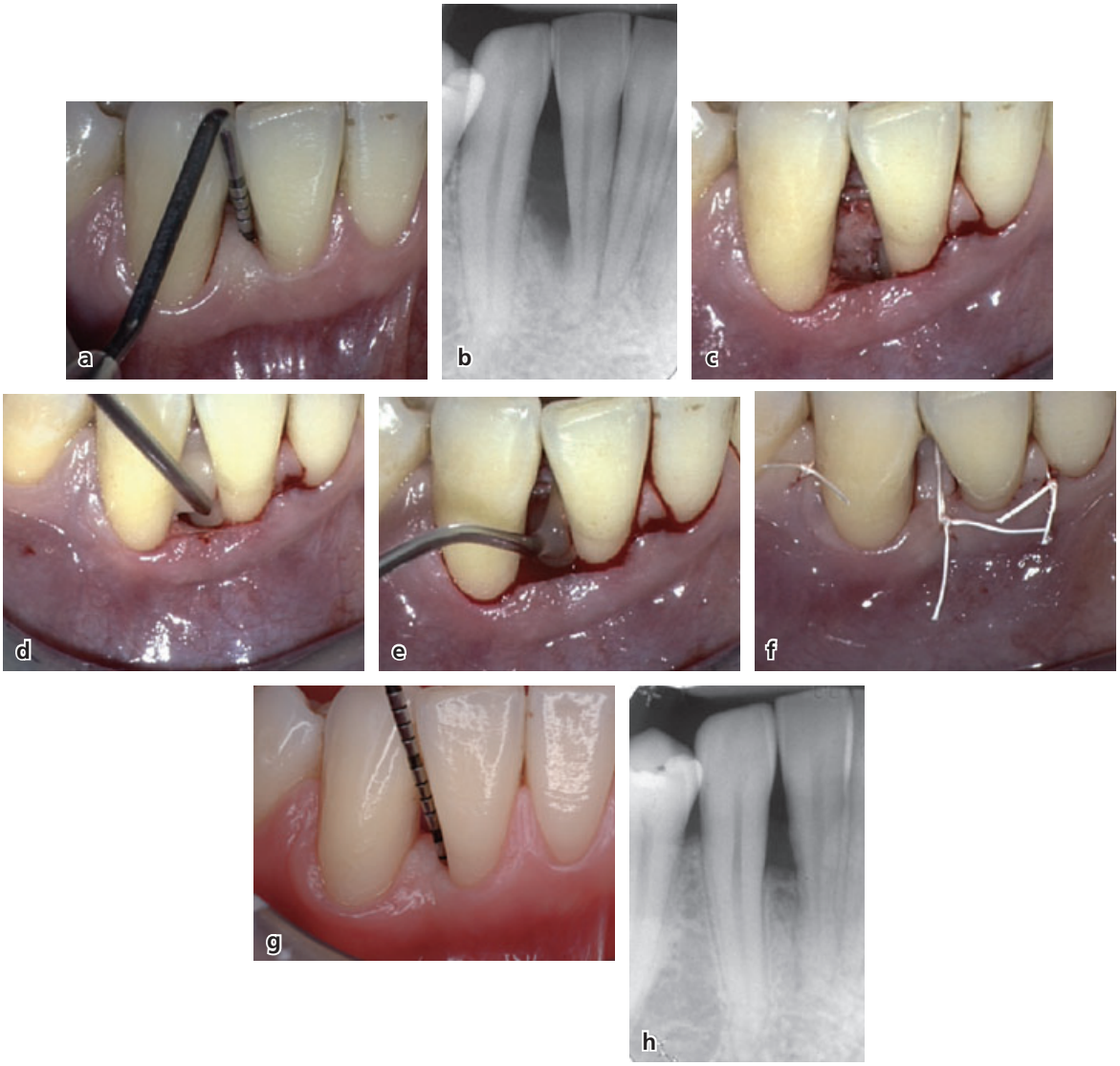


Fig. 43-20 Clinical case illustrating the application of the papilla preservation technique in conjunction with the application of enamel matrix derivative in gel form. A 10-mm pocket was detectable on the distal aspect of the lower lateral incisor following successful completion of initial cause-related therapy (a). The radiograph showed the presence of a deep intrabony defect extending to the apical third of the root (b). The defect was accessed with the modified papilla preservation technique (c) with limited mesial and distal extension of the flap. Following careful debridement, the root is conditioned with an EDTA gel according to the manufacturer's instructions for the application of enamel matrix derivative (d). After rinsing and drying of the defect and root surface, the enamel matrix derivative gel is applied on the root surface and to fill the defect (e), and flaps are sutured with a multilayer technique to achieve primary closure in the absence of tension (f). One year following regenerative surgery, shallow pockets and radiographic resolution of the defect are apparent (g,h).

application of a barrier membrane, primary closure of the interdental tissues above the membrane is attempted in the absence of tension, with the following sutures:

1. A first horizontal internal mattress suture (offset mattress suture) is positioned in the defect-associated interdental space running from the base (near to the mucogingival junction) of the keratinized tissue at the mid-buccal aspect of the tooth not involved with the defect to a symmetrical location at the base of the lingual/palatal flap. This suture frictions against the interdental root surface, hangs on the residual interdental bone crest and is anchored to the lingual/palatal flap. When tied, it allows the coronal positioning of the buccal flap. A relevant notation is that this suture, lying on the interdental bone crest, does not cause any compression at the mid-portion of the membrane, therefore preventing its collapse into the defect.
2. The interdental tissues above the membrane are then sutured to obtain primary closure with one of the following approaches: (a) one interrupted suture whenever the interdental space is narrow and the interdental tissues thin; (b) two interrupted sutures, when the interdental space is wider and the interdental tissues thicker; (c) an internal vertical/oblique mattress suture, when the interdental space is wide and the interdental tissues are thick.

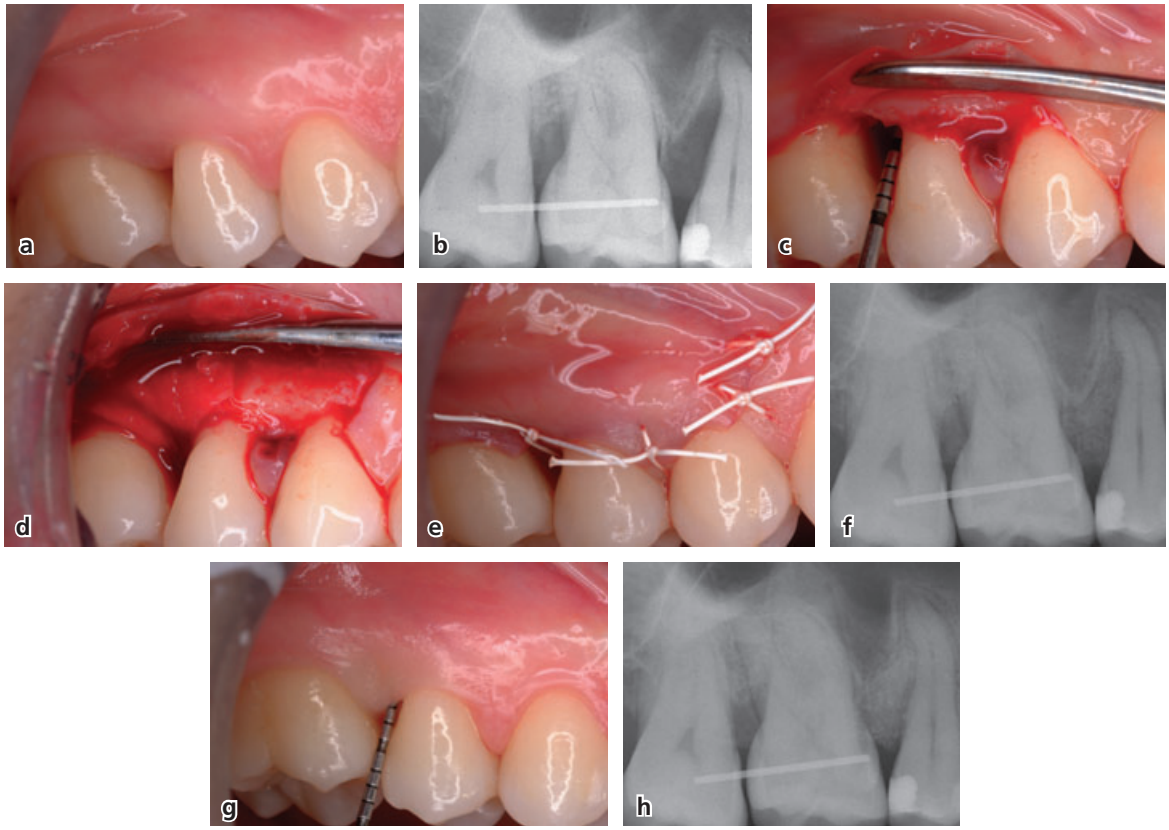


Fig. 43-21 Clinical case illustrating the application of the modified papilla preservation technique in conjunction with a bone replacement graft in combination with a bioresorbable membrane. After completion of initial cause-related therapy, a 9-mm pocket associated with an intrabony defect was present on the distal aspect of the upper second premolar (a,b). The defect reached the apical portion of the root and had a 9-mm intrabony component (c). Following careful root debridement, a bioresorbable membrane was adapted to the local anatomy and was positioned to contain the defect. A bone replacement graft was subsequently inserted under the membrane to provide additional support for the membrane and for the soft tissues (d). Primary closure was achieved with a single internal mattress suture (e). The control radiograph taken upon completion of the surgery shows the presence of the radio-opaque bone replacement graft in the defect (f). At 1-year follow-up, a 3-mm probing depth associated with resolution of the intrabony component of the defect is apparent (g,h). Please note that the radio-opaque bone replacement graft particles are still detectable but appear embedded in newly formed mineralized tissue.

Special care has to be paid to ensure that the first horizontal mattress suture would relieve all the tension of the flaps, and to obtain primary passive closure of the interdental tissues over the membrane with the last suture. When tension is observed, the sutures should be removed and the primary passive closure attempted a second time.

This approach has been preliminarily tested in a case series of 18 deep intrabony defects in combination with bioresorbable barrier membranes (Cortellini *et al*. 1999). The average clinical attachment level gain observed at 1 year was 4.9 ± 1.8 mm. In all the cases it was possible to obtain primary closure of the flap over the membrane, and 67% of the sites maintained primary closure over time. The same approach was then tested in a multi-center controlled randomized clinical trial involving 11 clinicians from seven different countries and a total of 136 defects (Tonetti *et al*. 1998). The average clinical attachment gain observed at 1 year in the 69 defects treated with the SPPF and a resorbable barrier membrane was 3 ± 1.6 mm. More than 60% of the treated sites maintained primary closure over time. It is important to underline that these results were obtained by different clinicians treating different populations of patients and defects, also involving narrow spaces and posterior areas of the mouth. The SPPF was successfully applied in conjunction with a variety of regenerative materials including biologically active materials such as EMD (Tonetti *et al.* 2002) (Fig. 43-23) and bone replacement grafts (Fig. 43-24) (Tonetti *et al*. 2004b; Cortellini & Tonetti 2004).

Minimally invasive surgical technique

In order to provide even greater wound stability and to further limit patient morbidity, a papilla preservation flap can be used in the context of a minimally invasive, high-power magnification-assisted surgical technique (Cortellini & Tonetti 2007a). Such a minimally invasive approach is particularly suited for treatment in conjunction with biologically active agents such as EMD or growth factors.

The defect-associated interdental papilla is accessed either with the simplified papilla preservation flap (SPPF) (Cortellini *et al*. 1999) or the modified

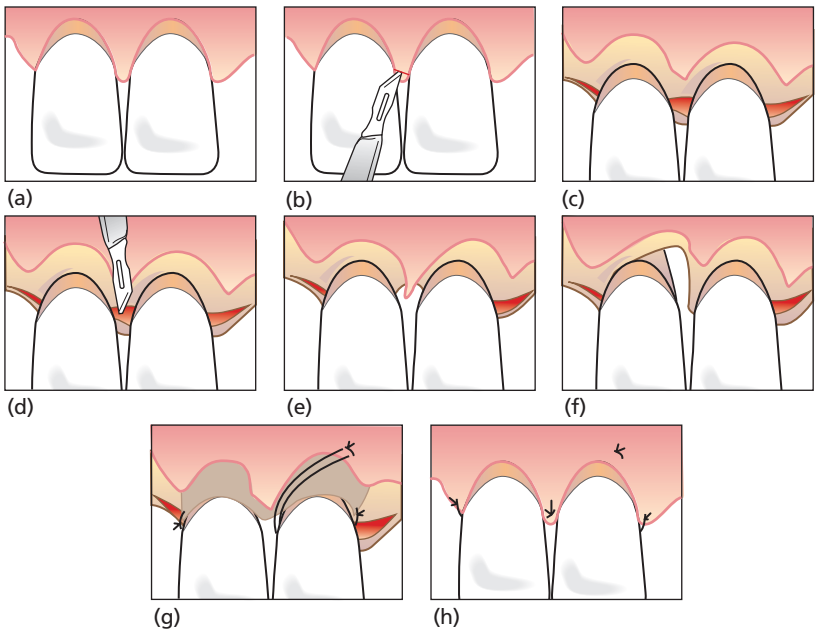


Fig. 43-22 (a) Pre-surgical appearance of the area that will be accessed with a simplified papilla preservation flap (SPPF). The defect is located on the mesial aspect of the maxillary right lateral incisor. (b) First oblique incision in the defect-associated papilla begins at the gingival margin of the mesio-buccal line angle of the lateral incisor. The blade is kept parallel to the long axis of the tooth and reaches the midpoint of the distal surface of the central incisor just below the contact point. (c) First oblique incision continues intrasulcularly in the buccal aspect of the lateral and central incisors, extending until the adjacent papillae, and a buccal full-thickness flap is elevated to expose 2–3 mm of bone. Note the defect-associated papilla still in place. (d) Bucco-lingual horizontal incision at the base of the papilla is as close as possible to the interproximal bone crest. Care is taken to avoid a lingual/palatal perforation. (e) Intrasulcular interdental incisions continue in the palatal aspect of the incisors until the adjacent partially dissected papillae. A full-thickness palatal flap including the interdental papilla is elevated. (f) Intrabony defect following debridement. Note the position of the bone crest on the distal aspect of the central incisor. (g) Membrane is positioned to cover the defect and 2–3 mm of remaining bone and secured to neighboring teeth. A horizontal internal mattress suture runs from the base of the keratinized tissue at the midbuccal side of the central incisor to a symmetric location at the base of the palatal flap. This suture causes no direct compression of the midportion of the membrane, preventing its collapse into the defect. (h) Primary closure and complete coverage of the membrane are obtained. From Cortellini *et al*. (1999) with permission from Quintessence Publishing Co. Inc.

papilla preservation technique (MPPT) (Cortellini *et al*. 1995d). The SPPF is performed whenever the width of the interdental space is 2 mm or narrower, while the MPPT is applied at interdental sites wider than 2 mm. The interdental incision (SPPF or MPPT) is extended to the buccal and lingual aspects of the two teeth adjacent to the defect. These incisions are strictly intrasulcular to preserve all the height and width of the gingiva, and their mesio-distal extension is kept at a minimum to allow the corono-apical elevation of a very small full-thickness flap with the objective of exposing just 1–2 mm of the defect-associated residual bone crest. When possible, only the defect-associated papilla is accessed and vertical releasing incisions are avoided. With these general rules in mind, different clinical pictures can be encountered in different defects.

The shortest mesio-distal extension of the incision and the minimal flap reflection occurs when the intrabony defect is a pure three-wall, or has shallow two- and/or one-wall subcomponents allocated entirely in the interdental area. In these instances the mesio-distal incision involves only the defect-associated papilla and part of the buccal and lingual aspects of the two teeth neighboring the defect. The full-thickness flap is elevated minimally, just to expose the buccal and lingual bone crest delineating the defect in the interdental area (Fig. 43-25).

A larger corono-apical elevation of the full-thickness flap is necessary when the coronal portion of the intrabony defect has a deep two-wall component. The corono-apical extension of the flap is kept to a minimum at the aspect where the bony wall is preserved (either buccal or lingual), and extends more apically at the site where the bony wall is missing (lingual or buccal), the objective being to reach and expose 1–2 mm of the residual bone crest (Fig. 43-26).

When a deep one-wall defect is approached, the full-thickness flap is elevated to the same extent on both the buccal and the lingual aspects.

When the position of the residual buccal/lingual bony wall(s) is very deep and difficult or impossible to reach with the above described minimal incision of the defect-associated interdental space, the flap(s) is(are) further extended mesially or distally involving one extra interdental space to obtain a larger flap reflection. The same approach is used when the bony

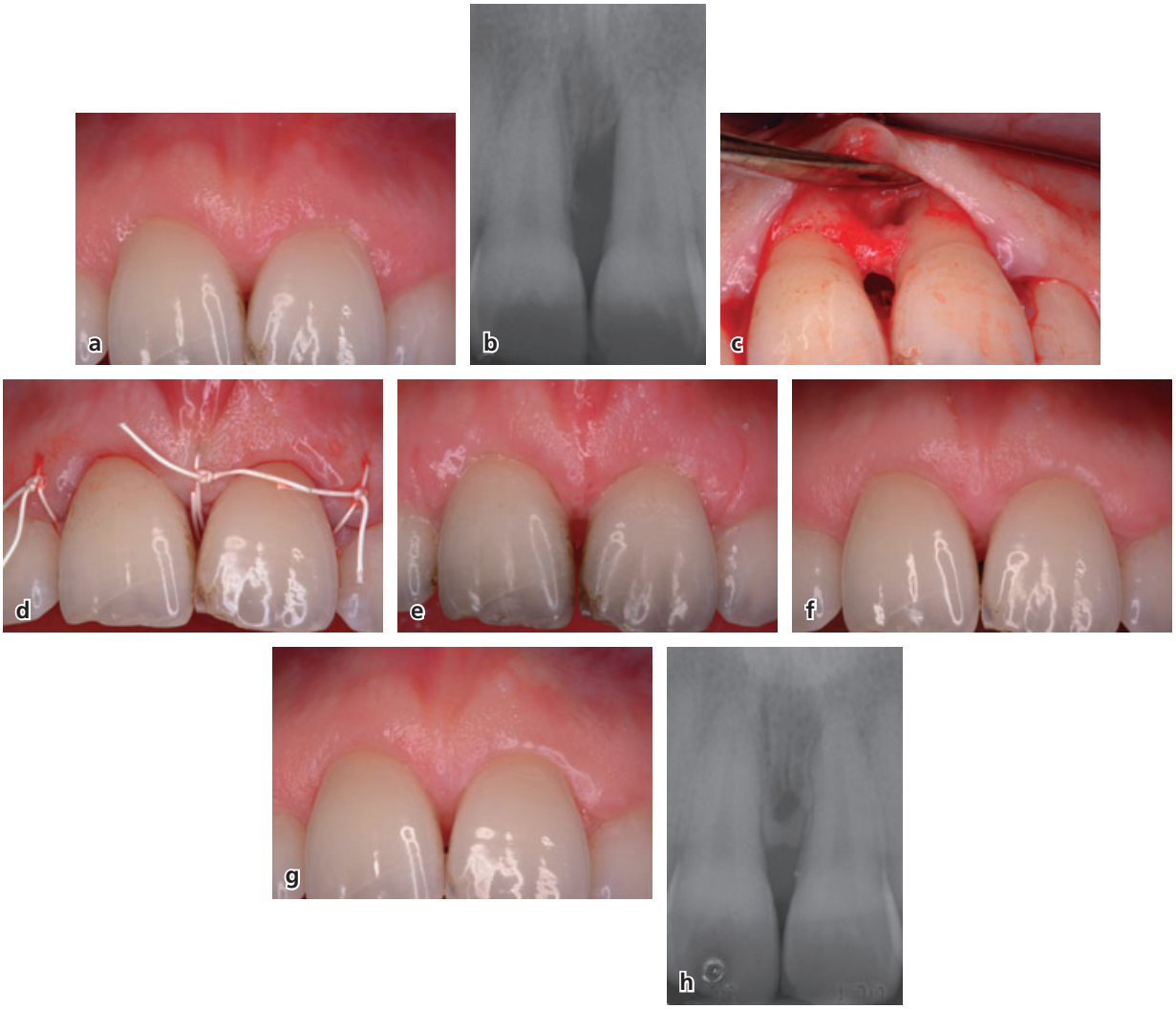


Fig. 43-23 Clinical case illustrating the clinical application of the simplified papilla preservation flap in conjunction with the application of a biologically active regenerative material (enamel matrix derivative in gel form). At re-evaluation following completion of successful initial cause-related therapy, an 8-mm pocket was detected on the mesial palatal aspect of the left central incisor (a). An angular defect was evidenced on a peri-apical radiograph (b). The complex anatomy of the defect is apparent following access to the defect with the modified papilla preservation technique: a buccal fenestration is apparent with the majority of the defect extending palatally to the apical third of the root (c). Following application of the enamel matrix derivative, primary closure of the flap was achieved with a multilayered suture (d). At the 1-week suture removal appointment, excellent maturation of the soft tissue healing is apparent (e). At 6 months, a well represented interdental papilla is present thanks to both the papilla preservation approach and the presence of a bony bridge that assisted in soft tissue support, in spite of the gel formulation of the enamel matrix derivative (f). Clinical and radiographic outcomes at 1 year show preservation of excellent esthetics and elimination of the defect (g,h). Probing depths were in the 2 to 3 mm range.

defect also extends to the buccal or the palatal side of the involved tooth, or when it involves the two interdental spaces of the same tooth (Fig. 43-27) or two approximal teeth (Fig. 43-28). In the latter instance a second interdental papilla is accessed, either with a SPPF or a MPPT, according to indications. Vertical releasing incisions are performed when flap reflection causes tension at the extremities of the flap(s). The vertical releasing incisions are always kept very short and within the attached gingiva (never involving the mucogingival junction). The overall aim of this approach is to avoid using vertical incisions whenever possible or to reduce their number and extent to a minimum when there is a clear indication for them. Periosteal incisions are never performed.

The defects are debrided with a combined use of mini curettes and power-driven instruments and the roots carefully planed. During the instrumentation the flaps are slightly reflected, carefully protected with periosteal elevators and frequent saline irrigations. At the end of instrumentation the biologically active agent is applied. Then the flaps are repositioned.

The suturing approach in most of the instances consists of a single modified internal mattress suture at the defect-associated interdental area to achieve primary closure of the papilla in the absence of any

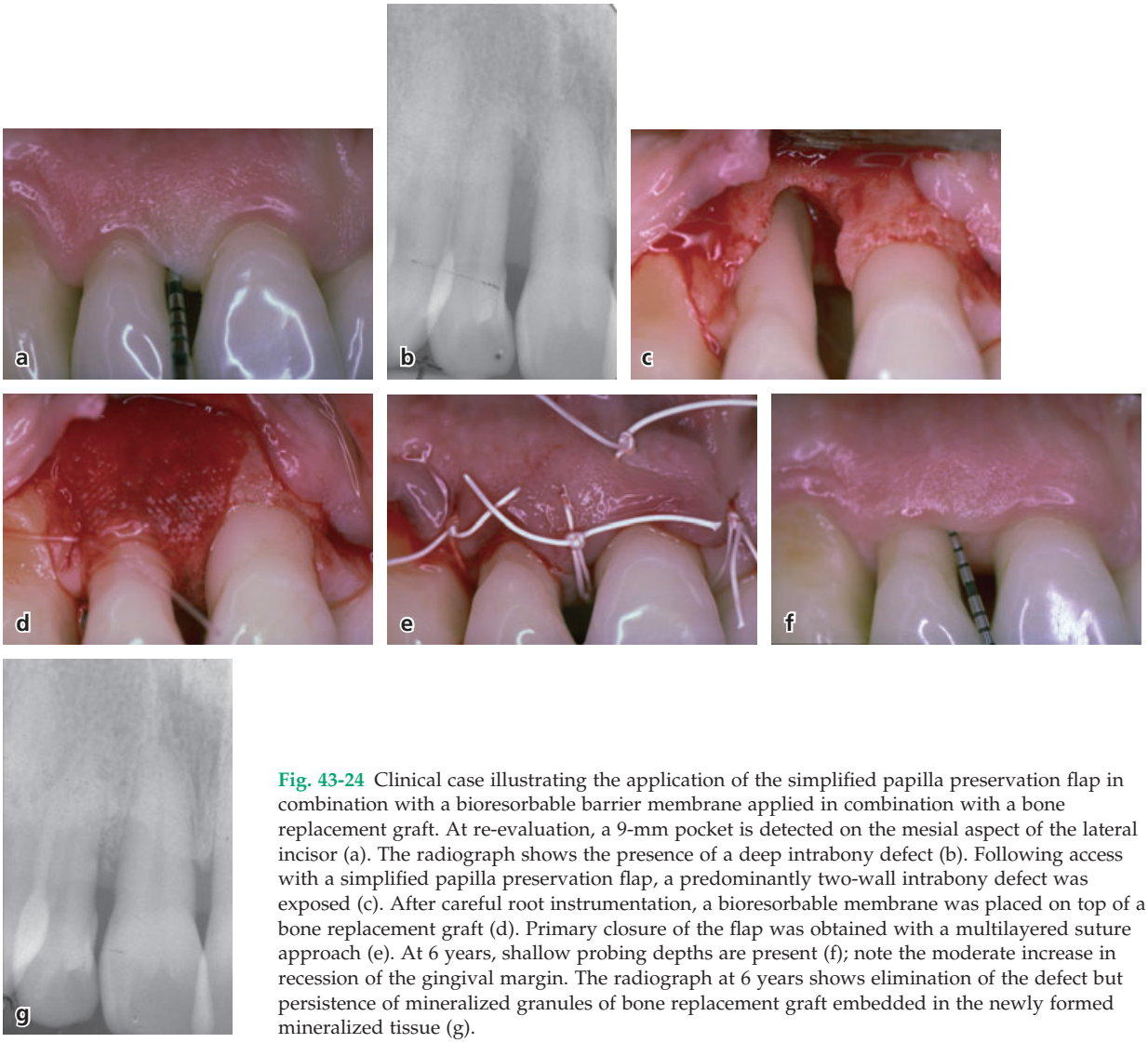


Fig. 43-24 Clinical case illustrating the application of the simplified papilla preservation flap in combination with a bioresorbable barrier membrane applied in combination with a bone replacement graft. At re-evaluation, a 9-mm pocket is detected on the mesial aspect of the lateral incisor (a). The radiograph shows the presence of a deep intrabony defect (b). Following access with a simplified papilla preservation flap, a predominantly two-wall intrabony defect was exposed (c). After careful root instrumentation, a bioresorbable membrane was placed on top of a bone replacement graft (d). Primary closure of the flap was obtained with a multilayered suture approach (e). At 6 years, shallow probing depths are present (f); note the moderate increase in recession of the gingival margin. The radiograph at 6 years shows elimination of the defect but persistence of mineralized granules of bone replacement graft embedded in the newly formed mineralized tissue (g).

tension (Cortellini & Tonetti 2001, 2005). When a second interdental space has been accessed, the same suturing technique is used to obtain primary closure in this area. Vertical releasing incisions are sutured with simple passing sutures. The buccal and lingual flaps are re-positioned at their original level, without any coronal displacement to avoid any additional tension in the healing area.

All the surgical procedures can be performed with the aid of an operating microscope or magnifying loops at a magnification of 4× to 16× (Cortellini & Tonetti 2001, 2005). Microsurgical instruments are utilized, whenever needed, as a complement to the normal set of periodontal instruments.

This approach has been preliminarly tested in two case series with a total of 53 deep intrabony defects (Cortellini & Tonetti 2007a,b). One-year results have shown clinically significant improvements (clinical attachment level gains of 4.8 ± 1.9 mm and 88.7 ± 20.7% clinical resolution of the defect) accompanied by greatly reduced morbidity.

Post-operative regime

The post-operative regime prescribed to the patients is aimed at controlling wound infection or contamination as well as mechanical trauma to the treated sites. A recent meta-analysis indicated that differences in regenerative outcomes are expected based on the post-operative care protocol: more frequent, intensive regimens were associated with better clinical attachment level gains in intrabony defects (Murphy *et al*. 2003) (Fig. 43-29). It generally includes the prescription of systemic antibiotics (doxycycline or amoxicillin) in the immediate post-operative period (1 week), 0.2 or 0.12% chlorhexidine mouthrinsing two or three times per day, and weekly professional tooth cleaning until the membrane is in place. Professional tooth cleaning consists of supragingival prophylaxis with a rubber cup and chlorhexidine gel. Patients are generally advised not to perform mechanical oral hygiene and not to chew in the treated area.

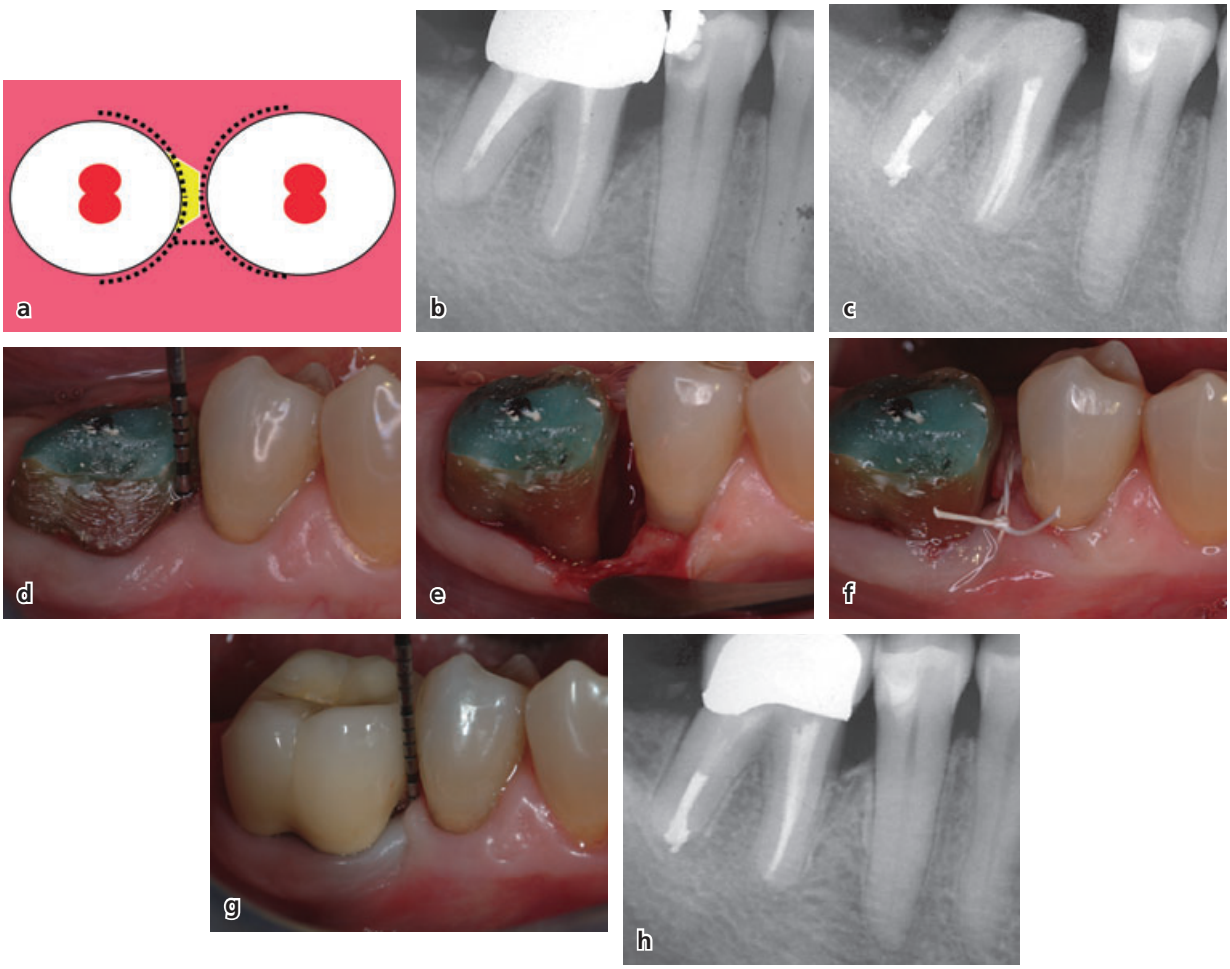


Fig. 43-25 Clinical illustration of the use of the minimally invasive surgical technique (MIST) in an isolated interdental three-wall defect. The diagram shows the extent of the incision performed according to the principles of the modified papilla preservation technique in the interdental space associated with the defect. Mesio-distal extension of the flap is limited to the buccal aspect of the teeth adjacent to the defect in order to optimize wound stability (a). The baseline radiograph shows the presence of dental diseases (peri-apical infection and caries) that need to be controlled during the initial cause-related phase of therapy (b). At re-evaluation, an 8-mm pocket associated with the presence of a deep intrabony defect was detected on the mesial aspect of the first molar (c,d). The defect was accessed in a minimally invasive fashion using a modified papilla preservation flap. The three-wall intrabony defect was exposed and carefully debrided (e). After application of enamel matrix derivative, primary closure was obtained with a single modified internal mattress suture (f). The 1-year outcomes show shallow probing depths and almost complete resolution of the defect (g,h).

Non-resorbable membranes are removed 4–6 weeks after placement, following elevation of partial-thickness flaps. Patients are re-instructed to rinse two or three times per day with chlorhexidine, not to perform mechanical oral hygiene and not to chew in the treated area for 3–4 weeks. In this period weekly professional control and prophylaxis are recommended. When bioresorbable membrane, bone replacement grafts or biologically active regenerative materials are used, the period of tight infection control regime is extended for 6–8 weeks. After this period, patients are re-instructed to resume mechanical oral hygiene gradually, including interdental cleaning, and to discontinue chlorhexidine. Patients are then enrolled in a periodontal care program on a monthly basis until 1 year. Probing or deep scaling in the treated area is generally avoided before the 1-year follow-up visit.

Post-operative morbidity

To date, little consideration has been given to critical elements that could contribute to the patient's assessment of the cost-benefit ratio of GTR procedures. These include post-operative pain, discomfort, complications, and the perceived benefits from the treatment. A parallel group, randomized, multicenter and controlled clinical trial designed to test the efficacy of GTR and flap surgery alone assessed these patient issues (Cortellini *et al*. 2001). During the procedure, 30.4% of the test and 28.6% of the controls reported moderate pain and subjects estimated the hardship of the procedure as 24 ± 25 units on a visual analog scale (VAS in a scale from 0 to 100) in the test group and 22 ± 23 VAS in the controls. Test surgery with membranes required longer chair time than flap surgery (on average 20 minutes longer). Among the

Fig. 43-26 Clinical illustration of the use of the minimally invasive surgical technique (MIST) in an isolated interdental defect extending towards the buccal aspect of the tooth. The diagram shows the extent of the incision performed according to the principles of the modified papilla preservation technique in the interdental space associated with the defect. Mesio-distal extension of the flap is limited to the buccal aspect of the teeth adjacent to the defect and to the interdental aspect adjacent to the buccal extension of the defect in order to optimize wound stability (a). Following completion of successful initial cause-related therapy, a 6-mm pocket associated with an intrabony defect was detected on the distal aspect of the lateral incisor (b,c). The attachment loss extended to the buccal aspect of the lateral incisor, suggesting the need to obtain access to the buccal aspect of this tooth. The defect was therefore accessed with a minimally invasive approach using the modified papilla preservation technique to access the interdental area and extending the incision to the papilla between the lateral and central incisors to ensure adequate access to the defect (d). Primary closure was obtained with a modified internal mattress suture and a simple passing suture (e). The 1-year outcomes show shallow probing depths, good preservation of the soft tissue heights, and resolution of the defect (f,g).

post-operative complications, edema was most prevalent at week 1 and most frequently associated with the GTR treatment, while post-operative pain was reported by fewer than 50% of both test and control patients. Pain intensity was described as mild and lasted on average 14.1 ± 15.6 hours in the test patients and 24.7 ± 39.1 hours in the controls. Post-operative morbidity was limited to a minority of subjects: 35.7% of the test and 32.1% of the controls reported that the procedures interfered with daily activities for an average of 2.7 ± 2.3 days in the test group and 2.4 ± 1.3 days in the control group. These data indicate that GTR adds almost 30 minutes to a flap procedure and is followed by a greater prevalence of post-surgical edema, while no difference could be observed between GTR and flap surgery alone in terms of post-operative pain, discomfort, and interference with daily activities.

To date, no comparative study has reported the morbidity associated with various regenerative approaches. Reports of multi-center trials on application of enamel matrix derivative or barrier membranes using the same methodology, however, show similar results for the application of these two regenerative materials (Tonetti *et al*. 1998, 2004a; Cortellini *et al*. 2001).

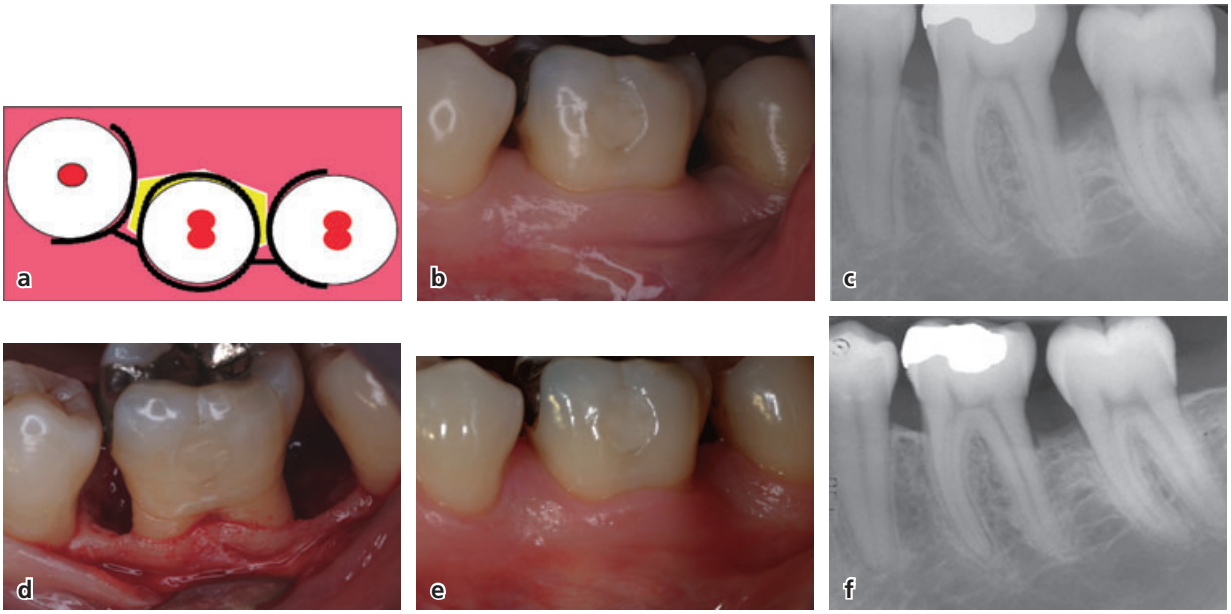


Fig. 43-27 Clinical illustration of the use of the minimally invasive surgical technique (MIST) in intrabony defects involving both interdental spaces of the same tooth. The diagram shows the extent of the incision performed according to the principles of the modified papilla preservation technique in the two interdental spaces associated with the defects. Mesio-distal extension of the flap is limited to the two interdental papillae associated with the defects (a) and reaches the line angle of the two adjacent teeth in order to limit the loss of wound stability while allowing adequate access to the defects. The clinical and radiographic appearance at baseline highlight the good control of inflammation obtained following completion of initial cause-related therapy and the presence of deep mesial and distal pockets with associated intrabony defects (b,c). Both the mesial and distal defects are accessed with papilla preservation flaps, the defects are debrided, and the root surfaces are carefully instrumented (d). Following application of enamel matrix derivative in the well contained defects, primary closure of the flap is achieved by modified internal mattress sutures. At 1-year follow-up, shallow pockets, preservation of soft tissues, and elimination of the defects are apparent (e,f).

Another important issue that has been addressed in a large multi-center trial has been the comparison of surgical complications (such as membrane exposure, flap dehiscence, or occurrence of suppuration) using resorbable barrier membranes or biologically active regenerative materials (EMD in gel form). Sanz *et al*. (2004) showed that all sites treated with membranes presented at least a surgical complication during healing, while this was observed in only 6% of sites treated with EMD. This study indicates that some regenerative materials/procedures may be less technique sensitive than others.

Barrier materials for regenerative surgery

In the first GTR attempts, a bacterial filter produced from cellulose acetate (Millipore®) was used as an occlusive membrane (Nyman *et al*. 1982; Gottlow *et al*. 1984; Magnusson *et al*. 1985b). Although this type of membrane served its purpose, it was not ideal for clinical application.

Non-absorbable materials

Later studies have utilized membranes of expanded polytetrafluoroethylene (e-PTFE) specially designed for periodontal regeneration (Gore Tex Periodontal Material®). The basic molecule of this material consists of a carbon–carbon bond with four attached fluorine atoms to form a polymer. It is inert and does not result in any tissue reaction when implanted in the body. This type of membrane persists after healing and must be removed in a second operation. Membranes of e-PTFE have been used successfully in animal experiments and in several clinical studies. From such studies it was found that for a barrier material to function optimally, it has to meet certain essential design criteria:

1. To allow for good tissue acceptance it is important that the material is biocompatible. The material should not elicit an immune response, sensitization or chronic inflammation that may interfere with healing and present a hazard to the patient. Biocompatibility, however, is a relative term since practically no materials are completely inert.
2. The material should act as a barrier to exclude undesirable cell types from entering the secluded space adjacent to the root surface. It is also considered an advantage that the material would allow the passage of nutrients and gases.
3. Tissue integration is another important property of a barrier material. Thus, tissue may grow into the material without penetrating all the way through. The goal of tissue integration is to prevent rapid epithelial downgrowth on the outer surface of the material or encapsulation of the material,

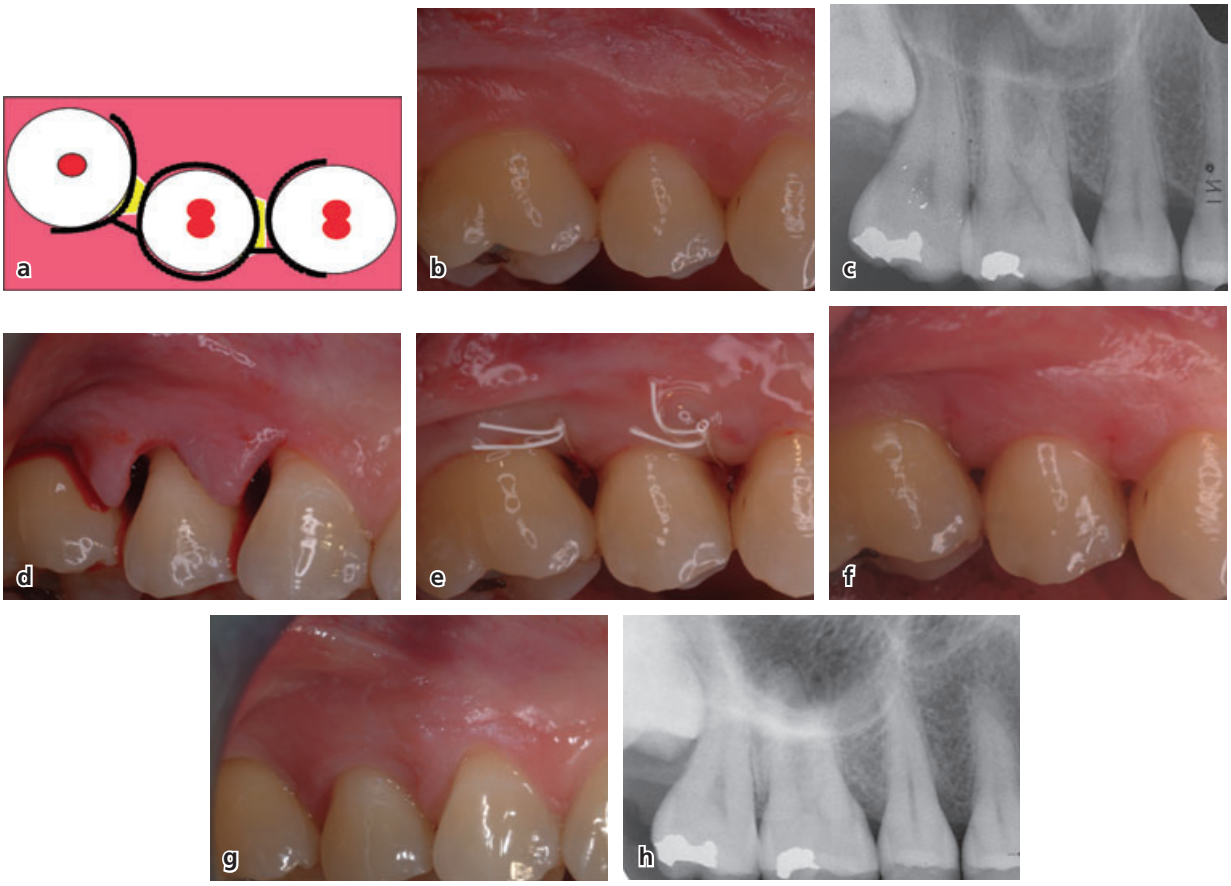
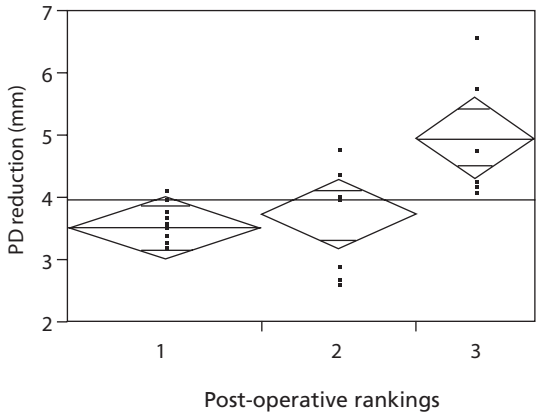


Fig. 43-28 Clinical illustration of the use of the minimally invasive surgical technique (MIST) in intrabony defects involving two adjacent teeth. The diagram shows the extent of the incision performed according to the principles of the papilla preservation flaps in the two interdental spaces associated with the defects. Mesio-distal extension of the flap is limited to the two interdental papillae associated with the defects (a) and reaches the line angle of the two adjacent teeth in order to limit the loss of wound stability and limit flap extension. After successful initial cause-related therapy, two defects are present on the mesial aspect of the first molar and second premolar (b,c). Simplified papilla preservation flaps are used to access the defects (d). Incisions are stopped at the distal line angle of the first premolar and on the buccal aspect of the first molar. Root debridement and application of enamel matrix proteins in gel form are performed before primary closure of the flap that was obtained by using two modified internal vertical mattress sutures (e). Excellent early healing in the absence of pain or discomfort is evident at the 1-week suture removal (f). At 1-year follow-up, absence of inflammation, shallow probing depths and resolution of the defects are evident (g,h).



Rank	Number of studies	Mean
1	10	3.52
2	8	3.73
3	6	4.97

Source	DF	Sum of squares	Mean square	F ratio	Prob F
Post-op rank	2	8.45	4.22	7.21	0.004
Error	21	12.29	0.58		
C. Total	23	20.75			

Fig. 43-29 Regression analysis of intrabony defect studies examining the relationship between post-operative care protocol ranking and the reduction (in mm) in probing depth (PD). Group 3 is statistically different from groups 1 and 2. From Murphy & Gunsolley (2003) with permission from the American Academy of Periodontology.

and to provide stability to the overlying flap. The importance of tissue integration was demonstrated in a study in monkeys (Warrer *et al*. 1992) in which bioabsorbable membranes of polylactic acid, a synthetic polymer, were used for treatment of circumferential periodontal defects. Due to the lack of tissue integration, the membranes in this study became surrounded by an epithelial layer and were often encapsulated and exfoliated.

4. It is also essential that the barrier material is capable of creating and maintaining a space adjacent to the root surface. This will allow the ingrowth of tissue from the periodontal ligament. Some materials may be so soft and flexible that they collapse into the defect. Other materials are too stiff and may perforate the overlying tissue.
5. Finally, there are clinical needs in the design of a barrier. It should be provided in configurations which are easy to trim and to place.

Bioabsorbable materials

In recent years, natural or synthetic bioabsorbable barrier materials for GTR have been introduced in order to avoid a second surgery for membrane removal. Barrier materials of collagen from different species and from different anatomic sites have been tested in animals and in humans (Blumenthal 1988, 1993; Pitaru *et al*. 1988; Tanner *et al*. 1988; Paul *et al*. 1992; Wang *et al*. 1994; Camelo *et al*. 1998; Mellonig 2000). Often the collagen used is a cross-linked variety of porcine or bovine origin. When a collagen membrane is implanted in the human body it is resorbed by the enzymatic activity of macrophages and polymorphnuclear leucocytes (Tatakis *et al*. 1999). Successful treatment following the use of such barrier materials has been demonstrated, but the results of the studies vary. Several complications, such as early degradation, epithelial downgrowth along the material, and premature loss of the material, were reported following the use of collagen materials. The varying results are probably due to differences in the properties of the material and the handling of the material at the time of implantation. Although probably very minimal, there is a risk that infectious agents from animal products can be transmitted to humans, and autoimmunization has also been mentioned as a risk.

Barrier materials of polylactic acid or copolymers of polylactic acid and polyglycolic acid were evaluated in animal and human studies and are commonly used (Magnusson *et al*. 1988; Caffesse *et al*. 1994; Caton *et al*. 1994; Gottlow *et al*. 1994; Laurell *et al*. 1994; Hugoson *et al*. 1995; Polson *et al*. 1995a; Hürzeler *et al*. 1997; Sculean *et al*. 1999a). These materials are biocompatible, but by definition they are not inert since some tissue reaction may be expected during degradation. The materials are degraded by hydrolysis and eliminated from the organism through the Krebs cycle as carbon dioxide and water (Tatakis *et al*. 1999).

The types of barrier materials tested in the studies differ regarding configuration and design. It appears that a number of bioabsorbable materials meet to a varying extent the requirements of a good barrier listed above. Indeed, there are several studies (Hugoson *et al*. 1995; Cortellini *et al*. 1996b; Smith *et al*. 1998; Tonetti *et al*. 1998; Cortellini & Tonetti 2000a) indicating that similar satisfactory results can be obtained with bioabsorbable barrier materials of polylactic and polyglycolic acid as with non-bioabsorbable materials.

Membranes in intrabony defects

Early evidence that GTR treatment of deep intrabony defects may produce clinical improvements in terms of clinical attachment gain was presented in several case reports (Nyman *et al*. 1982; Gottlow *et al*. 1986; Becker *et al*. 1988; Schallhorn & McClain 1988; Cortellini *et al*. 1990). In recent years, a number of clinical investigations have reported on a total of 1283 intrabony defects treated with GTR (Table 43-2). In these studies, the issue of evaluating the predictability of the clinical outcomes following application of GTR procedures was addressed. The weighted mean of the reported results indicates a mean gain in clinical attachment of 3.8 ± 1.7 mm, with a 95% confidence interval ranging from 3.7–4.0 mm (Cortellini & Tonetti 2000a). The reported clinical attachment gains following GTR treatment were significantly larger than the ones obtained from conventional flap surgery. A recent review (Lang 2000) on flap surgery reported a weighted mean of 1172 defects in 40 studies. CAL gains were 1.8 ± 1.4 mm, with a 95% confidence interval ranging from 1.6–1.9 mm.

Different types of non-bioabsorbable (Fig. 43-30) and bioabsorbable (Fig. 43-31) barrier materials were used in the studies summarized in Table 43-2. A subset analysis indicated that cases treated with non-bioabsorbable barrier materials (351 defects) showed a mean gain in clinical attachment of 3.7 ± 1.7 mm which did not differ from that obtained with bioabsorbable barrier materials of 3.6 ± 1.5 mm (592 defects).

Analysis of the results reported in some of the studies in Table 43-2 (i.e. 211 defects in 9 investigations: Proestakis *et al*. 1992; Cortellini *et al*. 1993b, 1995c, 1996b; Cortellini & Pini-Prato 1994; Laurell *et al*. 1994; Mattson *et al*. 1995; Mellado *et al*. 1995; Tonetti *et al*. 1996b) provides important information regarding the predictability of GTR in intrabony defects. Gains of 2–3 mm were observed in 29.2% of the defects, gains of 4–5 mm in 35.4% of the defects, and gains of 6 mm or more in 24.9% of the defects. Only in 10.5% of the treated defects was the gain less than 2 mm, while no change or attachment loss was observed in two cases.

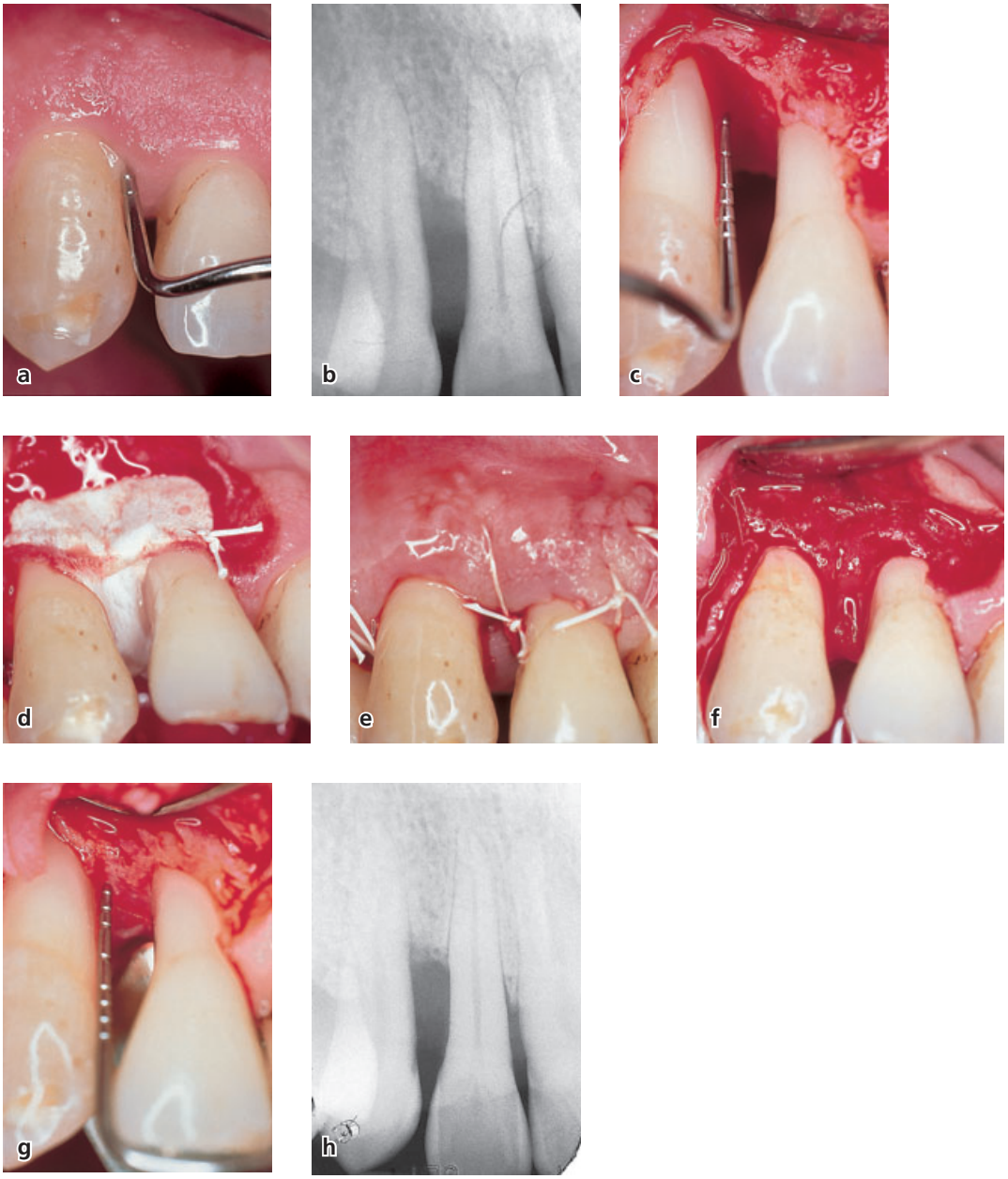


Fig. 43-30 Intrabony defect on the mesial aspect of a right maxillary canine treated with a non-bioabsorbable barrier membrane. (a) The pocket depth is 9 mm and the loss of clinical attachment is 10 mm. (b) Radiograph showing the presence of an interproximal intrabony defect. (c) After full-thickness flap elevation, defect debridement, and root planing, a 4-mm intrabony defect is evident. (d) An e-PTFE non-bioabsorbable barrier membrane has been tailored, positioned and tightly sutured around the teeth adjacent to the defect. (e) The flap has been repositioned and sutured to cover the membrane. Optimal preservation of the soft tissues has been accomplished with an intrasulcular incision. (f) After removal of the membrane at 5 weeks, the defect appears to be completely filled with newly formed tissue. (g) The treated site has been surgically re-entered after 1 year. The intrabony defect is completely filled with bone. (h) The 1-year radiograph confirms the complete resolution of the intrabony defect.

In some of the investigations, changes in bone levels were also reported (Becker *et al*. 1988; Handelsman *et al*. 1991; Kersten *et al*. 1992; Cortellini *et al*. 1993b,c; Selvig *et al*. 1993). Bone gains ranged between 1.1 and 4.3 mm and correlated with the reported gains in clinical attachment. In a study by Tonetti *et al*. (1993b), 1 year after GTR the bone was found to be located 1.5 mm apically to the position of the attained clinical attachment level.

Another important parameter related to the outcome of regenerative procedures is the residual pocket depth. In the studies reported in Table 43-2, shallow pockets were consistently found at 1 year. The weighted mean of residual pocket depth was 3.4 ± 1.2 mm, with a 95% CI ranging from 2.3–3.5 mm.

The reported outcomes indicate that GTR procedures predictably result in clinical improvements in intrabony defects beyond that of flap surgery. This was further confirmed in 11 controlled randomized clinical trials in which guided tissue regeneration was compared with conventional flap surgery (Table 43-3). A total of 267 defects were treated with flap

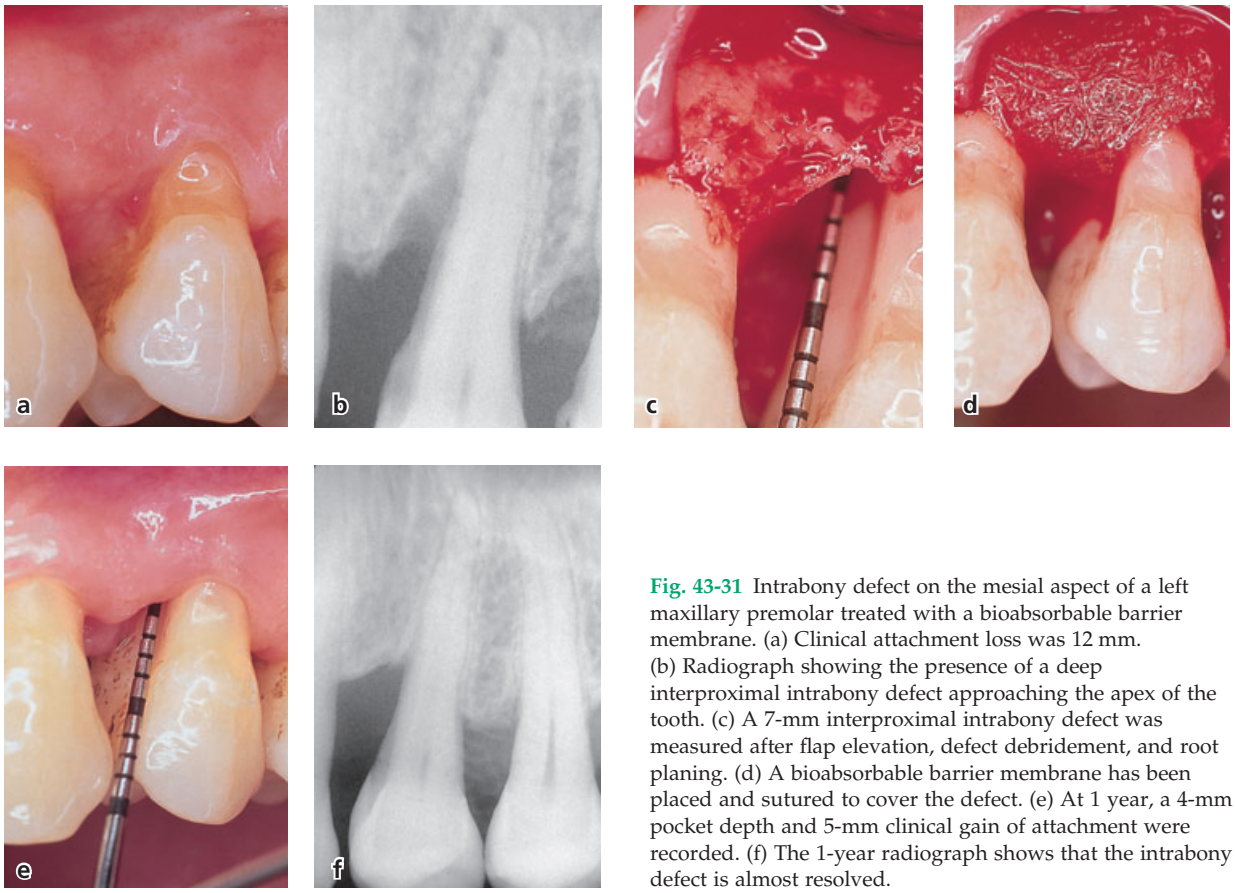


Fig. 43-31 Intrabony defect on the mesial aspect of a left maxillary premolar treated with a bioabsorbable barrier membrane. (a) Clinical attachment loss was 12 mm. (b) Radiograph showing the presence of a deep interproximal intrabony defect approaching the apex of the tooth. (c) A 7-mm interproximal intrabony defect was measured after flap elevation, defect debridement, and root planing. (d) A bioabsorbable barrier membrane has been placed and sutured to cover the defect. (e) At 1 year, a 4-mm pocket depth and 5-mm clinical gain of attachment were recorded. (f) The 1-year radiograph shows that the intrabony defect is almost resolved.

surgery and 317 with GTR. In 9 of the 11 investigations, GTR resulted in statistically significantly greater probing attachment level gains when compared to flap surgery. Similar results were also observed for residual pocket depth. It should be emphasized that one of the investigations reporting no significant differences between GTR and flap surgery was carried out in only nine pairs of defects (18 defects) located on maxillary premolars (Proestakis *et al*. 1992). In this study the intrabony component of the defects was shallow and 10 of the 18 defects had a furcation involvement. The weighted mean of the results reported in the 11 studies listed in Table 43-3 (Cortellini & Tonetti 2000a) indicated that the gain in clinical attachment in sites treated with GTR was 3.3 ± 1.8 mm (95% CI 2.8–3.6 mm), while the flap surgery resulted in a mean gain of 2.1 ± 1.5 mm (95% CI 1.8–2.4 mm). These clinical results strongly indicate that there is an added beneficial effect of placing a barrier material over an intrabony defect in conjunction with surgery.

Membranes for furcation involvement

The invasion of the furcation area of multi-rooted teeth by periodontitis represents a serious complication in periodontal therapy. The furcation area is often inaccessible to adequate instrumentation, and the roots frequently present concavities and furrows which make proper cleaning of the area impossible (see Chapter 39). As long as the pathologic process only extends a small distance (<5 mm; degree I and II involvements) into the furcation area, further progress of the disease can usually be prevented by scaling and root planing, provided a proper oral hygiene program is established after treatment. In more advanced cases (5–6 mm; degree II involvements), the initial cause-related treatment is frequently supplemented with surgery involving contouring of the inter-radicular bone (osteoplasty) or reduction of the tooth prominence at the furcation entrance by grinding (odontoplasty), in order to reduce the horizontal extension of the furcation involvement. In cases where the involvement extends deeper into the furcation area (>5 mm; degree II involvements), or a through-and-through defect (degree III involvements) has developed, tunnel preparation or root resection have been advocated as the choice of treatment. However, both of these latter treatments involve a risk of complications on a long-term basis. Following tunnel preparation, caries frequently develops in the furcation area and root-resected teeth often present complications of non-periodontal nature, although controversial reports exist regarding the long-term results of these treatment modalities (Hamp *et al*. 1975; Langer *et al*. 1981; Erpenstein 1983; Bühler 1988; Little *et al*. 1995; Carnevale *et al*. 1998).

Considering the complexity of current techniques for the treatment of furcation problems, and in view

Table 43-3 Controlled clinical trials comparing clinical outcomes of GTR procedures with access flap procedures in deep intrabony defects

Authors	Membranes	N	Gains in CAL ± SD (mm)		Residual PPD ± SD (mm)	
			GTR	Access flap	GTR	Access flap
Chung *et al*. 1990	Collagen	10	0.6 ± 0.6			
	Collagen	9	2.4 ± 2.1		4.0 ± 1.1	
	Control	14		–0.7 ± 0.9		
Proestakis *et al*. 1992	e-PTFE	9	1.2 ± 1.3		3.5 ± 0.9	
	Control	9		0.6 ± 1.0		3.7 ± 3.0
Quteish & Dolby 1992	Collagen	26	3.0 ± 1.5		2.2 ± 0.4	
	Control	26		1.8 ± 0.9		3.4 ± 0.6
Al-Arrayed *et al*. 1995	Collagen	19	3.9		2.5	
	Control	14		2.7		3.5
Cortellini *et al*. 1995c	e-PTFE	15	4.1 ± 1.9		2.7 ± 1.0	
	e-PTFE+titanium	15	5.3 ± 2.2		2.1 ± 0.5	
	Control	15		2.5 ± 0.8		3.7 ± 1.3
Mattson *et al*. 1995	Collagen	13	2.5 ± 1.5		3.6 ± 0.6	
	Control	9		0.4 ± 2.1		4.5 ± 1.8
Cortellini *et al*. 1996b	e-PTFE	12	5.2 ± 1.4		2.9 ± 0.9	
	Polylactic acid	12		4.6 ± 1.2		3.3 ± 0.9
	Control	12		2.3 ± 0.8		4.2 ± 0.9
Tonetti *et al*. 1998	Polylactic acid	69	3.0 ± 1.6		4.3 ± 1.3	
	Control	67		2.2 ± 1.5		4.2 ± 1.4
Pontoriero *et al*. 1999	Diff. barriers	30	3.1 ± 1.8		3.3 ± 1.3	
	Control	30		1.8 ± 1.5		4.0 ± 0.8
Ratka-Kruger *et al*. 2000	Polylactic acid	23	3.1 ± 2.3		4.7 ± 1.4	
	Control	21		3.3 ± 2.7		4.9 ± 2.1
Cortellini *et al*. 2001	Polylactic acid	55	3.5 ± 2.1		3.8 ± 1.5	
	Control	54		2.6 ± 1.8		4.7 ± 1.4
Weighted mean		**584**	**3.3 ± 1.8**	**2.1 ± 1.5**	**3.5 ± 1.1**	**4.1 ± 1.3**

CAL = clinical attachment level; PPD = probing pocket depth; SD = standard deviation.

of the long-term results and complications reported following treatment of advanced furcation involvements by traditional resective therapy, predictable regeneration of the periodontium at furcation-involved sites would represent a considerable progress in periodontics.

Mandibular degree II furcations

Pontoriero *et al*. (1988) reported a controlled randomized clinical trial in which significantly greater amounts of horizontal clinical attachment (H-CAL) gain (3.8 ± 1.2 mm) were obtained in 21 mandibular degree II furcations treated with e-PTFE membranes compared to those in a control group treated with open flap debridement alone (H-CAL gains of 2.0 ± 1.2 mm). Complete closure of the furcation was observed in 67% of the test sites and in only 10% of the control sites. Other studies, however, have failed to confirm these promising results to the same extent (Becker *et al*. 1988; Lekovic *et al*. 1989; Caffesse *et al*. 1990). Analysis of a series of studies published between 1988 and 1996 demonstrates a great variability in the clinical outcomes (Figs. 43-32, 43-33). Table 43-4 summarizes the outcomes of 21 clinical trials in which a total of 423 mandibular degree II furcations were treated with different types of non-bioabsorbable and bioabsorbable barrier membranes. The weighted mean of the reported results shows a H-CAL gain of 2.3 ± 1.4 mm with a 95% confidence interval ranging from 2.0–2.5 mm in defects with a baseline horizontal probing depth of 5.4 ± 1.3 mm. The reported number of complete furcation closures after GTR range from 0–67%. In three studies none of the treated furcations were closed (Becker *et al*. 1988; Yukna 1992; Polson *et al*. 1995b), in seven studies fewer than 50% were closed (Schallhorn & McClain 1988; Blumenthal 1993; Bouchard *et al*. 1993; Parashis & Mitsis 1993; Laurell *et al*. 1994; Mellonig *et al*. 1994; Hugoson *et al*. 1995), and in only one study were more than 50% of the treated furcations completely resolved (Pontoriero *et al*. 1988).

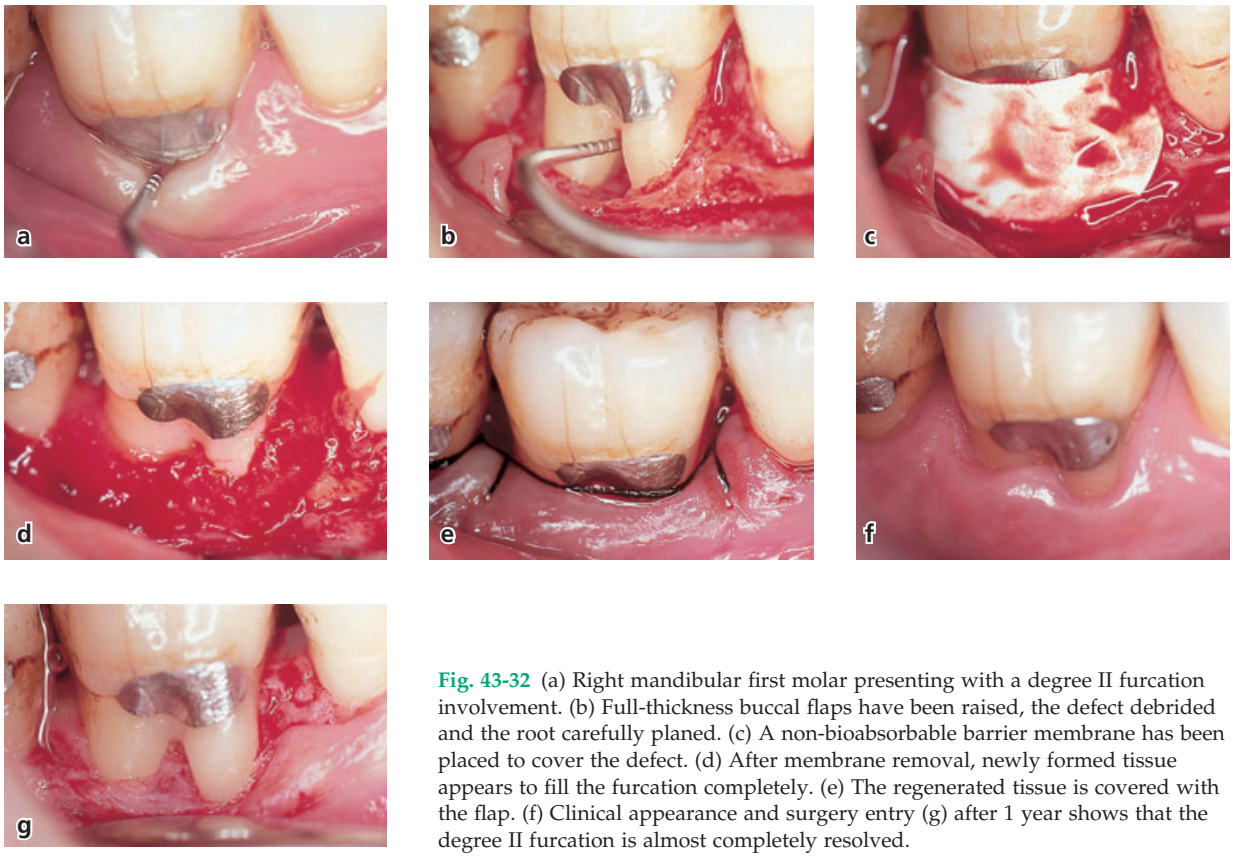


Fig. 43-32 (a) Right mandibular first molar presenting with a degree II furcation involvement. (b) Full-thickness buccal flaps have been raised, the defect debrided and the root carefully planed. (c) A non-bioabsorbable barrier membrane has been placed to cover the defect. (d) After membrane removal, newly formed tissue appears to fill the furcation completely. (e) The regenerated tissue is covered with the flap. (f) Clinical appearance and surgery entry (g) after 1 year shows that the degree II furcation is almost completely resolved.

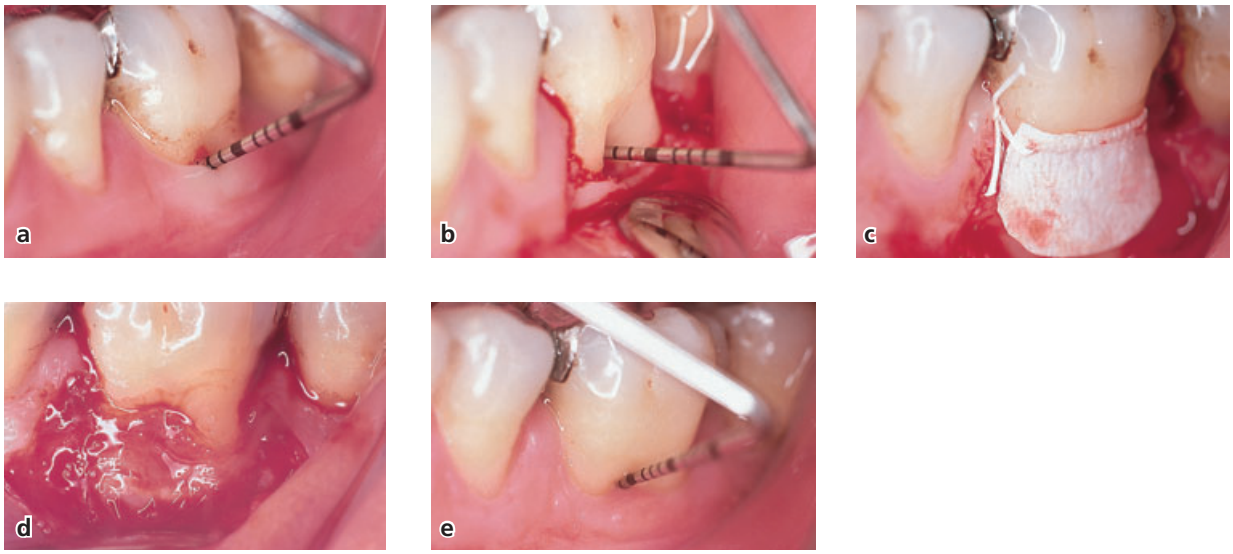


Fig. 43-33 (a) Left mandibular first molar presenting with a deep degree II furcation involvement. (b) Horizontal loss of tooth support of 7 mm was probed. (c) An e-PTFE barrier membrane has been trimmed and sutured to cover the furcation. (d) At membrane removal after 5 weeks, newly formed tissue fills the furcation completely. (e) At 1 year, a 3-mm gain of tooth support was measured, but a residual 4-mm degree II furcation involvement was still present.

A subset analysis of the studies reported in Table 43-4 indicated that furcations treated with non-bioabsorbable barrier membranes (287) showed a gain in horizontal clinical attachment of 1.8 ± 1.4 mm (95% CI 1.5–2.1 mm) as compared with 2.3 ± 1.2 mm H-CAL gain (95% CI 2–2.6 mm) in 174 defects treated with bioabsorbable barrier membranes. Five controlled clinical trials compared treatment with non-resorbable e-PTFE membranes and treatment with different types of bioabsorbable membranes (Table 43-5). In particular, one investigation reported significantly greater H-CAL gain in the non-bioabsorbable group (Bouchard *et al*. 1993), while another one (Hugoson *et al*. 1995) showed a significantly greater H-CAL gain in the bioabsorbable group. The remaining three investigations failed to

Table 43-4 Clinical outcomes and weighted mean of GTR treatment of mandibular degree II furcations

Authors	Type of study	Treatment	N	Defect depth (mm)	H-CAL gain (mm)	H-OPAL gain (mm)	No. of furca closed
Pontoriero *et al*. 1988	Controlled clinical trial	e-PTFE	21	4.4 ± 1.2	3.8 ± 1.2	NA	14 (67%)
Becker *et al*. 1988	Case cohort	e-PTFE	6	8.3 ± 2.3	NA	1.8 ± 1.5	0
Schallhorn & McClain 1988	Case cohort	e-PTFE	16	NA	NA	3.1 ± 1.7	5 (31%)
Lekovic *et al*. 1989	Controlled clinical trial	e-PTFE	6	NA	NA	0.2 ± 0.5	NA
Lekovic *et al*. 1990	Controlled clinical trial	e-PTFE	15	4.2 ± 0.2	NA	0.1 ± 0.1	NA
Caffesse *et al*. 1990	Controlled clinical trial	e-PTFE	9	4.8 ± ?	0.8 ± ?	NA	NA
Anderegg *et al*. 1991	Controlled clinical trial	e-PTFE	15	4.2 ± 2.2	NA	1.0 ± 0.8	NA
Yukna 1992	Controlled clinical trial	e-PTFE	11	3.0 ± ?	NA	1.0 ± ?	0
		FDDMA	11	4.0 ± ?	NA	2.0 ± ?	0
Blumenthal 1993	Controlled clinical trial	e-PTFE	12	4.4 ± 0.9	1.8 ± 1	1.7 ± 0.5	4 (33%)
		Collagen	12	4.5 ± 0.9	2.5 ± 0.8	2.5 ± 0.7	1 (8%)
Bouchard *et al*. 1993	Controlled clinical trial	e-PTFE	12	NA	2.8 ± 1.3	2.2 ± 1.4	4 (33%)
		Conn. graft	12	NA	1.5 ± 1.5	1.5 ± 1.1	2 (17%)
Machtei *et al*. 1993	Controlled clinical trial	e-PTFE	18	NA	2.3 ± 1.7	NA	NA
Parashis & Mitsis 1993	Controlled clinical trial	e-PTFE	9	5.7 ± 0.7	4.7 ± 1.5	NA	4 (44%)
Van Swol *et al*. 1993	Controlled clinical trial	Collagen	28	5.1 ± 1.4	2.3 ± 1	1.7 ± ?	NA
Wallace *et al*. 1994	Controlled clinical trial	e-PTFE	7	NA	NA	2.3 ± ?	NA
Black *et al*. 1994	Controlled clinical trial	e-PTFE	13	4.3 ± 2	0.8 ± 2.2	NA	NA
		Collagen	13	4.4 ± 1.5	1.5 ± 2	NA	NA
Laurell *et al*. 1994	Case cohort	Polylactic acid	19	NA	3.3 ± 1.4	NA	9 (47%)
Machtei *et al*. 1994	Controlled clinical trial	e-PTFE	30	7.7 ± 1.8	2.6 ± 1.7	NA	NA
Mellonig *et al*. 1994	Controlled clinical trial	e-PTFE	11	8.4 ± 1.2	NA	4.5 ± 1.6	1 (9%)
Wang *et al*. 1994	Controlled clinical trial	Collagen	12	6.0 ± 2.7	2.0 ± 0.4	2.5 ± ?	NA
Hugoson *et al*. 1995	Controlled clinical trial	e-PTFE	38	5.9 ± 1.3	1.4 ± 2.2	NA	4 (11%)
		Polylactic acid	38	5.6 ± 1.4	2.2 ± 2	NA	13 (34%)
Polson *et al*. 1995	Case cohort*	Polylactic Acid	29	5.4 ± 0.2	2.5 ± 0.1	NA	0
Weighted mean			**423**	**5.4 ± 1.3**†	**2.3 ± 1.4**‡	**1.9 ± 1**§	

H-CAL = horizontal clinical attachment; H-OPAL = horizontal open probing attachment; NA = data not available; e-PTFE = expanded polytetrafluoroethylene; FDDMA = freeze-dried dura mater allograft; Conn. graft = connective tissue graft.
* Mandibular and maxillary molars.
† N = Mean (340) ± S.D. (302); ‡ N = Mean (325) ± S.D. (316); § N = Mean (186) ± S.D. (177).

Table 43-5 Controlled clinical trials comparing clinical outcomes of GTR procedures with e-PTFE non-bioabsorbable barrier membranes with different types of bioabsorbable barrier membranes in mandibular degree II furcations

Authors	Design & treatment (GTR C/GTR T)	N C/T	Defect depth (mm)		H-CAL gain (mm)		H-OPAL gain (mm)	
			GTR C	GTR T	GTR C	GTR T	GTR C	GTR T
Yukna 1992	Intra-individual (e-PTFE/FDDMA)	11/11	3.0 ± ?	4.0 ± ?	NA	NA	1.0 ± ?	2.0 ± ?
Blumenthal 1993	Intra-individual (e-PTFE/collagen)	12/12	4.4 ± 0.9	4.5 ± 0.9	1.8 ± 1	2.5 ± 0.8	1.7 ± 0.5	2.5 ± 0.7
Bouchard *et al*. 1993	Intra-individual (e-PTFE/conn. graft)	12/12	NA	NA	2.8 ± 1.3*	1.5 ± 2	2.2 ± 1.4	1.5 ± 1.1
Black *et al*. 1994	Intra-individual (e-PTFE/collagen)	13/13	4.3 ± 2	4.4 ± 1.5	0.8 ± 2.2	1.5 ± 2	NA	NA
Hugoson *et al*. 1995	Intra-individual (e-PTFE/polytetrafluoroethylene)	38/38	5.9 ± 1.3	5.6 ± 1.4	1.4 ± 2.2*	2.2 ± 2.0*	NA	NA
Weighted mean		**86/86**	**4.9 ± 1.4**†	**5 ± 1.3**†	**1.6 ± 1.9**‡	**2 ± 1.7**‡1	**1.3 ± 1**§	**1.4 ± 0.9**§

GTR C = guided tissue regeneration control treatment; GTR T = guided tissue regeneration test treatment; N C/T = number of defects in the control (C) and in the test (T) treatment arm; H-CAL = horizontal clinical attachment; H-OPAL = horizontal open probing attachment; NA = data not available; e-PTFE = expanded polytetrafluoroethylene; FDDMA = freeze-dried dura mater allograft; Conn. graft = connective tissue graft.
* Difference between treatments statistically significant.
† N = Mean (74) ± S.D. (63); ‡ N = Mean (75) ± S.D. (75); § N = Mean (35) ± S.D. (24).

detect any significant differences between the outcomes of treatment with bioabsorbable or non-bioabsorbable membranes. Generally the results indicate that the predictability of GTR in the treatment of mandibular degree II furcations is questionable, if the treatment objective is the complete resolution of the furcation involvement.

Significant gain in vertical attachment level (VCAL) and reduction in pocket depth (PPD) was also reported by several investigators following treat-

Table 43-6 Controlled clinical trials comparing clinical outcomes of GTR procedures with access flap procedures in mandibular degree II furcations

Authors	Design (GTR treatment)	N C/T	Defect depth (mm)		H-CAL gain (mm)		H-OPAL gain (mm)	
			Access flap	GTR	Access flap	GTR	Access flap	GTR
Pontoriero *et al*. 1988	Intra-individual (e-PTFE)	21/21	4.0 ± 0.8	4.4 ± 1.2	2.0 ± 1.2*	3.8 ± 1.2*	NA	NA
Lekovic *et al*. 1989	Intra-individual (e-PTFE)	6/6	NA	NA	NA	NA	–0.1 ± 0.3	0.2 ± 0.5
Caffesse *et al*. 1990	Parallel (e-PTFE)	6/9	5.3 ± ?	4.8 ± ?	0.3 ± ?	0.8 ± ?	NA	NA
Van Swol *et al*. 1993	Parallel (collagen)	10/28	5.7 ± 2.5	5.1 ± 1.4	0.7 ± 1.2*	2.3 ± 1*	0.8 ± ?	1.7 ± ?
Mellonig *et al*. 1994	Intra-individual (e-PTFE)	6/6	7.5 ± 2.3	8.4 ± 1.2	NA	NA	1.1 ± 1.3*	4.5 ± 1.6*
Wang *et al*. 1994	Intra-individual (collagen)	12/12	5.6 ± 2.7	6.0 ± 2.7	1.1 ± 0.6*	2.0 ± 0.4*	1.5 ± ?	2.5 ± ?
Weighted mean		**66/87**	**5.4 ± 1.8†**	**5.5 ± 1.5‡**	**1.3 ± 1§**	**2.5 ± 1#**	**1 ± 1¶**	**2.3 ± 1.2****

N C/T = number of defects in the control (C) and in the test (T) treatment arm; H-CAL = horizontal clinical attachment; H-OPAL = horizontal open probing attachment; NA = data not available; e-PTFE = expanded polytetrafluoroethylene.
* Difference between treatments statistically significant.
† N = Mean (60) ± S.D. (54); ‡ N = Mean (81) ± S.D. (72); § N = Mean (49) ± S.D. (43); # N = Mean (70) ± S.D. (61); >3 N = Mean (39) ± S.D. (17);
** N = Mean (57) ± S.D. (17).

ment of mandibular degree II furcation defects (Pontoriero *et al*. 1988; Lekovic *et al*. 1989, 1990; Blumenthal 1993; Machtei *et al*. 1993, 1994; Black *et al*. 1994; Laurell *et al*. 1994; Mellonig *et al*. 1994; Wang *et al*. 1994; Hugoson *et al*. 1995; Polson *et al*. 1995b). The reported mean values ranged from 0.1 mm to 3.5 mm for V-CAL gain and from 1 mm to 4 mm for PPD reduction.

The effect of using barrier membranes for the treatment of mandibular degree II furcations was investigated in six controlled randomized clinical trials in which GTR procedures were directly compared to flap surgery (Table 43-6). Sixty-six furcations treated with flap surgery and 87 treated with GTR were included. Three of the four studies reporting H-CAL gains concluded that GTR resulted in statistically significantly greater horizontal attachment level gains than flap surgery (Pontoriero *et al*. 1988; Van Swol *et al*. 1993; Wang *et al*. 1994). The weighted mean of the results reported in Table 43-6 indicated that the H-CAL in furcations treated with GTR was 2.5 ± 1 mm (95% CI 2.1–2.9 mm) while the flap surgery resulted in a mean H-CAL gain of 1.3 ± 1 mm (95% CI 0.8–1.8 mm). These results indicate an added benefit from GTR in the treatment of mandibular degree II furcations.

Maxillary degree II furcations

Results reported in three controlled studies (Metzeler *et al*. 1991; Mellonig *et al*. 1994; Pontoriero & Lindhe 1995a) comparing GTR treatment of maxillary degree II furcations with non-bioabsorbable e-PTFE membranes and with open-flap debridement, indicate that GTR treatment of such defects is generally unpredictable. In a study including 17 pairs of degree II furcations Metzeler *et al*. (1991) measured CAL gains of 1.0 ± 0.9 mm in the GTR-treated sites versus 0.2 ± 0.6 mm in the control sites. Following re-entry, horizontal probing attachment gains (H-OPAL) of 0.9 ± 0.4 mm and 0.3 ± 0.6 mm were detected in the GTR- and flap-treated furcations, respectively. No differences were found and none of the furcations of the two groups were completely resolved. Similarly, Mellonig *et al*. (1994) treated eight pairs of maxillary degree II furcations which resulted in H-OPAL gains of 1.0 mm (GTR sites) and 0.3 mm (flap-treated sites). No differences were found and none of the treated furcations were completely closed. On the other hand, in a study on 28 maxillary degree II furcations Pontoriero and Lindhe (1995a) found a significant gain in CAL (1.5 mm) and horizontal bone (1.1 mm) in buccal degree II furcations.

Although these three investigations show a slight clinical improvement following treatment of degree II maxillary furcations with GTR, the results are generally inconsistent.

Degree III furcations

Four investigations on the treatment of mandibular degree III furcations (Becker *et al*. 1988; Pontoriero *et al*. 1989; Cortellini *et al*. 1990; Pontoriero & Lindhe 1995b) indicate that the treatment of such defects with GTR is unpredictable. A controlled study of Pontoriero *et al*. (1989) showed that only eight out of 21 "through-and-through" mandibular furcations treated with non-bioabsorbable barrier membranes healed with complete closure of the defect. Another ten defects were partially filled, and three remained open. In the control group, treated with open flap debridement, 10 were partially filled and 11 remained open. Similar results were reported by Cortellini *et al*. (1990) who, in a case cohort of 15 degree III mandibular furcations, found that 33% of the defects had healed completely, 33% were partially closed, and 33% were still through-and-through following treatment. Becker *et al*. (1988) did not observe complete closure of any of 11 treated degree III mandibular furcations. Similarly, in a controlled clinical trial by Pontoriero and Lindhe (1995b) on 11 pairs of maxillary degree III furcations randomly assigned to GTR

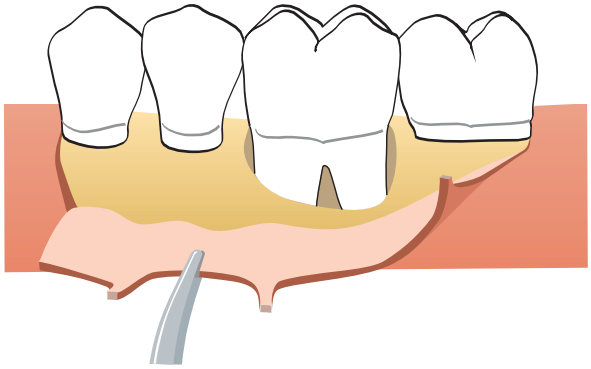


Fig. 43-34 Following marginal incisions and vertical releasing incisions on the buccal aspect of the jaw, buccal and lingual full-thickness flaps are elevated.

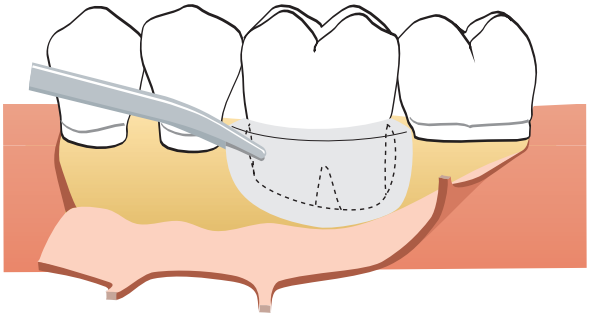


Fig. 43-35 The barrier material is placed in such a way that it completely covers the defect and extends at least 3 mm on the bone beyond the defect margin.

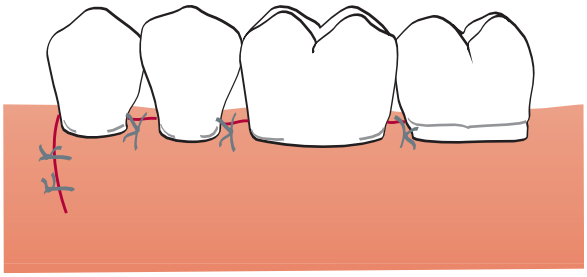


Fig. 43-36 The elevated tissue flaps are coronally displaced and sutured in such a way that the border of the barrier material is at least 2 mm below the flap margin.

or flap surgery, none of the furcation defects were closed.

Based on present evidence, it seems that mandibular degree II furcations in the first or second molars, either buccal or lingual, with deep pockets at baseline and a gingival thickness of >1 mm, may benefit from GTR treatment.

Surgical issues with barrier membranes

Surgery is initiated by sulcular incisions at both the buccal and lingual aspect of the jaw, followed by buccal and vertical releasing incisions, if necessary. For intrabony defects, the releasing incisions must be placed a minimum of one tooth anterior and/or posterior to the tooth that is being treated (Fig. 43-34). Care should be taken during this procedure to preserve the interdental papillae. All pocket epithelium is excised so that fresh connective tissue is left on the full-thickness flaps following reflection. After elevation of the tissue flaps, all granulation tissue is removed and thorough debridement of the accessed root surfaces is carried out using curettes, burs, etc.

Various types of bioabsorbable and non-bioabsorbable barrier materials are available in a variety of configurations designed for specific applications. The configuration most suitable for covering the defect is selected and additional adaptation of the material to the shape and extent of the defect is performed. The shaping of the material is carried out in such a way that it adapts closely to the tooth and completely covers the defect, extending at least 3 mm on the bone beyond the defect margins after placement (Fig. 43-35). This assures good stability of the material and protects the underlying blood clot during healing. At placement it is essential to ensure good adaptation of the barrier material to the alveolar bone surrounding the defect and to avoid overlaps or folds of the material.

Although exceptions exist, the barrier materials available are fixed to the tooth with a suture using a sling technique. For optimal performance, the barrier should be placed with its margin 2–3 mm apical to the flap margin. To maximize coverage of the barrier, a horizontal releasing incision in the periosteum may assist in the coronal displacement of the flap at the suturing of the wound. However, care should be taken not to compromise the blood supply to the flap. The interdental space near the barrier should be closed first. In order to achieve good closure, an internal vertical mattress suturing technique is advocated (Fig. 43-36).

To reduce the risk of infection and to assure optimal healing, the patient should be instructed to brush the area gently post-operatively with a soft bristle toothbrush and to rinse with chlorhexidine (0.2%) for a period of 4–6 weeks. In addition, systemic antibiotics are frequently administered immediately prior to surgery and for 1–2 weeks after surgery. When a non-bioabsorbable barrier is used, it should be removed after 4–6 weeks. However, if complications develop it may be necessary to remove it earlier.

Removal of the material requires a minor surgical procedure (Fig. 43-37). To obtain access to the barrier material, a small incision is made extending one tooth mesial and distal to the border of the barrier. The soft tissue flap is gently reflected and the barrier material dissected free from the flap using a sharp blade. During this procedure it is essential not to compromise the newly regenerated tissue. At removal of the barrier material there will usually be some pocket formation on the outer surface of the material. It is important that this epithelium is removed so

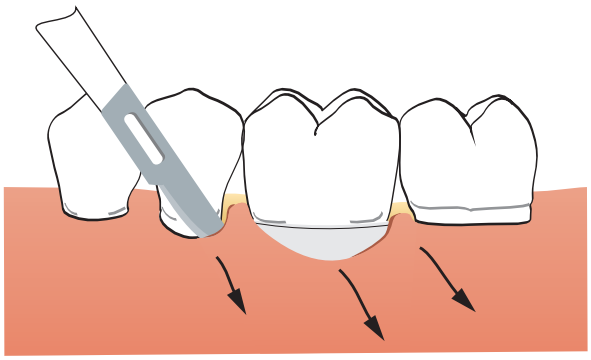


Fig. 43-37 In order to remove the barrier material an incision is made extending one tooth mesially and distally to the border of the barrier. After reflecting the covering tissue flaps, the barrier can be removed without compromising the newly regenerated tissue.

that fresh connective tissue is in contact with the newly regenerated tissue after wound closure. It is essential that the newly regenerated tissue is completely covered after suturing. The patient is instructed to rinse with chlorhexidine for 2–3 weeks during which period frequent visits for professional tooth cleaning are recommended. After this period, brushing and interdental cleaning can be resumed, chlorhexidine rinsing discontinued, and the patient enrolled in a regular periodontal maintenance program.

If the flap is excessively traumatized during surgery either part or all of it may slough during healing. Perforations may also occur, particularly in sites with sharp bony ledges. A minor osteoplasty during placement may help to allow the barrier to better follow the contours of the ridge. Abscess formation may also occur in the wound, probably due to severe bacterial contamination of the barrier. Dependent on the severity of such complications, early removal of the barrier may be indicated.

Bone replacement grafts

Bone replacement grafts (BRG) comprise a heterogeneous group of materials of human (autologous or allogeneic), animal or synthetic origin. Some consist of bone or exoskeletal mineral; others contain mainly bone matrix. Only few materials present evidence of periodontal regeneration. A randomized controlled clinical trial provided histologic support that the healing outcome following application of demineralized freeze-dried bone allograft (DFDBA) in intrabony defects has a regenerative component in the apical to middle portion of the depth of the defect (Bowers *et al*. 1989a,b,c). Isolated evidence also supports the fact that allograft and bovine bone mineral may yield a regenerative outcome when used alone (i.e. without other regenerative materials such as barrier membranes or biologically active regenerative materials (BARG) – see also Chapter 25) (Nevins *et al*. 2000).

Bone replacement grafts were the first periodontal regenerative materials to be applied clinically. Today they are widely used in North America as demineralized freeze-dried allografts and are frequently used in combination with other regenerative materials (GTR and/or BARG).

The clinical efficacy of allografts in terms of bone fill and clinical attachment level gains is supported by a meta-analysis indicating that an additional bone fill of 1 mm and additional clinical attachment level gains of 0.4 mm were observed (Reynolds *et al*. 2003). The total number of defects contributing to this meta-analysis however is relatively small (136 for clinical attachment level gain and 154 for bone fill). Furthermore no large-scale multi-center trial has ever been performed and hence the applicability of these results to clinical practice settings remains to be established.

As to their use, BRG can be applied alone following elevation of a papilla preservation flap for the treatment of intrabony defects. The graft is applied to overfill the defect to compensate for a degree of shedding of the graft expected in cases of imperfect containment of the graft by the closed flap. A study has suggested using BRG in combination with an antibiotic powder to enhance control of the bacterial contamination of the surgical wound (Yukna & Sepe 1982). This study reported improved outcomes from mixing the graft with tetracycline powder.

Biologically active regenerative materials

Preclinical and clinical evidence for the use of biologically active regenerative materials has been reviewed (see also Chapter 25). Currently, two preparations consisting of growth and/or differentiation factors are available for use in periodontal regeneration: enamel matrix derivative (EMD) in a gel form and platelet-derived growth factor (PDGF) mixed in a beta tricalcium phosphate bone replacement graft.

Significant preclinical evidence supports the positive effect of PDGF on periodontal wound healing and regeneration (Howell *et al*. 1997). Clinically, support for use of PDGF comes from a single multicenter trial performed in North America (Nevins *et al*. 2005). In that study 180 defects comprising both intrabony and furcation defects were treated with one of two concentrations of PDGF (0.3 mg/ml and 1.0 mg/ml) combined with the beta tricalcium phosphate delivery device or tricalcium phosphate alone. Results were assessed at 3 and 6 months and included both clinical and radiographic assessments. Clinical attachment level gains at 6 months failed to demonstrate a significant benefit of either concentration of PDGF compared to the bone replacement graft alone. With regards to radiographic assessments, however, the lower tested concentration of PDGF resulted in significantly higher percentages of radiographic bone

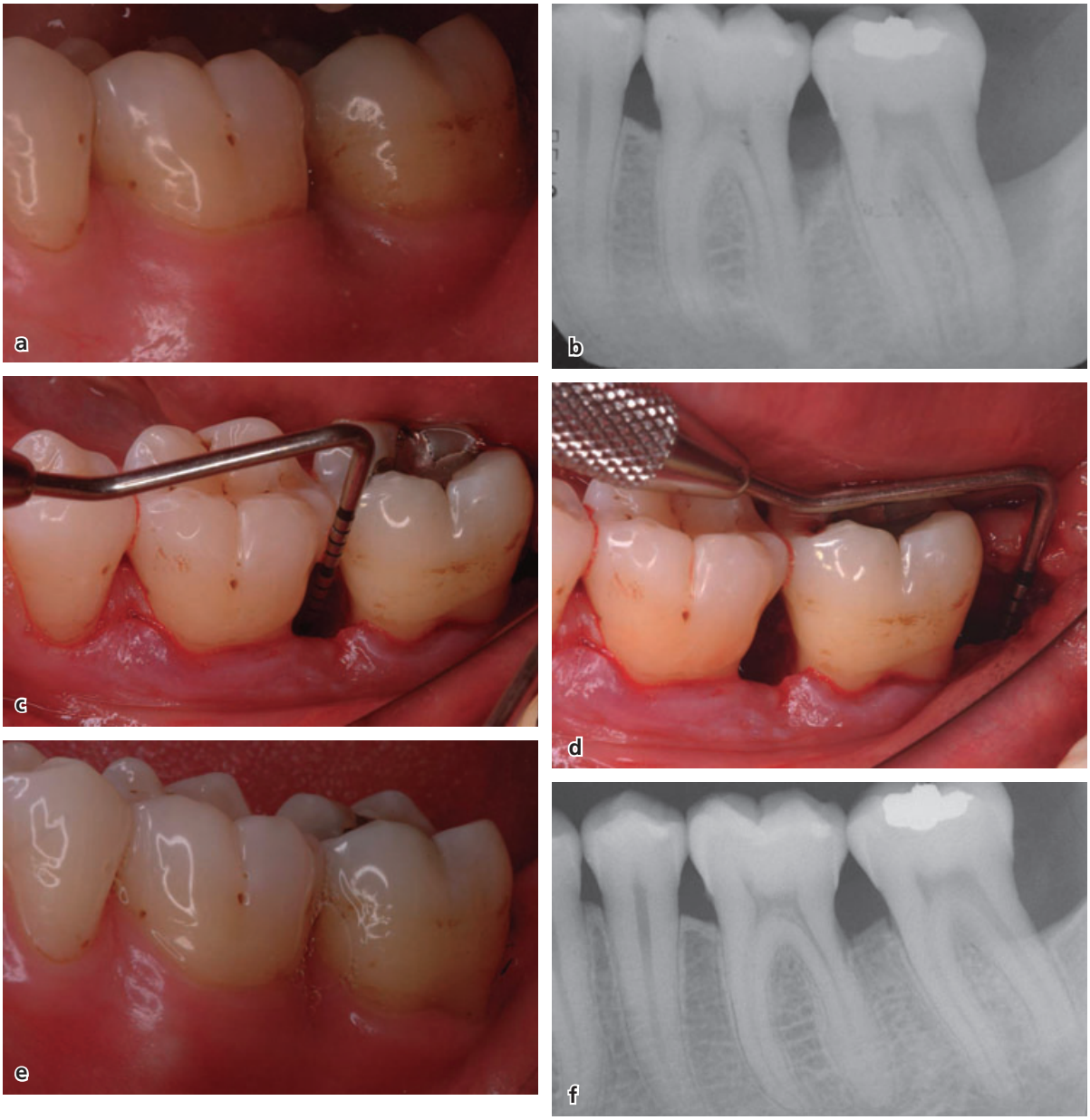


Fig. 43-38 Clinical case illustrating the use of enamel matrix derivative to regenerate defects located on two adjacent teeth. At re-evaluation, deep pockets associated with deep intrabony defects are evident on the distal aspect of the first and second molars (a,b). Defects were accessed with the modified papilla preservation technique on the distal aspect of the first molar and with the use of a crestal incision in the retromolar area (c,d). Deep defects were exposed following debridement and root instrumentation (c,d). Following application of enamel matrix derivative in gel form, primary closure was obtained with multilayered sutures. At 1-year follow-up, shallow probing depths associated with the elimination of the defects were observed (e,f).

fill of the defect (57% vs. 18%) and linear radiographic bone growth (2.6 mm vs. 0.9 mm). The results of this study led to the approval by the US Food and Drug Administration of this material. The authors interpreted the dichotomy represented by the significance of the added benefit in terms of radiographic parameters without the presence of significant changes in CAL as the result of biologic action of the growth factor formulation in shortening the healing time of the hard tissues. As of today, however, the results of this study have not been independently confirmed.

The benefit of use of EMD gel in the treatment of intrabony defects is supported by human histologic evidence, case report studies, meta-analysis of randomized controlled clinical trials, and a large multicenter trial (Heijl *et al*. 1997; Heden *et al*. 1999; Sculean *et al*. 1999b; Silvestri *et al*. 2000; Heden 2000; Tonetti *et al*. 2002; Giannobile & Somerman 2003; Heden & Wennstrom 2006) (Fig. 43-38).

Given their hydrophobic nature, enamel matrix proteins are mixed in a gel carrier at low pH for clinical use. Following an increase in pH in the periodontal wound and rapid elimination of the gel, EMD proteins (consisting mainly of amelogenins) are deposited in the wound environment and the root surface. While the mechanism(s) of action of EMD are

not fully understood, significant evidence suggests that periodontal ligament cells exposed to EMD switch their phenotype by increasing expression of a host of growth and differentiation factor related genes (Brett *et al*. 2002; Parkar & Tonetti 2004), including transforming growth factor beta (Lyngstadaas *et al*. 2001).

A secondary analysis of a multi-center trial has shown that, in intrabony defects, the added benefit of EMD was greater in three-wall defects than in one-wall defects (Tonetti *et al*. 2002). Furthermore, another secondary analysis of the same material assessing the effect of the radiographic defect angle on the outcome (Tsitoura *et al*. 2004) has uncovered a negative association between the ragiographic angle of the defect and the clinical attachment level gains observed at 1 year. These data have questioned the suitability of the gel formulation of the EMD for the treatment of defects with a non-supporting anatomy (wide defects with missing bony walls).

These observations have spurred considerable research interest in the incorporation of EMD in a variety of bone replacement grafts in order to enhance wound stability and space maintenance. At this stage, however, no systematic evidence is available to support the use of such combinations.

Clinically, the rate of wound healing following application of EMD seems to be enhanced. A study looking at soft tissue density in the surgical site by using underexposed radiographs (Tonetti *et al*. 2004b) has found that the rate of increase in soft tissue density following application of EMD may be faster than in the access flap control. Such modulation has been interpreted as the outcome of the local release of growth and differentiation factors by the cells involved in local wound healing.

Membranes combined with other regenerative procedures

Compromised results after GTR may be obtained in cases where the membrane collapses/falls (partially or totally) into the defect and/or towards the root surface, thereby reducing the space available for invasion of new tissue capable of forming periodontal ligament and bone in particular. Reduced amounts of regenerated bone due to membrane collapse were noticed in early studies of GTR. In the study of Gottlow *et al*. (1984), it was observed that collapse of the membrane towards the root surface resulted in new cementum formation on the entire exposed root surfaces, whereas bone regeneration was minimal. Although the authors reported that the degree of coronal regrowth of bone was unrelated to the amount of new cementum formation, they did not comment on what effect membrane collapse might have had. Experimental studies, however, recognized the negative effect of membrane collapse on periodontal regeneration generally and on bone formation in particular (Caton *et al*. 1992; Haney *et al*. 1993; Sigurdsson *et al*. 1994; Sallum *et al*. 1998). Haney *et al*. (1993) observed a highly significant correlation between the space provided by the membrane and the amount of regenerated alveolar bone using a supra-alveolar defect model in dogs. This finding corroborates that of Cortellini *et al*. (1995c) who reported that clinical application of self-supporting (reinforced with titanium) e-PTFE membranes, which could be positioned more coronally than ordinary e-PTFE membranes, yielded a statistically significant increase in PAL gain in intrabony defects. A particular risk for membrane collapse exists in cases where the configuration of the defect is incapable of supporting/preserving the membrane at the position where it was originally placed.

As already discussed, membrane materials must possess certain characteristics in order to be efficient. Among those it is important that the membrane is capable of keeping its shape and integral features, thereby maintaining the space created adjacent to the root surface. The e-PTFE membranes reinforced with titanium are the closest in meeting these requirements but they have the disadvantage that they are non-resorbable. At present there are no resorbable membranes available that fulfill this requirement sufficiently, which means that the placement of a resorbable membrane on, for instance, a wide one-wall defect involves the risk of membrane collapse. The collapse may be prevented by means of implantation of a biomaterial into the defect to support the membrane so that it maintains its original position (Fig. 43-39). However, the biomaterial to be used for this purpose must not interfere with the process of periodontal regeneration and ideally it may also promote bone regeneration.

As previously described, periodontal regeneration has been attempted with a variety of grafting materials, among which demineralized freeze-dried bone allografts (DFDBA) apparently facilitated regeneration in humans (Ouhayoun 1996). Schallhorn and McClain (1988) reported on improved clinical results in intrabony defects and degree II furcations, following a combination therapy including barrier membranes plus DFDBA and citric acid root conditioning.

In three controlled clinical trials, the treatment of a total of 45 pairs of intrabony defects with DFDBA grafting and GTR were compared to GTR alone (Table 43-7). The weighted mean of the results of the reported investigations showed similar gain in CAL in the GTR group (2.1 ± 1.1 mm, 95% CI 1.6–2.6 mm) and in the GTR plus DFDBA group (2.3 ± 1.4 mm, 95% CI 1.7–2.9 mm). The differences between the two treatments did not reach statistical significance, thus indicating no added effect of combining DFDBA with barrier materials in the treatment of intrabony defects. Guillemin *et al*. (1993) compared the effect of DFDBA alone with a combination of barrier materials and DFDBA in 15 pairs of intrabony defects. Both treatments resulted in significant amounts of CAL gains

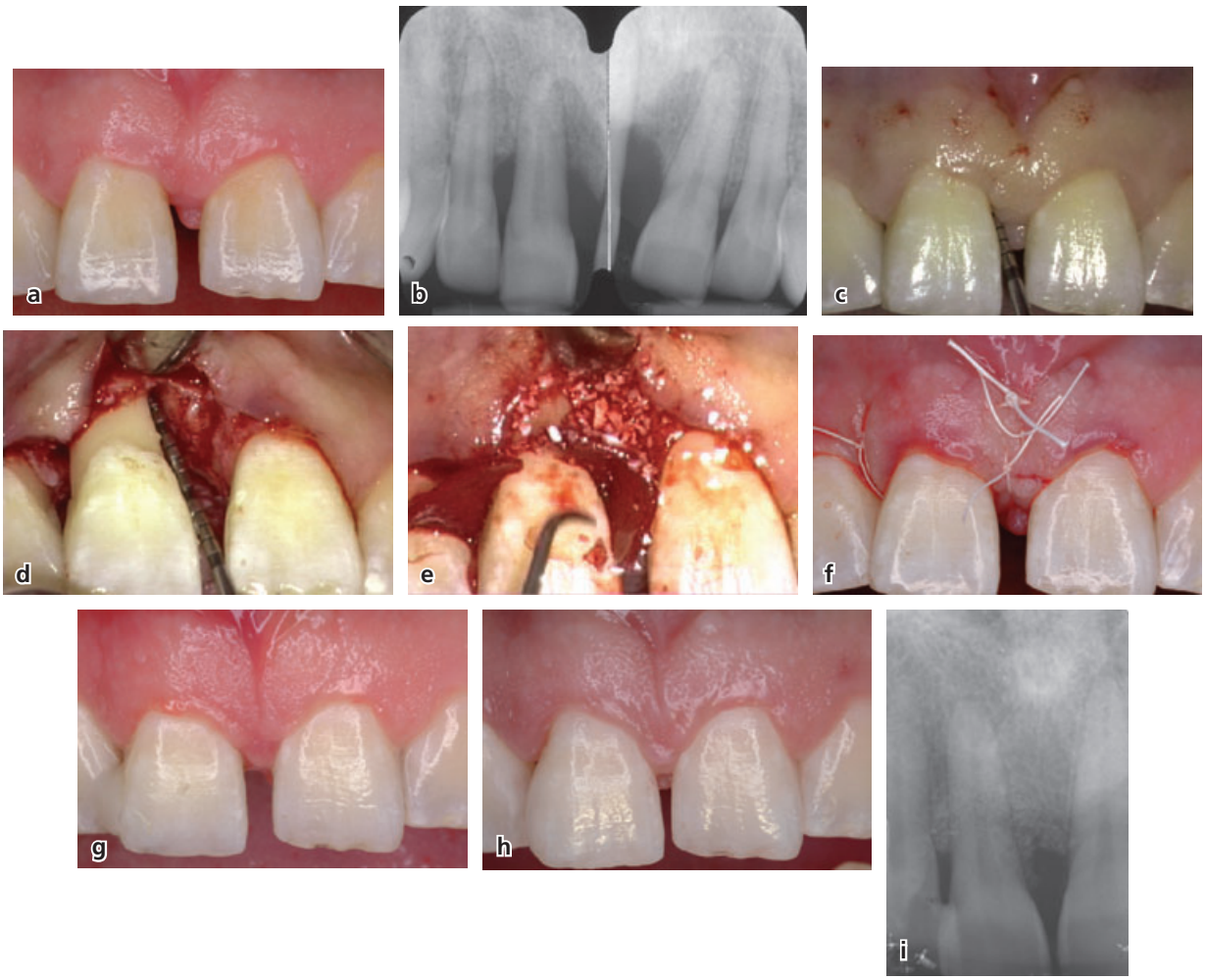


Fig. 43-39 Clinical case illustrating the application of bone replacement graft to support a bioresorbable membrane in a defect with poor space maintaining anatomy. Following control of periodontitis and risk factors, the upper right contral incisor presented with a 12-mm deep pocket associated with a defect extending close to the apex of the tooth (a–c). The defect was accessed with the modified papilla preservation flap to reveal an 8-mm intrabony component (d). A bone replacement graft was placed under a bioresorbable collagen membrane (e). Primary closure was achieved with a multilayered suture technique (f). Excellent early healing was observed already at the 2-week follow-up (g). At 1 year, periodontal regeneration resulted in shallow probing depths and good resolution of the intrabony defect (h,i). Radio-opaque bone replacement graft particles are visible within the newly formed mineralized tissue.

Table 43-7 Summary of controlled clinical trials evaluating the combined effects of decalcified freeze-dried bone allografts (DFDBA) and barrier membranes in deep intrabony defects

Authors	Design (GTR treatment)	N*	Gains in CAL (mm)		Significance	Residual PD (mm)		Significance
			GTR	GTR + DFDBA		GTR	GTR + DFDBA	
Chen *et al*. 1995	Intra-individual (Collagen)	8	2.0 ± 0.4	2.3 ± 0.5	P > 0.05, NS	4.2 ± 0.4	4.2 ± 0.5	P > 0.05, NS
Mellado *et al*. 1995	Intra-individual (e-PTFE)	11	2.0 ± 0.9	2.0 ± 1.4	P = 0.86, NS	NA	NA	NA
Gouldin *et al*. 1996	Intra-individual (e-PTFE)	26	2.2 ± 1.4	2.4 ± 1.6	NS	3.7 ± 1.6	3.7 ± 1.8	NS
Weighted mean		**45**	**2.1 ± 1.1**	**2.3 ± 1.4**		**3.8 ± 1.3**§	**3.8 ± 1.5**§	

* Defects per treatment arm.
CAL = clinical attachment level; PD = pocket depth; e-PTFE = expanded polytetrafluoroethylene; DFDBA = decalcified freeze-dried bone allograft; NS = not significant; NA = data not available.
§ N = mean (34) ± S.D. (34).

Table 43-8 Controlled clinical trials comparing clinical outcomes of GTR procedures with e-PTFE non-bioabsorbable barrier membranes with or without the adjunctive use of grafts in mandibular degree II furcations

Authors	Design & treatment (GTR C/GTR T)	N C/T	Defect depth (mm)		H-OPAL gain (mm)	
			GTR C	GTR T	GTR C	GTR T
Lekovic *et al*. 1990	Intra-individual (e-PTFE/e-PTFE + HA)	15/15	4.2 ± 0.2	4.3 ± 0.2	0.1 ± 0.1	1.6 ± 0.2
Anderegg *et al*. 1991	Intra-individual (e-PTFE/e-PTFE + DFDBA)	15/15	4.2 ± 2.2	5.3 ± 2.6	1.0 ± 0.8*	2.4 ± 1.5*
Wallace *et al*. 1994	Parallel (e-PTFE/e-PTFE + DFDBA)	7/10	6.0 ± ?	6.5 ± ?	2.3 ± ?	2.4 ± ?
Weighted Mean		**37/40**	**4.5 ± 1.2**†	**5.2 ± 1.4**‡	**0.9 ± 0.5**†	**2.1 ± 0.9**§

GTR C = guided tissue regeneration control treatment; GTR T = guided tissue regeneration test treatment; N C/T = number of defects in the control (C) and in the test (T) treatment arm; H-OPAL = horizontal open probing attachment; e-PTFE = expanded polytetrafluoroethylene; HA = hydroxyapatite; DFDBA = decalcified freeze-dried bone allograft.
* Difference between treatments statistically significant.
† N = Mean (37) ± S.D. (30); ‡ N = Mean (40) ± S.D. (30); § N = Mean (35) ± S.D. (24).

and bone fill at 6 months, but no difference was found between the treatments.

In three studies on mandibular degree II furcations, GTR treatment alone was compared with GTR treatment combined with hydroxyapatite or DFDBA (Table 43-8). In one of these investigations, a statistically significant improvement was found in terms of horizontal open probing attachment levels (H-OPAL) in the group of furcations treated with the combination therapy (Anderegg *et al*. 1991). In another of these three studies the difference between the two treatments was not statistically significant, but the combination therapy resulted in a greater extent of furcation fill (Lekovic *et al*. 1990). In the third investigation (Wallace *et al*. 1994), the two treatments were equivalent in terms of H-OPAL gains. The weighted mean of the cited studies showed greater H-OPAL gains in the cases treated with the combination therapy (2.1 ± 0.9 mm, 95% CI 1.6–2.6 mm) when compared to GTR treatment alone (0.9 ± 0.5 mm, 95% CI 0.6–1.1 mm), indicating a possible added benefit from the use of grafting materials in combination with non-bioabsorbable barrier membranes for the treatment of mandibular degree II furcations.

Promising clinical results with a PAL-gain of 1.0–5.5 mm were obtained in human case reports, in which the GTR technique was combined with grafting of Bio-Oss® for the treatment of intrabony periodontal defects (Lundgren & Slotte 1999; Mellonig 2000; Paolantonio *et al*. 2001). The combined Bio-Oss® and GTR treatment resulted in greater PPD reduction, PAL gain and defect fill than the mere implantation of Bio-Oss® in case series (Camelo *et al*. 1998) and than flap surgery alone in a split-mouth study (Camargo *et al*. 2000).

In a recent randomized controlled clinical study including 60 patients (Stavropoulos *et al*. 2003), Bio-Oss® alone or impregnated with gentamicin was used as an adjunct to GTR in the treatment of one-wall or two-wall intrabony defects, and the outcomes were compared to those obtained following GTR alone or flap surgery. Treatment with a membrane alone (Fig. 43-40) resulted in a mean PAL gain of 2.9 mm, while it was 3.8 and 2.5 mm, respectively, when Bio-Oss® grafts with or without gentamicin were placed in the defects prior to membrane coverage (Fig. 43-41). The control defects treated with flap surgery demonstrated a gain of PAL of only 1.5 mm. The clinical improvements in defects treated with GTR alone or in combination with Bio-Oss® grafting were significantly better than those obtained with flap surgery, whereas the differences between the groups treated with membranes were not statistically significant.

In a controlled study (Pietruska 2001), similar clinical improvements were obtained when Bio-Oss® combined with GTR was compared with biomodification of the root surface with enamel matrix protein (Emdogain®).

Camelo *et al*. (1998) and Mellonig (2000) presented histologic data indicating that the use of Bio-Oss® under a membrane may result in partial regeneration of the periodontal apparatus, but in all the cases, most of the defect was still occupied by deproteinized bone particles. Bone was not observed near the root, and the connective tissue fibers of the "new" periodontal ligament were mostly oriented parallel to the root surface. These results corroborate findings reported by Paolantonio *et al*. (2001), who observed only limited bone formation in the vicinity of the pre-existing bone in a biopsy, taken from a site treated 8 months earlier with Bio-Oss® and a collagen membrane. Most of the space in the defect was occupied by Bio-Oss® particles embedded in connective tissue. However, in a case report where intrabony defects were treated with Bio-Oss® combined with intraoral autogenous bone and GTR, new attachment formation had occurred consistently, but a major portion of the regenerated osseous tissue consisted of deproteinized bone particles (Camelo *et al*. 2001). The effect of combining citric acid root biomodification with GTR treatment was evaluated in two randomized controlled clinical trials in intrabony defects. The first investigation (Handelsman *et al*. 1991) demonstrated significant amounts of CAL gains in both the test (e-PTFE membranes and citric acid; CAL gain 3.5 ± 1.6 mm) and control sites (e-PTFE membranes alone; CAL gain 4.0 ±

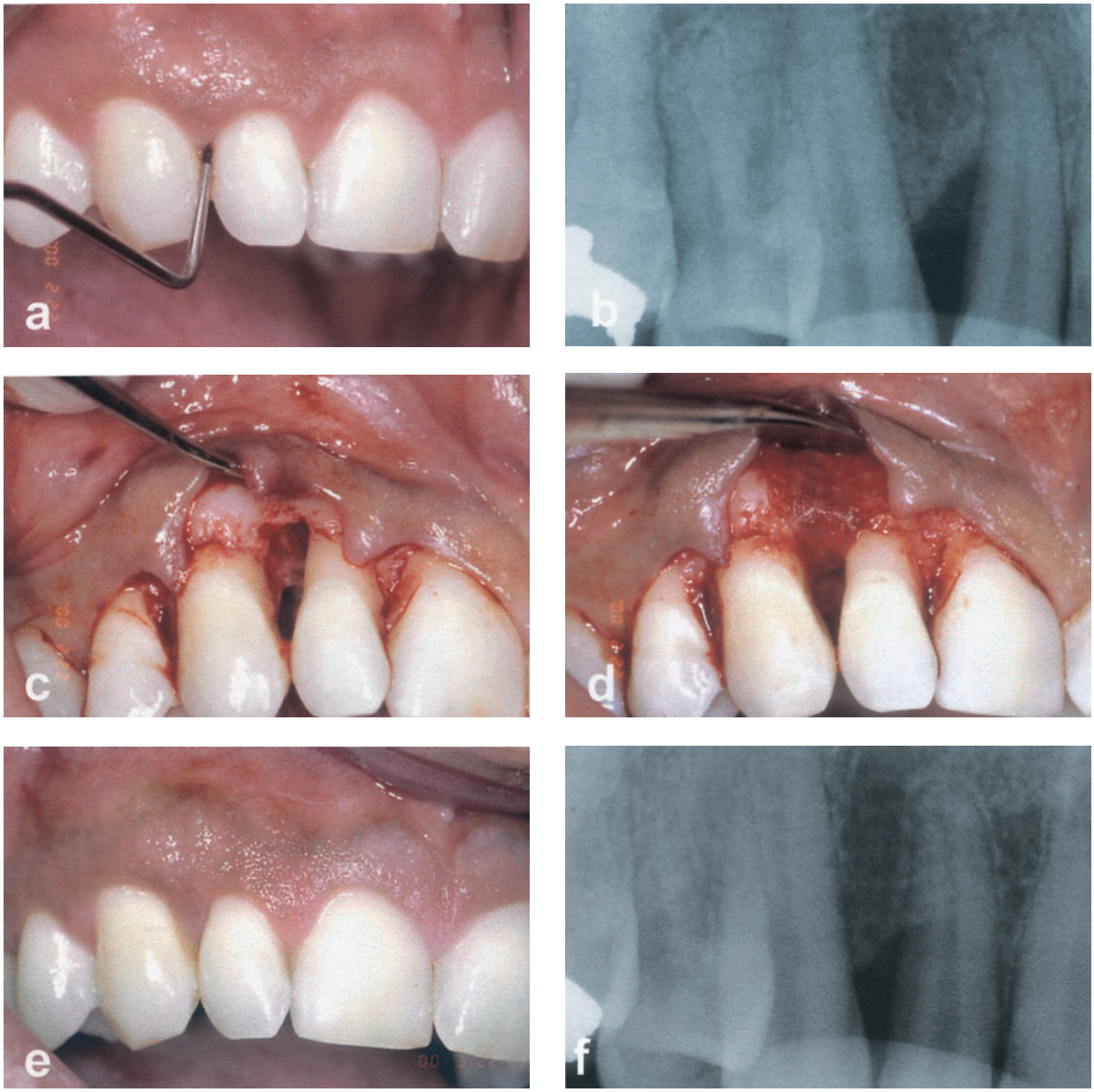


Fig. 43-40 Right lateral maxillary incisor with an 8-mm deep pocket associated with an intrabony defect on the distal aspect (a), as seen on the radiograph (b). Full-thickness buccal and palatal flaps have been raised and the defect has been debrided (c). A bioabsorbable membrane has been adopted over the defect (d). The level of the interdental gingiva is maintained after 1 year (e) and the intrabony defect (f) is resolved.

1.4 mm). Less favorable results following these two treatment modalities were reported by Kersten *et al*. (1992) who found CAL gains of 1.0 ± 1.1 mm in the test group, and CAL gains of 0.7 ± 1.5 mm in the control group. Both studies, however, failed to demonstrate any added effect of the use of citric acid in combination with non-bioabsorbable barrier membranes.

Root surface biomodification with tetracycline alone and in combination with GTR was evaluated in two controlled studies on degree II furcations (Machtei *et al*. 1993; Parashis & Mitsis 1993). Both investigations failed to show significant differences between sites treated with non-bioabsorbable barrier membranes alone or in combination with tetracycline root surface biomodification. Similarly, the use of other surface active chemicals like EDTA also failed to provide a significant added effect to GTR treatment in humans (Lindhe & Cortellini 1996).

Root surface biomodification

The suggested role of root surface biomodification for improving periodontal regeneration has been recently assessed in a systematic review (Mariotti *et al*. 2003). The results of that exhaustive review of the evidence indicated that there was no evidence of a measurable improvement following root conditioning with agents like citric acid, tetracycline HCl, phosphoric acid, fibronectin or EDTA.

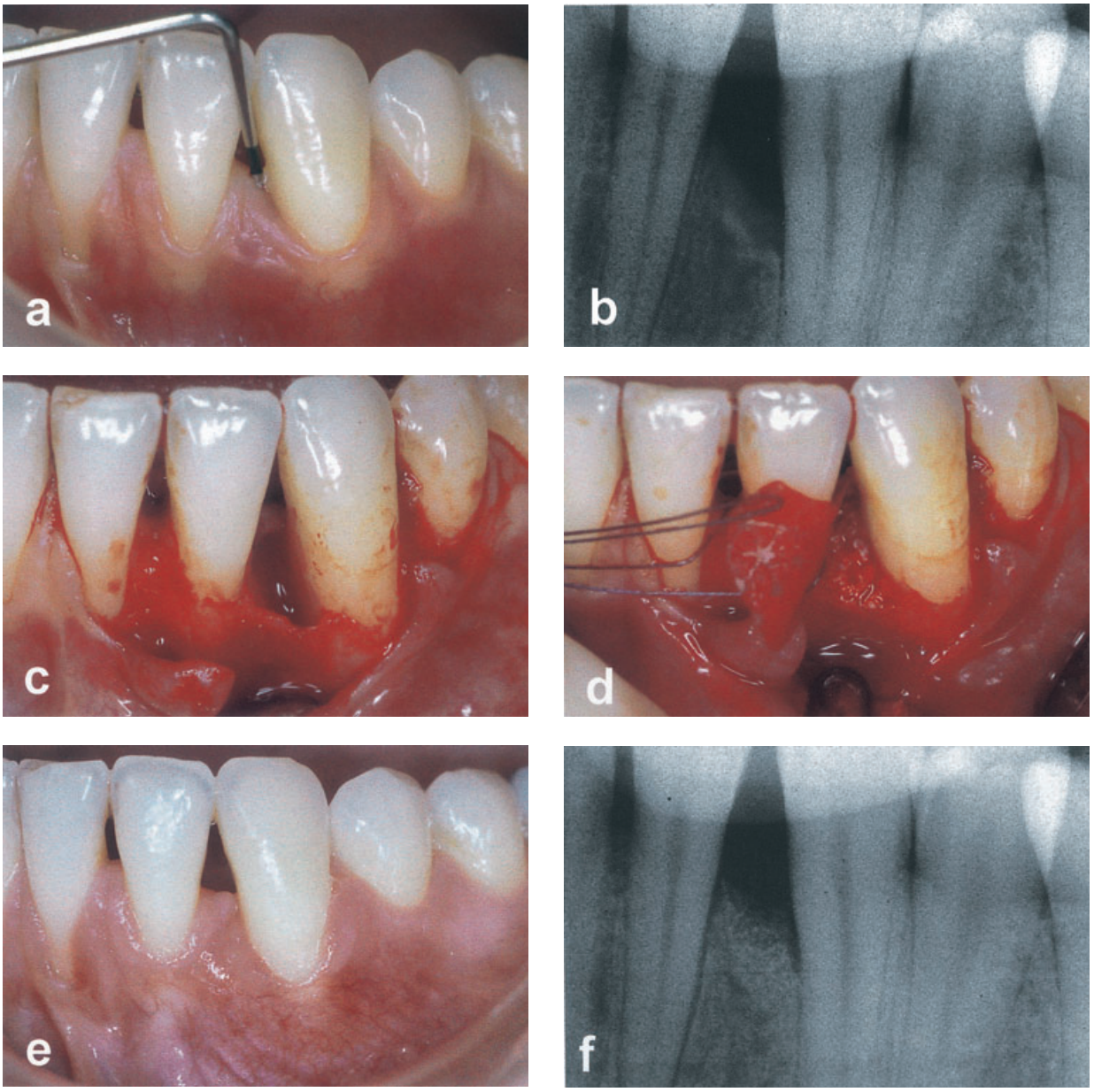


Fig. 43-41 Left mandibular canine with an 8-mm deep pocket (a) associated with an intrabony defect on its mesial aspect (b). The defect is debrided after flap elevation (c) and Bio-Oss® particles are placed in the defect (d) prior to placement of a bioabsorbable membrane. After 1 year (e), no gingival recession has occurred and the intrabony defect is almost resolved (f).

Clinical strategies

Periodontal regeneration in intrabony defects has been successfully attempted with a variety of different approaches. As discussed, meta-analyses of randomized controlled clinical trials as well as human and animal histologic findings support the potential of barrier membranes (Nyman *et al*. 1982; Gottlow *et al*. 1986), demineralized freeze dried bone allograft (DFDBA) (Bowers *et al*. 1989a,b,c), combination of barrier membranes and grafts (Camelo *et al*. 1998; Mellonig 2000), and the use of enamel matrix derivative (Mellonig 1999; Yukna & Mellonig 2000) to induce periodontal regeneration. Controlled clinical trials report that the above-mentioned approaches provide added benefits in terms of clinical attachment level (CAL) gain as compared to open-flap debridement alone (Needleman *et al*. 2002; Murphy *et al*. 2003; Trombelli *et al*. 2002; Giannobile & Somerman 2003; Tonetti *et al*. 2004a). Comparisons among some of the cited regenerative approaches failed to demonstrate a clear superiority of one of the tested materials (Murphy *et al*. 2003; Giannobile & Somerman 2003; Reynolds *et al*. 2003).

The existing evidence, therefore, does not support the choice of a single approach among the different regenerative possibilities. In addition, all the cited studies have shown a substantial degree of variability, in terms of CAL gains, reporting failures or unsatisfactory outcomes in part of the treated population.

Research conducted mostly in the past decade has clearly established that the variability observed in

outcomes of periodontal regenerative procedures is dependent on a variety of patient, defect, and surgical associated factors.

While relevant patient factors include cigarette smoking, residual periodontal infection, and oral hygiene, factors associated with the morphology of the defect are consistently found to be of relevance for the final outcome (Tonetti *et al*. 1998; Cortellini *et al*. 2001). Interestingly, however, the number of residual bony walls defining the defect seems to impact the outcomes of different periodontal regenerative materials in a divergent way. Non-resorbable (e-PTFE and titanium-reinforced e-PTFE) barrier membranes, and bioresorbable barriers supported by a graft do not seem to be affected by the number of residual bony walls of the defect (Tonetti *et al*. 1993a, 1996a, 2004b), while EMD results in better outcomes in three-wall defects (Tonetti *et al*. 2002). Furthermore, healing following application of bioresorbable barriers and non-resorbable e-PTFE barriers as well as EMD is associated with the radiographic width of the intrabony defect (Tonetti *et al*. 1993a; Falk *et al*. 1997; Tsitoura *et al*. 2004). No such association has been found for the use of a xenogenic bone replacement graft and resorbable barrier graft combination (Tonetti *et al*. 2004b).

Among the technical/surgical factors, membrane exposure and contamination have been associated with reduced outcomes (Selvig *et al*. 1992; Nowzari & Slots 1994; Nowzari *et al*. 1995; De Sanctis *et al*. 1996a,b). Similar problems were also encountered with bone grafting (Sanders *et al*. 1983). Reduced outcomes were also observed when the regenerated tissue was not properly protected with the flap at removal of non-resorbable barrier membranes (Tonetti *et al*. 1993a; Cortellini *et al*. 1995c).

A controlled clinical trial demonstrated that the combination of a papilla preservation flap and titanium-reinforced e-PTFE membrane resulted in greater amounts of clinical attachment level gains as compared to a conventional flap approach associated with an e-PTFE membrane (Cortellini *et al*. 1995c). This evidence, also partly supported by a systematic review (Murphy *et al*. 2003), strongly suggests that optimization of the surgical approach and control of surgical variables, particularly in relation to flap design and management and selection of the regenerative material, could improve outcomes. In the context of GTR, several specific flap designs aimed at the full preservation of the soft tissues during access to the defect have been described (Cortellini *et al*. 1995c,d, 1996c, 1999; Murphy 1996). Experimental testing of these regenerative flaps reported great improvements in achieving primary closure during the surgical session with optimal interdental closure being obtained in virtually all cases (Tonetti *et al*. 2004b; Cortellini *et al*. 1995c,d, 1999, 2001). During the subsequent healing, however, dehiscence of the interdental tissue and membrane exposure was observed in up to a third of the cases. The ability to accomplish and maintain primary closure of the tissues over a GTR membrane was further improved by the use of a microsurgical approach that resulted in maintenance of primary wound closure in 92.3% of the treated sites for the whole healing period (Cortellini & Tonetti 2001, 2007a,b).

This body of evidence can be utilized together with a degree of clinical experience to develop an "evidence-based regenerative strategy" to guide clinicians through a decision-making process aimed at the optimization of the clinical outcomes of periodontal regeneration in intrabony defects (Cortellini & Tonetti 2000a, 2005). Key steps of this process are the careful evaluation of the patient and of the defect, the access of the defect with a papilla preservation flap, the possibility of choosing the most appropriate regenerative technology/material, and the ability to seal the regenerating wound from the contaminated oral environment with optimal suturing techniques.

Two to three months after completion of periodontal therapy, baseline clinical measurements are recorded. The regenerative strategy is selected according to a decision-making process. Surgical procedures, according to the principles of periodontal regeneration, are performed. Patients are then enrolled in a stringent periodontal supportive care program for 1 year followed by regular supportive periodontal care.

The appropriate regenerative strategy for the individual case is selected according to a recently modified, evidence-based operative decision tree (Cortellini & Tonetti 2000a, 2005) (Figs. 43-42, 43-43, 43-44).

The surgical access to the intrabony defects is selected from among three different surgical approaches: the simplified papilla preservation flap (SPPF) (Cortellini *et al*. 1999), the modified papilla preservation technique (MPPT) (Cortellini *et al*. 1995d), and the crestal incision (Cortellini & Tonetti 2000a). The SPPF is chosen whenever the width of the interdental space is 2 mm or less, as measured at the level of the papilla; the MPPT is used at sites with an interdental width greater than 2 mm (Fig. 43-42); the crestal incision is applied next to an edentulous area.

Selection of the regenerative material is based on the defect anatomy (Figs. 43-43, 43-44). A non-resorbable titanium-reinforced e-PTFE membrane is used when the defect anatomy is not "supportive", such as in wide and one- or two-wall defects. Alternatively, a bioresorbable membrane supported with a bone replacement graft material can be used in these instances. The latter is preferred to titanium-reinforced e-PTFE when the non-supportive defects are associated with narrow interdental spaces. A bioresorbable membrane is applied alone in "supportive" defects, like the narrow and the two-to-three-wall ones. EMD is preferred in defects with a prevalent three-wall morphology or in well supported two-wall defects.

The suturing approach is chosen according to the defect anatomy and to the type of

Fig. 43-42 Decision-making algorithm illustrating the parameters to take into account when deciding how to access an interdental intrabony defect: the simplified papilla preservation flap (SPPF) is used for narrow interdental spaces (2 mm or narrower), while the modified papilla preservation technique (MPPT) is used to access defect associated with wider interdental spaces (3 mm or wider).

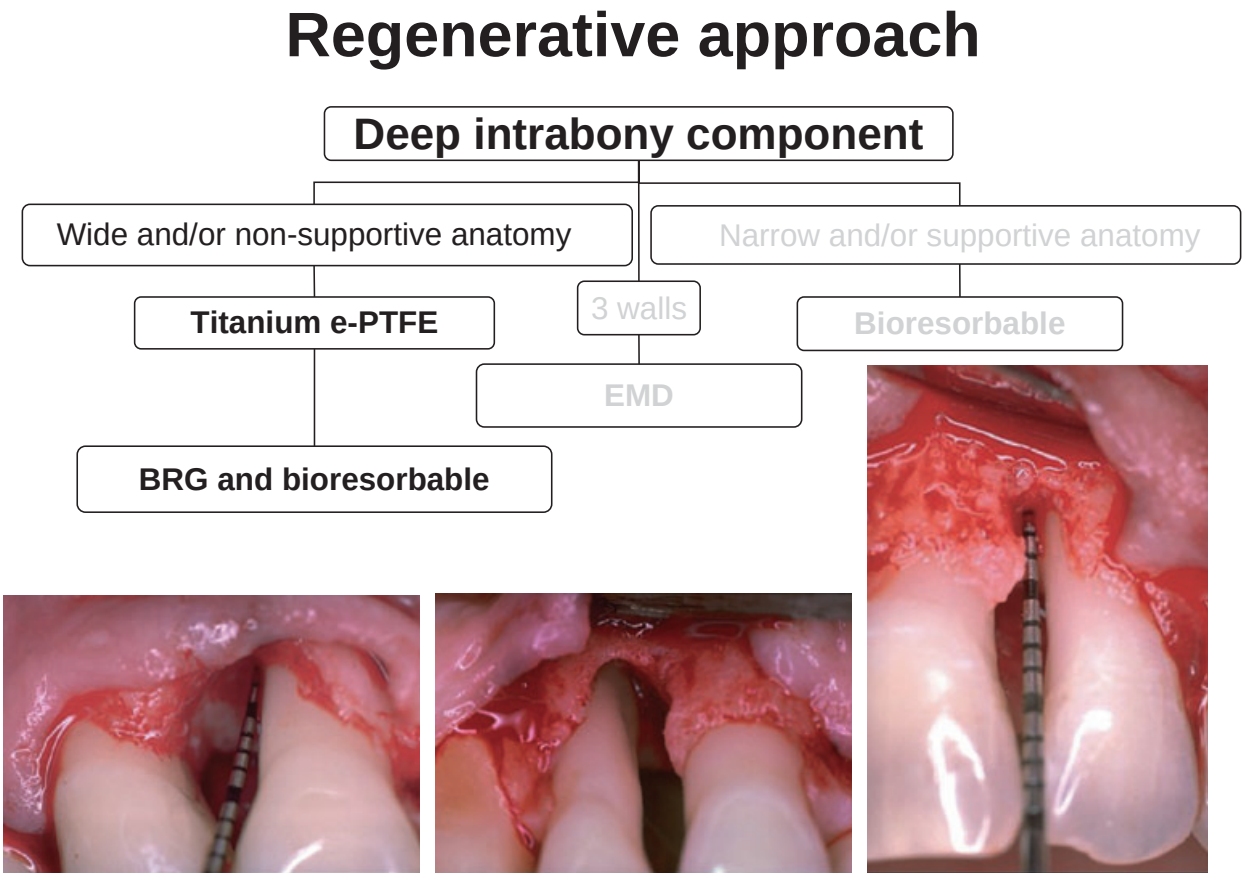


Fig. 43-43 Decision-making algorithm discussing the choice of currently available technologies for application in the treatment of intrabony defects with wide, non-space supporting anatomy. Either titanium-reinforced membranes or bioresorbable membranes are used to obtain a stable regenerative environment, provide space, and support the soft tissues.

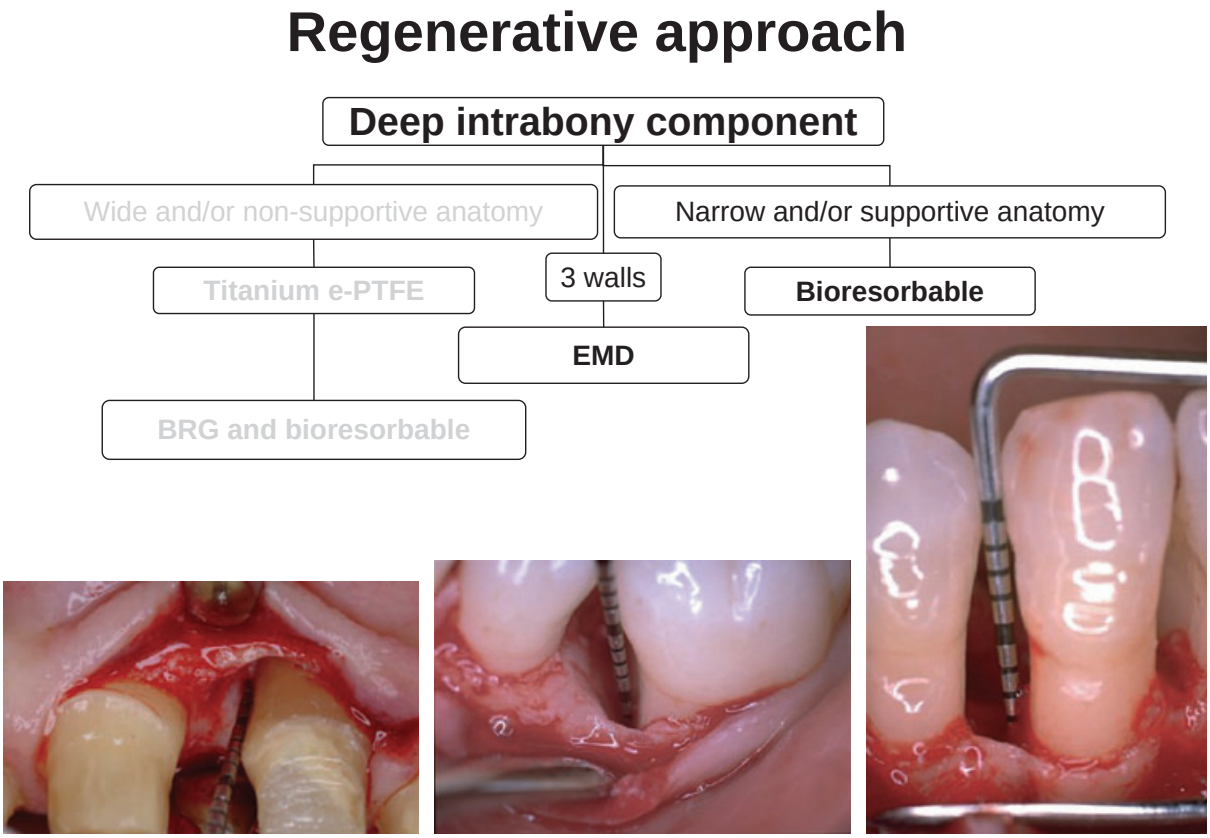


Fig. 43-44 Decision-making algorithm discussing the choice of currently available technologies for application in the treatment of intrabony defects with narrow, space-supporting anatomy. Enamel matrix derivative in gel form is preferred for three-wall defects, while bioresorbable membranes are used for the other narrow type of defects.

regenerative strategy used in each case. It consists of the combination of two sutures applied in the defect-associated interdental area to reach primary closure of the papilla in the absence of any tension. The first interdental suture is positioned between the apical part of the buccal gingiva, near the mucogingival junction, and an apical area of the lingual/palatal flap. In supportive defects (three-wall defects) or in the presence of a supportive membrane (titanium e-PTFE membrane), or a supported membrane (bioresorbable and bone replacement graft), an internal horizontal crossed mattress suture is used. In non-supportive defects and in the presence of bioresorbable membranes or EMD, an offset internal mattress suture is preferred. When a crestal incision is performed, internal horizontal mattress sutures can be conveniently applied. The aims of this first suture are to relieve the residual tension of the flaps in the defect-associated area and to displace the buccal flap coronally. A second, more coronal internal mattress suture is placed to close the interdental papilla passively over the regenerative material.

The surgical procedures can be performed with the aid of magnification such as loupes or an operating microscope. Microsurgical instruments can be utilized to complement the normal periodontal set of instruments.

An empirical protocol for the control of bacterial contamination consisting of doxycycline (100 mg bid for 1 week), 0.12% chlorhexidine mouth rinsing three times per day, and weekly prophylaxis is prescribed. Patients are requested to avoid brushing, flossing, and chewing in the treated area for 6–10 weeks. Non-resorbable membranes are removed after 6 weeks. Patients can resume full oral hygiene and chewing function in the treated area 2–4 weeks after membrane removal or when bioresorbable membranes are fully resorbed. Patients treated with EMD resume full oral hygiene after a period of 4–5 weeks. At the end of the "early healing phase", patients are placed on monthly recall for 1 year.

The performance of this clinical strategy has been recently assessed in a 40-patient consecutive case series (Cortellini & Tonetti 2005). Following completion of initial, cause-related periodontal therapy, subjects presented full-mouth plaque scores of 10.2 ± 2.7% and full-mouth bleeding scores at baseline of 7.9 ± 2.8%. At the intrabony defects, clinical attachment levels (CAL) were 10.2 ± 2.4 mm and probing depths (PD) amounted to 8.9 ± 1.8 mm. The radiographic defect angle was 29° ± 5.9°. Distance from the cemento-enamel junction to the bottom of the defect (CEJ-BD) was 11.2 ± 2.7 mm and the intrabony component of the defects (INFRA) was 6.6 ± 1.7 mm.

In this population the simplified papilla preservation flap could be used in 37.5% of sites, while the modified papilla preservation technique was selected in 45% of cases. The remaining sites, presenting with defects adjacent to edentulous areas, were accessed with a crestal incision.

Based on defect anatomy, non-resorbable titanium-reinforced e-PTFE barrier membranes were used in 30% of cases. In these cases defect angles ranged from 27–42° (average 32.4° ± 4.3°), and two out of three of the selected defects had a one-wall intrabony sub-component of 1–3 mm (average one-wall component of the 12 sites was 1.4 ± 1.2 mm).

Ten of the 11 defects treated with bioresorbable membranes supported with a bone replacement graft, presented a one-wall sub-component of 1–5 mm (average one-wall component of the 11 sites 1.8 ± 1.3 mm); defect angles in this group ranged from 21–45° (average 31.4° ± 7°).

Bioresorbable barriers alone were used in seven sites presenting with a prevalent two- and three-wall morphology and narrow defect angles, ranging from 20–28° (average 24.1° ± 3.7°). EMD was applied to ten defects with a prevalent three-wall component. The defect angle in this group ranged from 19–31° (average 26.5° ± 4.3°).

In all treated sites primary closure was obtained at completion of the surgical procedure. At the 1-week follow-up, when sutures were removed, two sites, both accessed with a SPPF, presented with a small interdental wound dehiscence: one had been treated with a bioresorbable membrane and bone replacement graft, the other with EMD. At week 2, two additional small wound dehiscences were detected: one accessed with MPPT and treated with a bioresorbable membrane and bone replacement graft, the other accessed with SPPF and treated with a bioresorbable barrier alone. All the other sites (90%) remained closed during the whole early healing phase.

The 40 patients presented at the 1-year follow-up visit with excellent levels of plaque control and low levels of bleeding on probing. The 1-year CAL clinical attachment gain was 6 ± 1.8 mm (range 4–11 mm). No sites gained less then 4 mm of CAL; 77.5% gained 5 mm or more and 40% more then 6 mm. Residual probing depths were 2.7 ± 0.6 mm, with an average pocket depth reduction of 6.1 ± 1.9 mm. Only four sites showed a residual probing depth of 4 mm; all the other sites resulted with a 1-year PPD of 3 mm or less. A minimal increase of 0.1 ± 0.7 mm in gingival recession between baseline and 1 year was recorded.

The performance of each of the four treatments was described in the study and it indicated that, whenever the choices were made according to the protocol (i.e. based on: width of the interdental space to chose the papilla preservation surgery; morphology of the defect to choose the regenerative material; and choice of the material and local anatomy to select the suturing approach) all four approaches gave excellent results with clinical attachment level gains equal to 88–95% resolution of the original depth of the intrabony component of the defect (Cortellini & Tonetti 2005).

The use of this decision-making protocol in the reported case series resulted in 6 ± 1.8 mm of CAL gain at 1 year. These results were obtained in defects with an intrabony component of 6.6 ± 1.7 mm. The percentage clinical attachment gain therefore was 92.1 ± 12%. This indicates that a large part of the intrabony component of the defects was resolved. Using the Ellegaard criteria (Ellegaard *et al*. 1971), resolution of the intrabony component of the defect was either satisfactory or complete in all treated cases. In particular 40.5% of defects had attachment level gains equal to or greater then the baseline depth of the intrabony component, while the defect with the worst response showed a 71.4% CAL gain. Historical comparison with clinical experiments using bone grafting or GTR clearly indicates that the results of this trial approach were in the top percentiles in terms of clinical attachment level gains and defect resolution (Cortellini & Tonetti 2000a; Rosen *et al*. 2000).

Conclusions

GTR represents the best documented regenerative procedure for obtaining periodontal regeneration in intrabony defects and in degree II furcations. GTR has demonstrated significant clinical improvement beyond that achieved with only debridement in such defects. Regarding degree II maxillary furcations, the results following GTR treatment are inconsistent, and the treatment of degree III furcation defects is unpredictable. An added benefit may be obtained by the use of grafting materials in combination with GTR in some situations: in particular in furcation defects or to support bioresorbable membranes.

DFDBA alone gives documented improvements in some type of intrabony defects, in particular three-wall and two-wall defects.

EMD in gel formulation gives significant benefits in the treatment of intrabony defects, particularly those with a supportive anatomy (three-wall defects and narrow two-wall defects).

Differences between individuals and studies regarding the results of treating intrabony defects and class II furcations are related to patient compliance, maintenance procedures, selection of defects, surgical management, etc.

Periodontal regeneration obtained following GTR is stable on a long-term basis, provided good oral hygiene is maintained and a proper recall program is established. Current data indicate that, in patients participating in a supportive periodontal care program, 96% of teeth with severe intrabony defects and treated with a periodontal regenerative procedure could be retained for a period up to 15 years.

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Chapter 44

Mucogingival Therapy – Periodontal Plastic Surgery

Jan L. Wennström, Giovanni Zucchelli, and Giovan P. Pini Prato

Introduction

Mucogingival therapy is a general term used to describe periodontal treatment involving procedures for correction of defects in morphology, position, and/or amount of soft tissue and underlying bone support at teeth and implants (*Glossary of Terms in Periodontology* 2001).

A more specific term, *mucogingival surgery*, was introduced in the 1950s by Friedman (1957) and was defined as "surgical procedures designed to preserve gingiva, remove aberrant frenulum or muscle attachments, and increase the depth of the vestibule". Frequently, however, the term "mucogingival surgery" was used to describe all surgical procedures that involved both the gingiva and the alveolar mucosa. Consequently, not only were techniques designed (1) to enhance the width of the gingiva and (2) to correct particular soft tissue defects regarded as mucogingival procedures but (3) certain pocket elimination approaches were also included in this group of periodontal treatment modalities. In 1993 Miller proposed the term *periodontal plastic surgery*, considering that mucogingival surgery had moved beyond the traditional treatment of problems associated with the amount of gingivae and recession type defects to also include correction of ridge form and soft tissue esthetics. Periodontal plastic surgery would accordingly be defined as "surgical procedures performed to prevent or correct anatomic, developmental, traumatic or disease-induced defects of the gingiva, alveolar mucosa or bone" (Proceedings of the World Workshop in Periodontics 1996). Among treatment procedures that may fall within this definition are various soft and hard tissue procedures aimed at:

- Gingival augmentation
- Root coverage
- Correction of mucosal defects at implants
- Crown lengthening
- Gingival preservation at ectopic tooth eruption
- Removal of aberrant frenulum
- Prevention of ridge collapse associated with tooth extraction
- Augmentation of the edentulous ridge.

The focus of this chapter is mainly on treatment procedures for corrections of soft tissue defects in relation to the tooth and the edentulous ridge, while bone augmentation procedures are covered in Chapter 49.

Gingival augmentation

A review of the literature on gingival augmentation reveals that the rationale for increasing the width of gingiva as a means of promoting gingival health and

improving attachment levels is poorly supported by scientific evidence. Usually clinical impressions, case reports, and anecdotal information have been used as the main reference to justify surgical intervention. In this perspective a discussion of the scientific evidence forming the basis for our current understanding of the role played by the gingiva in the protection of the periodontium proper seems appropriate.

Gingival dimensions and periodontal health

For many years the presence of an "adequate" zone of gingiva was considered critical for the maintenance of marginal tissue health and for the prevention of continuous loss of connective tissue attachment (Nabers 1954; Ochsenbein 1960; Friedman & Levine 1964; Hall 1981; Matter 1982). Clinicians had the "impression" that sites with a narrow zone of gingiva (Fig. 44-1) were often inflamed while the wide zone of gingiva found at neighboring teeth remained healthy. The prevailing concept was thus that a narrow zone of gingiva was insufficient (1) to protect the periodontium from injury caused by friction forces encountered during mastication and (2) to dissipate the pull on the gingival margin created by the muscles of the adjacent alveolar mucosa (Friedman 1957; Ochsenbein 1960). Moreover it was believed that an "inadequate" zone of gingiva would (1) facilitate subgingival plaque formation because of improper pocket closure resulting from the movability of the marginal tissue (Friedman 1962) and (2) favor attachment loss and soft tissue recession because of less tissue resistance to apical spread of plaque-associated gingival lesions (Stern 1976; Ruben 1979). It was also considered that a narrow gingiva in combination with a shallow vestibular fornix might (1) favor the accumulation of food particles during mastication, and (2) impede proper oral hygiene measures (Gottsegen 1954; Rosenberg 1960; Corn 1962; Carranza & Carraro 1970).

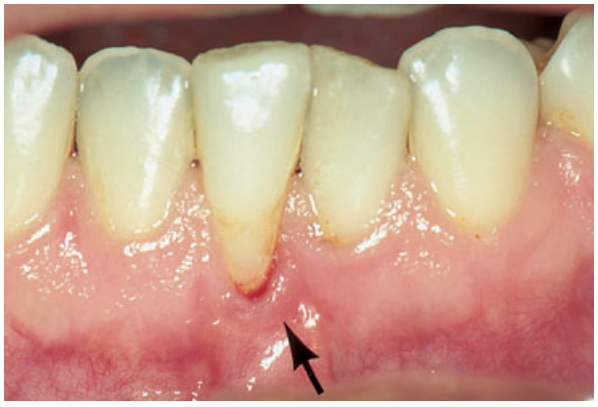


Fig. 44-1 A clinical photograph of a mandibular front tooth region. The gingiva on the buccal aspect of tooth 41 has a narrow width and shows more pronounced signs of inflammation than adjacent gingival units with a wider zone of gingiva.

The opinions expressed concerning what could be regarded as being an "adequate" or "sufficient" dimension of the gingiva varied. While some authors suggested that less than 1 mm of gingiva may be sufficient (Bowers 1963), others claimed that the apico-coronal height of keratinized tissue ought to exceed 3 mm (Corn 1962). A third category of authors had a more biologic approach to the question and stated that an adequate amount of gingiva is any dimension of gingiva which (1) is compatible with gingival health or (2) prevents retraction of the gingival margin during movements of the alveolar mucosa (Friedman 1962; De Trey & Bernimoulin 1980).

One of the first studies in which attempts were made to evaluate the significance of the gingival zone for the maintenance of periodontal health was carried out by Lang and Löe (1972) on dental students who had their teeth professionally cleaned once a day for 6 weeks. All buccal and lingual sites were examined for plaque, gingival conditions, and apico-coronal height of gingiva. The results showed that despite the fact that the tooth surfaces were free from plaque, all sites with less than 2 mm of gingiva exhibited persisting clinical signs of inflammation. Based on this observation the authors suggested that 2 mm of gingiva is an adequate width for maintaining gingival health. Subsequent clinical trials (Miyasato *et al*. 1977; Grevers 1977), however, failed to substantiate this concept of a required minimum dimension of gingiva. In fact, these clinical trials demonstrated that it is possible to maintain clinically healthy marginal tissues even in areas with less than 1 mm of gingiva.

The question whether a firmly attached portion of gingiva is critical for the protection of the periodontium proper was addressed by Wennström and Lindhe (1983a,b) utilizing the beagle dog model. In these studies dentogingival units with different clinical characteristics were experimentally established; (1) units with only a narrow and mobile zone of keratinized tissue and (2) units with a wide, firmly attached gingiva (Fig. 44-2). With daily performed mechanical plaque-control measures, the gingival units could be maintained free from clinical as well as histologic signs of inflammation irrespective of the presence or absence of an attached portion of gingiva. When bacterial plaque was allowed to accumulate (for 40 days), clinical signs of inflammation (redness and swelling) developed that were more pronounced in tooth regions with mobile gingiva (Fig. 44-3a) than in areas with presence of a wide and firmly attached gingival zone (Fig. 44-3b). However, histologic analysis revealed that the size of the inflammatory cell infiltrate and its extension in an apical direction (an assessment which indirectly may be used as an estimate of the apical migration of the bacterial plaque) were similar in the two categories of dentogingival units. The finding that the clinical signs of gingival inflammation did not correspond with the size of the inflammatory cell infiltrate illustrates the difficulties

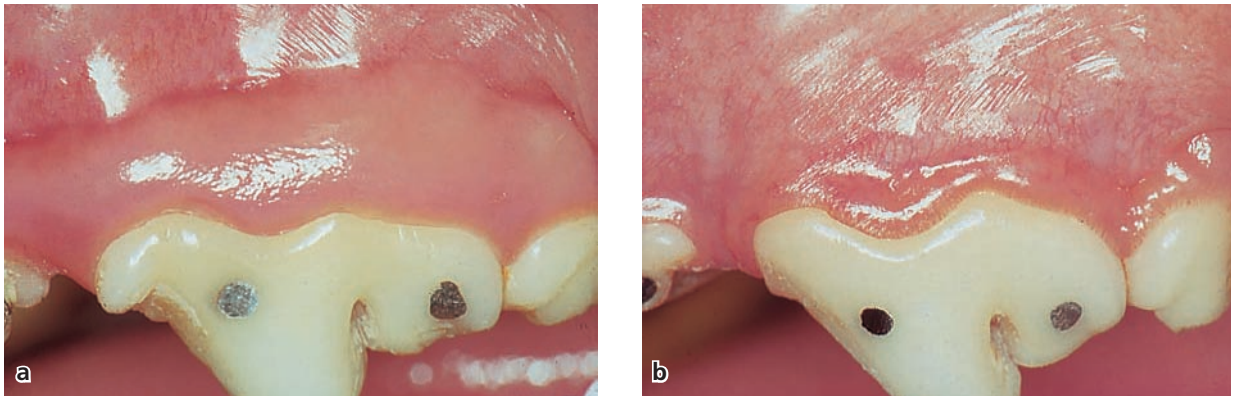


Fig. 44-2 Two teeth in a dog with varying dimensions of the marginal gingiva. (a) A buccal tooth site with a wide zone of attached gingiva. (b) A site with an unattached, narrow band of gingiva.

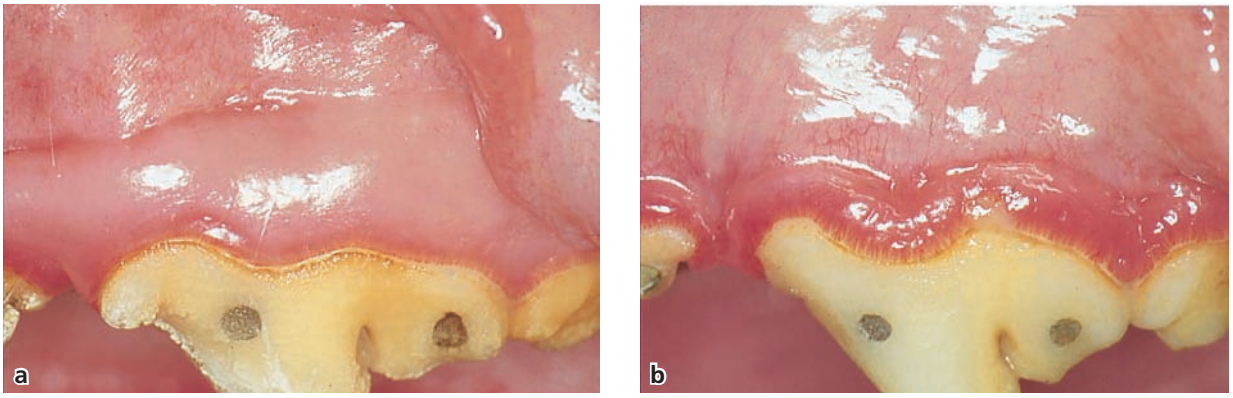


Fig. 44-3 The same teeth as in Fig. 44-2 after 40 days of plaque accumulation. The clinical signs of inflammation are more pronounced at the site with the narrow band of gingiva (b) than at the site with the wide zone of attached gingiva (a).

inherent in the interpretation of data from clinical examinations made in areas with varying width of gingiva. This should be kept in mind when interpreting the data by Lang and Löe (1972) showing that clinically visible signs of inflammation, such as redness and swelling, were more frequent in areas with less than 2 mm of gingiva than in areas with a wider zone of gingiva.

The necessity for and effectiveness of gingival augmentation in maintaining periodontal attachment was examined by Dorfman *et al*. (1980). Ninety-two patients with bilateral facial tooth surfaces exhibiting minimal keratinized tissue (i.e. less than 2 mm) had a free gingival graft placed on one side, while the contralateral side served as the untreated control. Prior to and after surgery the patients were subjected to scaling and root planing and instruction in oral hygiene measures. Not surprisingly, the investigators found a significant increase (approximately 4 mm) in the width of keratinized tissue at the grafted sites. This increased width of gingiva, as well as the clinical attachment level, was maintained throughout the 2 years of follow-up. In the control sites the width of gingiva was less than 2 mm and did not vary significantly during the observation period. However, the attachment level was also maintained unchanged in the non-grafted areas. Thus, the resistance to continuous attachment loss was not linked to the height (width) of gingiva, a conclusion that was further substantiated by subsequent 4- and 6-year follow-up reports of this patient material (Dorfman *et al*. 1982; Kennedy *et al*. 1985).

Further support for the conclusion that a minimal zone of gingiva may not compromise periodontal health is available in a number of other longitudinal clinical studies (e.g. Hangorsky & Bissada 1980; De Trey & Bernimoulin 1980; Lindhe & Nyman 1980; Schoo & van der Velden 1985; Kisch *et al*. 1986; Wennström 1987; Freedman *et al*. 1999). Hence, Hangorsky and Bissada (1980), who evaluated the long-term clinical effect of free soft tissue grafts, concluded that while the free gingival graft is an effective means to widen the zone of the gingiva, there is no indication that this increase has direct influence upon periodontal health.

Conclusion

Gingival health can be maintained independent of its dimensions. Furthermore, there is evidence from both experimental and clinical studies that, in the presence of plaque, areas with a narrow zone of

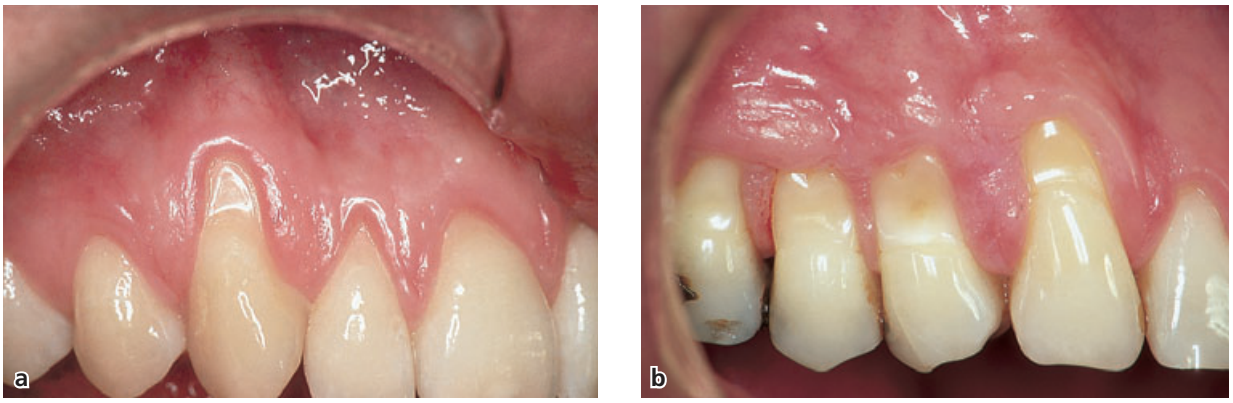


Fig. 44-4 Recessions associated with toothbrushing trauma. The marginal gingiva is clinically healthy and abrasion defects of various extension can be noted in the exposed roots.

gingiva possess the same "resistance" to continuous attachment loss as teeth with a wide zone of gingiva. Hence, the traditional dogma of the need of an "adequate" width (in millimeters) of gingiva, or attached portion of gingiva, for prevention of attachment loss is not scientifically supported.

Marginal tissue recession

Marginal tissue recession, i.e. displacement of the soft tissue margin apical to the cemento-enamel junction (CEJ) with exposure of the root surface, is a common feature in populations with high standards of oral hygiene (e.g. Sangnes & Gjermo 1976; Murtomaa *et al*. 1987; Löe *et al*. 1992; Serino *et al*. 1994), as well as in populations with poor oral hygiene (e.g. Baelum *et al*. 1986; Yoneyama *et al*. 1988; Löe *et al*. 1992; Susin *et al*. 2004). In populations maintaining high standards of oral hygiene, loss of attachment and marginal tissue recession are predominantly found at buccal surfaces (Löe *et al*. 1992; Serino *et al*. 1994), and are frequently associated with the presence of a "wedge-shaped defect in the crevicular area of one or several teeth" (Sangnes & Gjermo 1976). In contrast, all tooth surfaces are usually affected with soft tissue recession in periodontally untreated populations, although the prevalence and severity is more pronounced at single-rooted teeth than at molars (Löe *et al*. 1978; 1992; Miller *et al*. 1987; Yoneyama *et al*. 1988).

Tissue trauma caused by vigorous toothbrushing is considered to be a predominant causative factor for the development of recessions, particularly in young individuals. Traumatizing toothbrushing and tooth malposition are the factors most frequently found to be associated with marginal tissue recession (Sangnes 1976; Vekalahti 1989; Checchi *et al*. 1999). In addition, Khocht *et al*. (1993) showed that recessions are related to the use of hard toothbrushes. Other local factors that have been associated with marginal tissue recession are (1) alveolar bone dehiscences (Bernimoulin & Curilivic 1977; Löst 1984), (2) high muscle attachment and frenal pull (Trott & Love 1966), (3) plaque and calculus (van Palenstein Helderman *et al*. 1998; Susin *et al*. 2004), and (4) iatrogenic factors related to restorative and periodontal treatment procedures (Lindhe & Nyman 1980; Valderhaug 1980).

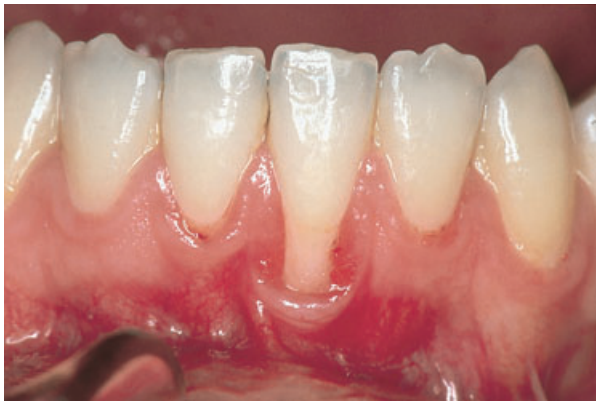


Fig. 44-5 A recession associated with localized plaque-induced inflammatory lesion.

At least three different types of marginal tissue recessions may exist:

- *Recessions associated with mechanical factors, predominately toothbrushing trauma* (Fig. 44-4). Recessions resulting from improper toothbrushing techniques are often found at sites with clinically healthy gingiva and where the exposed root has a wedge-shaped defect, the surface of which is clean, smooth and polished.
- *Recessions associated with localized plaque-induced inflammatory lesions* (Fig. 44-5). Such recessions may be found at teeth that are prominently positioned, i.e. the alveolar bone is thin or absent (bone dehiscence), and where in addition the gingival tissue is thin (delicate). An inflammatory lesion that develops in response to subgingival plaque occupies the connective tissue adjacent to the dentogingival epithelium. Measurements made by Waerhaug (1952) suggest that the distance between the periphery of microbial plaque on the tooth surface and the lateral and apical extension of the

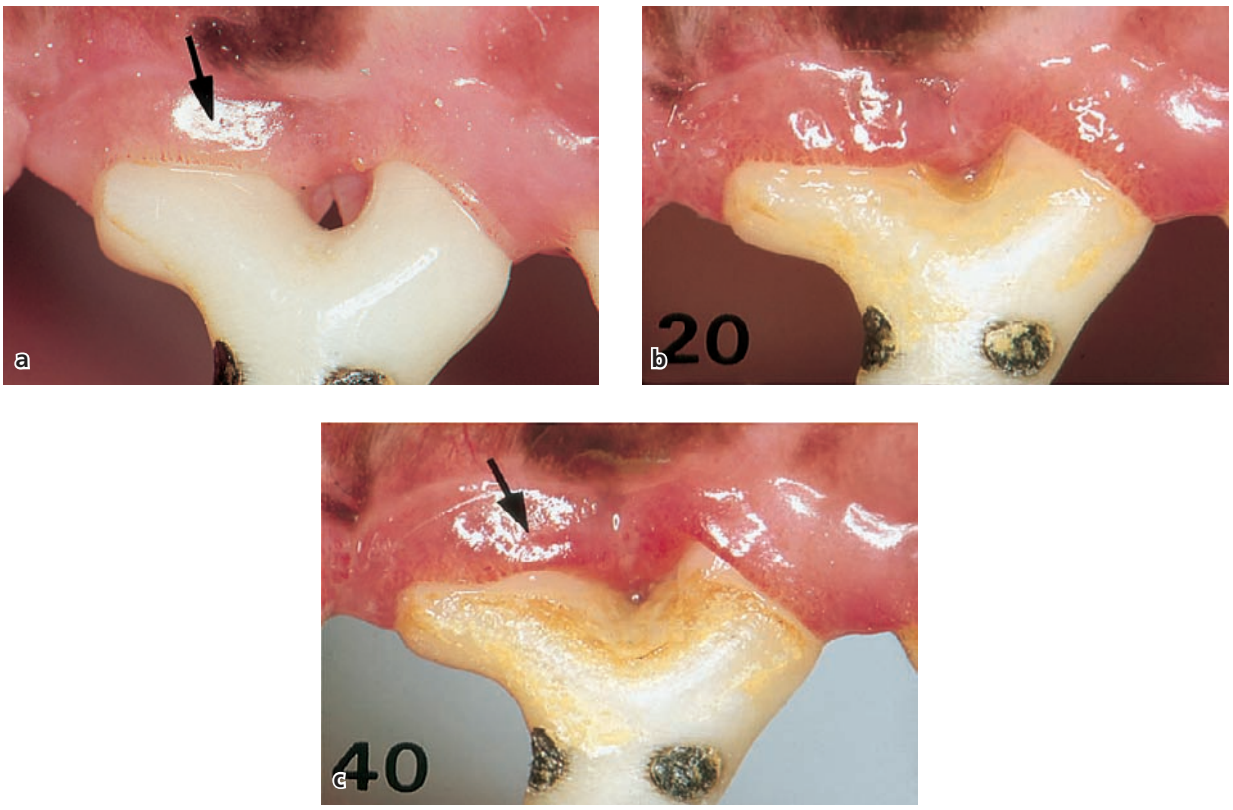


Fig. 44-6 Clinical photographs illustrating the development of a soft tissue recession as a result of plaque-induced inflammation in a beagle dog. (a) Note the thin but healthy gingiva (arrow) at the start of the plaque accumulation period. (b) Pronounced clinical signs of inflammation are seen after 20 days. (c) After 40 days of no tooth cleaning, the gingival margin has receded.

inflammatory cell infiltrate seldom exceeds 1–2 mm. Thus, if the free gingiva is voluminous the infiltrate will occupy only a small portion of the connective tissue. In a thin and delicate gingiva, on the other hand, the entire connective tissue portion may be engaged. Proliferation of epithelial cells from the oral as well as the dentogingival epithelium into the thin and degraded connective tissue may bring about a subsidence of the epithelial surface which clinically becomes manifest as recession of the tissue margin (Baker & Seymour 1976) (Fig. 44-6).

- *Recessions associated with generalized forms of destructive periodontal disease* (Fig. 44-7). The loss of periodontal support at proximal sites may result in compensatory remodeling of the support at the buccal/lingual aspect of the teeth leading to an apical shift of the soft tissue margin (Serino *et al*. 1994).

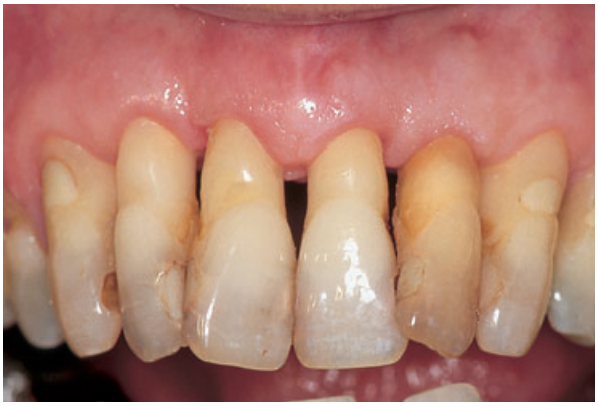


Fig. 44-7 Recessions associated with generalized forms of destructive periodontal disease. Recession of the soft tissue is found not only at the facial aspect of the teeth but also at proximal sites.

Cross-sectional studies showing that a correlation exists between the presence of recession defects and the height (width) of the gingiva (e.g. Stoner & Mazdyasna 1980; Tenenbaum 1982) have often been interpreted as an evidence that a narrow zone of gingiva is a contributing factor in the development of soft tissue recessions (Fig. 44-8). It should be realized, however, that data derived from cross-sectional studies can neither prove nor disprove a cause–effect relationship. Consequently, the data reported from such studies may equally well be interpreted to demonstrate that the formation of a recession defect results in a reduced height of the gingiva. Fig. 44-1 illustrates a lower incisor tooth region with a localized gingival recession at the buccal aspect of tooth 41. The gingiva apical to the recession defect is narrow ("insufficient") while at neighboring teeth the gingival height may be considered "adequate". It is reasonable to assume that the gingiva at tooth 41, *before*

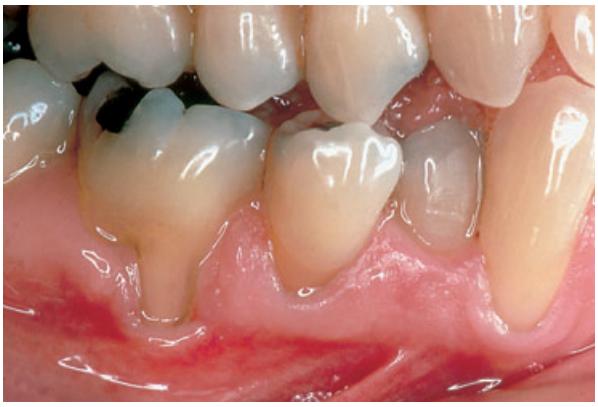


Fig. 44-8 A mandibular tooth segment with multiple buccal recessions illustrating the association proposed between recession depth and height of gingiva.

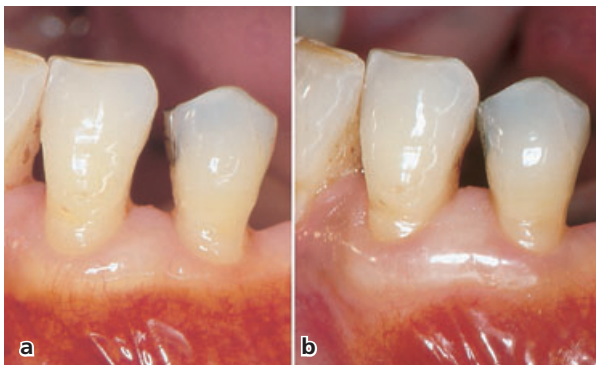


Fig. 44-9 (a) Clinical photographs of a canine and a first premolar in the mandibular jaw with <1 mm of attached portion of gingiva 6 months after surgical treatment. (b) Note the increase of the width of the gingiva at the facial aspect of the teeth and the more coronally positioned gingival margin 5 years later.

the recession defect developed, had a height that was similar to that found at tooth 31 and tooth 42. In other words, the narrow zone of gingiva found at tooth 41 may be the result of *loss of gingival tissue during the period of recession development*, rather than being the cause of the formation of the defect. If this interpretation is valid, the rationale for increasing the height of the gingiva in an area *apical to the existing defect* as a means of preventing further recession may appear somewhat obscure. In fact, data obtained from prospective, longitudinal studies of patients showing areas with only a minimal zone of gingiva favor the conclusion that a certain quantity of gingiva is not essential for the preclusion of soft tissue recessions.

Lindhe and Nyman (1980) examined the alterations of the position of the gingival margin following periodontal surgery in 43 patients with advanced periodontal breakdown. Following active treatment, all patients were recalled once every 3–6 months for maintenance care. The position of the soft tissue margin in relation to the CEJ was assessed on the facial aspect of all teeth after initial healing and after 10–11 years of maintenance. The presence or absence of keratinized tissue after surgical treatment was also determined. The results showed that both in areas with and without visible keratinized tissue after healing, a small coronal regrowth (≈1 mm) of the soft tissue margin had occurred during the period of maintenance. In other words, no recession was observed in this group of patients maintained on a careful prophylaxis program.

Dorfman *et al*. (1982) reported a 4-year follow-up study including 22 patients with bilateral tooth areas exhibiting gingival recession and lack of firmly attached marginal soft tissue. In conjunction with scaling and root planing a free gingival graft was placed on one side, while the contralateral control side was treated by scaling and root planing only. All patients were recalled for prophylaxis once every 3–6 months during a 4-year period. The data obtained from the examinations of the non-grafted control areas revealed that no further recession of the soft tissue margin or loss of probing attachment had occurred despite the lack of attached marginal tissue. In fact, there was a slight gain of probing attachment. The authors concluded that recession sites without attached gingiva might not experience further attachment loss and recession if the inflammation is controlled. In a subsequent report (Kennedy *et al*. 1985), the authors reported data on 10 patients who had not participated in the maintenance program for a period of 5 years. In these patients plaque and clinical signs of inflammation as well as some further recession were noted at the 5-year examination as compared with the data obtained after termination of active treatment. However, except for the clinical signs of inflammation, which were more pronounced in non-grafted sites, no differences were observed between control sites with <1 mm or complete lack of attached gingiva and grafted sites.

The lack of relationship between the height of gingiva and the development of soft tissue recession is further validated by results from longitudinal clinical studies (Schoo & van der Velden 1985; Kisch *et al*. 1986; Wennström 1987; Freedman *et al*. 1999). The study by Wennström (1987) reports observations made at 26 buccal sites surgically deprived of all keratinized tissue. A baseline examination carried out 6 months after treatment revealed that these sites had regained a zone of gingiva which was, however, not attached or had only a minimal (<1 mm) portion attached to the underlying hard tissues (Figs. 44-9a and 44-10a). Adjacent teeth with a broad zone of attached gingiva were also included in the examinations. In most sites the position of the soft tissue margin had been maintained unchanged over 5 years (Figs. 44-9b and 44-10b). A further apical displacement of the soft tissue margin had occurred at two out of 26 sites with no/minimal attached portion of gingiva and at three out of 12 adjacent control sites with a wide attached zone of gingiva. Since four of these five sites were found in one patient (Fig. 44-11), and all sites were free from clinical signs of inflam-

mation, excessive toothbrushing was considered to be the causative factor, and following correction of the brushing technique no further progression was observed. Furthermore, the development of soft tissue recession at the control sites resulted in a decreased width of the gingiva, an observation that supports the concept that a narrow zone of gingiva apical to a localized recession is a consequence rather than a cause of the recession.

Conclusion

Marginal soft tissue recession is a common feature in populations with good as well as poor standards of oral hygiene. There is evidence to suggest that the predominant cause for localized recessions in young individuals is toothbrushing trauma, while periodontal disease may be the primary cause in older adults. Evidence from prospective longitudinal studies shows that the gingival height is not a critical factor for the prevention of marginal tissue recession, but that the development of a recession will result in loss of gingival height.

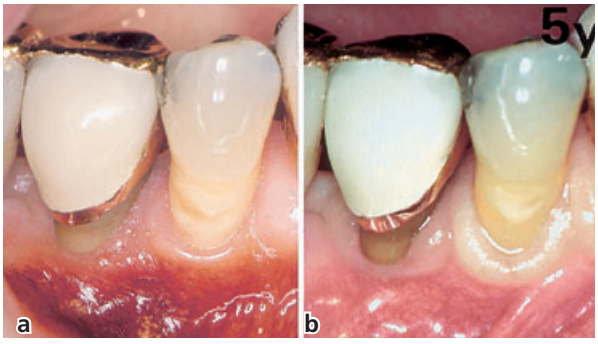


Fig. 44-10 (a) A mandibular canine and first premolar tooth region showing a very narrow zone of gingiva 6 months after surgical therapy. (b) No major change in the position of the soft tissue margin has occurred during a 5-year period despite the lack of attached gingiva.

Marginal tissue recession and orthodontic treatment

Results from clinical and experimental research have documented that most forms of orthodontic therapy are innocuous to the periodontium (see Chapter 57). The clinician may experience, however, that some patients respond to frontal movements of incisors and lateral movements of posterior teeth by gingival recession and loss of attachment (Maynard & Ochsenbein 1975; Coatoam *et al*. 1981; Foushee *et al*. 1985) (Fig. 44-12). Based on the clinical observation that recession may occur during orthodontic therapy involving sites that have an "insufficient" zone of gingiva, it was suggested that a grafting procedure to increase the gingival dimensions should precede the initiation of orthodontic therapy in such areas (Boyd 1978; Hall 1981; Maynard 1987).

As discussed previously, the presence of an alveolar bone dehiscence is considered to be a prerequisite for the development of a marginal tissue recession, i.e. a root dehiscence may establish an environment that is conducive for loss of gingival tissue. With respect to orthodontic therapy, this would imply that as long as a tooth is moved exclusively within the alveolar bone, soft tissue recession will not develop (Wennström *et al*. 1987). On the other hand, predisposing alveolar bone dehiscences may be induced by uncontrolled facial expansion of a tooth through the cortical plate, thereby rendering the tooth liable to development of soft tissue recession. In this context it is interesting to note that experimental studies have shown that labial bone will reform in the area of a dehiscence when the tooth is retracted towards a proper positioning of the root within the alveolar process (Engelking & Zachrisson 1982; Karring *et al*. 1982) (Fig. 44-13). It is therefore likely that the reduction in recession seen at a previously prominently positioned tooth that has been moved into a more proper position within the alveolar process (Fig. 44-14) is also accompanied by bone formation.

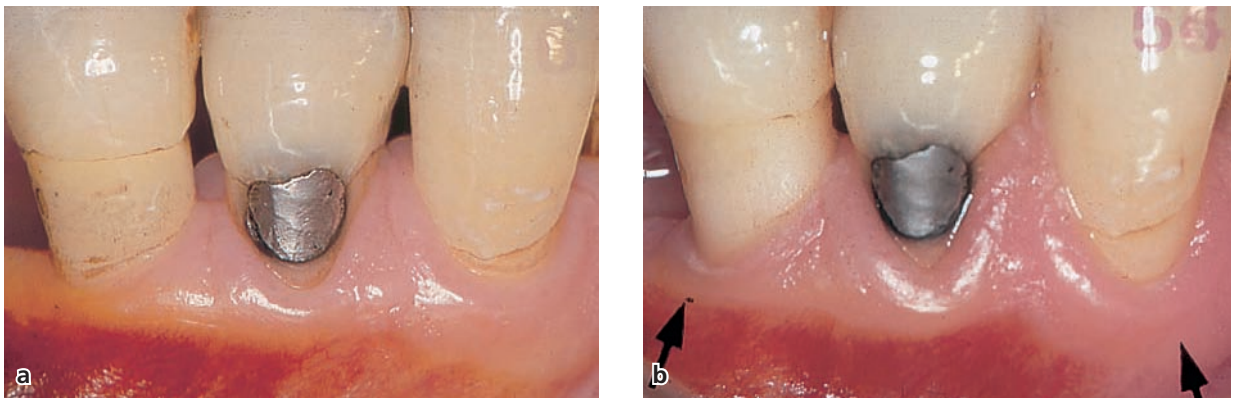


Fig. 44-11 Clinical photographs of the mandibular right canine–premolar tooth region in a patient showing several sites with apical displacement of the soft tissue margin during the 5 years of observation. (a) At the initial examination the two premolars had <1 mm and the canine >1 mm of attached portion of gingiva. (b) After 5 years, recession and loss of keratinized tissue can be seen on the buccal aspect of the canine, which initially had a broad zone of gingiva (black arrow). The second premolar also showed further apical displacement of the soft tissue margin (white arrow).

Alterations occurring in gingival dimensions and marginal tissue position in conjunction with orthodontic therapy are related to the *direction of tooth movement*. Facial movement results in reduced facial gingival dimensions, while an increase is observed following lingual movement (Coatoam *et al*. 1981; Andlin-Sobocki & Bodin 1993). Recession of the labial gingival margin and loss of attachment was demonstrated in experimental studies in the monkey following either tipping and extrusion movements or bodily movements of incisors (Batenhorst *et al*. 1974; Steiner *et al*. 1981). However, similarly designed studies carried out in dogs (Karring *et al*. 1982; Nyman *et al*. 1982) and humans (Rateitschak *et al*. 1968) failed to demonstrate that labial tooth movement is accompanied by marginal tissue recession and attachment loss. The conflicting results may be related to differences with respect to e.g. (1) the amount of labial tooth displacement, (2) the presence/absence of plaque and gingival inflammation in the regions subjected to tooth movement, and/or (3) differences in gingival dimensions. Steiner *et al*. (1981) speculated on mechanisms by which gingival tissue could be lost as a result of labial tooth movement and suggested that tension in the marginal tissue created by the forces applied to the teeth could be an important factor. If this hypothesis were valid, obviously the volume (thickness) of the gingival tissue at the pres-

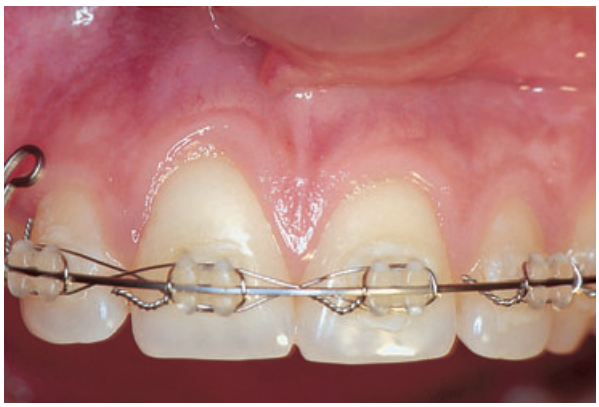


Fig. 44-12 Soft tissue recession at tooth 11 observed during the course of active orthodontic treatment.

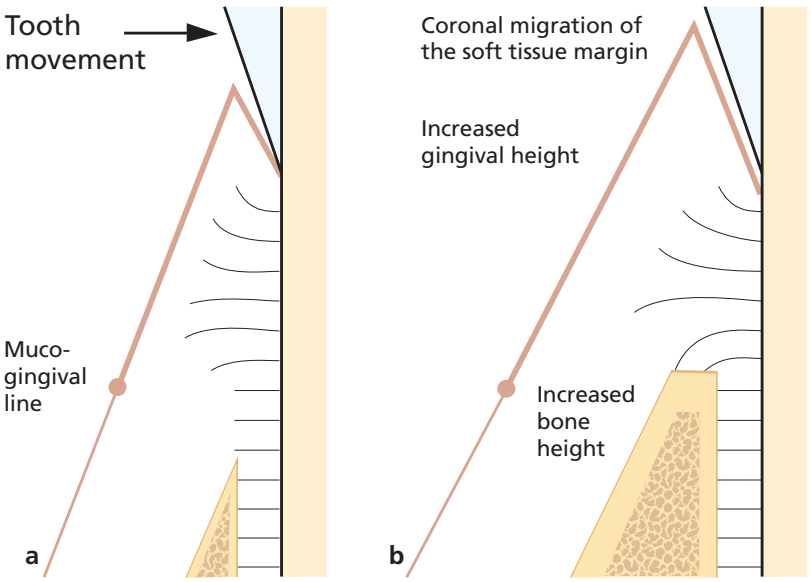


Fig. 44-13 (a) Schematic drawing illustrating alterations occurring in the marginal periodontal tissues following lingual movement of a tooth prominently positioned in the arch and having a bone dehiscence. (b) An increase in bone height and gingival height will be seen as well as a coronal migration of the soft tissue margin following lingual positioning of the tooth.

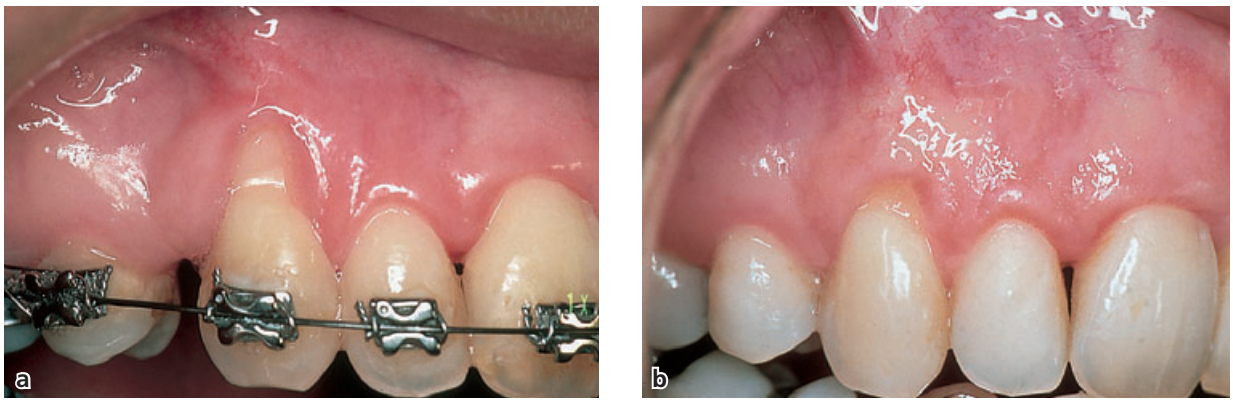


Fig. 44-14 (a) A prominently positioned 13 showing soft tissue recession. (b) The same tooth following the completion of the orthodontic tooth movement. Note the reduction of the recession that has taken place as a consequence of the changed position of the tooth.

sure side, rather than its apico-coronal height, would determine whether or not marginal tissue recession develops during orthodontic therapy.

Support for the hypothesis is obtained from an experimental study in monkeys (Wennström *et al*. 1987) in which teeth were orthodontically moved into areas with varying thickness and quality of the marginal soft tissue. Following extensive bodily movement of incisors in a labial direction through the alveolar bone (Fig. 44-15), most teeth showed a small apical displacement of the soft tissue margin but no loss of connective tissue attachment (Fig. 44-16). In other words, the apical displacement of the gingival margin was the result of a reduced height of the free gingiva (Fig. 44-17), which in turn may be related to tension ("stretching") in the soft tissues during the facial tooth movement and reduced bucco-lingual tissue thickness. Similar to results presented by Foushee *et al*. (1985) from a study in humans, no relationship was found between the initial apico-coronal width (height) of the gingiva and the degree of apical displacement of the soft tissue margin during orthodontic therapy. Thus, the findings do not lend support to the concept of a certain zone of gingiva as essential for the prevention of recession during orthodontic therapy, but rather collaborate observations reported by Coatoam *et al*. (1981) that the integrity of the periodontium can also be maintained during orthodontic therapy in areas which have only a minimal zone of gingiva.

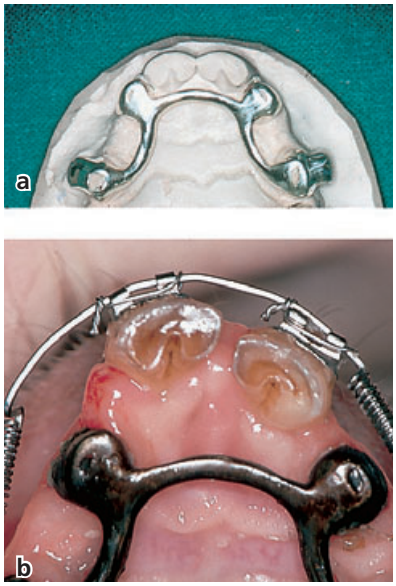


Fig. 44-15 Occlusal view of the maxillary jaw in a monkey showing the position of the central incisors before (a) and after (b) bodily movement in labial direction. The canines and lateral incisors were joined in an individual fabricated silver splint and used as anchorage teeth.

In the experimental studies by Steiner *et al*. (1981) and Wennström *et al*. (1987) it was observed that teeth, which experienced loss of connective tissue attachment when orthodontically moved facially, showed obvious clinical signs of inflammation throughout the experimental period. Since it has been demonstrated that, in presence of plaque-induced suprabony lesions, orthodontic forces generating bodily tooth movement are not capable of causing accelerated destruction of the connective tissue attachment (Ericsson *et al*. 1978), a decreased bucco-lingual dimension of the border tissue due to "stretching" of the facial gingiva may have favored the destructive effect of the plaque-associated inflammatory lesion. This assumption is validated by the observations that, in the presence of plaque-induced gingivitis, a thin marginal soft tissue is more susceptible to complete breakdown than a thick one (Baker & Seymour 1976). Furthermore, no difference in attachment loss was observed at plaque-infected teeth that were bodily moved *within the alveolar bone*, irrespective of the type of bordering soft tissue (gingiva or lining mucosa) (Wennström *et al*. 1987). Hence, the *thickness rather than the quality* of the marginal soft tissue on the pressure side of the tooth may be the determining factor for the development of the recession. The interpretation is supported by findings of recent clinical studies in humans analyzing factors of importance for the development of recessions during labial movement of mandibular incisors. Melsen and Allais (2005) found that gingival inflammation and a "thin gingival

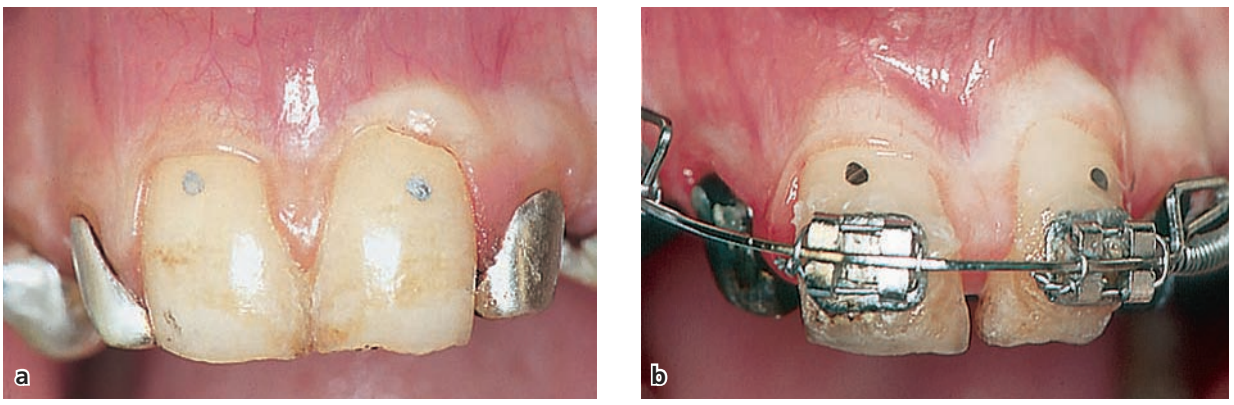


Fig. 44-16 The buccal aspect of the central incisors shown in Fig. 44-15, before (a) and after (b) the labial tooth movement. No obvious change in the location of the gingival margin has occurred despite the pronounced labial displacement of the incisors.

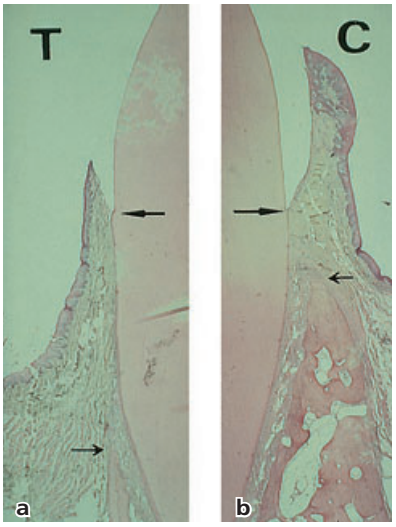


Fig. 44-17 Histologic specimens showing (a) reduced alveolar bone height at an incisor bodily moved in labial direction and (b) normal alveolar bone height at a non-moved control tooth. Note the maintained level of connective tissue attachment and the reduced height of the free gingiva at the labially displaced incisor (a). Large arrows indicate the position of the cemento-enamel junction and small arrows the position of the alveolar bone crest.

biotype" were significant predictors for gingival recession, and Yared *et al*. (2006) reported that 93% of the teeth that developed recession had a gingival thickness less than 0.5 mm. Hence, the observations made in the studies discussed strongly emphasize the importance of adequate infection control during orthodontic treatment.

Conclusion

The clinical implication of the results from the studies discussed is that labial tooth movement should be preceded by careful examination of the dimensions of the tissues covering the facial aspect of the teeth to be moved. As long as the tooth can be moved within the envelope of the alveolar process, the risk of harmful side effects in the marginal tissue is minimal, irrespective of the dimensions and quality of the soft tissue surrounding the tooth. If, however, the tooth movement is expected to result in the establishment of an alveolar bone dehiscence, the volume (thickness) of the covering soft tissue should be considered as a factor that may influence the development of soft tissue recession during, as well as after, the phase of active orthodontic therapy. A thin gingiva may serve as a *locus minorus resistentia* to developing soft tissue defects in the presence of plaque-induced inflammation or toothbrushing trauma.

Gingival dimensions and restorative therapy

The placement of restoration margins subgingivally may not only create a direct operative trauma to the tissues (Donaldson 1974), but may also facilitate subgingival plaque accumulation, with resultant inflammatory alterations in the adjacent gingiva and recession of the soft tissue margin (Parma-Benfenati *et al*. 1985; Lang 1995; Günay *et al*. 2000). Over a 10-year period, Valderhaug (1980) evaluated longitudinally the soft tissue alterations taking place at facial sites of 286 teeth with subgingivally or supragingivally placed crown margins in 82 patients. The re-examination performed 1 year after insertion of the restorations revealed that the gingivae at teeth with subgingival restoration margins were more inflamed than at those with supragingivally placed borders. Of the 150 teeth which had the facial crown margin located subgingivally at the time of cementation, 40% already showed supragingival exposure of the crown margin after 1 year, and at the 10-year examination as many as 71% had become supragingivally positioned due to recession of the soft tissue margin. Compared to teeth with supragingivally placed crown margins the amount of recession and clinical attachment loss was greater at sites with subgingivally placed restoration margins.

Stetler and Bissada (1987) evaluated the periodontal conditions at teeth with subgingivally placed restoration margins on teeth with varying apico-coronal height of gingiva and found that teeth having a narrow (<2 mm) band of gingiva showed more pronounced clinical signs of inflammation than restored teeth with a wide gingival zone, but that there was no difference in loss of probing attachment. However, if subgingivally placed restorations favor plaque accumulation and the adjacent gingiva is thin, there may be a potential risk for the development of soft tissue recession. In fact, an experimental study in the beagle dog (Ericsson & Lindhe 1984), in which metallic strips were inserted subgingivally in areas with varying width of gingiva, showed that in sites with a thin gingival margin, recession was a more likely consequence of the combined tissue trauma caused by the insertion of the strip and subsequent plaque accumulation during a 6-month period than in sites with a broad gingival zone. The authors suggested that the placement of restorations in a subgingival position might favor plaque retention and at sites with a thin gingiva this will lead to loss of tissue height, i.e. an apical displacement of the soft tissue margin. Accordingly, if such an apical displacement as a consequence of plaque-induced inflammation is to be prevented, either the plaque-control standard has to be improved or the *thickness* of the gingival margin has to be increased. However, an increased gingival dimension will not prevent the apical propagation of the plaque-associated lesion and the associated loss of periodontal attachment.

Conclusion

Subgingival placement of the margin of a restoration is likely to result in soft tissue recession over time.

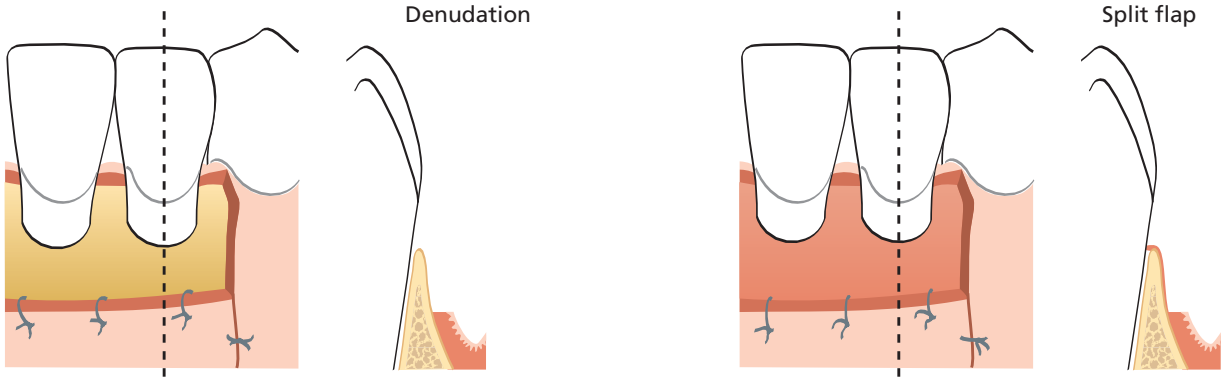


Fig. 44-18 The use of vestibular extension operations for increasing the width of the gingiva involves the production of a wound extending from the gingival margin to a level some millimeters apical to the mucogingival junction. With the "denudation" technique all soft tissue is removed leaving the alveolar bone exposed. With the "split flap" procedure only the superficial portion of the oral mucosa is removed leaving the bone covered with connective tissue.

Experimental and clinical data suggest that the thickness of the marginal gingiva, but not the apico-coronal width of the gingiva, may influence the magnitude of recession taking place as a result of direct mechanical trauma during tooth preparation and bacterial plaque retention.

Indications for gingival augmentation

Scientific data obtained from well controlled clinical and experimental studies have unequivocally demonstrated that the apico-coronal width of gingiva and the presence of an attached portion of gingiva are not of decisive importance for the maintenance of gingival health and the height of the periodontal tissues. Consequently, the presence of a narrow zone of gingiva *per se* cannot justify surgical intervention (Proceedings of the 1st European Workshop on Periodontology 1994; Proceedings of the World Workshop in Periodontics 1996). However, gingival augmentation should be considered in situations where, for example, the patient experiences discomfort during toothbrushing and/or chewing due to an interfering lining mucosa. Furthermore, when orthodontic tooth movement is planned and the final positioning of the tooth can be expected to result in an alveolar bone dehiscence, an increase of the *thickness* of the covering soft tissue may reduce the risk for development of soft tissue recession. An increase of the *thickness* of the gingival margin may also be considered in certain situations when subgingival restorations are placed in areas with a thin marginal tissue.

Gingival augmentation procedures

Gingival augmentation operations comprise a number of surgical techniques, the majority of which have been developed mainly on an empiric basis and without sufficient knowledge about the biology of the involved tissues. The earliest of these techniques are the "vestibular extension operations" which were designed mainly with the objective of extending the depth of the vestibular sulcus (Bohannan 1962a,b). In recent years, however, the use of pedicle or free soft tissue grafts have become the most commonly used techniques in the management of "insufficient" gingival dimensions, because of higher predictability of the healing result.

Vestibular/gingival extension procedures

The "denudation techniques" included the removal of all soft tissue within an area extending from the gingival margin to a level apical to the mucogingival junction leaving the alveolar bone completely exposed (Ochsenbein 1960; Corn 1962; Wilderman 1964) (Fig. 44-18). Healing following this type of treatment resulted often in an increased height of the gingival zone, although in some cases only a very limited effect was observed. However, the exposure of alveolar bone produced severe bone resorption with permanent loss of bone height (Wilderman *et al*. 1961; Costich & Ramfjord 1968). In addition, the recession of marginal gingiva in the surgical area often exceeded the gain of gingiva obtained in the apical portion of the wound (Carranza & Carraro 1963; Carraro *et al*. 1964). Due to these complications and severe postoperative pain for the patient, the use of the "denudation technique" can hardly be justified.

With the "periosteal retention" procedure or "split flap" procedure (Fig. 44-18) only the superficial portion of the oral mucosa within the wound area was removed leaving the bone covered by periosteum (Staffileno *et al*. 1962, 1966; Wilderman 1963; Pfeifer 1965). Although the preservation of the periosteum implies that less severe bone resorption will occur than following the "denudation technique", loss of crestal bone height was also observed following this type of operation unless a relatively thick layer of connective tissue was retained on the bone surface (Costich & Ramfjord 1968). If a thick layer was not secured, the periosteal connective tissue tended to undergo necrosis and the subsequent

healing closely resembled that following the "denudation technique" described above.

Other described gingival extension procedures may be considered as modifications of the "denudation" and "split flap" techniques or combinations of these procedures. The apically repositioned flap procedure (Friedman 1962), for instance, involved the elevation of soft tissue flaps and their displacement during suturing in an apical position, often leaving 3–5 mm of alveolar bone denuded in the coronal part of the surgical area. This resulted in the same risk for extensive bone resorption as other "denudation techniques". It was proposed by Friedman (1962) that a post-surgical increase of the width of the gingiva can be predicted with the "apically repositioned flap", but several studies indicated that the presurgical width most often was retained or became only slightly increased (Donnenfeld *et al*. 1964; Carranza & Carraro 1970).

The vestibular/gingival extension procedures referred to were based on the assumption that it is the frictional forces encountered during mastication that determines the presence of a keratinized tissue adjacent to the teeth (Orban 1957; Pfeifer 1963). Therefore, it was believed that by the displacement of muscle attachments and the extension of vestibular depth, the regenerating tissue in the surgical area would be subjected to physical impacts and adapt to the same functional requirements as those met by "normal" gingiva (Ivancie 1957; Bradley *et al*. 1959; Pfeifer 1963). Later studies, however, showed that the characteristic features of the gingiva are determined by some inherent factors in the tissue rather than being the result of functional adaptation and that the differentiation (keratinization) of the gingival epithelium is controlled by morphogenetic stimuli from the underlying connective tissue (see Chapter 1).

Grafting procedures

The gingival and palatal soft tissues will maintain their original characteristics after transplantation to areas of the alveolar mucosa (see Chapter 1). Hence, the use of transplants offers the potential to predict the post-surgical result. The type of transplants used can be divided into (1) pedicle grafts, which maintain their connection with the donor site after placement at the recipient site (Fig. 44-19), and (2) free grafts that are completely deprived of their connection with the donor area (Fig. 44-20). For gingival augmentation free grafts have been used most commonly (Haggerty 1966; Nabers 1966; Sullivan & Atkins 1968a; Hawley & Staffileno 1970; Edel 1974). Acellular freeze-dried dermal matrix (ADM) allografts may be utilized

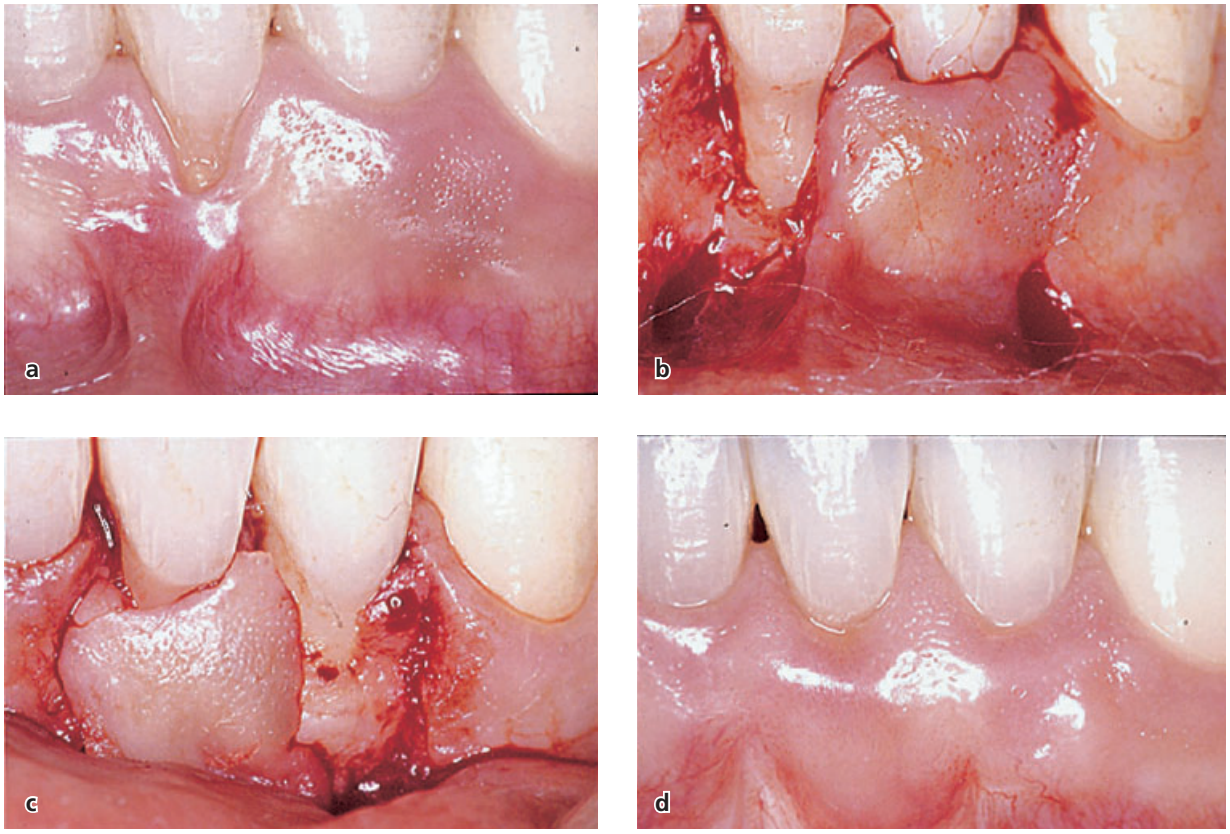


Fig. 44-19 Pedicle graft procedure for gingival augmentation. (a) A lower central incisor with facial soft tissue recession associated with high attachment of a frenulum. (b) The frenulum is released and a split flap of keratinized tissue is dissected from the area of the neighboring tooth. (c) The mobilized soft tissue flap is laterally moved and secured in position at the recipient site. (d) The healing result 1 year post-treatment shows the establishment of a broad zone of keratinized tissue without interfering frenulum.

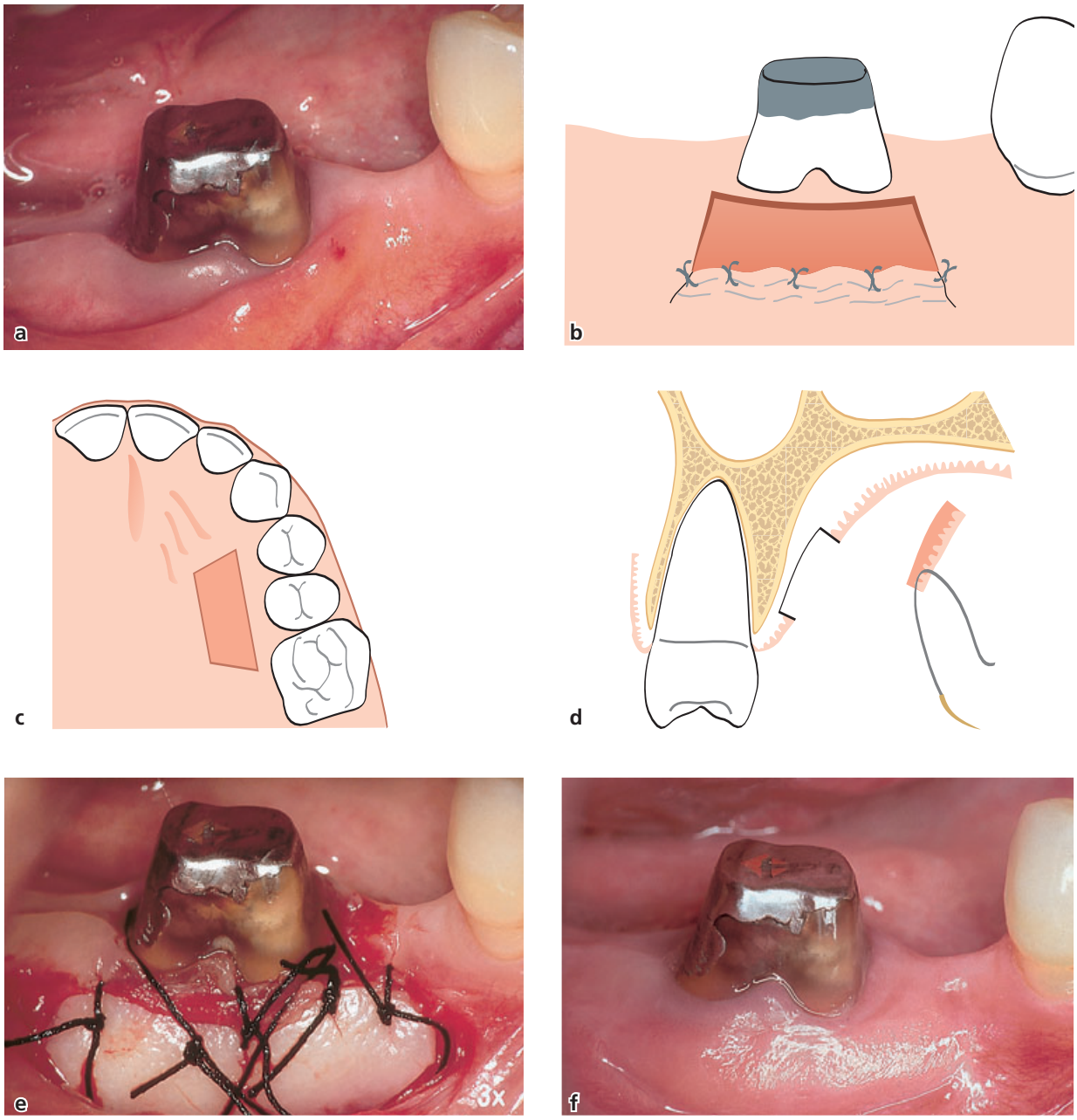


Fig. 44-20 Grafting procedure for gingival augmentation. (a) A lower molar at which the patient experiences discomfort during toothbrushing due to interfering lining mucosa and high attachment of a frenulum. Decision was made to displace the attachment of the frenulum apically and augment the gingival zone through the placement of a free graft. (b) A partial-thickness flap is dissected to prepare a recipient bed. The flap is displaced apically and sutured. (c,d) A graft with a thickness of 1.5–2 mm and of sufficient size and contour (a foil template of the recipient site may be used) is dissected from the palatal mucosa in the region of the premolars. (e) The graft is immediately transferred to the prepared recipient bed and anchored by sutures to secure a close adaptation of the graft to the recipient bed. (f) A periodontal dressing is applied to protect the graft. Following healing a broad zone of keratinized tissue has been established.

as an alternative to the use of an autogenous mucosal graft from the palate (Wei *et al*. 2000; Harris 2001), but the increase in the width of keratinized tissue following the use of these grafts may not be as predictable as with the use of autogenous grafts.

Technique

- The surgical procedure is initiated with the preparation of the recipient site (Fig. 44-20a-b). A periosteal bed free from muscle attachment and of sufficient size is prepared by sharp dissection. The partial-thickness flap is displaced apically and sutured.
- In order to ensure that a graft of sufficient size and proper contour is removed from the donor area, usually the palatal mucosa in the region of the premolars, it is recommended to produce a foil template over the recipient site. The template is transferred to the donor site where it is outlined by a shallow incision (Fig. 44-20c). A graft with a thickness of approximately 1.5–2 mm is then dissected from the donor area (Fig. 44-20d). It is

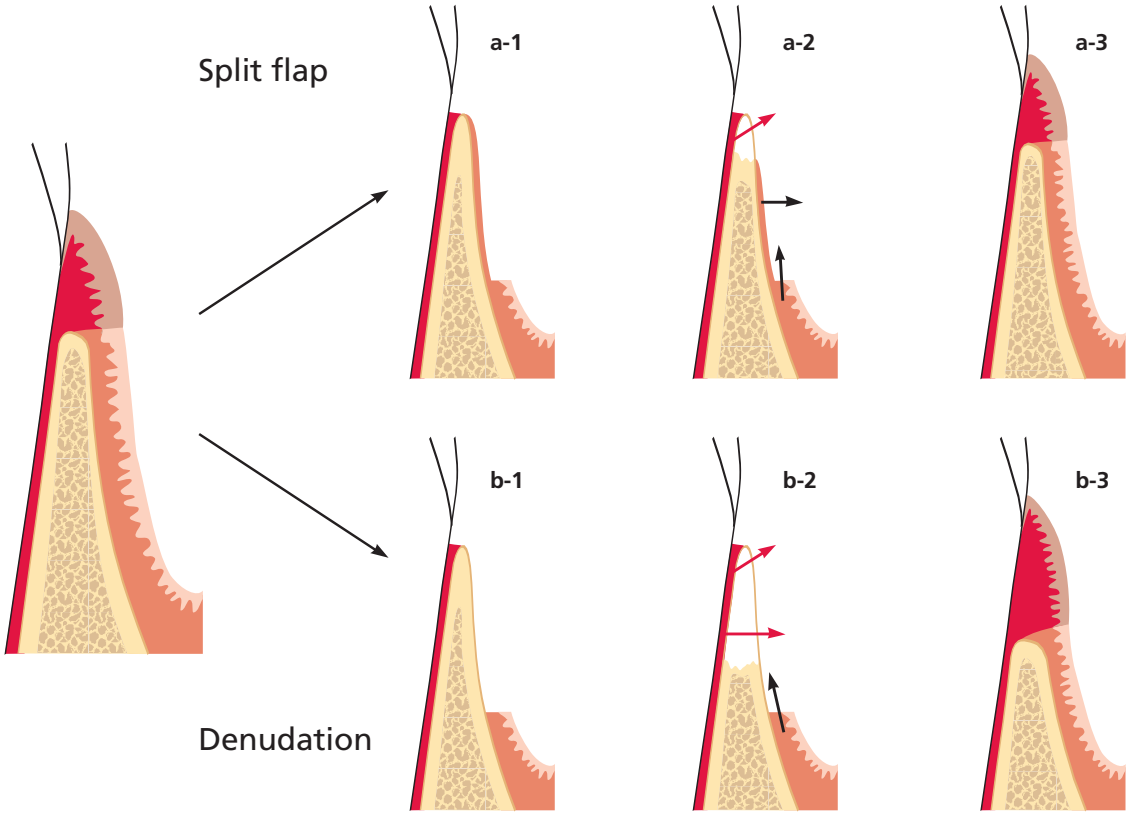


Fig. 44-21 Schematic drawing illustrating different stages of healing following the "split-flap" (a) and "denudation" (b) techniques. Cells from the oral mucosa, bone, and periodontal ligament (arrows) participate in granulation tissue formation. Due to the difference in the degree of bone resorption (a-2, b-2), a larger area of the coronal portion of the wound is filled with granulation tissue from the periodontal ligament following "denudation" than following the "split-flap" technique. Since granulation tissue from the periodontal ligament possesses the ability to induce a keratinized epithelium, "denudation" usually results in a wider zone of keratinized tissue than is the case following the "split-flap" technique (a-3, b-3).

advocated to place the sutures in the graft before it is cut completely free from the donor area since this may facilitate its transfer to the recipient site.

- The graft is immediately transferred to the prepared recipient bed and sutured (Fig. 44-20e). In order to immobilize the graft at the recipient site the sutures must be placed in the periosteum or the adjacent attached gingiva. After suturing, pressure is exerted against the graft for 5 minutes in order to eliminate blood and exudate from between the graft and the recipient bed. The graft and the palatal wound are protected with a periodontal dressing. To retain the dressing in the palatal site, a stent usually has to be used.
- The sutures and periodontal dressing are removed after 1–2 weeks.

For description of the pedicle graft procedure, see "Root coverage procedures".

Healing following gingival augmentation procedures

Vestibular/gingival extension procedures

Since the specificity of the gingiva is determined by some inherent factor in the tissues, the post-operative results of vestibular extension procedures depend on the degree to which the various tissues contribute to the formation of granulation tissue in the wound area (Karring *et al*. 1975). Following the "denudation" or "split flap technique", the wound area is filled with granulation tissue derived from the periodontal ligament, the tissue of the bone marrow spaces, the retained periosteal connective tissue, and the surrounding gingiva and lining mucosa (Fig. 44-21). The degree of bone resorption induced by the surgical trauma influences the relative amount of granulation tissue that grows into the wound from these various tissue sources. The resorption of crestal bone exposes varying amounts of the periodontal ligament tissue in the marginal area allowing granulation tissue from the periodontal ligament to fill out the coronal portion of the wound. The greater the bone loss, the greater is the portion of the wound that becomes filled with granulation tissue from the periodontal ligament. This particular tissue possesses the capability to induce keratinization of the covering epithelium. This means that the widening of the keratinized tissue following "denudation" and "split flap" operations is achieved at the expense of a reduced bone height. The "denudation technique" usually results in more bone loss than the "split flap technique". Therefore, a greater amount of granulation tissue

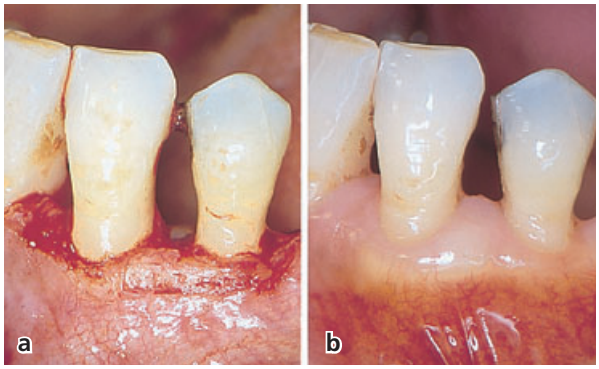


Fig. 44-22 (a) Clinical photograph of the buccal aspect of a canine and a premolar following the removal of the entire zone of gingiva by a gingivectomy procedure. (b) The healing result 9 months after surgery shows the regain of keratinized tissue.

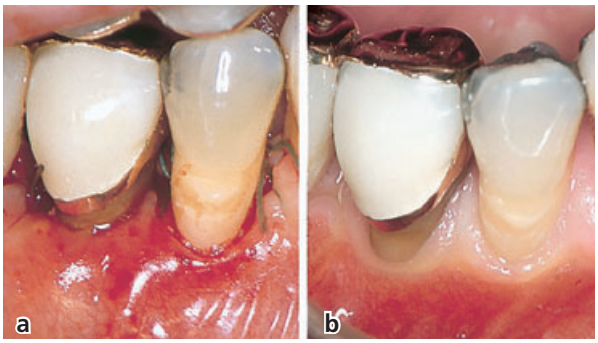


Fig. 44-23 Clinical photographs of a tooth region subjected to excision of the entire zone of gingiva by a flap procedure. (a) The alveolar mucosa has been displaced coronally to achieve complete coverage of the surgically exposed alveolar bone. (b) Healing has resulted in the reformation of a narrow zone of gingiva on the buccal aspect of the teeth, 9 months post surgery.

with the capability of inducing a keratinized epithelium develops in the marginal area following the "denudation technique" than following the "split flap technique". This is in accordance with the clinical observation that the "denudation technique" usually is superior to the "split flap technique" in increasing the width of keratinized tissue (Bohannan 1962a,b).

In a clinical study by Wennström (1983) periodontal pockets were eliminated by the use of a "gingivectomy" or a "flap" procedure which both involved the complete removal of the keratinized tissue. In the "gingivectomy" procedure the wounded area was left to heal by second intention, while in the "flap" procedure the alveolar mucosa was repositioned to achieve complete coverage of the surgically exposed alveolar bone (Figs. 44-22a and 44-23a). Irrespective of the surgical technique used, healing resulted in the reformation of keratinized tissue, the width of which, however, was greater following the "gingivectomy" procedure than following the "flap" procedure (Figs. 44-22b and 44-23b). The gingiva was formed because granulation tissue from the periodontal ligament, with the capacity of inducing a keratinized epithelium, had proliferated coronally along the root surface. This granulation tissue formation was obviously favored by a more pronounced bone resorption during the healing following the "gingivectomy" procedure.

It can be concluded that the success or failure in extending the width of keratinized tissue by the "denudation" or "split flap" techniques rests with the origin of granulation tissue, which is related to the extent of bone loss induced by the surgical trauma. This in turn means that the result with respect to increasing the gingival width by methods involving periosteal exposure or denudation of the alveolar bone is unpredictable. The use of such methods is therefore not justified in periodontal therapy. The procedures discussed merely represent examples on how lack of knowledge about basic biologic principles may lead to the development of inappropriate therapeutic methods.

Grafting procedures

Healing of free soft tissue grafts placed entirely on a connective tissue recipient bed were studied in monkeys by Oliver *et al*. (1968) and Nobuto *et al*. (1988). According to these authors healing can be divided into three phases (Fig. 44-24):

1. *The initial phase (from 0–3 days)*. During these first days of healing a thin layer of exudate is present between the graft and the recipient bed. During this period the grafted tissue survives with an avascular "plasmatic circulation" from the recipient bed. Therefore, it is essential for the survival of the graft that a close contact is established to the underlying recipient bed at the time of operation. A thick layer of exudate or a blood clot may hamper the "plasmatic circulation" and result in rejection of the graft. The epithelium of the free graft degenerates early in the initial healing phase, and subsequently it becomes desquamated. In placing a graft over a recession, part of the recipient bed will be the avascular root surface. Since the graft is dependent on the nature of its bed for diffusion of plasma and subsequent revascularization, the utilization of free grafts in the treatment of gingival recessions involves a great risk of failure. The area of the graft over the avascular root surface must receive nutrients from the connective tissue bed that surrounds the recession. Thus, the amount of tissue that can be maintained over the root surface is limited by the size of the avascular area.
2. *Revascularization phase (from 2–11 days)*. After 4–5 days of healing, anastomoses are established between the blood vessels of the recipient bed and those in the grafted tissue. Thus, the circulation of blood is re-established in the pre-existing blood vessels of the graft. The subsequent time period is

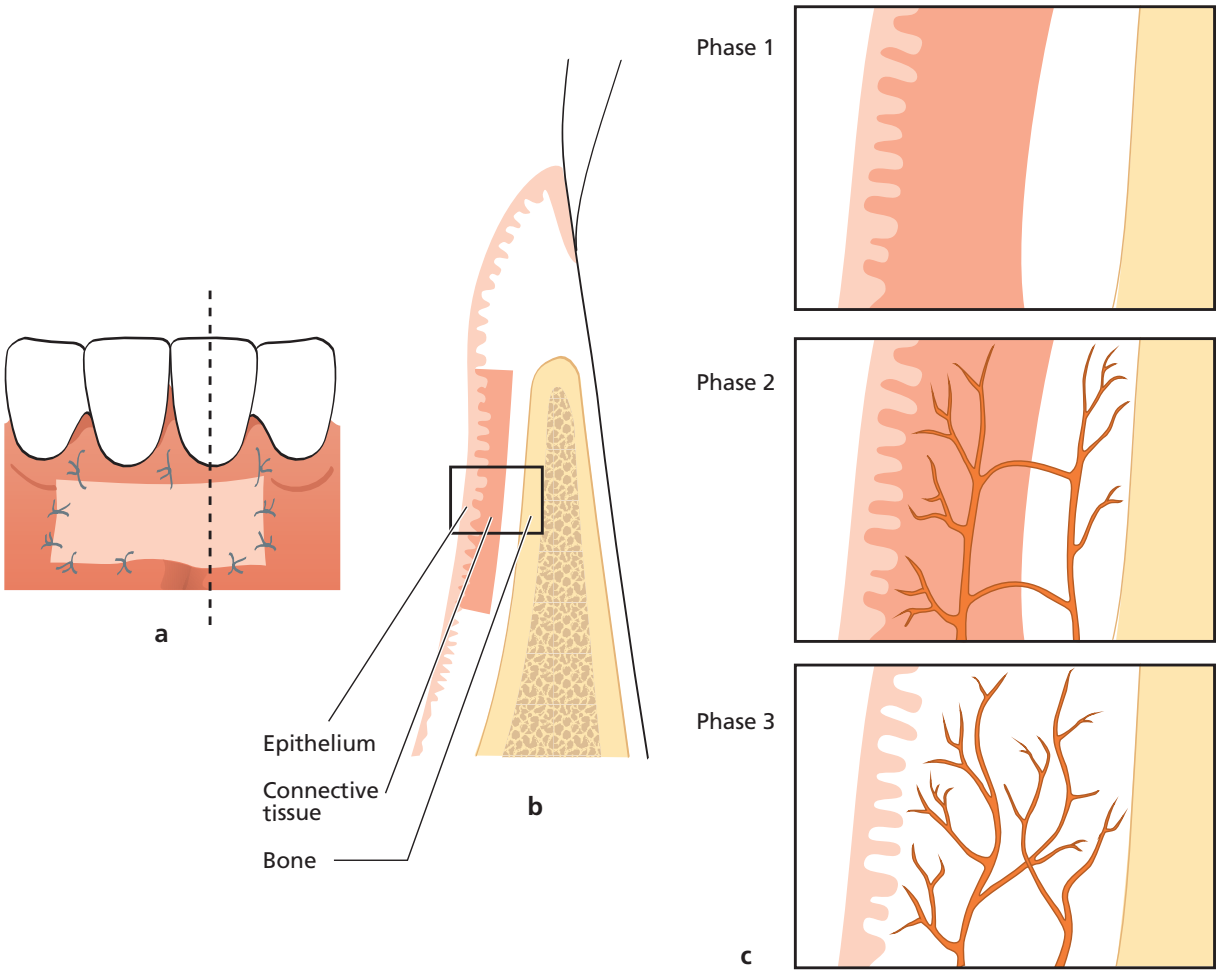


Fig. 44-24 Schematic drawings illustrating healing of a free gingival graft placed entirely on a connective tissue recipient bed (a). A cross-section through the area is shown in (b). The framed areas (c) illustrate the three phases into which the healing process can be divided.

characterized by capillary proliferation, which gradually results in a dense network of blood vessels in the graft. At the same time a fibrous union is established between the graft and the underlying connective tissue bed. The re-epithelialization of the graft occurs mainly by proliferation of epithelium from the adjacent tissues. If a free graft is placed over the denuded root surface, apical migration of epithelium along the tooth-facing surface of the graft may take place at this stage of healing.

3. *Tissue maturation phase (from 11–42 days).* During this period the number of blood vessels in the transplant becomes gradually reduced, and after approximately 14 days the vascular system of the graft appears normal. Also, the epithelium gradually matures with the formation of a keratin layer during this stage of healing.

The establishment and maintenance of a "plasmatic circulation" between the recipient bed and the graft during the initial phase of healing is critical for the result of this kind of therapy. Therefore, in order to ensure ideal conditions for healing, blood between the graft and the recipient site must be removed by exerting pressure against the graft following suturing.

Root coverage

The main indications for root coverage procedures are esthetic/cosmetic demands (Fig. 44-25) and root sensitivity. Changing the topography of the marginal soft tissue in order to facilitate plaque control is also a common indication for root coverage procedures (Fig. 44-26).

It should be recalled that the two major causative factors in the development of marginal tissue recession are trauma caused by toothbrushing and plaque-induced periodontal inflammation. The control of these factors will prevent further progression of the recession in most cases. This means that in tooth regions with a thin covering soft tissue, with or without an incipient recession, the patient should be encouraged to carry out effective but at the same time non-traumatic plaque-control measures. With respect to toothbrushing, the Bass method (Chapter 35) should be avoided and the patient should be

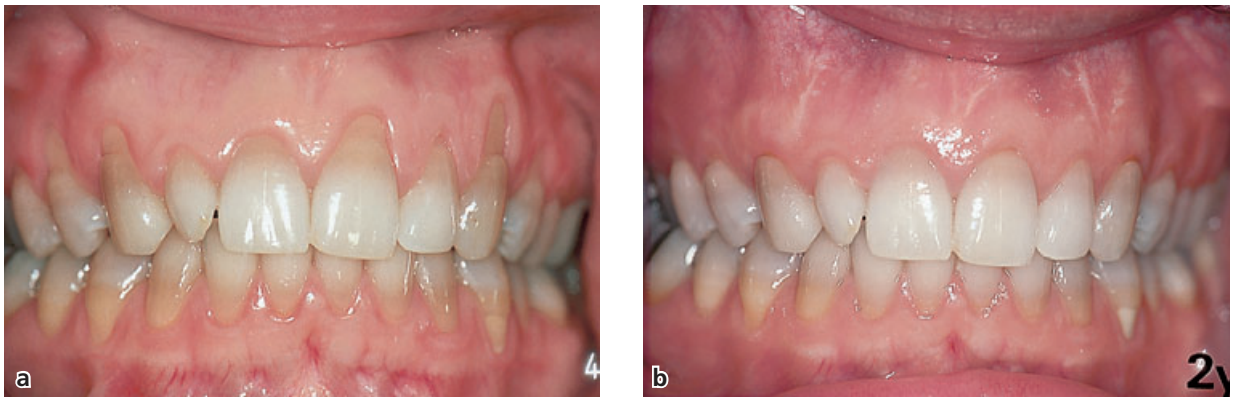


Fig. 44-25 (a) A 25-year-old woman with esthetic concerns due to multiple soft tissue recessions in the maxilla and a high lip line. The gingiva is healthy and several of the exposed root surfaces show abrasion defects, indicating toothbrushing trauma as the causative factor for the development of the recessions. The brushing technique was altered and root coverage was achieved surgically. (b) The 2-year post-treatment view.

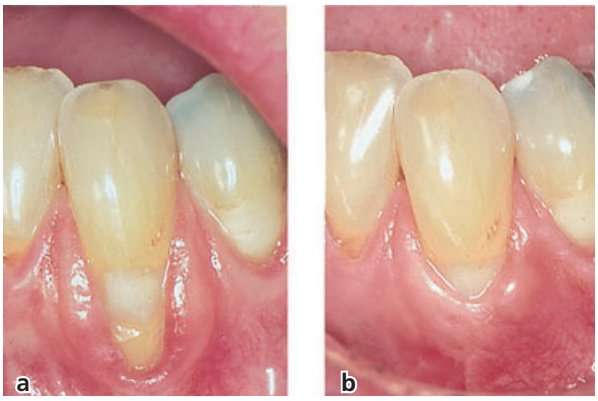


Fig. 44-26 (a) A mandibular canine with a deep recession, which offers problems with respect to self-performed plaque control. (b) To facilitate plaque control the position of the soft tissue margin was altered surgically.

instructed to use a technique creating as little apically directed pressure on the soft tissue margin as possible. A soft toothbrush should, of course, be used.

Miller (1985a) described a useful classification of recession defects taking into consideration the anticipated root coverage that is possible to obtain (Fig. 44-27):

- Class I: marginal tissue recession not extending to the mucogingival junction. No loss of interdental bone or soft tissue.
- Class II: marginal tissue recession extends to or beyond the mucogingival junction. No loss of interdental bone or soft tissue.
- Class III: marginal tissue recession extends to or beyond the mucogingival junction. Loss of interdental bone or soft tissue is apical to the CEJ, but coronal to the apical extent of the marginal tissue recession.
- Class IV: marginal tissue recession extends beyond the mucogingival junction. Loss of interdental bone extends to a level apical to the extent of the marginal tissue recession.

While complete root coverage can be achieved in class I and II defects, only partial coverage may be expected in class III. Class IV recession defects are not amenable to root coverage. Consequently, the critical clinical variable to assess in order to determine the possible outcome of a root coverage procedure is the level of periodontal tissue support at the proximal surfaces of the tooth.

Recession defects in the child need particular attention. In the growing child recession defects may be eliminated spontaneously, provided adequate plaque control is established and maintained (Fig. 44-28). Andlin-Sobocki *et al*. (1991) reported from a 3-year prospective study that 25 out of 35 recession defects with an initial depth of 0.5–3.0 mm healed spontaneously following improvement of the oral hygiene standard. Furthermore, all but three remaining recessions showed a decrease and no site demonstrated an increase in depth. Hence, reparative surgical treatment of soft tissue recessions in the developing dentition may not be necessary and should preferably be postponed until the growth is completed.

In an orthodontic case showing a recession defect and a thin (delicate) gingiva associated with a prominent, facially positioned tooth (Fig. 44-29a), surgical treatment for root coverage should be postponed until the orthodontic therapy is completed. The recession, as well as the dehiscence, will decrease as a consequence of the lingual movement of the tooth into a more proper position within the alveolar bone (Fig. 44-29b), and, if still indicated, the root coverage procedure will show higher predictability if performed after rather than before the tooth movement.

Root coverage procedures

Surgical procedures used in the treatment of recession defects may basically be classified as (1) *pedicle soft tissue graft procedures* and (2) *free soft tissue graft procedures*.

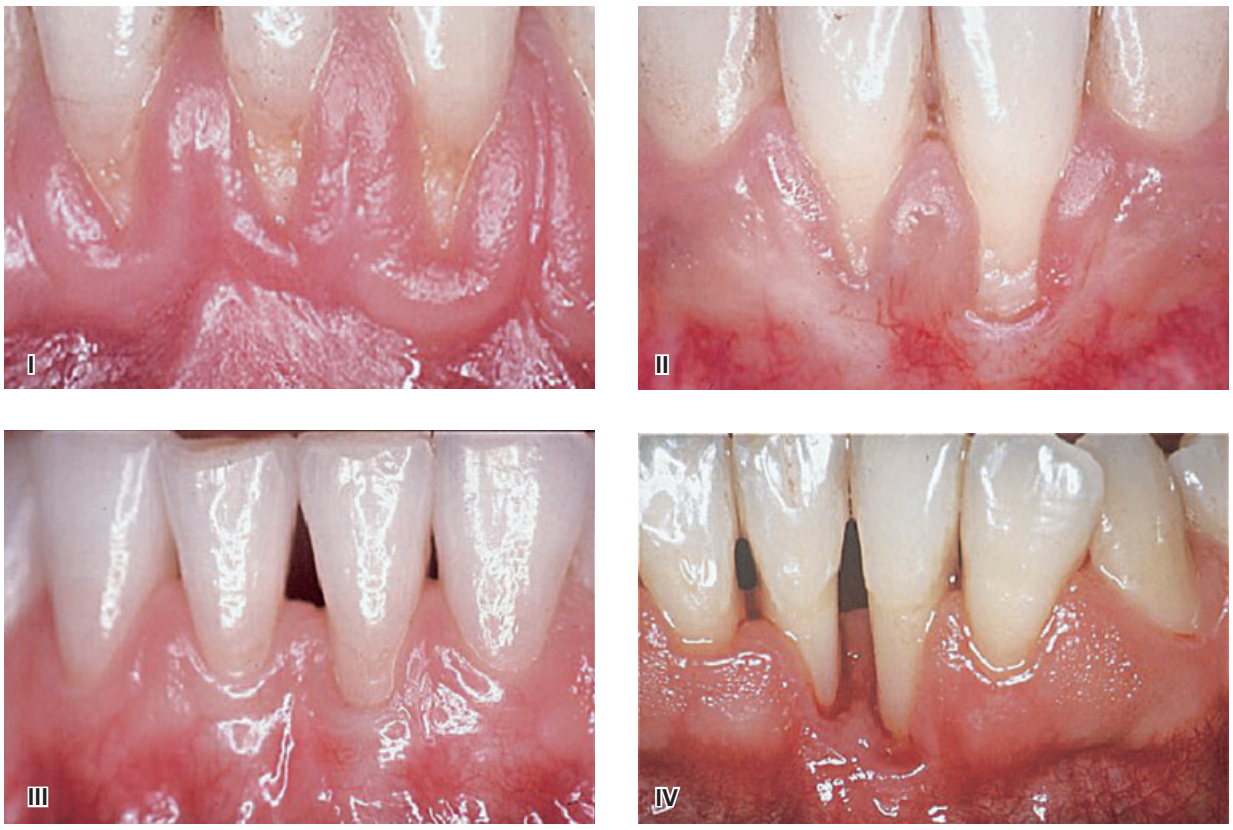


Fig. 44-27 The Miller classification of recession defects (see text).

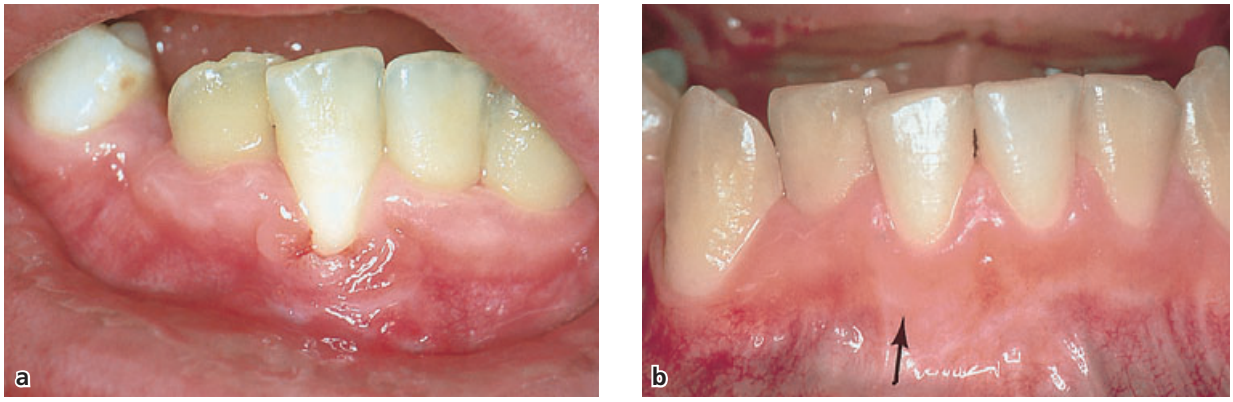


Fig. 44-28 A 9-year-old boy showing recession at tooth 41. (a) The tooth is rotated and buccally positioned. The minimal amount of gingiva found apical to the recession shows pronounced signs of inflammation. The plaque control in the region was improved but surgical intervention was postponed. (b) The same tooth area at the age of 14 years. Note the spontaneous soft tissue repair that has taken place at tooth 41 as a consequence of the improved plaque control and the growth in the alveolar process.

The pedicle graft procedures are, depending on the direction of transfer, grouped as (1) *rotational flap procedures* (e.g. laterally sliding flap, double papilla flap, oblique rotated flap) or (2) *advanced flap procedures* (e.g. coronally repositioned flap, semilunar coronally repositioned flap). The latter procedures do not include rotation or lateral movement of the pedicle graft. Regenerative procedures are also included within the group of pedicle graft procedures, i.e. rotational and advanced flap procedures involving the placement of a barrier membrane between the graft and the root or the application of enamel matrix proteins.

The autogenous free soft tissue graft procedure may be performed as (1) an epithelialized graft or as (2) a subepithelial connective tissue graft (non-epithelialized graft), both usually taken from the area of the masticatory mucosa in the palate.

Factors, such as depth and width of recession, availability of donor tissue, presence of muscle

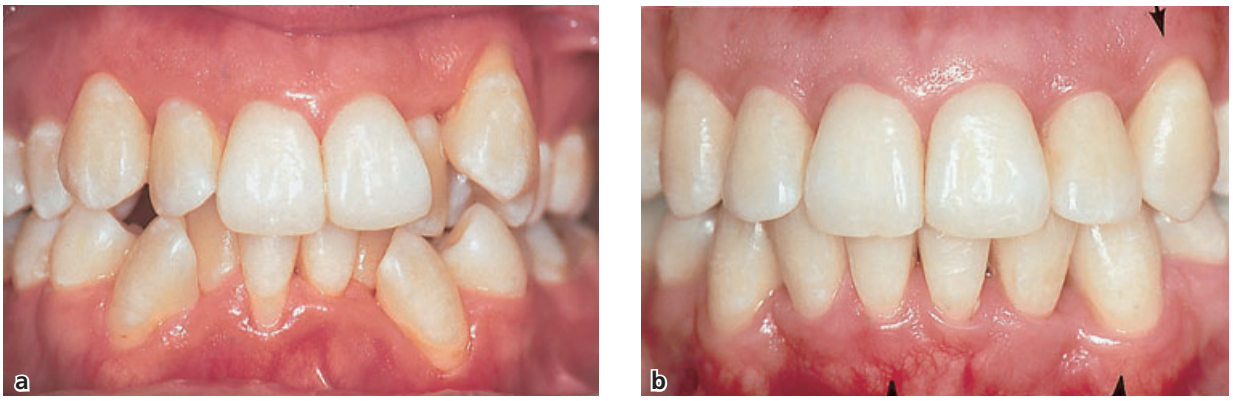


Fig. 44-29 Spontaneous repair of soft tissue recessions following orthodontic tooth movement. (a) A 22-year-old woman showing recessions and thin marginal tissues at prominently positioned teeth, particularly 23, 33, 41, and 43. (b) Following proper alignment of the teeth, the recessions have spontaneously been resolved and an increased gingival height can be noted.

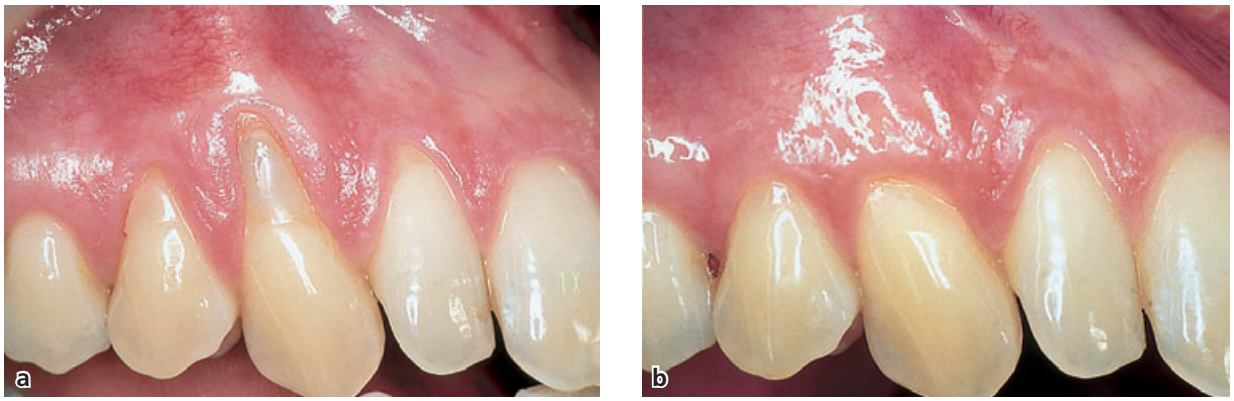


Fig. 44-30 (a) A canine showing pronounced recession and a composite resin restoration in the exposed root. Following removal of the restoration the exposed root was surgically covered with soft tissue (pedicle graft). (b) 2-year post-operative healing result.

attachments, and esthetics, have to be taken into consideration in the selection of treatment procedure.

Treatment of the exposed root surface

Before root coverage is attempted the exposed portion of the root should be rendered free from bacterial plaque. Preferably, this is achieved by the use of a rubber cup and a polishing paste. Controlled clinical trials have shown no differences in terms of root coverage or residual probing depth between teeth that had been instrumented (root planed) or polished only (Oles *et al*. 1988; Pini Prato *et al*. 1999). Extensive root planing may therefore only be performed in situations where a reduced root prominence would be considered beneficial for graft survival or tissue regeneration, or if a shallow root caries lesion is diagnosed. The presence of a filling in the root does not preclude the possibility for root coverage (Fig. 44-30), but the filling should be removed before the root is covered with soft tissue.

The use of root surface demineralization agents has been advocated as important not only for the removal of the smear layer, but also to facilitate the formation of a new fibrous attachment through exposure of collagen fibrils of the dentine matrix and to allow subsequent interdigitation of these fibrils with those in the covering connective tissue. However, controlled clinical trials comparing the clinical outcome of root coverage procedures with and without root conditioning (Ibbott *et al*. 1985; Oles *et al*. 1985; Bertrand & Dunlap 1988; Laney *et al*. 1992; Bouchard *et al*. 1997; Caffesse *et al*. 2000) failed to demonstrate a beneficial effect from the use of acid root biomodification. Gottlow *et al*. (1986) evaluated the healing following treatment of localized gingival recessions with coronally positioned flaps and citric acid root biomodification in a controlled study in dogs. Histologic analysis after 3 months of healing disclosed no differences in the amount of root coverage or new connective tissue attachment between citric acid-treated sites and saline-treated control sites. Although root resorption was a common finding among the citric acid-treated teeth in this dog model, such a finding has not been reported to be common in humans. In conclusion, the literature clearly indicates that the inclusion of root conditioning does not improve the healing outcome of root coverage procedures.

Pedicle soft tissue graft procedures

Rotational flap procedures

The use of a laterally repositioned flap to cover areas with localized recession was introduced by Grupe and Warren (1956). This technique, which was called *the laterally sliding flap* operation, involved the reflection of a full-thickness flap in a donor area adjacent to the defect and the subsequent lateral displacement of this flap to cover the exposed root surface (Fig. 44-19). In order to reduce the risk for recession on the donor tooth, Grupe (1966) suggested that the marginal soft tissue should not be included in the flap. Staffileno (1964) and Pfeifer and Heller (1971) advocated the use of a split-thickness flap to minimize the potential risk for development of dehiscence at the donor tooth. Other modifications of the procedure presented are *the double papilla flap* (Fig. 44-31) (Cohen & Ross 1968), *the oblique rotational flap* (Pennel *et al*. 1965), *the rotation flap* (Patur 1977), and *the transpositioned flap* (Bahat *et al*. 1990).

The technique is as follows:

- The rotational flap procedure (Fig. 44-32) is initiated with the preparation of the recipient site. A reverse bevel incision is made all along the soft tissue margin of the defect (Fig. 44-32a). After removal of the dissected pocket epithelium, the exposed root surface is thoroughly curetted.
- At a distance of approximately 3 mm from the wound edge, which delineates the defect at the side opposite the donor area, a superficial incision is performed extending from the gingival margin to a level approximately 3 mm apical to the defect (Fig. 44-32b). Another superficial incision is placed horizontally from this incision to the opposite wound edge. The epithelium together with the outer portion of the connective tissue within the area delineated by these incisions and the wound edges is removed by sharp dissection (Fig. 44-32c). In this way a 3 mm wide recipient bed is created at the one side of the defect, as well as apical to the defect.
- A tissue flap to cover the recession is then dissected in the adjacent donor area. The preparation of this flap is initiated by a vertical superficial incision placed parallel to the wound edge of the recession and at a distance that exceeds the width of the recipient bed and the exposed root surface by approximately 3 mm (Fig. 44-32c). This incision is extended beyond the apical level of the recipient bed and is terminated within the lining mucosa with an oblique releasing incision directed towards the recession site. An incision connecting the vertical incision and the incision previously made around the recession is placed approximately 3 mm apical to the gingival margin of the donor site.

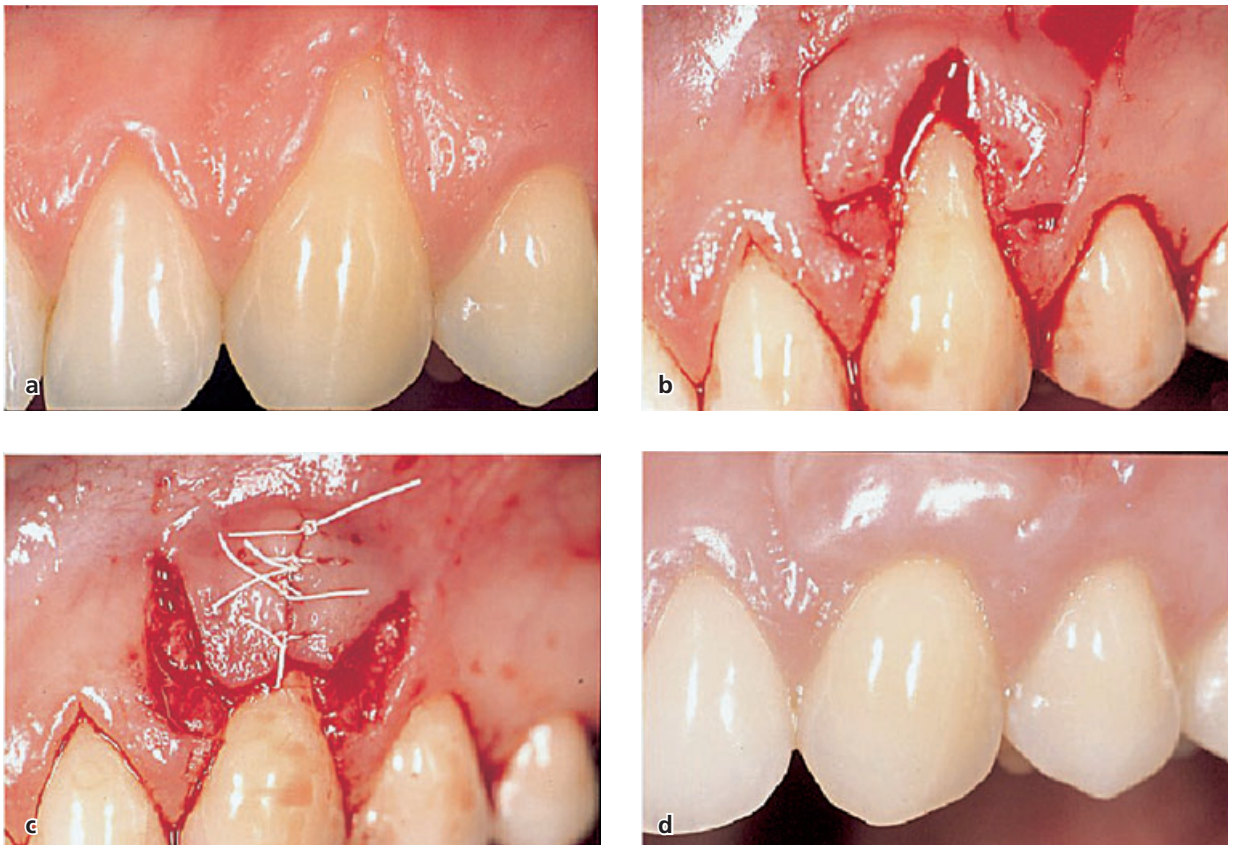


Fig. 44-31 Double papilla flap procedure. (a) Pre-treatment view of a maxillary canine with facial soft tissue recession. Using split incisions, soft tissue flaps are mobilized from both sides of the recession (b) and sutured together for coverage of the exposed root (c). The healing result 6-month post-operatively shows complete root coverage (d).

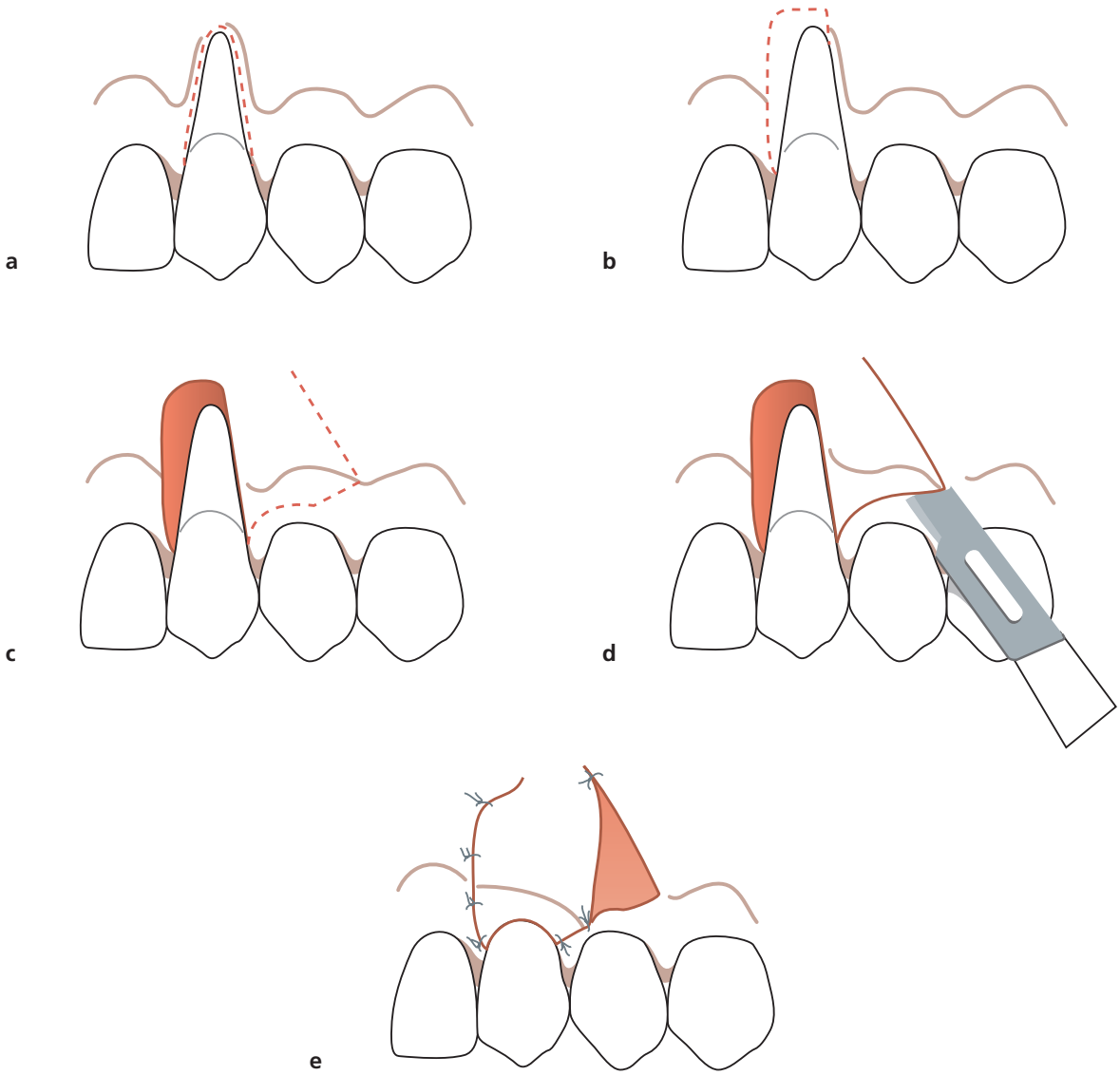


Fig. 44-32 Rotational flap procedure. Schematic drawings illustrating the surgical technique in utilizing rotational pedicle grafts to cover localized recession defects (see the text for explanation).

- A split-thickness flap is then prepared by sharp dissection within the area delineated by these incisions so that a layer of connective tissue is left covering the bone in the donor area when the flap is displaced laterally over the denuded root surface (Fig. 44-32d). It is important that the oblique releasing incision is made so far apically that the tissue flap can be placed on the recipient bed without being subjected to tearing forces when adjacent soft tissues are moved. The prepared tissue flap is rotated about 45° when sutured at the recipient bed (Fig. 44-32e).
- The suturing of the flap should secure a close adaptation of the pedicle graft to the underlying recipient bed. Pressure is applied against the flap for 2–3 minutes in order to further secure a good adaptation. To protect the surgical area during the initial phase of healing, a periodontal dressing may be applied. A light-cured dressing material, e.g. Barricaid™ (Dentsply International Inc., Milford, DE, USA), is preferably used since this can be applied without dislocating the flap and has, in addition, a favorable esthetic appearance.
- Following removal of the dressing and the sutures, usually after 10–14 days, the patient is instructed to avoid mechanical tooth cleaning for further 2 weeks, but to use twice daily rinsing with a chlorhexidine solution as a means of infection control.

Advanced flaps

Since the lining mucosa is elastic, a mucosal flap raised beyond the mucogingival junction can be stretched in coronal direction to cover exposed root surfaces (Harvey 1965; Sumner 1969; Brustein 1979; Allen & Miller 1989; Wennström & Zucchelli 1996; De Sanctis & Zucchelli 2007). The coronally advanced flap can be used for root coverage of a single tooth as well as multiple teeth, provided suitable donor tissue is available. In situations with only shallow

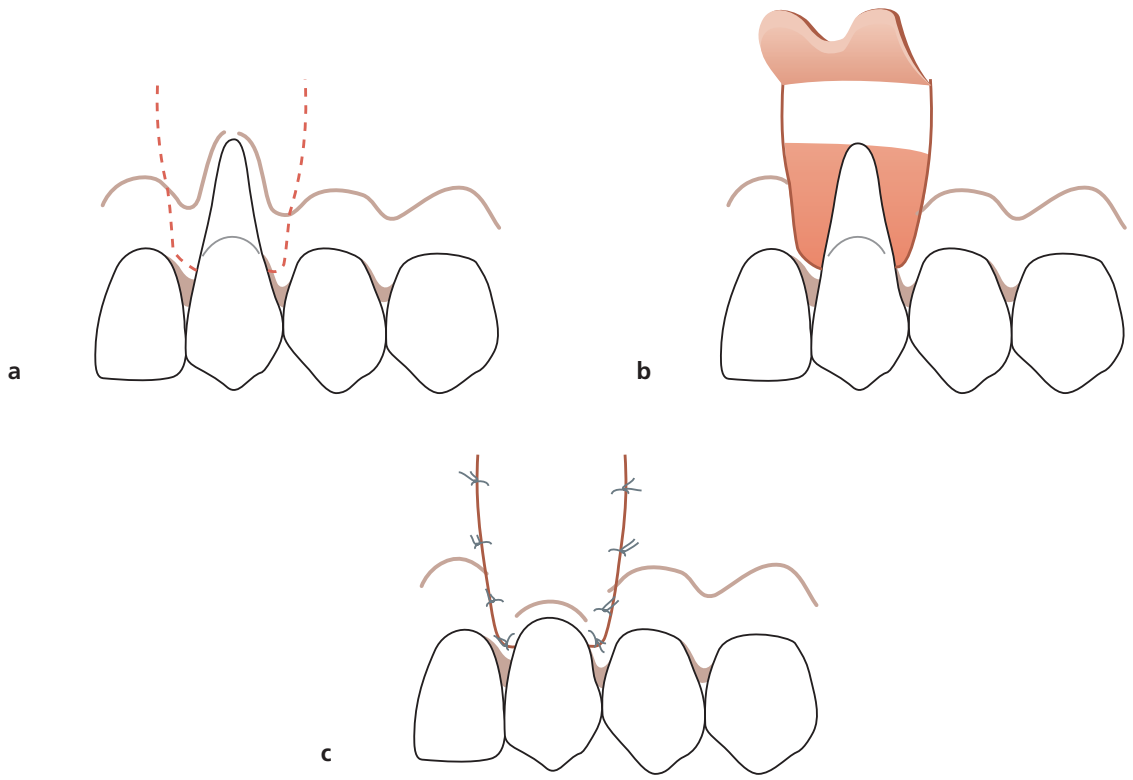


Fig. 44-33 Coronally advanced flap procedure. Schematic drawings illustrating the surgical technique in utilizing coronally advanced pedicle grafts to cover localized recession defects (see the text for explanation).

recession defects and minimal probing pocket depth labially, the *semilunar coronally repositioned flap* may offer an alternative approach (Harlan 1907; Tarnow 1986). For the treatment of an isolated deep gingival recession affecting a lower incisor, or the mesial root of the first maxillary molar, Zucchelli *et al*. (2004) suggested the use of a *laterally moved and coronally advanced flap*.

The technique for a *coronally advanced flap procedure* is as follows (Fig. 44-33):

- The coronally advanced flap procedure is initiated with the placement of two apically divergent vertical releasing incisions, extending from a point coronal to the CEJ at the mesial and distal line axis of the tooth and apically into the lining mucosa (Fig. 44-33a).
- A split-thickness flap is prepared by sharp dissection mesial and distal to the recession and connected with an intracrevicular incision. Apical to the receded soft tissue margin on the facial aspect of the tooth, a full-thickness flap is elevated to maintain maximal thickness of the tissue flap to be used for root coverage (Fig. 44-33b). Approximately 3 mm apical to the bone dehiscence, a horizontal incision is made through the periosteum, followed by blunt dissection into the vestibular lining mucosa to release muscle tension. The blunt dissection is extended buccally and laterally to such an extent that the mucosal graft is tension-free when positioned coronally at the level of the CEJ. The facial portion of the interdental papillae may be de-epithelialized to allow for a final placement of the flap margin coronal to the CEJ.
- The tissue flap is coronally advanced, adjusted for optimal fit to the prepared recipient bed, and secured at the level of the CEJ by suturing the flap to the connective tissue bed in the papilla regions (Fig. 44-33c). Additional lateral sutures are placed to carefully close the wound of the releasing incisions. Mechanical tooth cleaning is avoided during the first 3–4 weeks of healing (rinsing with a chlorhexidine solution is prescribed), and when re-instituted, instructions in the use of a tooth-brushing technique creating minimal apically directed trauma to the soft tissue margin is given.

Figure 44-34 illustrates the treatment of a recession defect with the use of the coronally advanced flap procedure. To allow the positioning of the flap margin coronal to the CEJ at the buccal surface the interdental papillae have to be de-epithelialized before suturing (Fig. 44-35).

The technique for a *laterally moved, coronally advanced flap* is as follows (Fig. 44-36):

- A vertical incision is made approximately 3 mm from the lateral edge of the recession defect at the side opposite the donor area, and parallel to the lateral border of the recession defect. The incision is extended from the level of the CEJ to a point

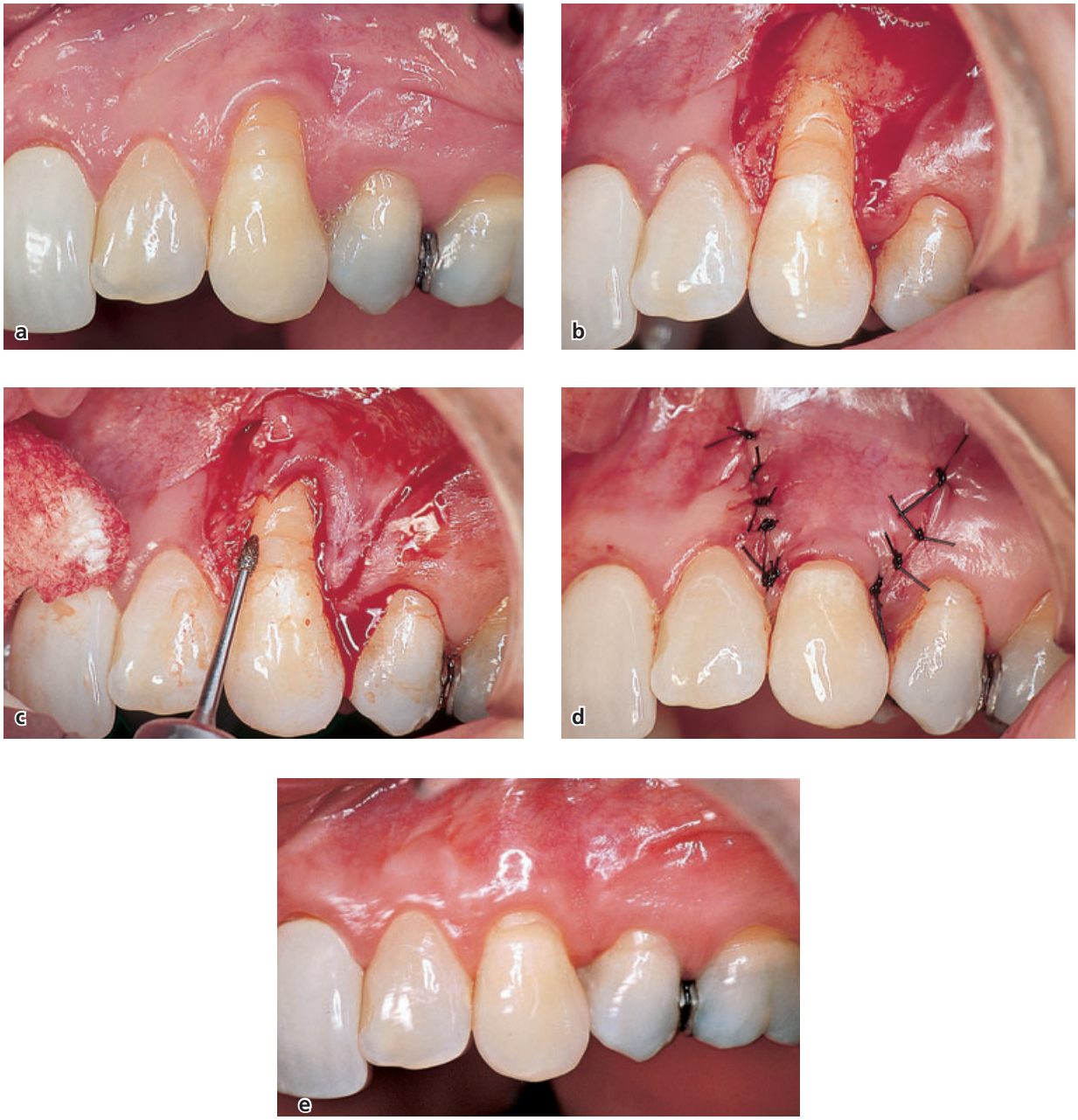


Fig. 44-34 Coronally advanced flap procedure. (a) A deep and wide recession defect on a canine with a composite resin restoration in the exposed root portion. Before preparation of the pedicle graft, the root is polished with pumice and a rubber cup. (b) A split flap has been dissected mesial and distal to the root, and a full-thickness flap apical to the recession. Approximately 4 mm apical to the bone dehiscence the periosteum has been cut and a blunt dissection performed to facilitate the coronal positioning of the pedicle graft. (c) The composite resin restoration is removed. (d) Close suturing of the pedicle graft to cover the exposed root surface. (e) Healing outcome 1 year post-operatively.

approximately 3 mm apical to the defect. At the marginal end of the vertical incision (at the level of the CEJ), a horizontal incision is made towards the recession defect. A third incision is made parallel to the lateral soft tissue margin of the recession defect on the donor side, from the bottom of the defect to the apical termination of the vertical incision on the recipient side. The area delineated by these incisions is de-epithelialized. In this way a 3 mm wide recipient bed is created lateral as well as apical to the defect.

- A pedicle graft is harvested from the adjacent tooth site by the use of three incisions: (1) a beveled intrasulcular incision along the lateral edge of the recession defect, (2) a horizontal submarginal incision with a 6 mm greater length than the width of the recession defect, and (3) a beveled oblique vertical incision extending into the alveolar mucosa and parallel to the first incision. The outline of the submarginal incision should preserve 3 mm of marginal soft tissue at the donor tooth, and preferably provide at least 2 mm of keratinized tissue

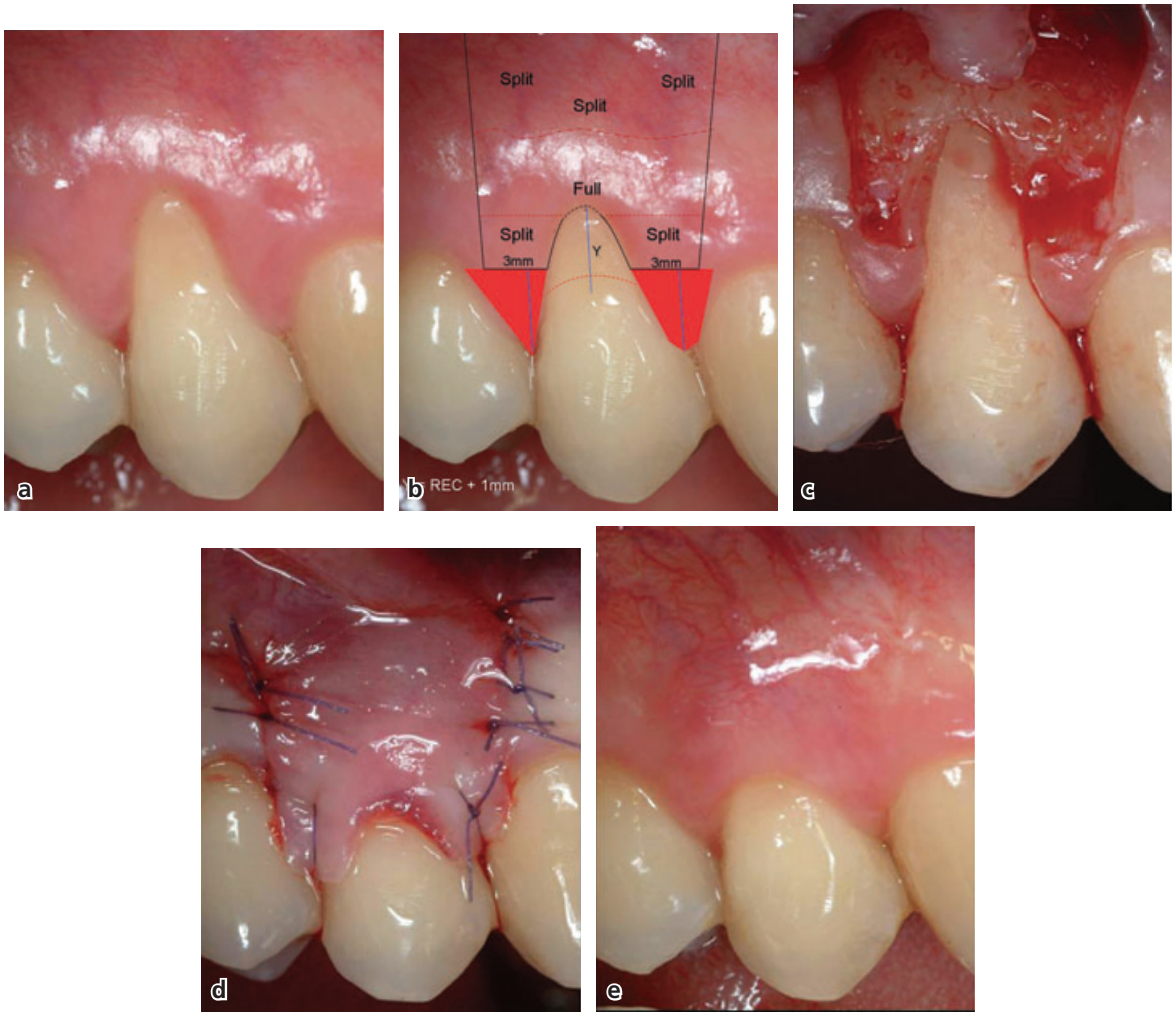


Fig. 44-35 Coronally advanced flap procedure. (a) A recession defect affecting a first premolar. (b) Schematic outline of the flap preparation. Blue line = amount (in mm) of intended coronal advancement of the flap; dotted red area = de-epithelialized papillae; Split = split-thickness elevation; Full = full-thickness elevation. (c) Flap elevated. The papilla areas are then de-epithelialized to allow anchorage of the flap coronal to the cemento-enamel junction (CEJ). (d) The flap is advanced and anchored at a level coronal to the CEJ with a sling suture. (e) Clinical healing at 1 year.

along the entire mesial–distal extension of the flap.

- The flap is mobilized as a split-thickness flap in its lateral parts, while the center part, which will be placed over the exposed root, is elevated as a full-thickness flap. Apical to the mucogingival line, the elevation is continued as split-thickness until it is possible to passively move the mucosal graft laterally to the recipient site.
- Blunt dissection is performed into the vestibular mucosa to release muscle tension to permit coronal advancement and passive adaptation of the flap to a level coronal to the CEJ.
- The facial surface of the interdental papillae is de-epithelized to create connective tissue beds to which the laterally moved, coronally advanced flap can be sutured.
- The suturing of the flap starts with the placement of two interrupted periosteal sutures in the most apical end of the vertical releasing incisions, and continues with a series of interrupted sutures, directed in a apical–coronal direction from the flap to the adjacent wound edge. A horizontal double mattress periosteal suture is placed apical to the vertical incisions to reduce lip tension on the root coverage portion of the flap. The coronal suture is a sling suture, which permits a precise adaptation of the flap against the root surface and the interdental connective tissue beds.

Figure 44-37 illustrates the treatment of a recession defect at a maxillary molar with the use of the *laterally moved, coronally advanced flap* procedure.

Zucchelli and De Sanctis (2000) described a flap design for the treatment of multiple recessions, which allows for optimal adaptation of the flap following its coronal advancement without placement of vertical releasing incisions. The technique for this *coronally advanced flap procedure for multiple recessions* is as follows (Fig. 44-38):

Fig. 44-36 The laterally moved, coronally advanced flap (see text for explanation). (a) A cenral insicor with recession defect. (b) Schematic outline of the preparation of the recipient site and the pedicle graft. Dotted pink area = receiving area for lateral flap; dotted red area = de-epithelialized papillae; x = recession width at the level of the cemento-enamel junction; Split = split-thickness elevation; Full = full-thickness elevation. (c,d) The flap is transpositioned laterally and coronally, and secured in position by sutures. A horizontal double mattress suture is performed to reduce lip tension on the marginal portion of the flap. (e) Clinical healing at 1 year.

- Oblique submarginal incisions are made in the interdental areas and connected with intracrevicular incisions at the recession defects. The incisions are extended to include one tooth on each side of the teeth to be treated to facilitate coronal repositioning of the flap. The oblique incisions over the interdental areas are placed in such a manner that the "surgically created papillae" mesial to the midline of the surgical field are dislocated apically and distally, while the papillae of the flap distal to the midline are shifted in a more apical and mesial position (Fig. 44-37a).
- Starting at the oblique interdental incisions, a split-thickness flap is dissected (Fig. 44-38c). Apical to the level of the root exposures, a full-thickness flap is raised to provide maximum soft tissue thickness of the flap to be positioned coronally over the roots (Fig. 44-38d).
- At the most apical portion of the flap, the periosteum is incised and followed by dissection into the vestibular lining mucosa to eliminate all muscle tension. The mobilized flap should be able to passively reach a level coronal to the CEJ at each single tooth in the surgical field.
- The remaining facial portion of the interdental papillae is de-epithelialized to create connective tissue beds to which the flap can be sutured.
- Sutures are placed to accomplish a precise adaptation of the coronally advanced flap against the teeth and to the interdental connective tissue beds (Fig. 44-38e). In addition, a horizontal double mattress suture is placed to reduce lip tension on the marginal portion of the flap.

The technique for a *semilunar coronally repositioned flap procedure* is as follows (Fig. 44-39):

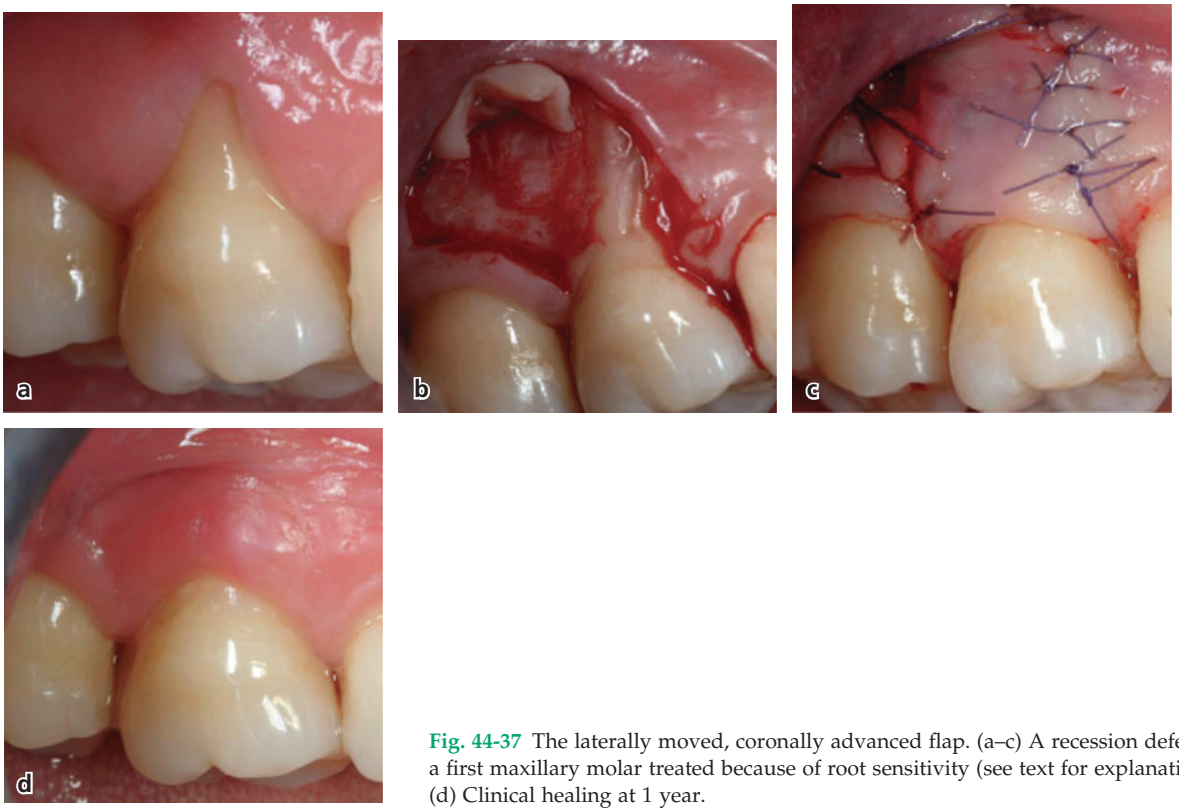


Fig. 44-37 The laterally moved, coronally advanced flap. (a–c) A recession defect at a first maxillary molar treated because of root sensitivity (see text for explanation). (d) Clinical healing at 1 year.

- A semilunar incision is placed apical to the recession and at a distance from the soft tissue margin, which should be approximately 3 mm greater than the depth of the recession. The outline of the incision should be parallel to the curvature of the gingival margin (Fig. 44-39a). The incision is extended into the papilla region on each side of the tooth, but care should be taken to maintain a broad base of anchorage to secure a collateral blood supply to the pedicle graft.
- A split-thickness dissection of the facially located tissue is then made by an intracrevicular incision extending apically to the level of the semilunar incision (Fig. 44-39b). The mid-facial soft tissue graft is coronally repositioned to the level of the CEJ (Fig. 44-39c) and stabilized by light pressure for 5 minutes.
- No suturing is needed but a light-cured dressing may be applied for wound protection.

Pedicle soft tissue graft procedures combined with a barrier membrane

The use of a barrier membrane, according to the principles of guided tissue regeneration (GTR, see Chapter 25), in conjunction with pedicle soft tissue graft procedures was introduced as a treatment modality for root coverage by Pini Prato *et al*. (1992). In order create space for tissue formation between the facial root surface and the membrane Pini Prato *et al*. (1992) suggested that extensive root planing should be carried out to produce concave root morphology. Specially designed membranes for the treatment of recession type defects are available, such as non-absorbable titanium-reinforced expanded polytetrafluoroethylene (e-PTFE) membranes (Fig. 44-40c). In addition, a variety of bioabsorbable membranes are commercially available, but many of these may not be rigid enough for maintaining required space during healing.

The pedicle graft used in the GTR procedure is generated through the preparation of a coronally advanced flap (Fig. 44-40):

- Apically divergent vertical releasing incisions are made at the mesial and distal line axis of the tooth, extending from a point coronal to the CEJ and apically into the lining mucosa. A trapezium-shaped full-thickness flap is raised beyond the bone dehiscence (Fig. 44-40b). The periosteum at the base of the raised mucoperiosteal flap is incised, followed by a blunt supraperiosteal dissection to such a depth that the trapezoidal flap easily can be advanced coronally to the desired position. Depending on the degree of coronal repositioning, the facial portion of the interdental papillae may need to be de-epithelialized to prepare proper recipient beds for the pedicle graft.
- The root is extensively planed or ground to obtain a concave profile of the root surface, thereby providing space for tissue formation. If a titanium-reinforced membrane is used, the root profile may not need to be changed to establish the required space between the root and the membrane.

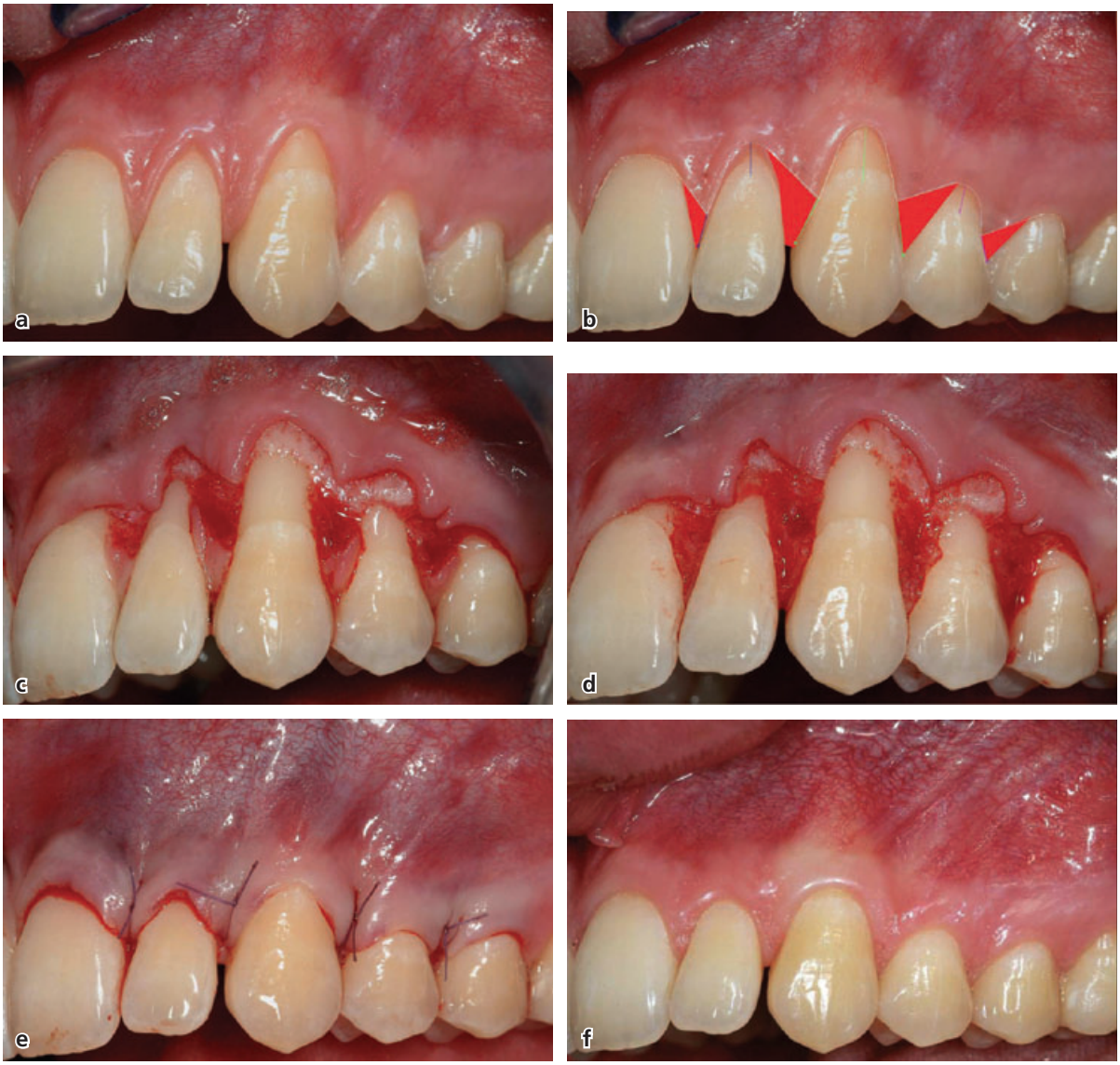


Fig. 44-38 Coronally advanced flap procedure for multiple recessions (see text for explanation). (a–e) The oblique incisions over the interdental areas are placed in such a manner that the "surgically created papillae" mesial to the midline of the surgical field are dislocated apically and distally, while the papillae of the flap distal to the midline are shifted in a more apical and mesial position. (f) The 1-year post-treatment view.

- The membrane barrier to be used is trimmed to cover the exposed root and approximately 3 mm of the bone lateral and apical to the dehiscence (Fig. 44-40c) and anchored to the tooth by a sling suture placed at the level of the CEJ.
- The mobilized flap is positioned coronally and secured by interdentally placed interrupted sutures (Fig. 44-40d). The membrane should be completely covered by the flap to reduce the risk for bacterial contamination during healing. Additional sutures are placed to close the lateral wound of the releasing incisions.
- The patient is advised to use a chlorhexidine mouth rinse for infection control and not to use any mechanical cleaning devices for at least 6 weeks in the tooth region subjected to surgery.
- The use of non-biodegradable membrane barriers requires a second surgery for membrane removal, usually after 5–6 weeks (Fig. 44-40e,f). A partial-thickness trapezoidal flap is raised to expose the membrane. Following its removal, the flap is repositioned at the level of the CEJ to completely cover the newly formed tissue. Mechanical plaque control is reinstituted 4 weeks after membrane removal.

Pedicle soft tissue graft procedures combined with enamel matrix proteins

Abbas *et al*. (2003) described a surgical procedure for periodontal regenerative therapy of recession defects utilizing enamel matrix derivative bioactive material (Emdogain®):

- The surgical technique utilized is the coronally advanced flap as described above (Fig. 44-33). The interdental papillae should be de-epithelialized to

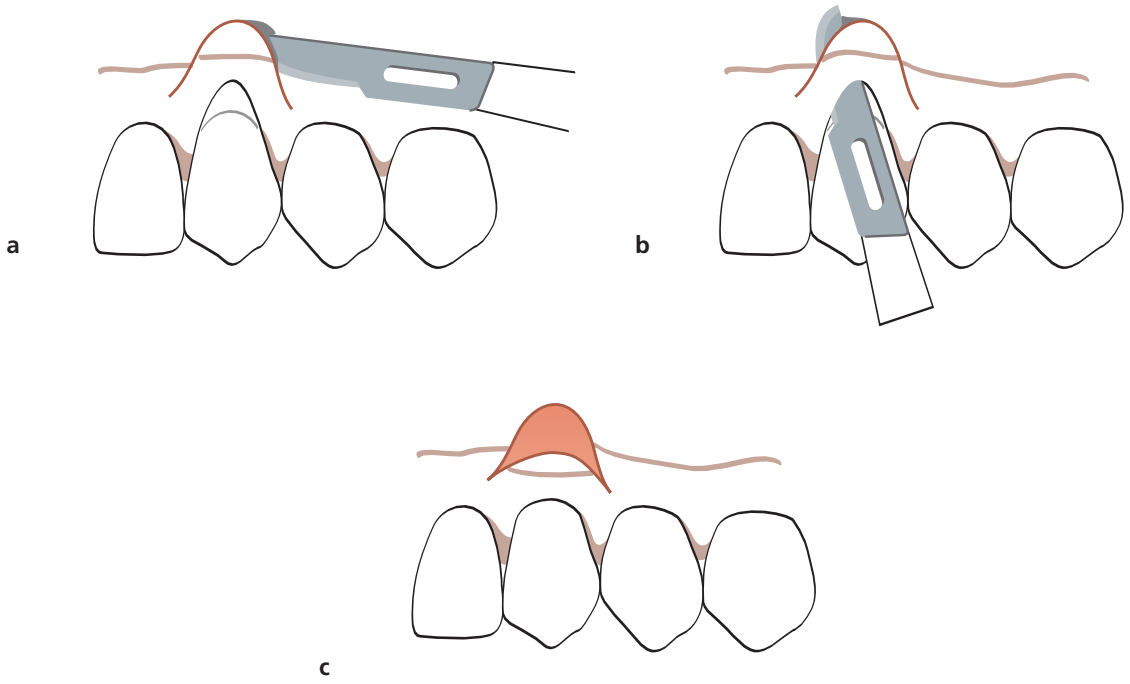


Fig. 44-39 Semilunar coronally repositioned flap procedure. Schematic drawings illustrating the surgical technique in utilizing coronally displaced pedicle grafts to cover shallow localized recession defects (see text for explanation).

allow for maximum coronal positioning of the tissue flap over the exposed root surface at suturing.

- Following preparation of the coronally advanced flap, the exposed root surface is conditioned with PrefGel™ (24% EDTA-gel, pH 6.7; Straumann Biologics, Switzerland) for 2 minutes to remove the smear layer.
- After thorough rinsing with sterile saline, the enamel matrix protein gel (Emdogain®, Straumann Biologics, Switzerland) is applied to the exposed root surface. The pedicle graft is advanced coronally and secured at a level slightly coronal to the CEJ by suturing the flap to the de-epithelialized papilla regions using non-irritating sutures. The vertical incisions are then closed with two to three sutures. Mechanical tooth cleaning is avoided during the first 3–4 weeks of healing (rinsing with a chlorhexidine solution is prescribed), and when re-instituted, a toothbrushing technique creating minimal apically directed trauma to the soft tissue margin is used.

Free soft tissue graft procedures

A free soft tissue graft of masticatory mucosa is usually selected when there is no acceptable donor tissue present in the area adjacent to the recession defect or when a thicker marginal tissue is desirable. The procedure can be used for the treatment of a single tooth as well as for groups of teeth. The graft used may either be (1) an *epithelialized graft* or (2) a *subepithelial connective tissue graft* of palatal masticatory mucosa.

Epithelialized soft tissue graft

The epithelialized free soft tissue graft procedure can be performed either as a two-step surgical technique, where an epithelialized free soft tissue graft is placed apical to the recession and following healing is positioned coronally over the denuded root (Fig. 44-41) (Bernimoulin *et al*. 1975; Guinard & Caffesse 1978), or as a one-step technique by which the graft is placed directly over the root surface (Sullivan & Atkins 1968a,b; Miller 1982) (Fig. 44-42). The latter of the two techniques has been most commonly used.

The principles of utilizing free mucosal grafts were outlined by Sullivan and Atkins (1968a,b) and later modified by Miller (1982):

- Before any incisions the exposed root surface is carefully scaled and root planed (Fig. 44-42a). The convexity of the root may be reduced to minimize the mesio-distal avascular recipient bed.
- As in the treatment with pedicle grafts, the preparation of *the recipient bed* is crucial for the success of free graft procedure. A 3–4 mm wide recipient connective tissue bed should be prepared apical and lateral to the recession defect (Fig. 44-42b). The area is demarcated by first placing a horizontal incision, at the level of the CEJ, in the interdental tissue on each side of the tooth to be treated. Subsequently, two vertical incisions, extending from the incision line placed in the interdental tissue to a level approximately 4–5 mm apical to the recession, are placed. A horizontal incision is then made connecting the two vertical incisions at their apical termination. Starting from an intracrevicular incision, a split incision is made to sharply dissect the

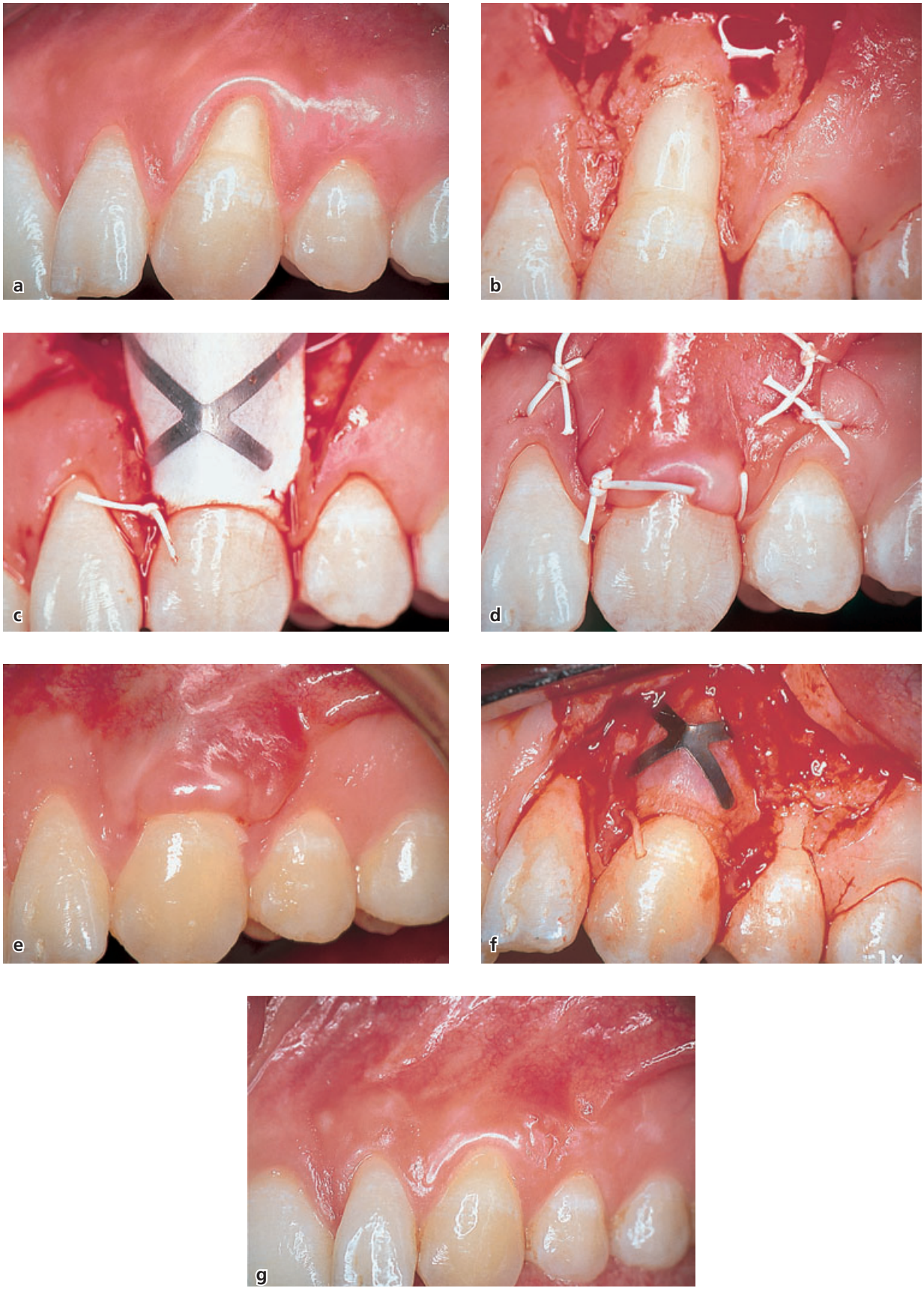


Fig. 44-40 Coronally advanced flap procedure combined with a titanium-reinforced non-biodegradable membrane barrier. (a–f) A recession defect at tooth 23 requiring treatment due to the patient's esthetic demands (see the text for explanation). (g) The 1-year post-operative result.

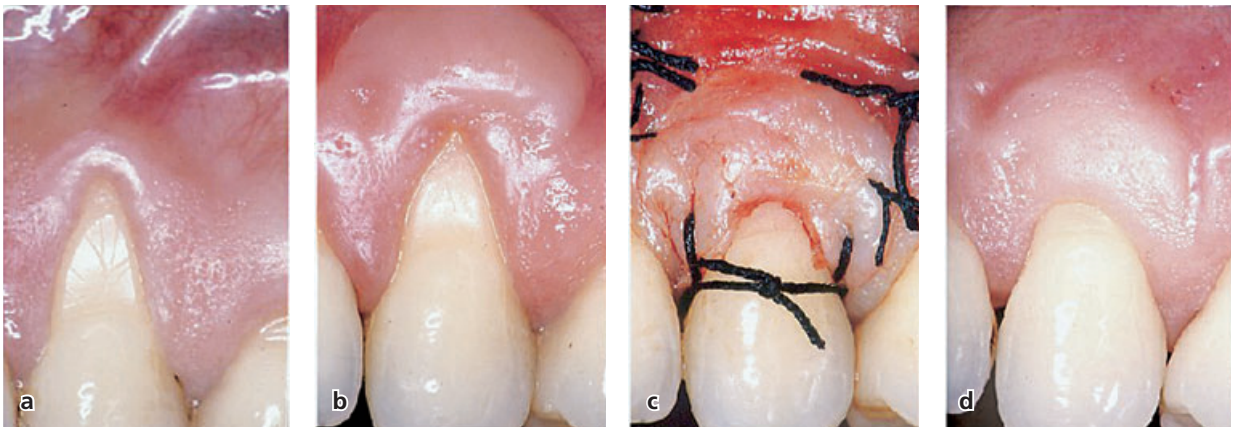


Fig. 44-41 Two-stage epithelialized free soft tissue graft procedure. (a–c) An epithelialized soft tissue graft is placed apical to the recession and allowed to heal. At a second stage surgery, a coronally advanced flap procedure is performed to achieve coverage of the denuded root. (d) The 1-year post-operative result.

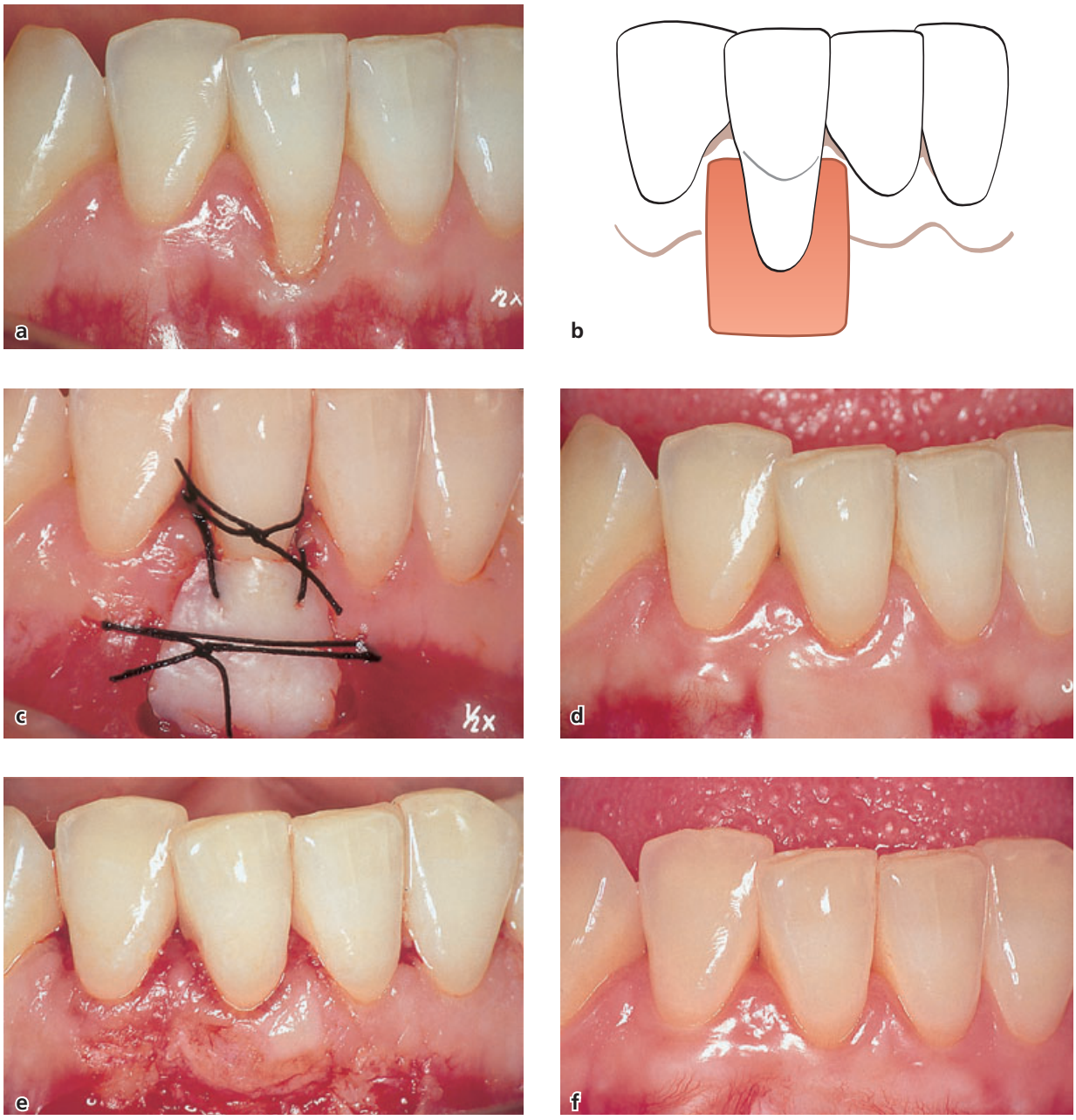


Fig. 44-42 Epithelialized free soft tissue graft procedure. A recession defect at a mandibular central incisor treated with the free graft procedure (see the text for explanation).

epithelium and the outer portion of the connective tissue within the demarcated area.

- To ensure that a graft of sufficient size and proper contour is removed from the donor area, a foil template of the recipient site is prepared. This template is transferred to the donor site, the palatal mucosa in the region of the premolars, and the required size of the graft is outlined by a shallow incision. A graft with a thickness of 2–3 mm is then dissected from the donor area (Fig. 44-20c–d). It is advocated to place sutures in the graft before it is cut completely free from the donor area since this may facilitate its transfer to the recipient site. Following the removal of the graft, pressure is applied to the wound area for control of bleeding.
- The graft is immediately placed on the prepared recipient bed. In order to immobilize the graft at the recipient site, sutures must be anchored in the periosteum or in the adjacent attached gingiva. Adequate numbers of sutures are placed to secure close adaptation of the graft to the underlying connective tissue bed and root surface (Fig. 44-42c). Before the placement of a periodontal dressing, pressure is exerted against the graft for some minutes in order to eliminate blood from between the graft and the recipient bed. Following the control of bleeding, the wound in the donor area in the palate is covered by a periodontal dressing. An acrylic plate may be required to maintain the dressing in place during healing phase.
- The sutures and periodontal dressing are usually maintained for 2 weeks. The appearance of a grafted area after 3 months of healing is shown in Fig. 44-42d. A gingivoplasty may be indicated to achieve a satisfactory esthetic appearance of the grafted area (Fig. 44-42e,f).

Connective tissue graft

The techniques utilizing a subepithelial soft tissue graft, i.e. the connective tissue, involve the placement of the graft directly over the exposed root and the mobilization of a mucosal flap coronally (Fig. 44-43) or laterally (Fig. 44-44) for coverage of the graft (Langer & Langer 1985; Nelson 1987; Harris 1992; Bruno 1994; Zucchelli *et al*. 2003). An alternative technique is to place the base of the connective tissue graft within an "envelope" prepared by an undermining partial-thickness incision from the soft tissue margin, i.e. part of the graft will rest on the root surface coronal to the soft tissue margin (Fig. 44-45) (Raetzke 1985; Allen 1994). For the treatment of multiple adjacent recessions, a multi-envelope recipient bed ("tunnel") may be prepared (Zabalegui *et al*. 1999). The subepithelial connective tissue graft is harvested from the palate or the retromolar pad by the

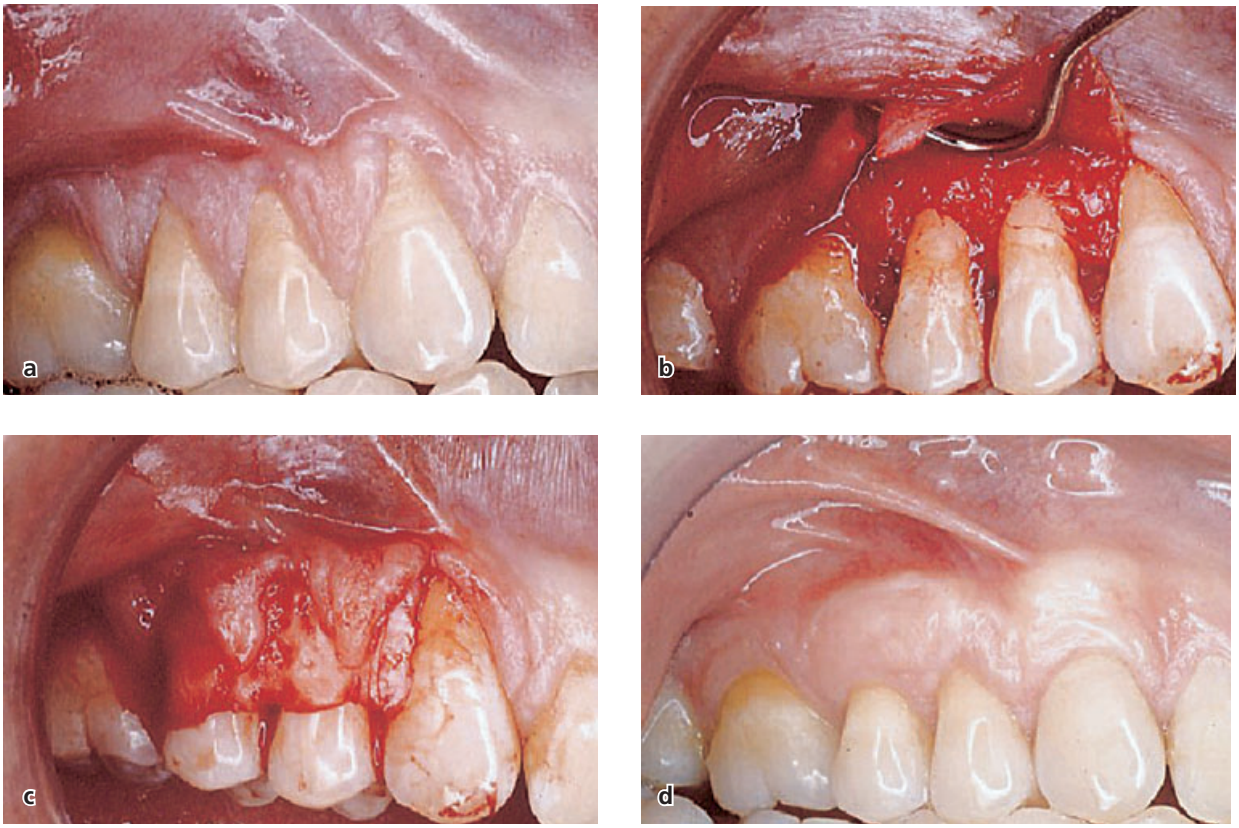


Fig. 44-43 Free connective tissue graft combined with a coronally advanced flap procedure – single recession (see the text for explanation). (a) Deep gingival recession at a cuspid with minimal height of keratinized tissue apical to the root exposure. (b) The graft has been sutured to leave an area between the cemento-enamel junction and the graft available for the marginal keratinized tissue of the flap. (c) The flap has been advanced coronally and sutured. (d) Clinical healing at 1 year.

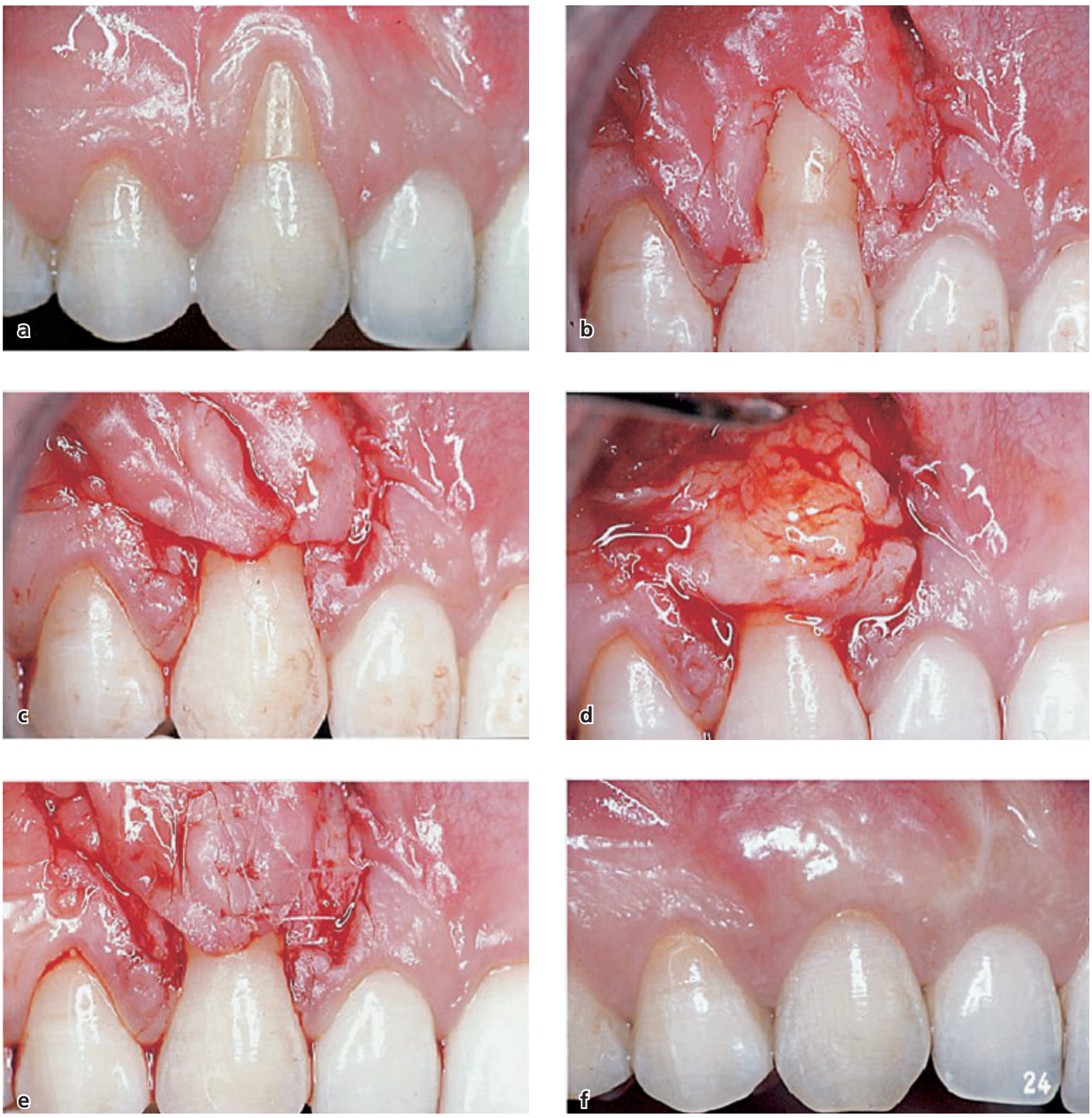


Fig. 44-44 (a–e) Free connective tissue graft combined with a double papilla flap procedure. (f) The 1-year post-treatment result.

use of a "trap door" approach (Fig. 44-46). Compared to the epithelialized graft, the connective tissue graft is preferable due to a less invasive palatal wound and an improved esthetic result.

The technique for the *connective tissue graft combined with a coronally advanced flap* is as follows (Fig. 44-43):

- The surgical technique utilized is the coronally advanced flap as described above, but with the difference that the flap is elevated entirely as a split-thickness flap. The interdental papillae should be de-epithelialized to allow for maximum coronal positioning of the tissue flap over the exposed root surface at suturing (Fig. 44-43b).
- A subepithelial connective tissue graft of masticatory mucosa is harvested on the palatal aspect of the maxillary premolars/first molar (or from the retromolar pad) by the use of a "trap door" approach (Fig. 44-46). Before incisions are placed, the available thickness of the mucosa is estimated by the use of the tip of the syringe. A horizontal incision, perpendicular to the underlying bone surface, is made approximately 3 mm apical to the soft tissue margin (Fig. 44-46a). The mesio-distal extension of the incision is determined by the graft size required, which is 6 mm longer than the width of the dehiscence measured at the level of the CEJ. To facilitate the removal of the graft, a vertical releasing incision may be made at the mesial termination of the primary incision. An incision is then placed from the line of the first incision and directed apically to perform a split incision of the palatal mucosa (Fig. 44-46b–f). A small periosteal

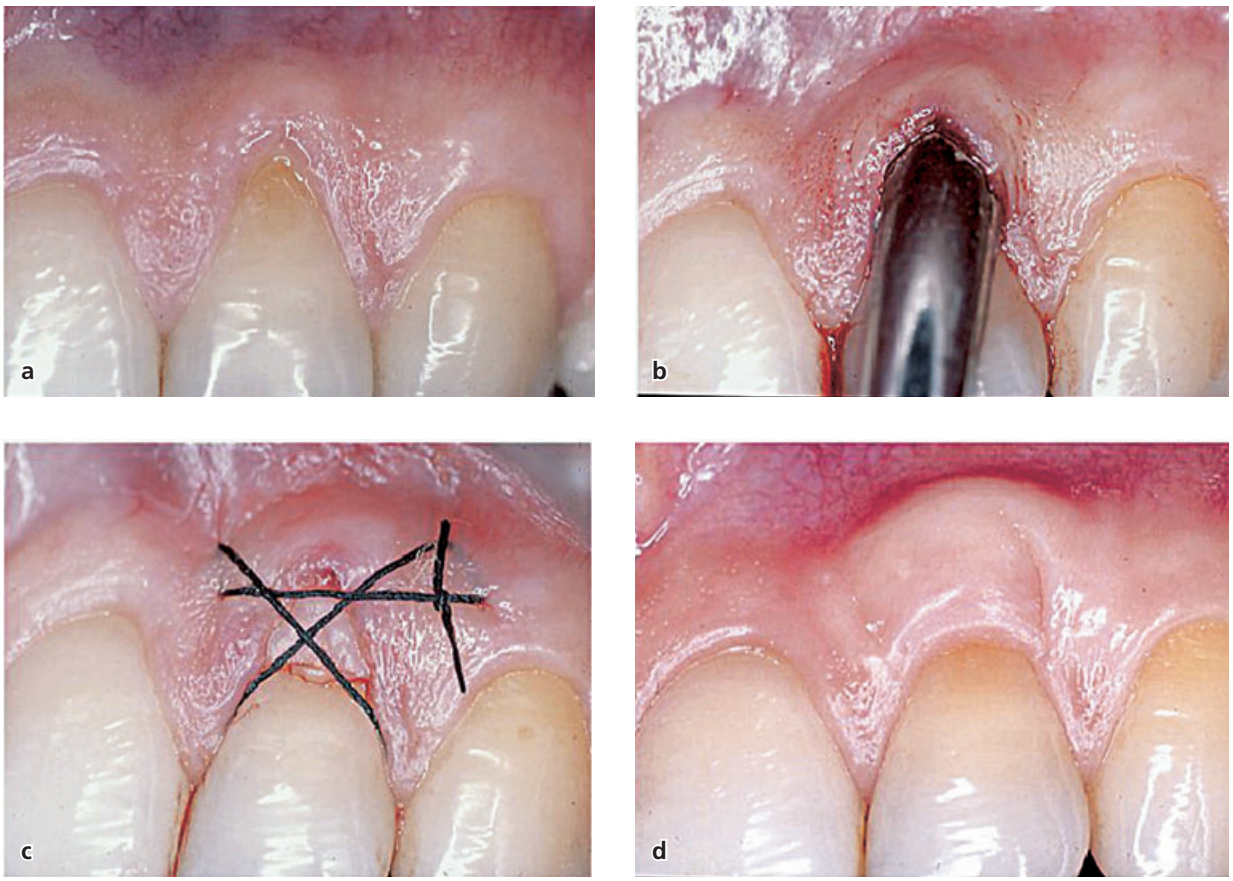


Fig. 44-45 (a–c) Free connective tissue graft procedure – the "envelope technique" (see text for explanation). (d) The 1-year post-treatment result. (Courtesy of Dr. P. Cortellini, Italy.)

elevator or scalpel is used to release the connective tissue graft from the bone.

- The graft is immediately transferred to the recipient site and positioned at a distance from the CEJ equal to the height of keratinized tissue originally present apical to the recession defect. The graft is secured in position with two double vertical mattress sutures to adjacent soft tissue lateral to the dehiscence (Fig. 44-43c). A sling suture is placed in the papilla regions to position the margin of the covering advanced flap about 1 mm coronal to the CEJ. Interrupted sutures are used to close the wound along the vertical incisions (Fig. 44-43d).

Figure 44-47 illustrates the procedure applied to a case with multiple recession sites.

The "envelope" technique (Fig. 44-48) is as follows:

- With the use of the "envelope" technique the recipient site is prepared by first eliminating the sulcular epithelium by an internal beveled incision (Fig. 44-48a). Secondly, an "envelope" is prepared apically and laterally to the recession by split incisions (Fig. 44-48b). The depth of the preparation should be 3–5 mm in all directions. In an apical direction, the preparation of the site should extend beyond the mucogingival junction to facilitate the placement of the connective tissue graft and to allow for coronal advancement of the mucosal flap at time of suturing.
- A foil template may be used for the harvest of an appropriately sized connective tissue graft. The graft, which is obtained by the "trap door" approach described above (Fig. 44-46), is inserted into the prepared "envelope" and positioned to cover the exposed root surface (Fig. 44-48c–d).
- Sutures are placed to secure graft in position (Fig. 44-48d). A crossed sling suture may be placed to advance the mucosal flap coronally. Pressure is applied for 5 minutes to adapt the graft closely to the root surface and covering soft tissue.

Figure 44-45 shows the treatment of a recession defect with the "envelope" technique.

The "tunnel" technique (Fig. 44-49) is as follows:

- In case multiple adjacent recessions are to be treated, "envelopes" are prepared for each tooth as described above. However, the lateral split incisions are extended so that the multi-envelopes are connected mesially and distally to form a mucosal tunnel. Care should be taken to avoid detachment of the papillae.
- The graft is gently positioned inside the tunnel and its mesial and distal extremities are fixed with two interrupted sutures. Sling sutures may be placed

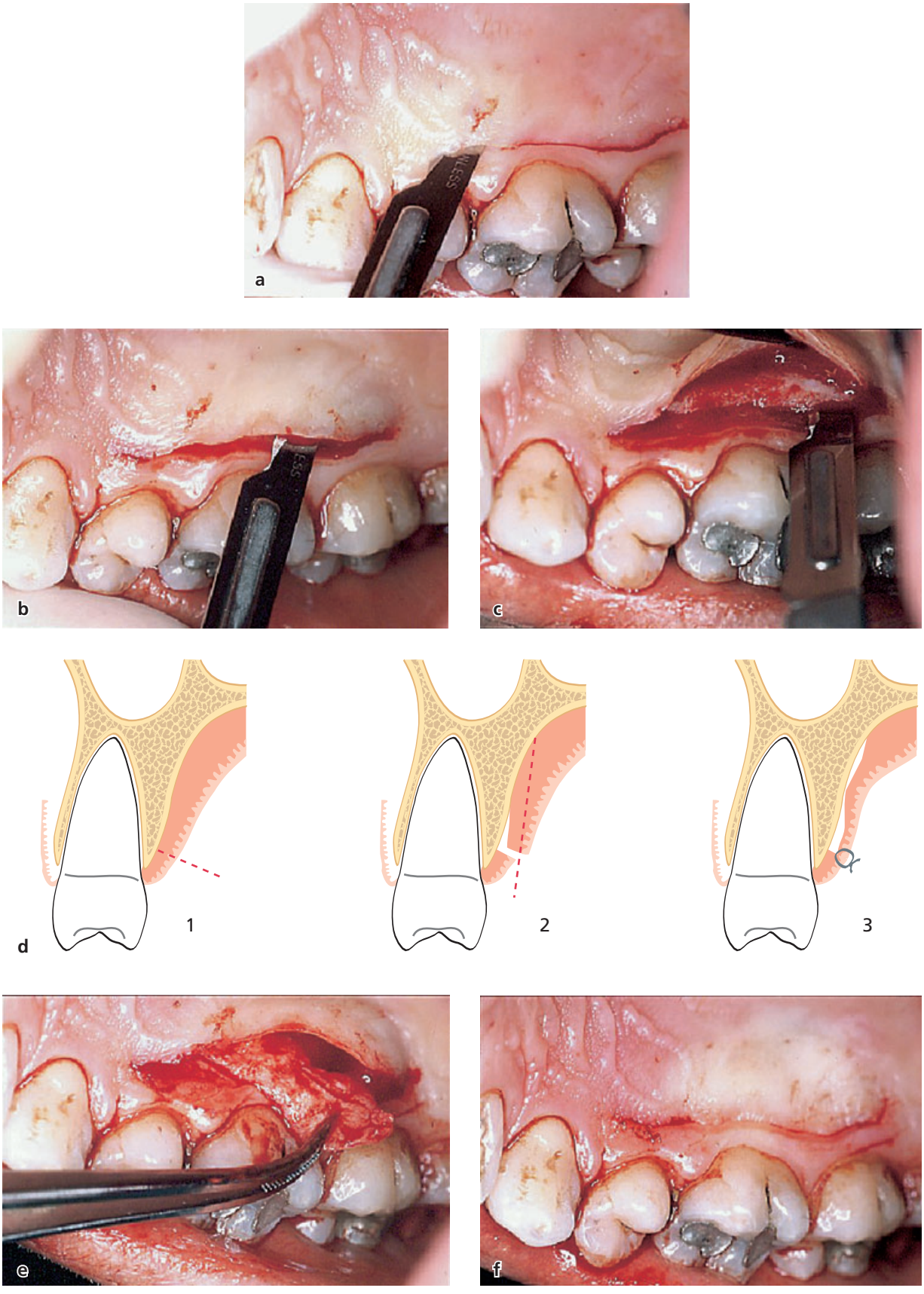


Fig. 44-46 "Trap-door" technique for harvest of a free connective tissue graft (see text for explanation).

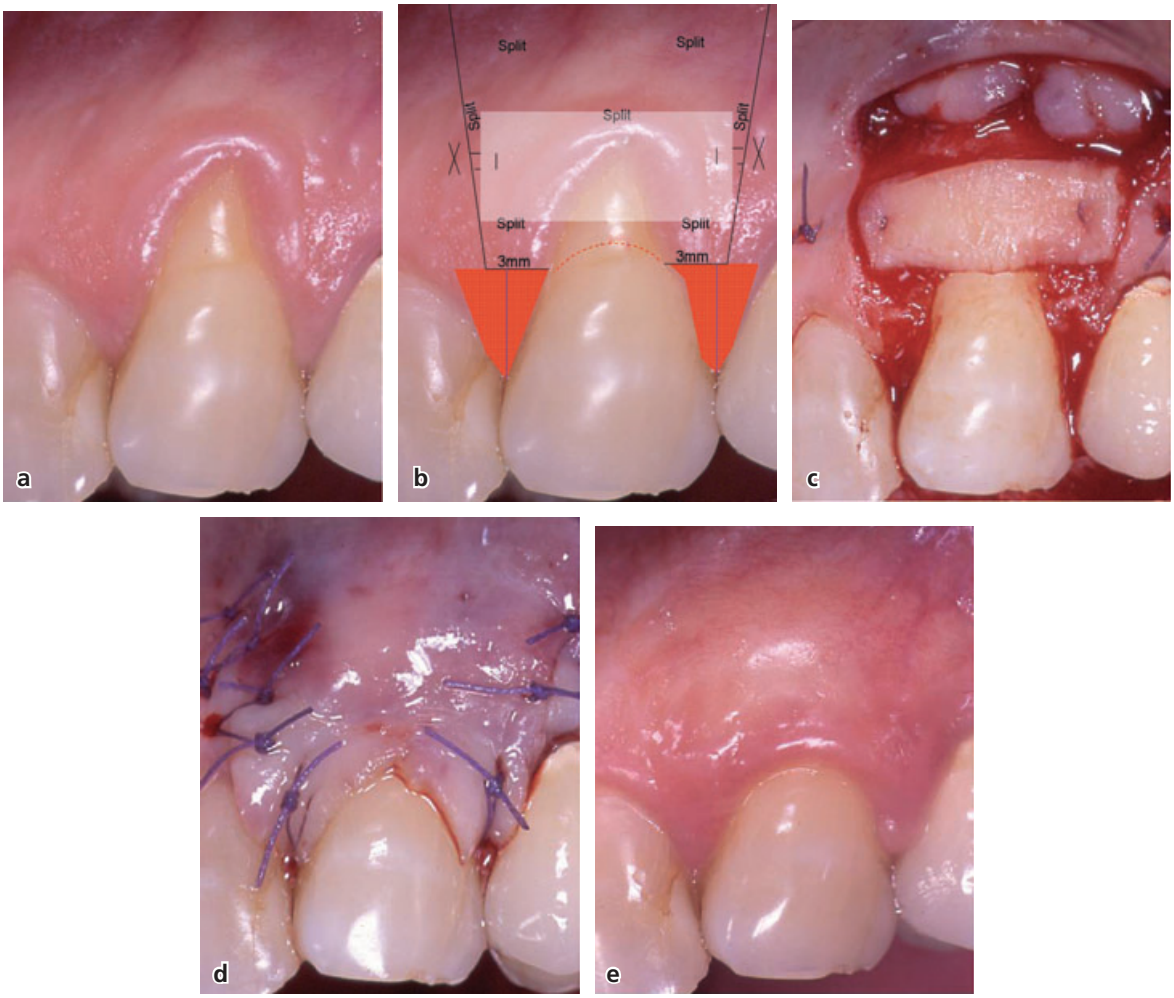


Fig. 44-47 (a–d) Free connective tissue graft combined with a coronally advanced flap procedure – multiple recessions (see the text for explanation). (e) The 1-year post-treatment result.

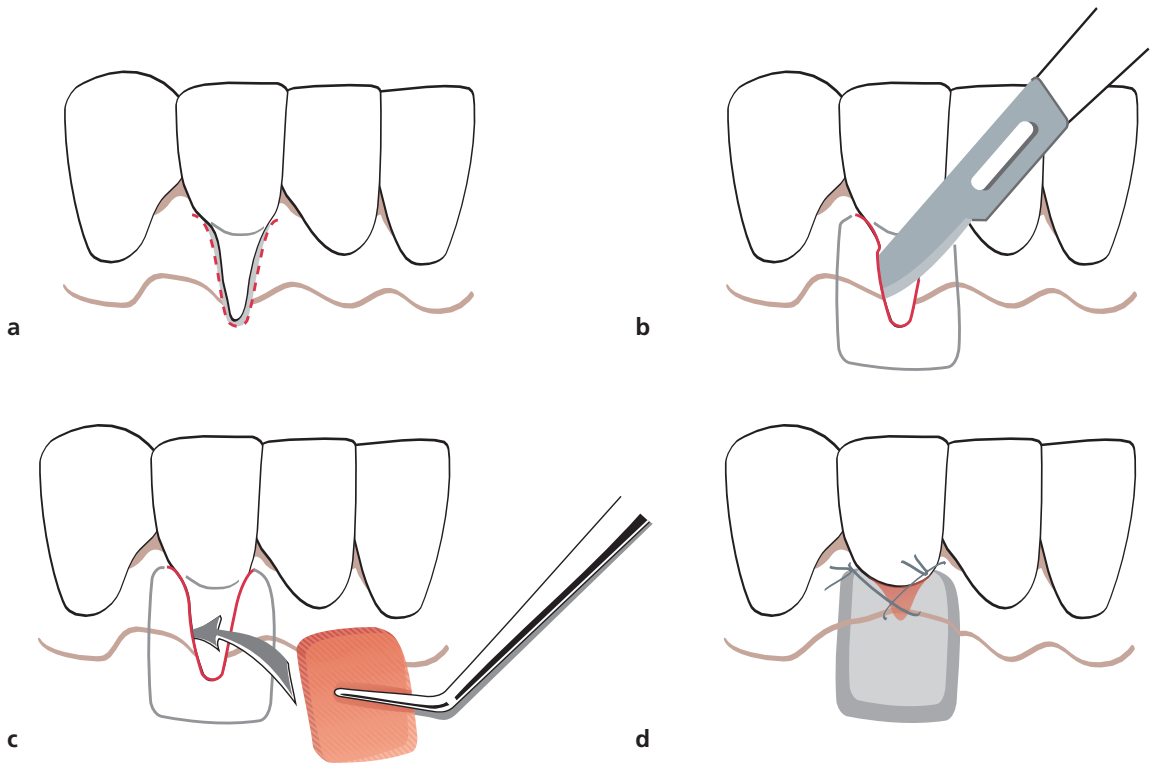


Fig. 44-48 Free connective tissue graft procedure – the "envelope technique". Schematic drawings illustrating the surgical technique (see the text for explanation).

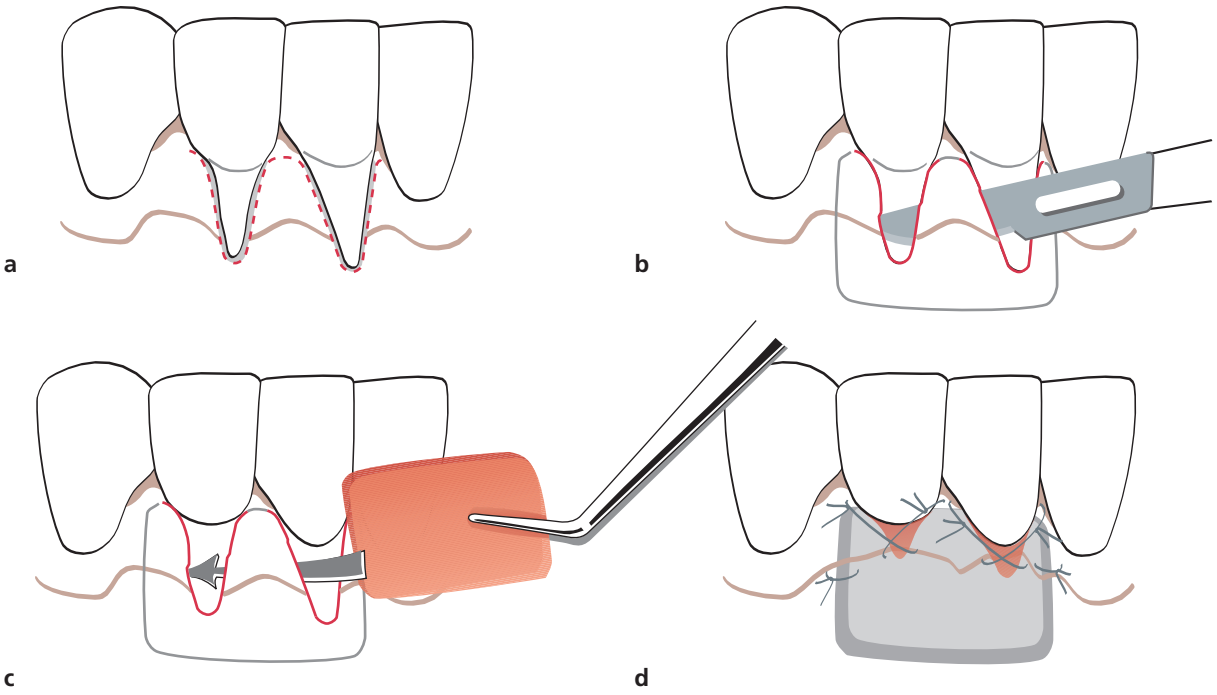


Fig. 44-49 Free connective tissue graft procedure – the "tunnel technique". Schematic drawings illustrating the surgical technique (see the text for explanation).

Table 44-1 Summary of the data available in the literature on the amount of root coverage obtainable with various procedures (Miller class I–II defects)

Root coverage procedure	No. of studies	No. of patients/teeth	Root coverage	
			Mean % of initial recession	Range
Rotational flaps	10	222/235	68	41–74
Coronally advanced flap	17	315/527	79	55–99
Guided tissue regeneration	35	589/695	75	48–94
Enamel matrix proteins	10	207/219	86	72–94
Free connective tissue graft	33	683/890	86	53–98
Epithelialized free soft tissue graft	16	335/491	63	11–87

to advance the mucosal flap coronally over the exposed portions of the connective tissue graft. Pressure is applied for 5 minutes to closely adapt the graft to the root surface and covering soft tissue. Application of a periodontal dressing is often not required.

Clinical outcome of root coverage procedures

Independent of the modality of surgical procedure used to obtain soft tissue root coverage, shallow residual probing depths, gain in clinical attachment, and an increase in gingival height are the common characteristics of treatment outcome. Although the major indication for performing root coverage procedures is esthetic/cosmetic demands by the patient, few studies have included assessments of esthetics as an end-point of success. Instead, the common outcome variables used are the amount of root coverage achieved, expressed in percentage of the initial depth of the recession defect, and the proportion of treated sites showing complete root coverage.

Root coverage

An overall comparison of the treatment outcome of various root coverage procedures is hampered by the fact that comparatively few studies have presented well documented clinical data and that there is substantial heterogeneity between studies (Roccuzzo *et al*. 2002; Oates *et al*. 2003). A summary with regard to the average amount of initial Miller class I–II recession defects that was successfully covered following treatment, based on the data published in a systematic review by Pagliaro *et al*. (2003) and relevant data from studies published between 2003 and 2006 (Table 44-1), shows that an average of 63–86% root coverage may be expected. However, the variability in the treatment outcome for the various procedures, both within and between studies, is large. This indicates that the procedures are operator sensitive and/or that various factors influencing the treatment outcome have not been adequately considered.

Complete coverage of the recession defect is the ultimate goal of the therapy. Table 44-2 summarizes

Table 44-2 Summary of the data available in the literature on the predictability of complete root coverage following the use of various procedures (Miller class I–II defects)

Root coverage procedure	No. of studies	No. of patients/teeth	Complete root coverage	
			Mean % of teeth	Range
Rotational flaps	1	30/30	43	–
Coronally advanced flap	15	287/499	48	9–95
Guided tissue regeneration	24	357/453	36	0–75
Enamel matrix proteins	7	138/150	72	53–90
Free connective tissue graft	26	549/732	61	0–93
Epithelialized free soft tissue graft	10	253/380	28	0–90

data on the predictability of this event with the use of the various surgical procedures. The average percentage of complete root coverage following pedicle or free graft procedures varies between 28 and 72%, with large variability between studies irrespective of surgical procedure used. According to the systematic reviews by Roccuzzo *et al*. (2002) and Oates *et al*. (2003), coronally advanced flaps with connective tissue grafts result in significantly greater root coverage compared to guided tissue regeneration. The lower mean predictability of complete root coverage achieved with the GTR procedure has been associated with the problem of membrane exposure during healing (Trombelli *et al*. 1995), but whether a bioabsorbable or a non-biodegradable barrier membrane is used does not seem to affect the treatment outcome (Roccuzzo *et al*. 1996).

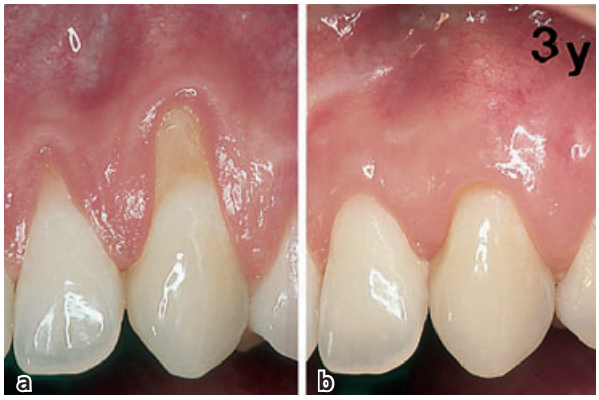


Fig. 44-50 (a) Buccal recession defects but no loss of periodontal support at proximal surfaces. Complete root coverage can be achieved. (b) 3-year follow-up.

Factors influencing the degree of root coverage

Patient-related factors. As with other surgical periodontal treatment procedures, poor oral hygiene is a factor that will negatively influence the success of root coverage procedures (Caffesse *et al*. 1987). Further, the predominant causative factor in the development of gingival recession is toothbrushing trauma, and hence this factor has to be corrected to secure an optimal outcome of any root coverage procedure. Treatment outcome in terms of root coverage is usually less favorable in smokers than in non-smokers (Trombelli & Scabbia 1997; Zucchelli *et al*. 1998; Martins *et al*. 2004; Erley *et al*. 2006; Silva *et al*. 2006), although some studies showed no differences (Tolmie *et al*. 1991; Harris 1994).

Site related factors. Among site-specific factors, the level of interdental periodontal support may be of greatest significance for the outcome of root coverage procedures. From a biological point of view complete root coverage is achievable in class I–II recession defects (Fig. 44-50), while when loss of connective tissue attachment also involves proximal tooth sites (class III–IV recession defects), only partial facial root coverage is obtainable (Miller 1985b) (Fig. 44-51).

An additional factor shown to influence the degree of attainable root coverage is the dimensions of the recession defect. Less favorable treatment outcome has been reported at sites with wide (>3 mm) and deep (≥5 mm) recessions (Holbrook & Ochsenbein 1983; Pini Prato *et al*. 1992; Trombelli *et al*. 1995). In a study comparing the treatment effect of coronally advanced flap and free connective tissue graft procedures, Wennström and Zucchelli (1996) reported that complete root coverage was observed in only 50% of the defects with an initial depth of ≥5 mm compared

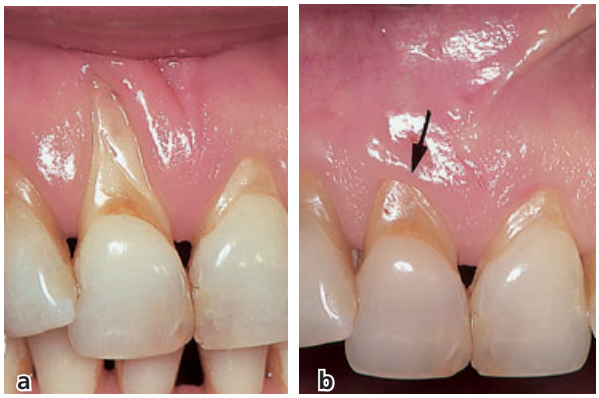


Fig. 44-51 (a) A deep buccal recession at tooth 11. The tooth has loss of support at proximal sites (Miller class III) and complete root coverage is not achievable. Also neighboring teeth show recessions at all tooth surfaces. (b) 2-year healing result following attempted root coverage at the facial aspect of tooth 11. The coronal position of the soft tissue margin is defined by the extension of proximal loss of periodontal support.

to 96% in shallower defects. Pini Prato *et al*. (1992) suggested, based on clinical observations in a controlled clinical trial, that a more favorable result with respect to root coverage might be obtained with the GTR procedure in sites with deep (≥5 mm) recession defects as compared to the coronally advanced flap. At the 18-month examination the average coverage was 77% with and 66% without the inclusion of a membrane barrier. However, data presented from recent systematic reviews and meta-analyses (Roccuzzo *et al*. 2002; Oates *et al*. 2003) showing that the predictability of root coverage is significantly reduced with the use of barrier membranes, limit the justification of using the GTR procedure in the treatment of recession defects. The pre-treatment gingival height apical to the recession defect is not correlated to the amount of root coverage obtained (Romanos *et al*. 1993; Harris 1994).

Technique-related factors. Several technique-related factors may influence the treatment outcome of a pedicle graft procedure. In a systematic review including data from 15 studies (Hwang & Wang 2006) a positive correlation was demonstrated between the thickness of the tissue flap and recession reduction. For complete root coverage the critical threshold thickness was found to be about 1 mm. However, whether a full- or split-thickness pedicle graft is used for root coverage may not influence the treatment outcome (Espinel & Caffesse 1981).

Elimination of flap tension is considered an important factor for the outcome of the coronally advanced flap procedure. Pini Prato *et al*. (2000a) measured the tension in coronally advanced flaps to compare the amount of root coverage in sites with and without residual flap tension. At sites that had residual tension (mean 6.5 g) the root coverage amounted to 78% 3 months post-surgically and 18% of the treated sites showed complete root coverage. Sites without tension demonstrated mean root coverage of 87% and complete root coverage in 45% of the cases. Furthermore, a statistically significant negative association was shown between the magnitude of residual tension in the flap and the amount of recession reduction.

Although the connective tissue areas lateral to the recession defect are considered important for the retention of the advanced flap when positioned over the root surface, the dimension of the interdental papilla is not a prognostic factor for the clinical outcome of the root coverage procedure (Saletta *et al*. 2001). As can be expected, the position of the gingival margin relative to the CEJ after suturing affects the probability of complete root coverage following healing. Pini Prato *et al*. (2005) demonstrated that for 100% predictability of complete root coverage in the treatment of Miller class I recessions with a coronally advanced flap procedure the flap margin has to be positioned at least 2 mm coronal to the CEJ.

With regard to free graft procedures, the thickness of the graft is a factor influencing the success of treatment procedure (Borghetti & Gardella 1990). A thickness of the free graft of about 2 mm is recommended.

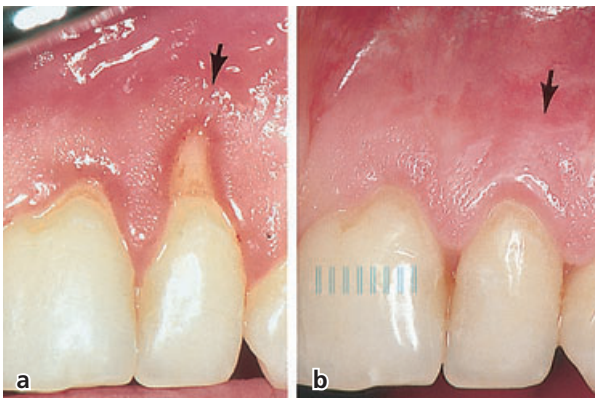


Fig. 44-52 Increased dimension of keratinized tissue 1 year following root coverage with a coronally advanced flap procedure. Before (a) and 1-year post-operatively (b). Arrows indicate the position of the mucogingival line.

Increased gingival height

An increased apico-coronal height of the gingiva is found following all procedures in which pedicle grafts of adjacent gingiva or free grafts from the palate have been placed over the recession defect. It is interesting to note, however, that an increased gingival height is also a common finding following a coronally advanced flap procedure only involving the existing gingiva apical to the recession (Fig. 44-52). This finding may be explained by several events taking place during the healing and maturation of the marginal tissue. Granulation tissue formation derived from the periodontal ligament tissue will form a connective tissue similar to the one of gingiva and with the potential to induce keratinization of the covering epithelium (Karring *et al*. 1971). A second factor to consider is the tendency of the mucogingival line to regain its "genetically" defined position following its coronal "dislocation" with the coronally advanced flap procedure used to achieve root coverage. Support for the concept that the mucogingival line will regain its original position over time is generated from a study by Ainamo *et al*. (1992). The authors performed an apically repositioned flap procedure in the lower anterior tooth region, which resulted in a 3 mm apical displacement of the mucogingival line. Re-examination after 18 years showed no differences in position of the mucogingival line between sites treated with the apically repositioned flap and contralateral control sites treated with a procedure not interfering with the mucogingival line, indicating that the mucogingival line had regained its original position.

Soft tissue healing against the covered root surface

Treatment of gingival recessions by pedicle grafts or free grafts may be clinically successful, but does the

treatment result in a healing characterized by the formation of a connective tissue attachment or an epithelial attachment? Independent of the quality of attachment formed, however, root coverage procedures evidently rarely result in the formation of a deep periodontal pocket.

Healing of pedicle soft tissue grafts

In the areas surrounding the recession defect, i.e. where the recipient bed consists of bone covered by connective tissue, the pattern of healing is similar to that observed following a traditional flap operation. Cells and blood vessels from the recipient bed as well as from the tissue graft invade the fibrin layer, which gradually becomes replaced by connective tissue. After 1 week a fibrous reunion is already established between the graft and the underlying tissue.

Healing in the area where the pedicle graft is in contact with the denuded root surface was studied by Wilderman and Wentz (1965) in dogs. According to these authors the healing process can be divided into four different stages (Fig. 44-53):

1. *The adaptation stage (from 0–4 days).* The laterally repositioned flap is separated from the exposed root surface by a thin fibrin layer. The epithelium covering the transplanted tissue flap starts to proliferate and reaches contact with the tooth surface at the coronal edge of the flap after a few days.
2. *The proliferation stage (from 4–21 days).* In the early phase of this stage the fibrin layer between the root surface and the flap is invaded by connective tissue proliferating from the subsurface of the flap. In contrast to areas where healing occurs between two connective tissue surfaces, growth of connective tissue into the fibrin layer can only take place from one surface. After 6–10 days a layer of fibroblasts is seen in apposition to the root surface. These cells are believed to differentiate into cementoblasts at a later stage of healing. At the end of the proliferation stage, thin collagen fibers are formed adjacent to the root surface, but a fibrous union between the connective tissue and the root has not been observed. From the coronal edge of the wound, epithelium proliferates apically along the root surface. According to Wilderman and Wentz (1965), the apical proliferation of epithelium may stop within the coronal half of the defect although further downgrowth of epithelium was also frequently observed.
3. *The attachment stage (from 27–28 days).* During this stage of healing thin collagen fibers become inserted in a layer of new cementum formed at

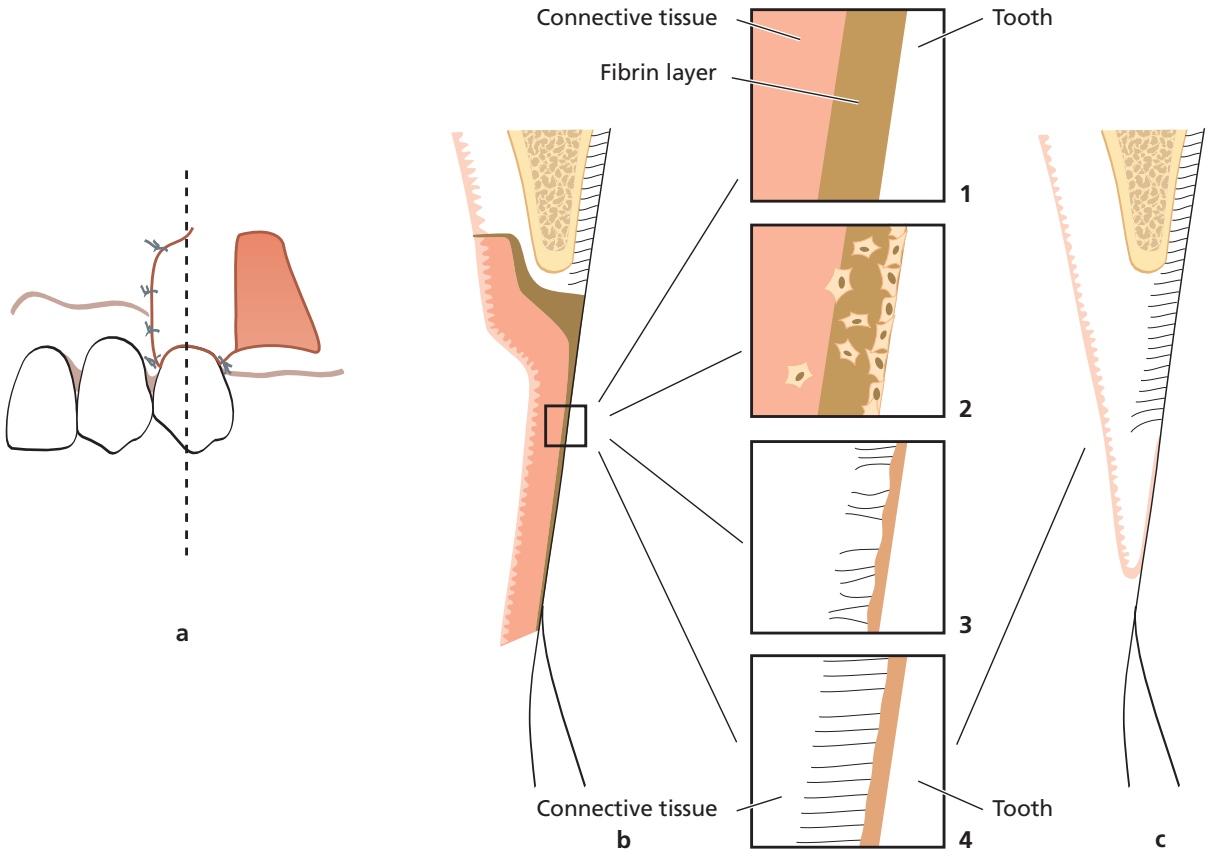


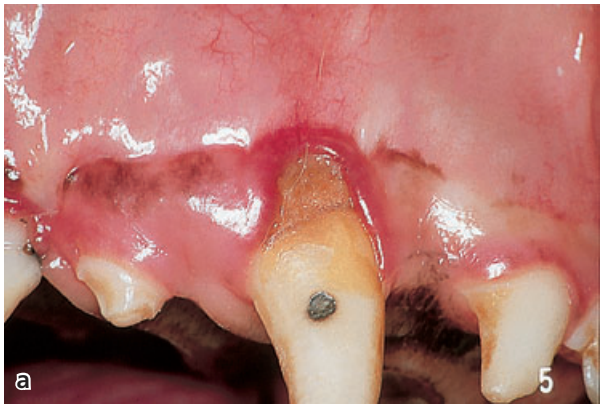
Fig. 44-53 (a) Schematic drawing illustrating healing following treatment of a localized soft tissue recession with a pedicle graft. (b) Cross section through the area immediately after operation. The framed areas (1–4) illustrate the four stages into which the healing process can be divided. (c) Area after healing. Approximately 50% of the successfully covered defect may show new connective tissue attachment.

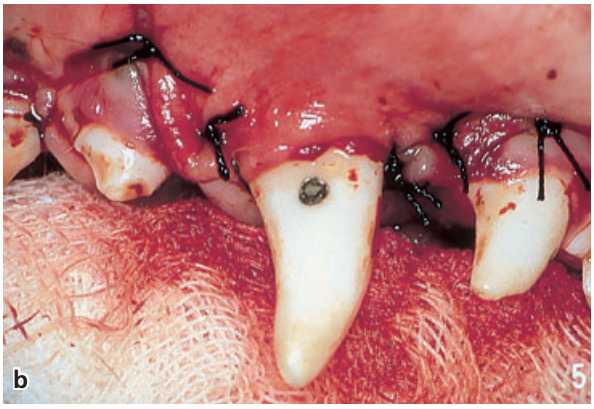
the root surface in the apical portion of the recession.

4. *The maturation stage.* This last stage of healing is characterized by continuous formation of collagen fibers. After 2–3 months bundles of collagen fibers insert into the cementum layer on the curetted root surface in the apical portion of the recession.

Results of experimental studies in monkeys and dogs on the healing characteristics of the periodontal wound have been interpreted to indicate that gingival connective tissue lacks the ability to form a new connective tissue attachment to the root, but may induce root resorption (see Chapter 25). This finding is of particular interest when considering the rationale for the treatment of recession defects by free or pedicle soft tissue grafts. Since, in these surgical procedures, gingival connective tissue is placed in contact with a denuded root surface, root resorption should be expected to occur. The reason why it is not a common complication following this type of treatment can be explained by two possible events. Either cells from the periodontal ligament form a fibrous attachment to the root surface or epithelial cells proliferate apically, forming a root-protective barrier (long junctional epithelium) towards the gingival connective tissue.

Histologic studies on whether it is the one or the other type of attachment that results following treatment of recessions with pedicle grafts indicate that new connective tissue attachment may be formed in part of the defect. In the study by Wilderman and Wentz (1965) a connective tissue attachment of around 2 mm and an epithelial attachment of the same height had formed in the soft tissue covered portion of the defect, i.e. about 50% of the successfully covered defect showed new connective tissue attachment. Gottlow *et al*. (1986) examined the result of healing following treatment of experimentally produced recession type defects with a coronally advanced flap in dogs (Fig. 44-54). The histologic analysis after 3 months of healing disclosed that, on average, 20% of the apico-coronal length of the original defect had been exposed due to recession during healing (i.e. about 80% root coverage was achieved), 40% was covered by epithelium and 40% demonstrated connective tissue attachment with cementum formation (Fig. 44-55). Determining factors for the type of healing result were the size and the shape of the defect. The possibility of achieving a new connective tissue attachment in the apical portion of the defect seemed to be considerably better in narrow recession defects than in wider ones, most likely because the periodontal ligament at the lateral parts of the defect will serve as a source of granulation





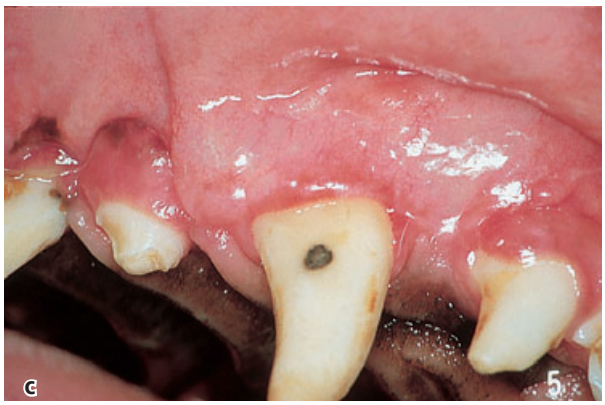


Fig. 44-54 Clinical photographs illustrating the treatment of an experimentally induced localized recession defect in a dog with a coronally displaced flap. (a) Presurgical appearance of the localized recession defect. (b) The site following flap closure of the defect and (c) following 3 months of healing.

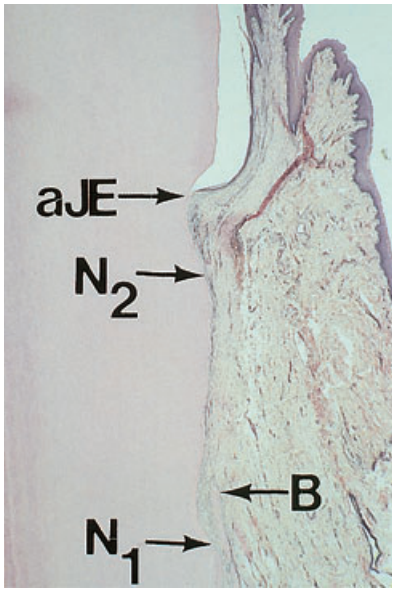


Fig. 44-55 Microphotograph of the healing following a coronally displaced flap in the dog as illustrated in Fig. 44-54. A new connective tissue attachment is formed and extends coronally from the apical border of the notch prepared at the bottom of the bone dehiscence (N_1) to the apical termination of the epithelium (aJE) located within the notch indicating the presurgical level of the soft tissue margin (N_2). B = alveolar bone crest.

tissue from which a new connective tissue attachment can develop.

Healing following pedicle graft procedures has also been histologically studied in monkeys (Caffesse *et al*. 1984; Gottlow *et al*. 1990), and in these studies 38–44% of the successfully covered recession defects demonstrated formation of new connective tissue attachment. The study by Gottlow *et al*. (1990) also showed that the use of a GTR membrane between the root surface and the pedicle graft generated significantly more new connective tissue attachment (79% of the covered part of the recession defect). A significantly increased amount of cementum formation with inserting collagen fibers was also demonstrated following the utilization of enamel matrix proteins in combination with a coronally advanced flap for treatment of experimentally produced recession defects in dogs (Sallum *et al*. 2004).

Some case reports with human block sections provide further evidence that new connective tissue attachment may be formed following pedicle graft procedures. Histologic evaluation of two teeth treated with a laterally positioned flap revealed that connective tissue attachment was re-established in the apical quarter of the successfully covered portion of the root (Sugarman 1969). Cortellini *et al*. (1993) examined histologically a tooth treated with the GTR procedure and showed that connective tissue faced 74% of the length of the recession defect. New cementum with inserting collagen fibers, i.e. new connective tissue attachment, covered 48% of the distance between the apical border of the root instrumentation and the soft tissue margin. In addition, histomorphometric assessments of a tooth treated with enamel matrix proteins revealed that new cementum covered 73% of the original defect (Heijl 1997).

Healing of free soft tissue grafts

Survival of a free soft tissue graft placed over a denuded root surface depends on diffusion of plasma and subsequent revascularization from those parts of the graft that are resting on the connective tissue bed surrounding the dehiscence. The establishment of collateral circulation from adjacent vascular borders of the bed allows the healing phenomenon of "bridging" (Sullivan & Atkins 1968a). Hence, the amount of tissue that can be maintained over the root surface is limited by the size of the avascular area (Oliver *et al*. 1968; Sullivan & Atkins 1968). Other factors considered critical for the survival of the tissue graft placed over the root surface are that a sufficient vascular bed is prepared around the dehiscence and that a thick graft is used (Miller 1985b).

Another healing phenomenon frequently observed following free graft procedures is "creeping attachment", i.e. coronal migration of the soft tissue margin. This occurs as consequence of tissue maturation during a period of about 1 year post treatment.

There are few histologic evaluations of the nature of the attachment established to the root surface following the use of free grafts for root coverage. Sugarman (1969) reported from a histologic evaluation of a human tooth treated with a free soft tissue graft that new connective tissue attachment was found in the apical quarter of the successfully covered recession defect. Harris (1999) and Majzoub *et al*. (2001), each reporting the histologic outcome of free connective tissue grafts in two cases, found only minimal amounts of new cementum formation in the most apical part of the recession defect and that healing resulted in a long junctional epithelium occupying the interface between the covering soft tissue and the root. Carnio *et al*. (2002) performed histologic evaluation of four cases of root coverage with a connective tissue graft combined with application of enamel matrix proteins (Emdogain®). They reported that the healing resulted in connective tissue adhesion to the root surface and that the formation of new cementum was observed only in the most apical end of the grafted area.

Thus, the limited histologic information available from humans on the healing of free soft tissue grafts indicates that a healing pattern similar to the one discussed above following pedicle graft procedures may result, namely that connective tissue attachment may be established in the most apical and lateral parts of the recession defect, but that an epithelial attachment is formed along the major portion of the root. Further, the application of enamel matrix proteins may prevent the apical migration of the epithelium but may not favor the formation of a true

connective tissue attachment between the free graft and the root surface.

Interdental papilla reconstruction

There may be several reasons for loss of papilla height and the establishment of "black triangles" between teeth. The most common reason in the adult individual is loss of periodontal support due to plaque-associated lesions. However, abnormal tooth shape, improper contours of prosthetic restorations, and traumatic oral hygiene procedures may also negatively influence the outline of the interdental soft tissues.

Nordland and Tarnow (1998) proposed a classification system regarding the papillary height adjacent to natural teeth, based on three anatomic landmarks: the interdental contact point, the apical extent of the facial CEJ, and the coronal extent of the proximal CEJ (Fig. 44-56):

- *Normal*: the interdental papilla occupies the entire embrasure space apical to the interdental contact point/area.
- *Class I*: the tip of the interdental papilla is located between the interdental contact point and the level of the CEJ on the proximal surface of the tooth.
- *Class II*: the tip of the interdental papilla is located at or apical to the level of the CEJ on the proximal surface of the tooth but coronal to the level of the CEJ mid-buccally.
- *Class III*: the tip of the interdental papilla is located at or apical to the level of the CEJ mid-buccally.

In an observational study in humans, Tarnow *et al*. (1992) analyzed the correlation between the presence of interproximal papillae and the vertical distance between the contact point and the interproximal bone crest. When the vertical distance from the contact point to the crest of bone was 5 mm or less, the papilla was present almost 100% of the time, whereas if the distance was 6 mm or more only partial papilla fill of the embrasure between the teeth was most commonly found. Considering that a supracrestal connective tissue attachment zone of approximately 1 mm is normally found (Gargiulo 1961), the observation indicates that the biologic height of the interdental papilla may be limited to about 4 mm. This interpretation is supported by the observation that in interdental areas denuded following an apically repositioned flap procedure, an up-growth of around 4 mm of soft tissue had taken place 3 years after surgery (Van der Velden 1982). Hence, before attempts are made to surgically reconstruct an interdental papilla, it is important to carefully assess both (1) the vertical distance between the bone crest and the apical point of the contact area between the crowns and (2) the soft tissue height in the interdental area. If the distance bone crest–contact point is ≤5 mm and the papilla height is less than 4 mm, surgical intervention for increasing the volume of the papilla could be justified in order to solve the problem of an interdental "black triangle". However, if the contact point is located >5 mm from the bone crest, because of loss of periodontal support and/or an inappropriate interdental contact relationship between the crowns, means to lengthen the contact

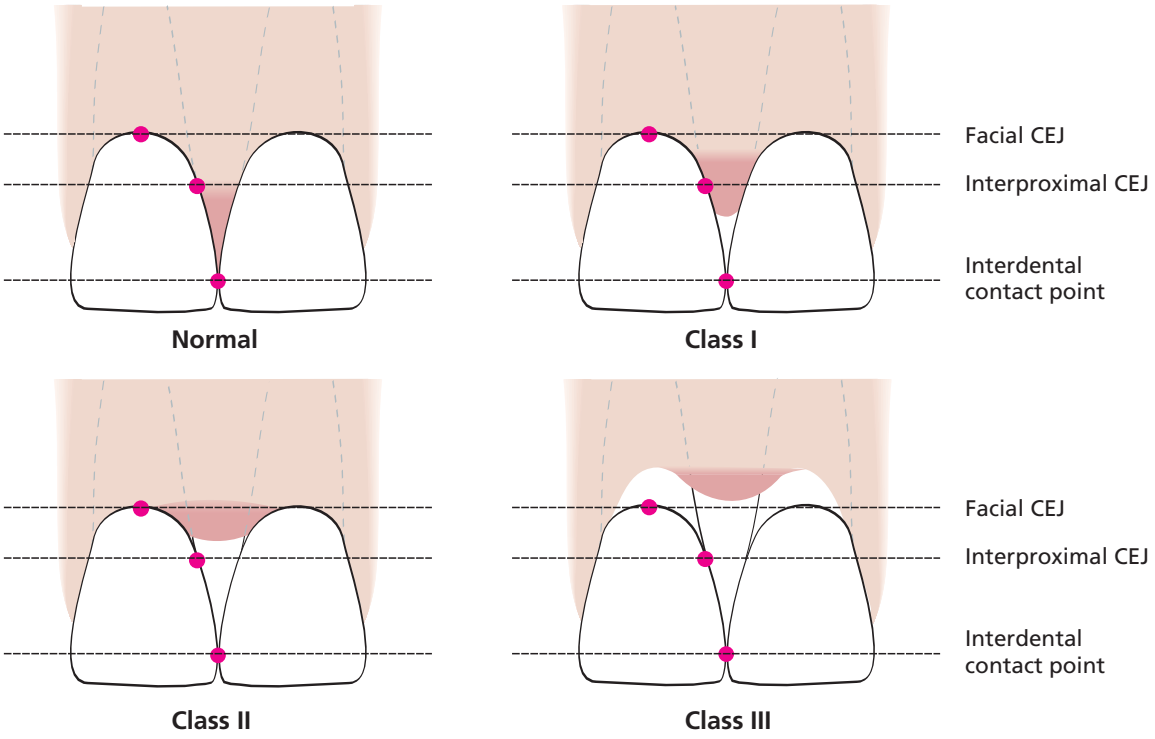


Fig. 44-56 Schematic drawing illustrating the classification system for papilla height (Nordland & Tarnow 1998).

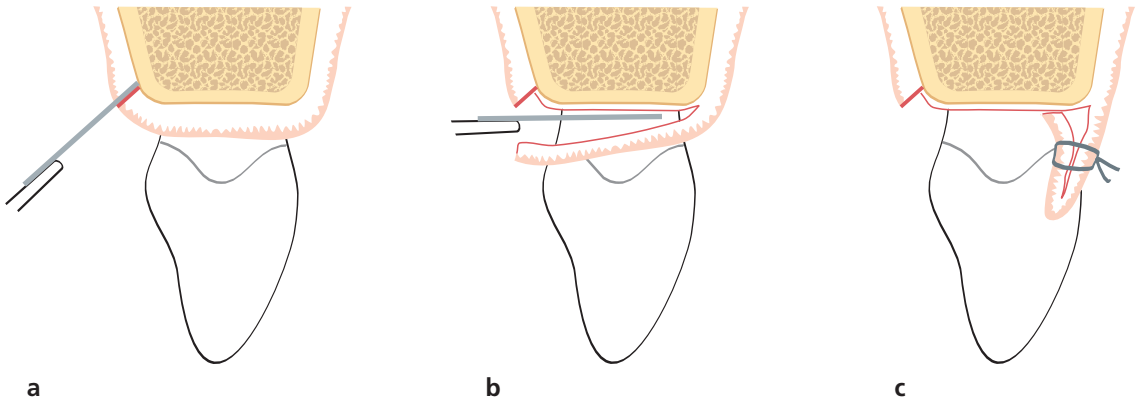


Fig. 44-57 Papilla reconstruction – pedicle graft technique. Schematic drawings illustrating the surgical technique (see the text for explanation).

area apically between the teeth should be selected rather than a surgical attempt to improve the topography of the papilla.

If loss of papilla height is only caused by soft tissue damage from oral hygiene devices, interproximal hygiene procedures must be initially discontinued to allow soft tissue recovery and then successively modified in order to eliminate/minimize traumatic injury to the papillae.

Surgical techniques

Several case reports have been published regarding surgical techniques for reconstruction of deficient papillae (e.g. Beagle 1992; Han & Takei 1996; Azzi *et al*. 1999). However, the predictability of the various procedures has not been documented and no data are available in the literature providing information on the long-term stability of surgically regained interdental papillae.

Beagle (1992) described a pedicle graft procedure utilizing the soft tissues palatal to the interdental area (Fig. 44-57). A split-thickness flap is dissected on the palatal aspect of the interdental area. The flap is elevated labially, folded, and sutured to create the new papilla at the facial part of the interdental area. A periodontal dressing is applied on the palatal aspect only, in order to support the papilla.

Han and Takei (1996) proposed an approach for papilla reconstruction ("semilunar coronally repositioned papilla") based on the use of a free connective tissue graft (Fig. 44-58). A semilunar incision is placed in the alveolar mucosa facial to the interdental area and a pouch-like preparation is performed into the interdental area. Intrasulcular incisions are made around the mesial and distal half of the two adjacent teeth to free the connective tissue from the root surfaces to allow coronal displacement of the gingival–papillary unit. A connective tissue graft, taken from the palate, is placed into the pouch to support the coronally positioned interdental tissue.

Azzi *et al*. (1999) described a technique in which an envelope-type flap is prepared for coverage of a connective tissue graft (Fig. 44-59). An intrasulcular incision is made at the tooth surfaces facing the interdental area to be reconstructed. Subsequently, an incision is placed across the facial aspect of the interdental area and an envelope-type split-thickness flap is elevated into the proximal site as well as apically to a level beyond the mucogingival line. A connective tissue graft is harvested from the tuberosity area, trimmed to adequate size and shape, and placed under the flaps in the interdental papilla area. The flaps are brought together and sutured with the connective tissue graft underneath.

Crown-lengthening procedures

Excessive gingival display

In most patients, the lower edge of the upper lip assumes a "gum-wing" profile which limits the amount of gingiva that is exposed when a person smiles. Patients who have a high lip line expose a broad zone of gingival tissue and may often express concern about their "gummy smile" (Fig. 44-60a). The form of the lips and the position of the lips during speech and smiling cannot be easily changed, but the dentist may, if necessary, modify/control the form of the teeth and interdental papillae as well as the position of the gingival margins and the incisal edges of the teeth. In other words, it is possible by a combination of periodontal and prosthetic treatment measures to improve dentofacial esthetics in this category of patient.

As a base for treatment decisions, a careful analysis of the dentofacial structures and how they may affect esthetics should be performed. It should include the following features:

- Facial symmetry
- Interpupillary line; even or uneven
- Smile line: low, median or high
- Dental midline in relation to facial midline
- Gingival display during speech and during broad, relaxed smile
- Harmony of gingival margins

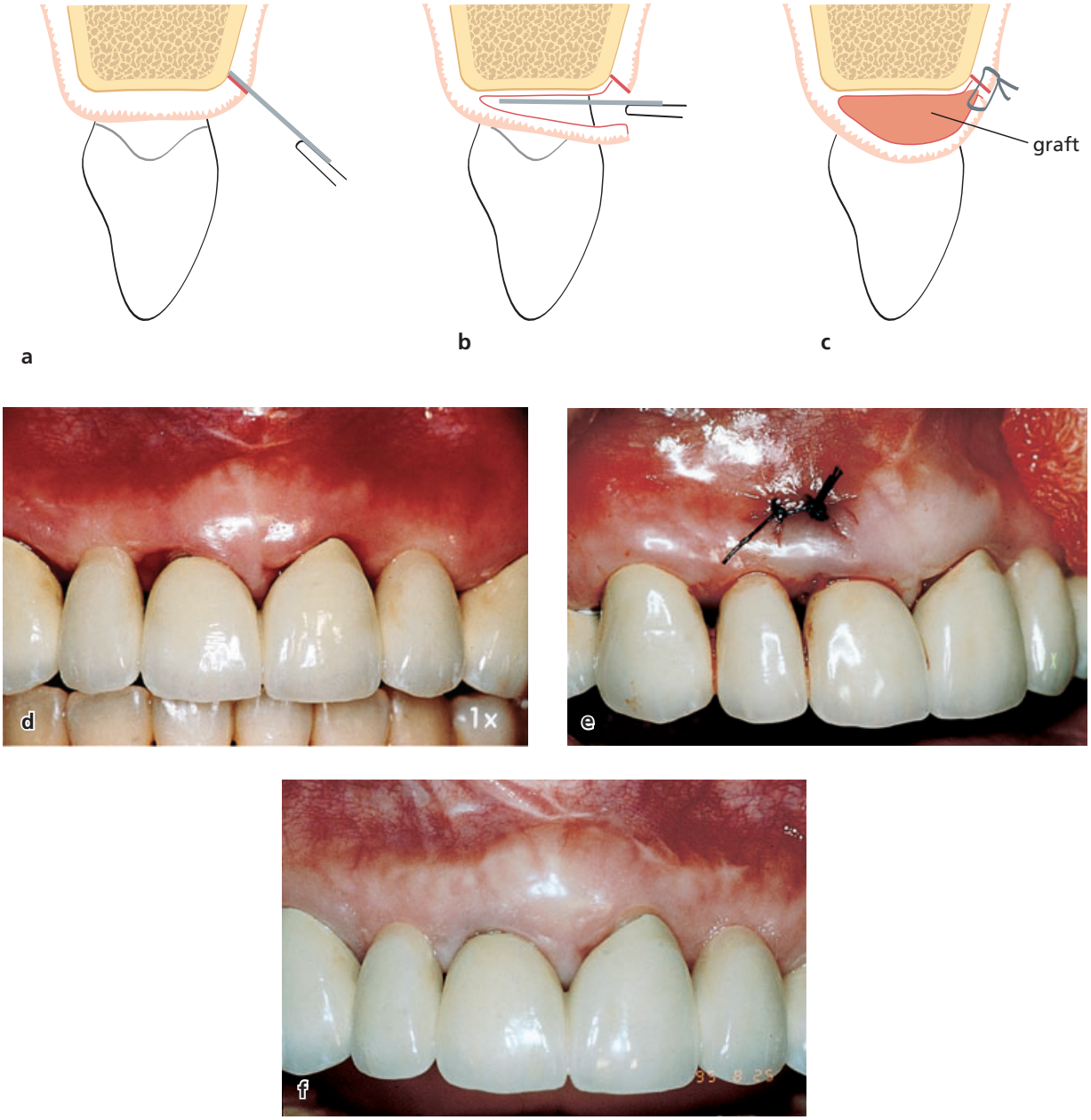


Fig. 44-58 Papilla reconstruction – the "semilunar coronally repositioned papilla" technique. (a–c) Schematic drawings illustrating the surgical technique (see the text for explanation). (d–f) Reconstruction of papillae distal to the central incisors with the use of the semilunar coronally repositioned papilla technique in a patient with a fixed bridge reconstruction.

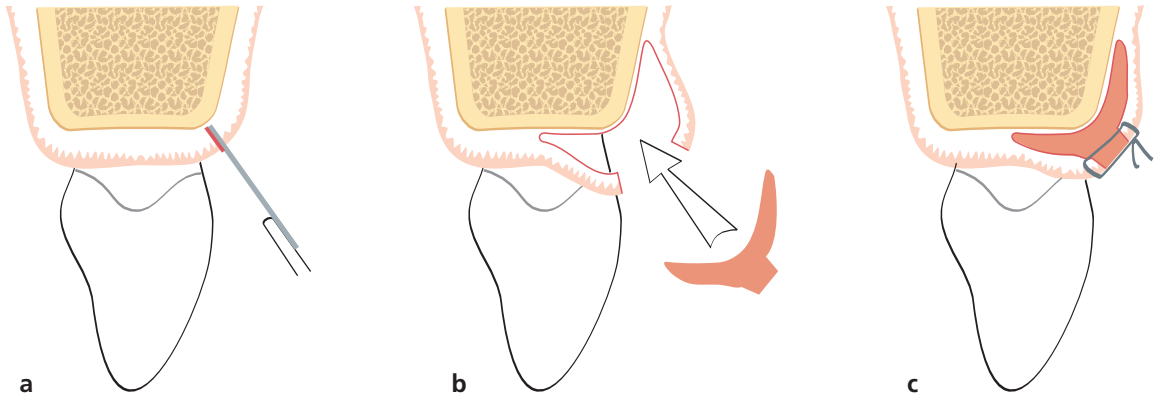


Fig. 44-59 Papilla reconstruction – "envelope" technique. Schematic drawings illustrating the surgical technique (see the text for explanation).

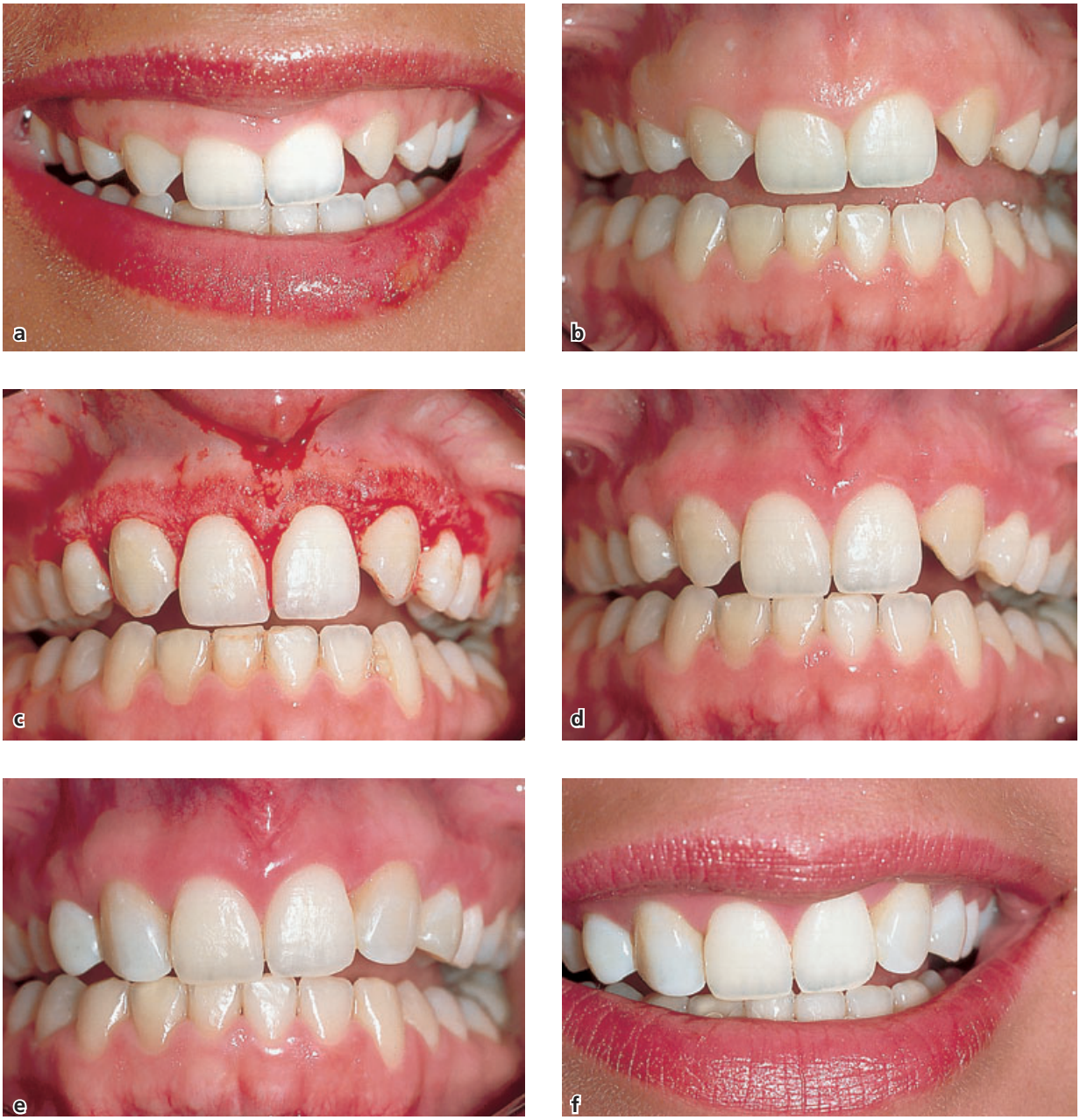


Fig. 44-60 Crown-lengthening procedure. (a,b) Pretreatment views. The clinical crowns are considerably shorter than the anatomic crowns. The lateral incisors were congentially missing and orthodontic treatment had been carried out to move the posterior teeth anteriorly. The canine teeth in the position of the lateral incisors added to the esthetic disharmony. (c) A gingivectomy was performed to expose the anatomic crowns of the teeth. (d) One month post surgery. At this appointment, the canine and first premolar teeth were reshaped and bonded. (e) Tooth form and proportional balance were improved by bonding. (f) At 3 years post-treatment, the gingival tissues exhibited no rebound and retained the architectural form sculpted into the tissue at the time of the surgical procedure.

- Location of gingival margins in relation to the CEJs
- Tooth size and proportions/harmony
- Incisal plane/occlusal plane.

If excessive gingival exposure is due to insufficient length of the clinical crowns, a crown-lengthening procedure is indicated to reduce the amount of gingiva exposed, which in turn will favorably alter the shape and form of the anterior teeth. To select the proper treatment approach for crown lengthening, an analysis of the individual case with regard to crown–root–alveolar bone relationships should also be included.

In the young adult with an intact periodontium the gingival margin normally resides about 1 mm coronal to the CEJ. However, some patients may have a height of free gingiva that is greater than 1 mm, resulting in an disproportional appearance of the clinical crown. If such a patient complains about their "small front teeth" and the periodontium is of a thin biotype, full exposure of the anatomic crown

Fig. 44-61 (a) Pretreatment view. The patient disliked her "small front teeth" and diastema. Radiographs and probing indicated the gingival tissues were covering the cervical one third of the crowns. Crestal bone was thin and in normal relationship to the cemento-enamel junctions. The patient preferred "pink gums" if she could possibly have them. (b) A long externally beveled path of incision was used to accomplish the gingivectomy. (c) This view shows the color changes and pleasing architecture produced in the anterior gingiva at 2 months post surgery. The diastema was partially closed by direct bonding at this time. (d) Post-treatment view showing the enhancement of esthetic values for the patient.

can be accomplished by a gingivectomy/gingivoplasty procedure (Fig. 44-60).

An assessment should also be made regarding the amount and pattern of pigmentation existing within the gingival tissues, and the patient's desire to maintain or lessen the pigmentation contained within the tissues. The externally beveled path of incision that is usually employed in a gingivectomy procedure will remove the pigmentation and produce pink gingival tissue upon initial healing (Fig. 44-61). The surgically induced color change in the tissues comes about rapidly and markedly affects esthetic values. For this reason, an externally beveled gingivectomy procedure should not be terminated at the midline in patients that have pigmented gingival tissues. It should be extended across the midline to the premolar area to avoid a color mismatch in the esthetic zone of the anterior teeth. The color change may be permanent or the pigmentation may slowly return over a period of a year or more. Patients should be informed of the changes in tissue color that will occur and be allowed to make a choice as to the color of the tissue they will have post-surgically. If they wish to maintain their pigmentation, an internally beveled path of incision (internal gingivectomy) should be employed (Fig. 44-62).

If the periodontium is of the thick biotype and there is a bony ledge at the osseous crest, an apically positioned flap procedure (see Chapter 38) should be performed. This will allow for osseous recontouring (Fig. 44-63).

More extensive bone recontouring is required to solve esthetic problems found in patients who do indeed have short anatomic crowns in the anterior section of the dentition. In this category of patients, prosthetic measures must be used after resective periodontal therapy to increase the apico-coronal dimension of the crowns (Fig. 44-64). Patients who are candidates for this kind of resective therapy can be divided into two categories:

1. Subjects who have normal occlusal relationships and incisal guidance. In this category the incisal line of the front teeth must remain unaltered but the clinical crowns can be made longer by surgically exposing root structure and by locating the cervical margins of the restorations apical to the CEJ (Fig. 44-64).
2. Subjects who have abnormal occlusal relationships with excessive interocclusal space in the posterior dentition when the anterior teeth are in edge-to-edge contact. In this category of patients

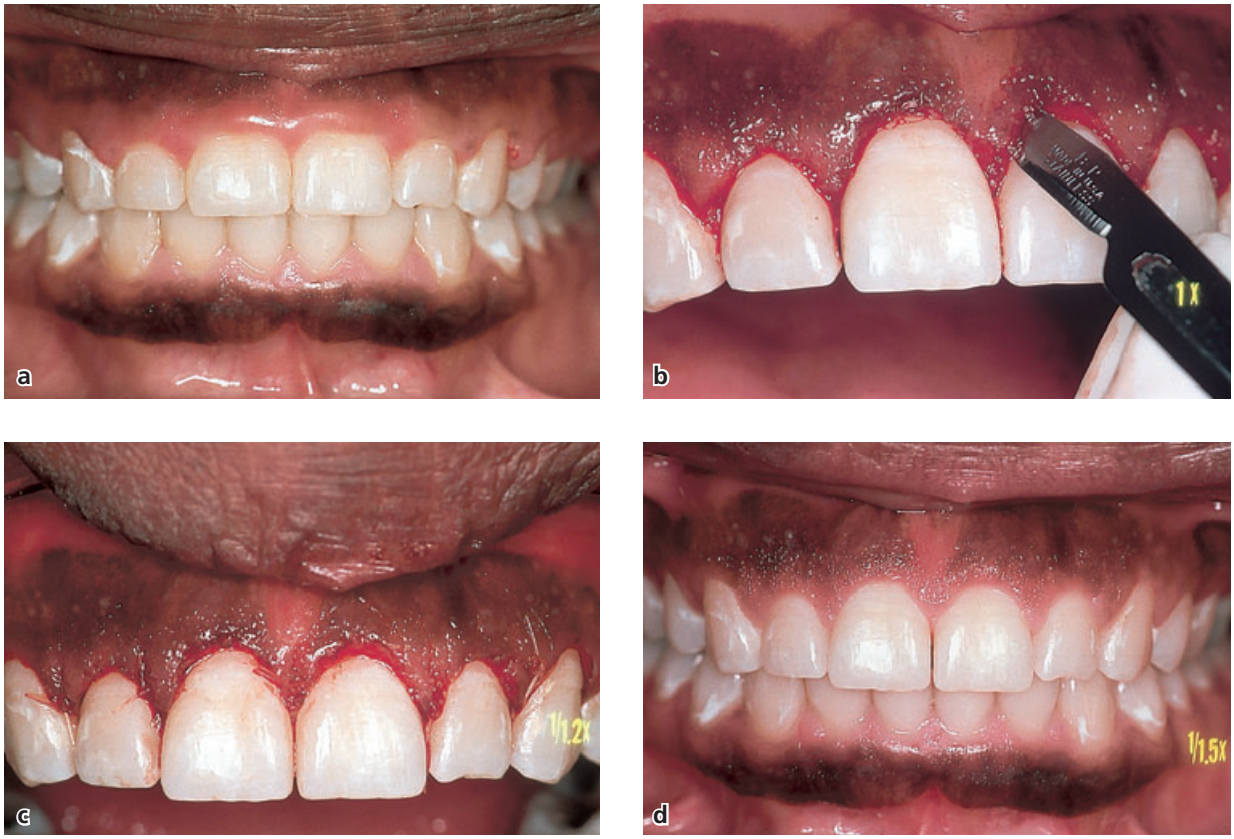


Fig. 44-62 (a) Pretreatment view. This patient disliked the looks of her "small front teeth"; she sought consultation to have her teeth made longer by crowning them. Probing and radiographs revealed normal osseous morphology and a wide zone of attached gingiva that covered the cervical one third of the incisors. It was explained to the patient that a surgical solution was preferred to restorative procedures to make her teeth longer. The patient made a request that the color of her gingival tissues remain unchanged. (b) An internally beveled path of incision was use to effect an "internal gingivectomy" to maintain the pigmentation in the tissues. This created mini flaps in the areas of the papillae. (c) 5-0 gut sutures were used to stabilize the papillae. (d). The crown lengthening that was achieved with maintenance of color harmony can be seen in this view at 3 months post surgery. (Courtesy of Dr. E. Saacks, Pennsylvania, USA.)

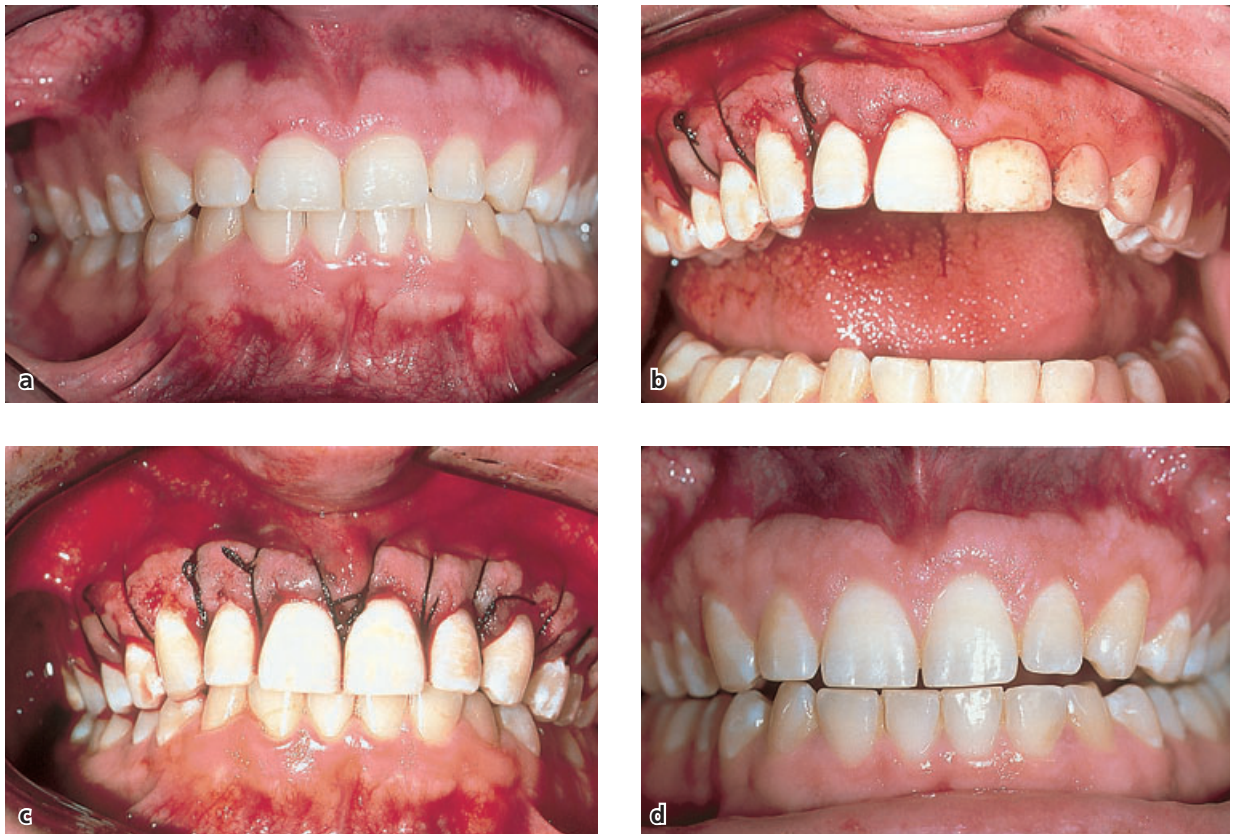


Fig. 44-63 (a) Pretreatment view. The patient, a dentist, requested crown lengthening to lessen his "gummy smile" and give him a more masculine appearance. The patient had a wide zone of attached gingiva and thick crestal bone. Palpation indicated bony exostoses. (b) An apically positioned flap and osseous resective surgery, from second premolar to second premolar, were used to lengthen the teeth. The surgery was confined to the labial surfaces. This view shows one half of the surgery completed. (c) Vertical mattress sutures were utilized to hold the flap apically. (d) Three years post-treatment. Note that the gingival tissues retain the morphology created at the time of surgery.

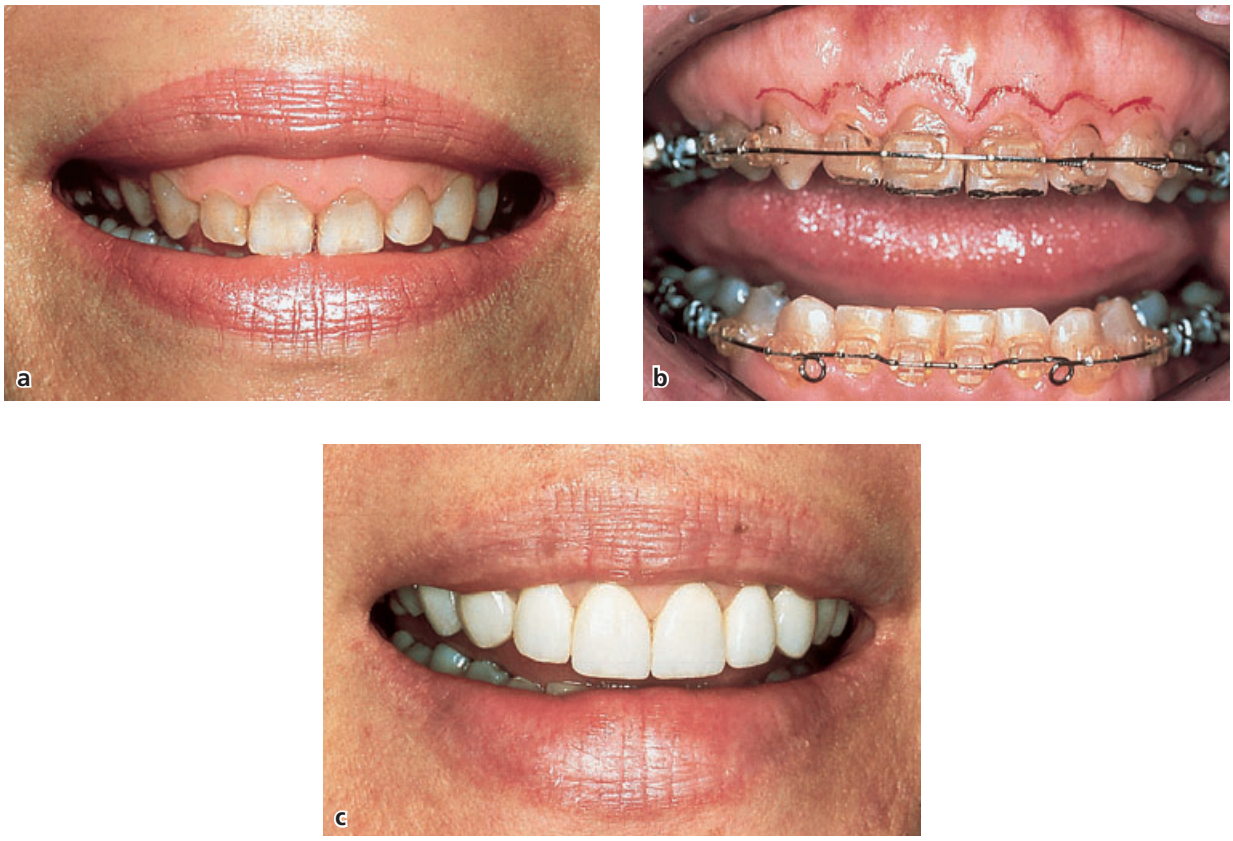


Fig. 44-64 Crown lengthening by surgical and prosthetic procedures. (a) Pretreatment view. The patient displayed "short front teeth" and a broad exposure of gum tissue. The full anatomic crown is exposed in this case and the surgically induced recession will expose root structure. (b) The patient had an unusually wide zone of attached gingiva. The gingival margins were positioned apically by making an internally beveled flap with a submarginal entrance incision as outlined in red ink. The crest of the bone was reduced in height. (c) After the tissues had matured following surgery, individual crowns were prepared for each of the anterior teeth. Crown lengthening was achieved and the patient no longer exposed a broad expanse of gum tissue. (Courtesy of Dr. D. Garber, Atlanta, GA, USA.)

the length of the maxillary front teeth can be reduced without inducing posterior occlusal interferences. In addition, the marginal gingiva can be resected or relocated to an apical position before crown restorations are made.

In some individuals with an excessive display of gingiva, the size and shape of the teeth and the location of the gingival margins may be perfectly normal. The excessive display of gingiva in these cases is often caused by vertical maxillary excess and a long mid-face (Fig. 44-65). Periodontal crown lengthening procedures will not suffice to solve their problems, but rather the maxilla must be altered by a major maxillofacial surgical procedure. The risk–benefit and cost–benefit ratios must be thoroughly evaluated before recommending this type of surgical therapy to correct esthetic problems.

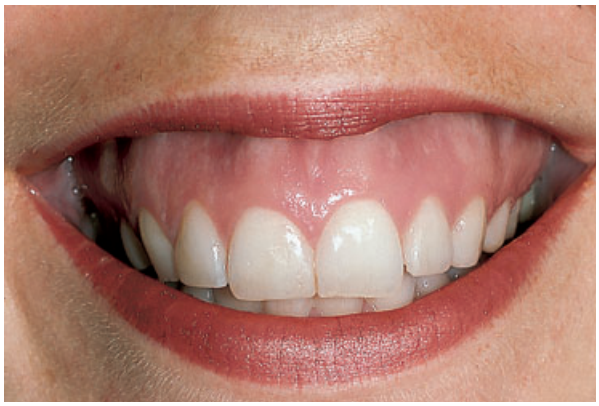
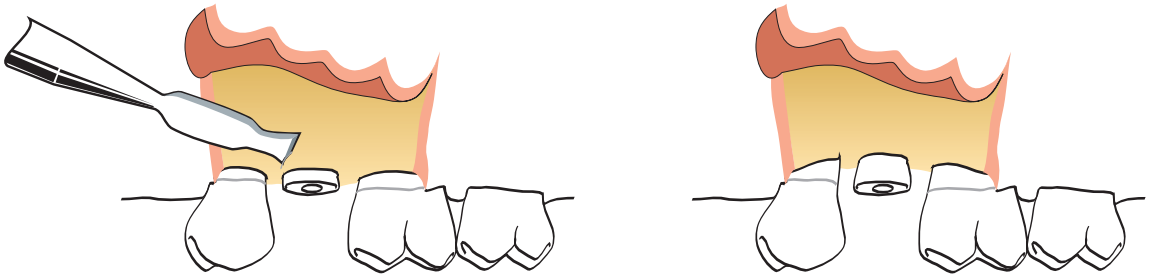


Fig. 44-65 This patient displays a large expanse of gingival tissue when smiling or speaking. The patient has a long mid-face and vertical maxillary excess. The gingival margins reside 1 mm coronal to the cemento-enamel junction and the anatomic and clinical crowns are approximately equal.

Exposure of sound tooth structure

Crown-lengthening procedures may be required to solve problems such as (1) inadequate amount of tooth structure for proper restorative therapy, (2) subgingival location of fracture lines, and (3) subgingival location of carious lesions. The techniques used to accomplish crown lengthening include (1) apically positioned flap procedure including bone resection and (2) forced tooth eruption with or without fiberotomy.



a b

Fig. 44-66 Surgical resective therapy for crown lengthening cannot be confined to the tooth in need of treatment. The principles of osseous resection require that bone be removed from the adjacent teeth to create a gradual rise and fall in the profile of the osseous crest. This causes a loss of attachment apparatus and recession of the adjacent teeth as well.

Apically positioned flap with bone recontouring

The apically positioned flap technique with bone recontouring (resection) may be used to expose sound tooth structure. As a general rule, at least 4 mm of sound tooth structure must be exposed at the time of surgery. During healing the supracrestal soft tissues will proliferate coronally to cover 2–3 mm of the root (Herrero *et al*. 1995; Pontoriero & Carnevale 2001; Lanning *et al*. 2003), thereby leaving only 1–2 mm of supragingivally located sound tooth structure. When this technique is used for crown lengthening it must also be realized that gingival tissues have an inherent tendency to bridge abrupt changes in the contour of the bone crest. Thus, in order to retain the gingival margin at its new and more apical position, bone recontouring must be performed not only at the problem tooth but also at the adjacent teeth to gradually reduce the osseous profile (Fig. 44-66). Consequently, substantial amounts of attachment may have to be sacrificed when crown lengthening is accomplished with an apically positioned flap technique. It is also important to remember that, for esthetic reasons, symmetry of tooth length must be maintained between the right and left sides of the dental arch. This may, in some situations, call for the inclusion of even more teeth in the surgical procedure.

- *Indication:* crown lengthening of multiple teeth in a quadrant or sextant of the dentition.
- *Contraindication:* surgical crown lengthening of single teeth in the esthetic zone (Fig. 44-67).
- *Technique:* The apically positioned flap technique and methods used for bone recontouring are discussed in Chapter 38.

Forced tooth eruption

Orthodontic tooth movement can be used to erupt teeth in adults (Reitan 1967; Ingber 1974, 1976; Potashnick *et al*. 1982). If moderate eruptive forces are used, the entire attachment apparatus will move in unison with the tooth. The tooth must be extruded a distance equal to or slightly longer than the portion of sound tooth structure that will be exposed in the subsequent surgical treatment. After the tooth has reached the intended position and has been stabilized, a full-thickness flap is elevated and bone recontouring is performed to expose sound root structure. For esthetic reasons it is important that the bone and soft tissue levels at adjacent teeth remain unchanged.

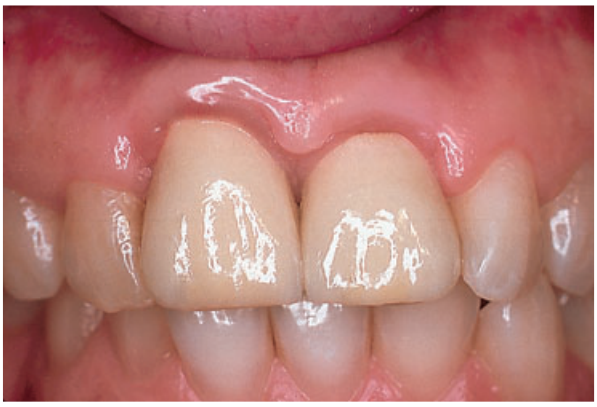


Fig. 44-67 A deformity which interfered with dentofacial esthetics was created at the right central incisor by using a surgical crown lengthening procedure at one single tooth to expose sound tooth structure. The soft tissues cannot follow the abrupt and steep changes in the osseous profile. The crown preparation invaded the zone of normal supracrestal connective tissue. This created a chronic periodontal pocket and adversely affected esthetics. (Courtesy of Dr. A. Winnick, Toronto, Canada.)

Forced tooth eruption can also be used to level and align gingival margins and the crowns of teeth to obtain esthetic harmony. Instead of using surgical procedures to position the gingival margins of unaffected normal teeth apically to the level of a tooth with recession or orthodontic malalignment, the tooth that is malpositioned or has sustained recession is erupted to the level of the normally positioned teeth. The entire attachment apparatus and dentogingival junction will follow the root of the tooth as it is moved coronally (Fig. 44-68).

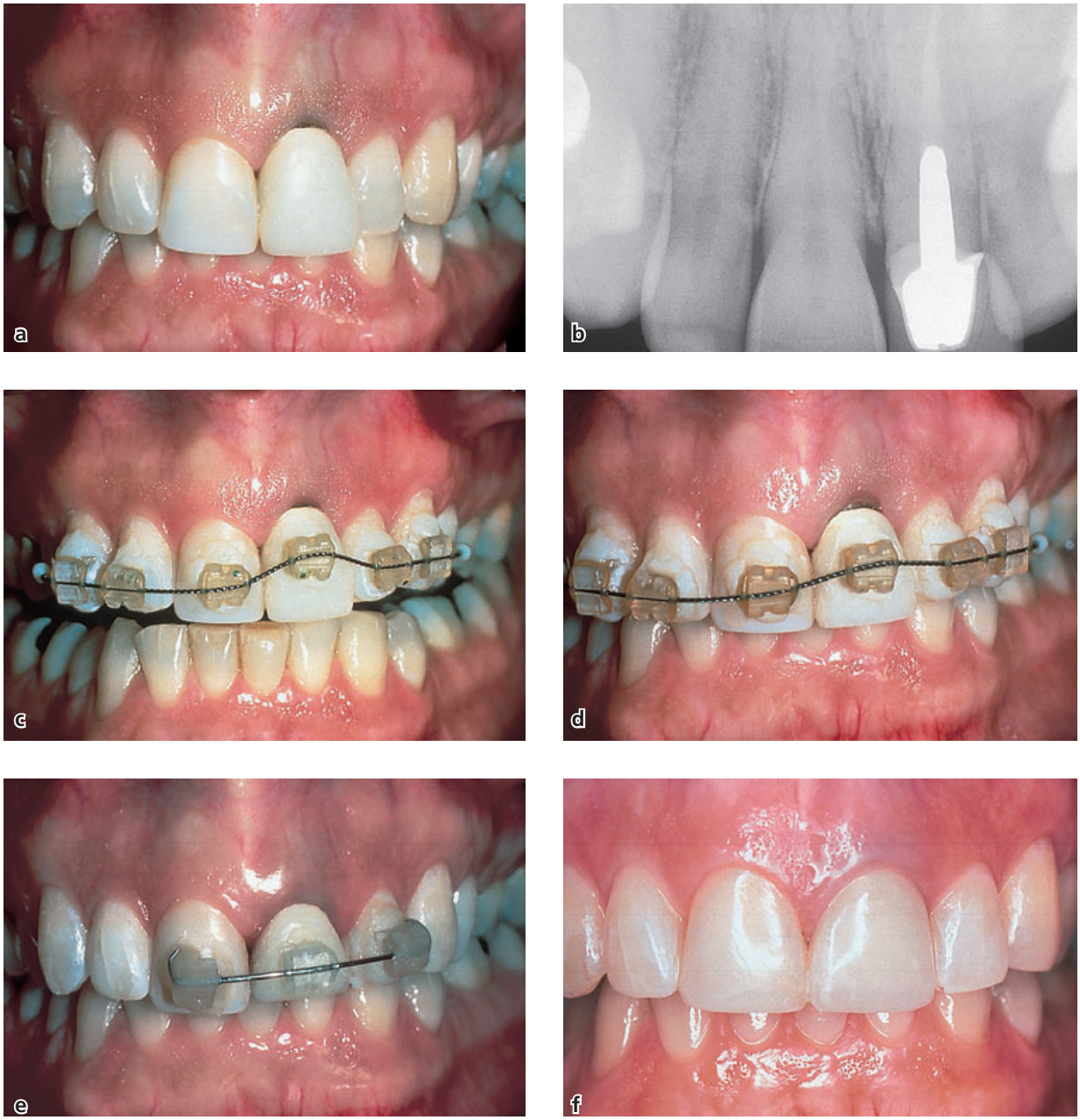


Fig. 44-68 Forced tooth eruption (show method) used to level gingival margins, treat recession on a single tooth and create esthetic harmony. (a,b) Recession on the left central incisor exposed the root surface darkened from root canal treatment. The uneven gingival margins and dark root surface detracted from an otherwise attractive smile. (c) A nitol wire with an offset bracket was used to slowly extrude the incisor. (d) Occlusal adjustment was done on the lingual side of the crown to create room for the tooth to erupt. This view, at 1 month in tooth movement, shows the gingival tissues moving with the root of the tooth. (e) Sufficient eruption had occurred by 3 months to level the gingival margins. The orthodontic brackets were used for temporary stabilization and a new crown was prepared. (f) The new crown masked the show-through of the dark root. The even gingival margins and beautiful crown created esthetic harmony. (Courtesy of Dr. J. Ingber, Philadelphia, PA, USA.)

- *Indication:* crown lengthening at sites where removal of attachment and bone from adjacent teeth must be avoided. The forced eruption technique can also be used as a means of reducing pocket depth at sites with angular bony defects (Brown 1973; Ingber 1974, 1976). The angular bony defect at the problem tooth can be reduced while the attachment level at the adjacent tooth surface remains unchanged (Fig. 44-69).
- *Contraindication:* the forced eruption technique requires the use of fixed orthodontic appliances. Thus, in patients who only have a few teeth remaining, an alternative approach for crown lengthening has to be selected.
- *Technique:* orthodontic brackets are bonded to the problem tooth and to adjacent teeth and are combined with an arch wire. Another type of mechanical system can be utilized by placing a heavy gauge bar or wire in grooves prepared in the adjacent teeth and over the problem tooth. A power elastic is tied from the bracket to the arch wire (or the bar), which pulls the tooth coronally. If most of the

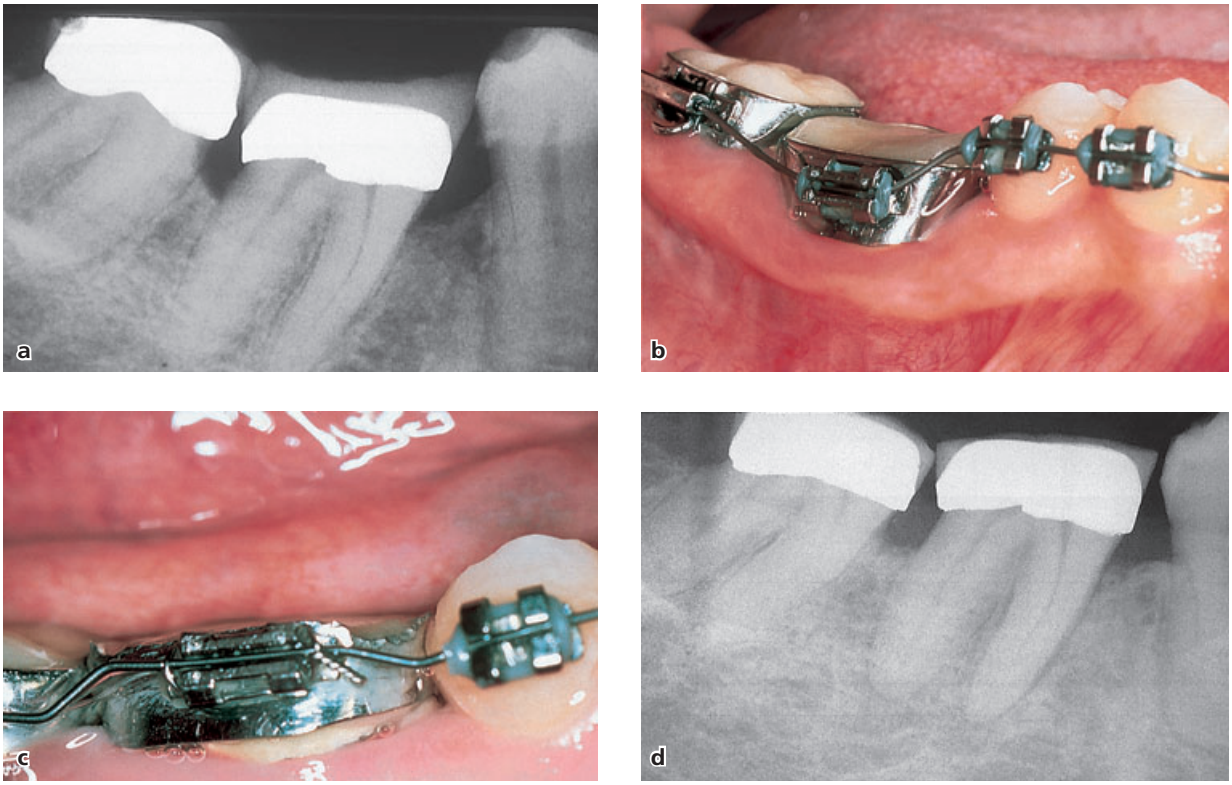


Fig. 44-69 Slow tooth eruption procedure used to level cemento-enamel junctions and angular bone crests. (a) Pretreatment radiograph. (b) A nitol wire was used to erupt the molar. (c) The crown was shortened over a period of 4 months by selective grinding. (d) Radiograph taken 8 months after the start of treatment. The angular bone defects were leveled.

crown structure is lost, root canal therapy is required. A post placed in the root canal is fitted with a power elastic, which is also joined with the arch wire. The direction of the tooth movement must be carefully checked to ensure that the problem tooth is not tilted or moved toward the adjacent tooth surfaces.

Forced tooth eruption with fiberotomy

If fiberotomy is performed during the forced tooth eruption procedure the crestal bone and the gingival margin are retained at their pre-treatment locations, and the tooth–gingiva interface at adjacent teeth is unaltered. Fiberotomy is performed by the use of a scalpel at 7–10-day intervals during the forced eruption to sever the supracrestal connective tissue fibers, thereby preventing the crestal bone from following the root in coronal direction. In the case presented in Fig. 44-70, fiberotomy was performed only at the mesial half of the root. Radiographs obtained after 9 weeks demonstrate that crestal bone migration has occurred at the distal but not at the mesial surface of the erupted tooth (Pontoriero *et al*. 1987).

- *Indication:* crown lengthening at sites where it is important to maintain the location of the gingival margin at adjacent teeth unchanged.
- *Contraindication:* fiberotomy should not be used at teeth associated with angular bone defects.
- *Technique:* similar to the technique described for the forced tooth eruption procedure. Fiberotomy is performed once every 7–10 days during the phase of forced tooth eruption.

Ectopic tooth eruption

Surgical intervention is often indicated for teeth erupting ectopically, i.e. with an eruption position facial to the alveolar ridge (Fig. 44-71). To create a satisfactory width of the gingiva for the permanent tooth, the tissue entrapped between the erupting tooth and the deciduous tooth is usually utilized as donor tissue (Agudio *et al*. 1985; Pini Prato *et al*. 2000b).

Three different techniques have been described for the interceptive mucogingival treatment of buccally erupting teeth, depending on the distance from the donor site (entrapped gingiva) to the recipient site (area located facially–apically to the erupting permanent tooth) (Agudio *et al*. 1985; Pini Prato *et al*. 2000b):

- *Double pedicle graft* (Fig. 44-72). This flap procedure is indicated when the permanent tooth erupts within the zone of keratinized tissue but close to the mucogingival junction. An intrasulcular incision is performed at the deciduous tooth and extended laterally to the gingival crevice of the adjacent teeth and apically to the erupting

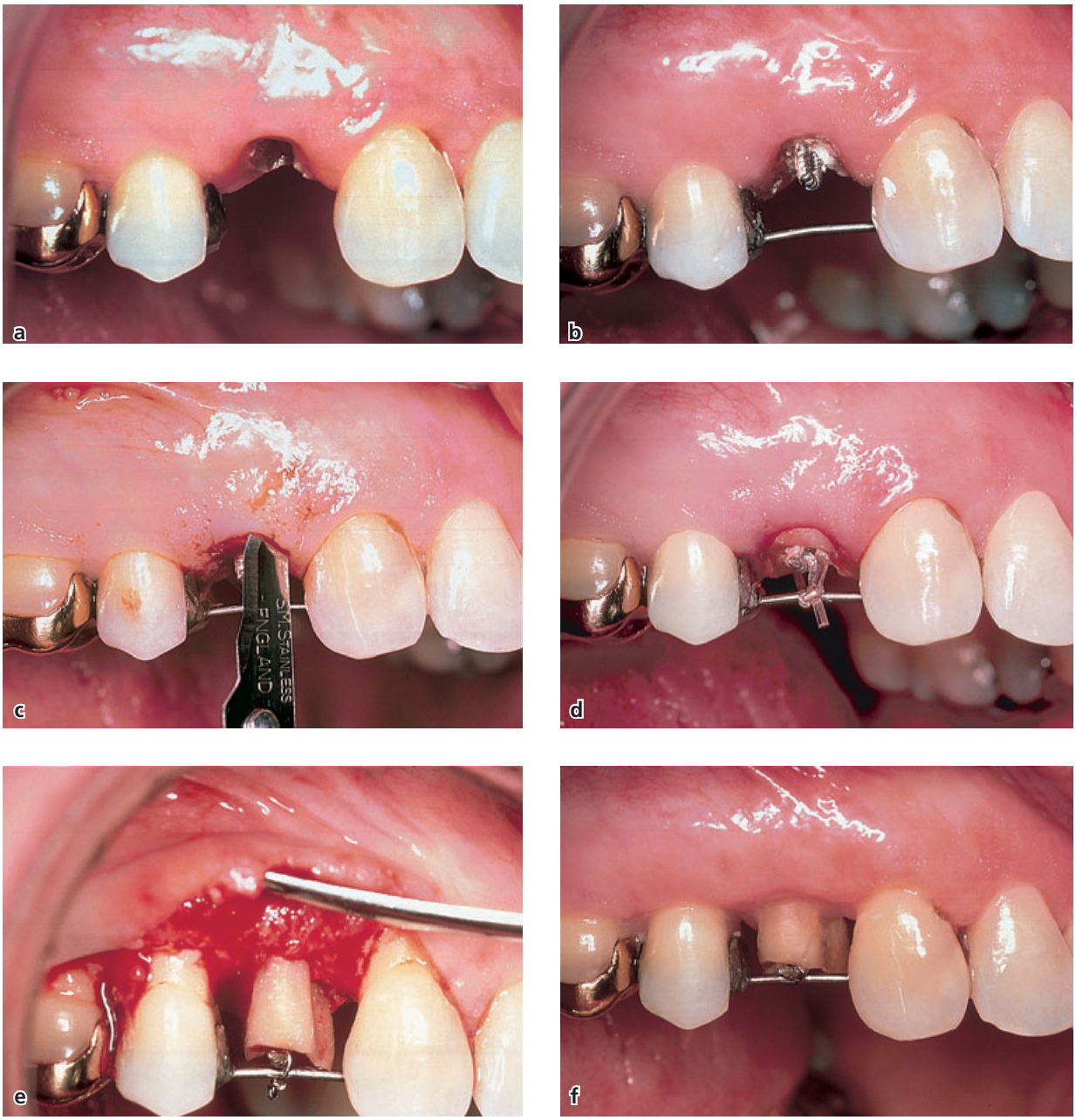


Fig. 44-70 Rapid tooth eruption procedure in conjunction with fiberotomy procedure. (a) Buccal view, the fracture on the first premolar extended subgingivally. (b) Soft tooth structure was excavated and a twisted wire with an occlusal hook was temporarily cemented in the root canal. A bar was placed into the amalgam restoration on the premolar and bonded to the lingual surface of the canine. (c,d) Sulcular fiber resection was performed at the mesial half of the tooth to the level of the bone crest. The distal half remained as a control surface. The fiber resection was repeated once a week during the 3-week eruption phase. (e) The tooth was stabilized for 6 weeks, and at that time a full-thickness flap was raised. The bone crest had a "positive" angulation at the distal surface and remained unchanged at the "test" mesial surface. Osseous resection was used to level the bony septum on the distal surface. (f) Ample crown lengthening was obtained and the gingival margins healed to their former shape and location. (g) Pretreatment radiograph enlarged to show the normal shape of the crests of the interdental septae. (h) Enlargement of the post-eruption radiograph (3 weeks of rapid eruption and 6 weeks of stabilization) to show the "positive" angular crest on the "control" distal side and the unchanged crest on the mesial "test" side. (Courtesy of Dr. R. Pontoriero, Milan, Italy.)

permanent tooth. By mobilization of the flap apical to the mucogingival line, the entrapped gingiva can be elevated and transposed for positioning apically to the erupting tooth. Sutures may be placed to secure the position of the gingival tissue facial to the erupting tooth.

- *Apically positioned flap* (Fig. 44-73). When the permanent tooth is erupting apical to the mucogingival junction, vertical releasing incisions have to be placed to allow for apical positioning of the keratinized tissue. Two lateral releasing incisions are made and extended apically beyond the mucogin-

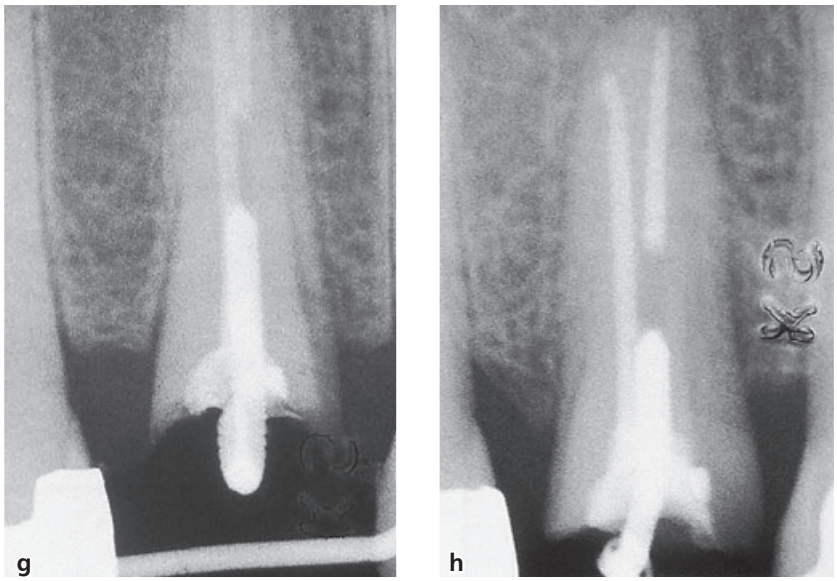


Fig. 44-70 *Continued*

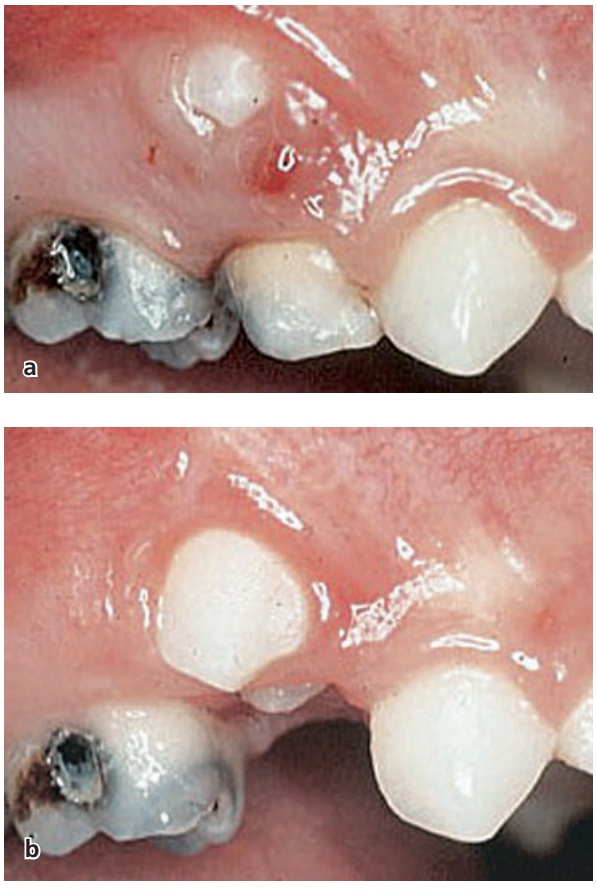


Fig. 44-71 Ectopic tooth eruption. The permanent tooth is erupting close to the mucogingival junction.

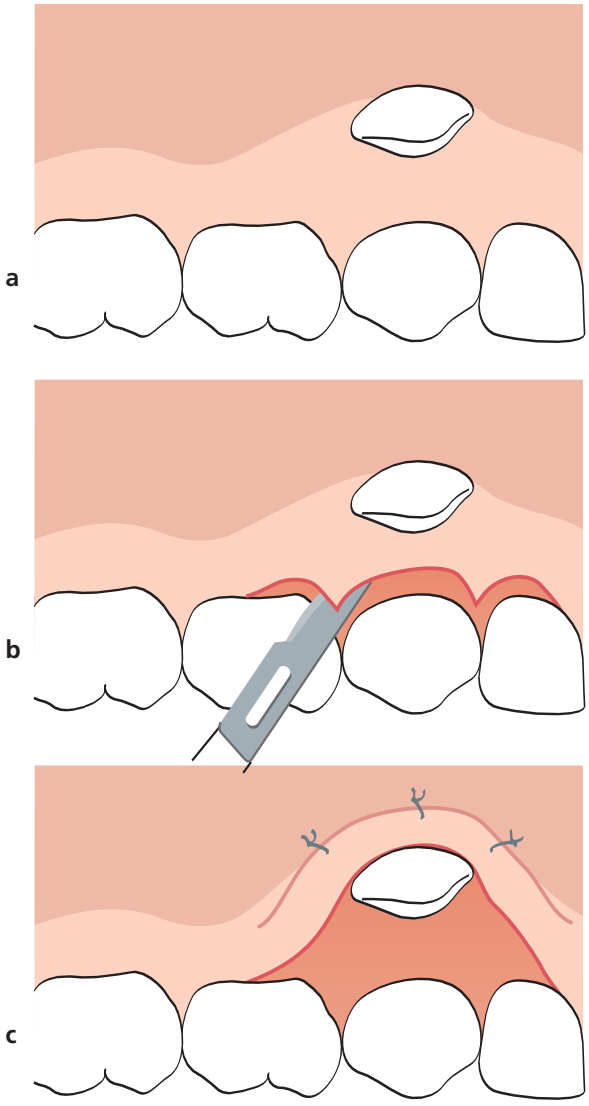


Fig. 44-72 Ectopically erupting tooth – double pedicle graft. Schematic drawings illustrating the surgical technique (see text for explanation).

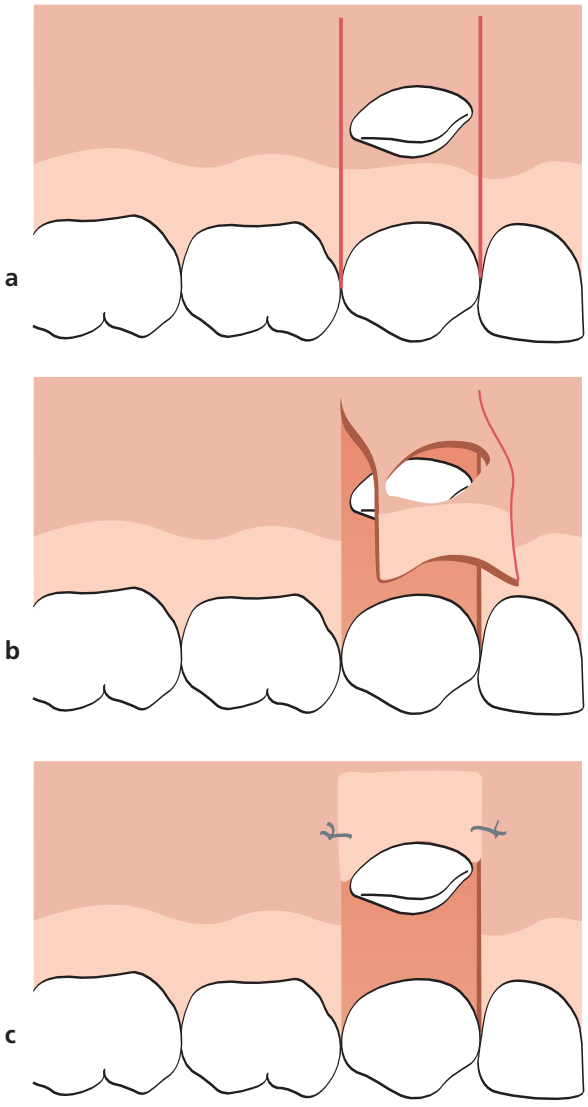


Fig. 44-73 Ectopically erupting tooth – apically positioned flap. Schematic drawings illustrating the surgical technique (see text for explanation).

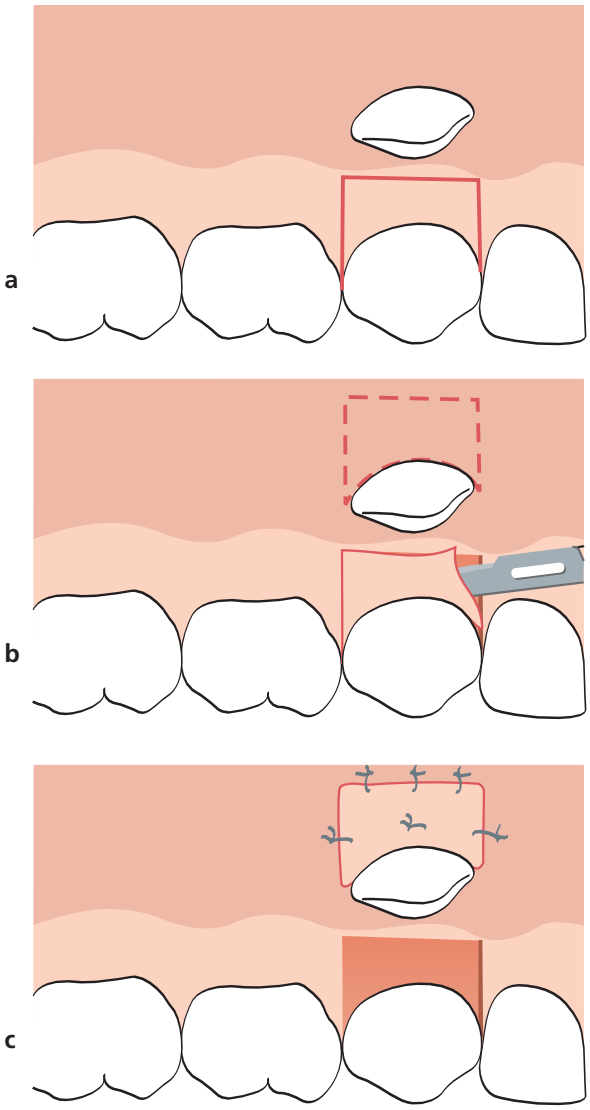


Fig. 44-74 Ectopically erupting tooth – free gingival graft. Schematic drawings illustrating the surgical technique (see text for explanation).

gival junction. An intrasulcular incision is performed at the deciduous tooth and a partial-thickness flap is elevated beyond the ectopically erupting tooth. The mobilized gingival flap is moved apical to the erupting tooth and secured in position by sutures.

- *Free gingival graft* (Fig. 44-74). If the tooth is erupting within the alveolar mucosa distant to the mucogingival junction, a free gingival graft procedure may be selected. The entrapped gingiva is removed by a split incision and used as an epithelialized connective tissue graft. The free gingival graft is placed at a prepared recipient site facial/apical of the erupting tooth. Careful suturing is performed to secure close adaptation of the graft to the underlying connective tissue bed.

All the described procedures have been proven to be effective in establishing a facial zone of gingiva following the alignment of teeth erupting in an ectopic position (Pino Prato *et al*. 2000b,c).

The deformed edentulous ridge

A partially edentulous ridge may retain the general shape of the alveolar process. Such a ridge is traditionally referred to as a normal ridge. Even though this normal ridge has retained the bucco-lingual and apico-coronal dimensions of the alveolar process, it is not normal in many other respects; the eminences that existed in the bone over the roots are no longer present, and the interdental papillae are missing.

The smooth contours of the normal ridge create problems for the restorative dentist. In a fixed bridge the pontics (1) frequently give the impression that they rest on the top of the ridge rather than emerge from within the alveolar process, (2) lack a root eminence, and (3) lack marginal gingivae and interdental papillae. Dark triangles, which almost always inter-

fere with dentofacial esthetics, are present in the embrasure area between the pontics and between the abutments and the pontics. In other words, in the presence of a normal ridge it may be difficult or impossible to produce a fixed prosthesis which truly restores the esthetics and function of the natural dentition.

Prevention of soft tissue collapse following tooth extraction

Following extraction of a tooth, the topography of the surrounding soft and hard tissues will be altered. The soft tissue margin will collapse and the height of the adjacent papillae will be reduced. This soft tissue collapse may be prevented by immediate post-extraction placement of an ovate pontic to support the soft tissues. Figure 44-75 illustrates such a situation where a central incisor had to be extracted due to root fracture. With the immediate placement of the pontic the facial soft tissue margin and the papillae were maintained almost unchanged following the healing of the extraction site. Also, in situations where several adjacent teeth have to be extracted, insertion of ovate pontics may facilitate the preservation of the outline of the soft tissue ridge (Fig. 44-76).

Prevention of ridge collapse due to alveolar bone resorption following tooth extractions must also be considered. Borghetti and Laborde (1996) recommended means for prevention of bone ridge collapse after tooth extraction in any case of:

1. Fracture of the vestibular osseous plate during tooth extraction or due to trauma
2. Resorption of the vestibular osseous plate
3. Presence of a thin vestibular bone plate.

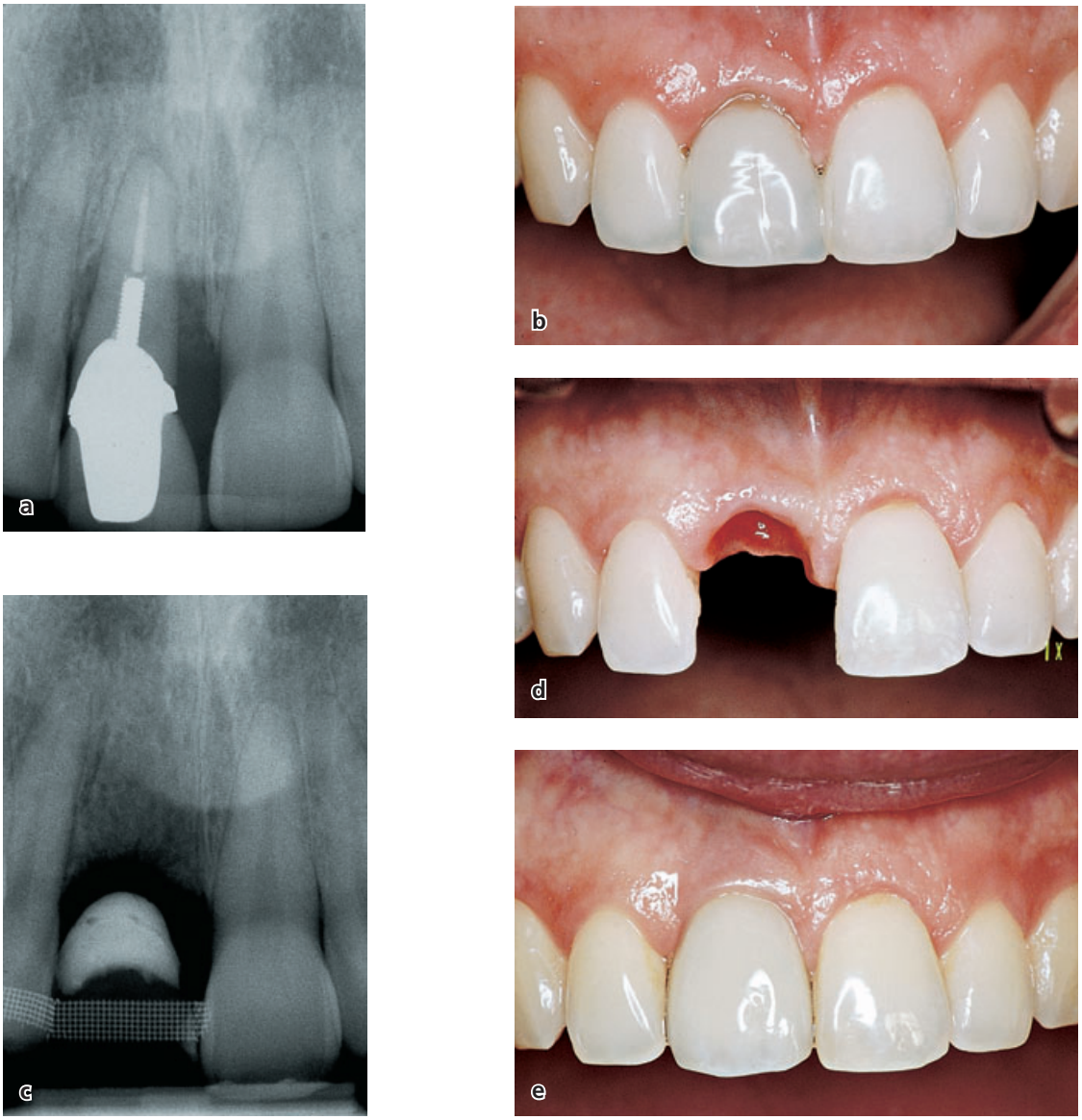


Fig. 44-75 (a) A central incisor that cannot be maintained because of root fracture which also caused pronounced periodontal destruction. (b) Immediately following tooth extraction, an ovate pontic was inserted to support the facial and proximal soft tissues. (c,d) Radiographic and clinical view of the area 6 weeks after tooth extraction. (e) Follow-up 1 year after the placement of permanent prosthetic reconstruction (single implant).

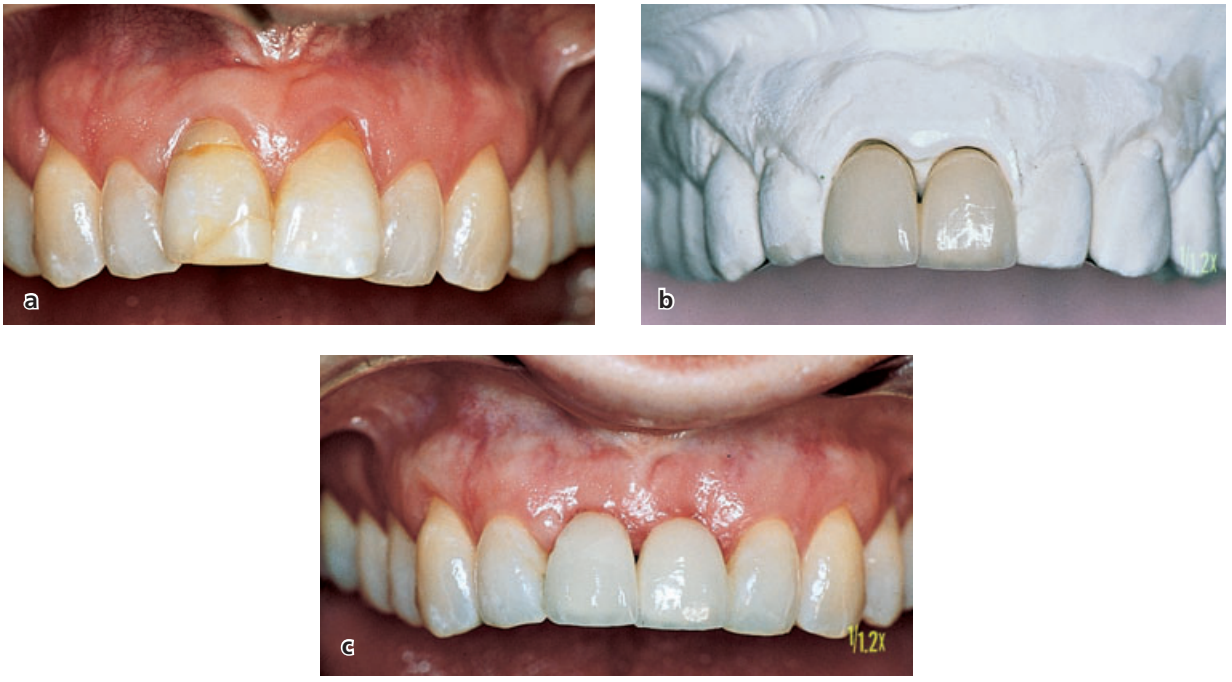


Fig. 44-76 (a) A 26-year-old female patient who had a trauma against the maxillary central incisors. Due to root fracture and endodontic complications both central incisors had to be extracted. (b) A Rochette bridge with ovate pontics was fabricated as a temporary replacement for the incisors. (c) Clinical view if the front tooth region 8 weeks after tooth extraction and placement of the resin bonded temporary bridge.

Among procedures proposed for prevention of ridge collapse in conjunction with tooth extractions are (1) flap elevation for complete soft tissue closure of the extraction sites (Borghetti & Glise 2000), (2) placement of connective tissue grafts over the extraction sites (Nevins & Mellonig 1998), (3) placement of bone grafts (Becker *et al*. 1994), and (4) utilization of barrier membranes (Lekovic *et al*. 1997). Procedures for preservation of the bone dimensions following tooth extraction are discussed in Chapter 49.

Correction of ridge defects by the use of soft tissue grafts

A deformed ridge may result from tooth extractions, advanced periodontal disease, abscess formations, etc. The deformity that exists in the ridge is directly related to the volume of root structure and associated bone that is missing or has been destroyed. According to Siebert (1983) ridge defects can be divided into three classes:

- Class I: loss of bucco-lingual width but normal apico-coronal height
- Class II: loss of apico-coronal height but normal bucco-lingual width
- Class III: a combination of loss of both height and width of the ridge.

Ridge augmentation procedures should be preceded by careful surgical–prosthetic treatment planning with joint consultations involving the surgeon and the restorative dentist in order to attain an optimal esthetic result. The following factors should be determined prior to the initiation of therapy:

- Volume of tissue required to eliminate the ridge deformity
- Type of graft procedure to be used
- Timing of various treatment procedures
- Design of the provisional restoration
- Potential problems with tissue discolorations and matching tissue color.

Ideally, a provisional restoration should be made prior to surgery. The shape of the teeth in the provisional restoration, the axial inclination and emergence profile of the teeth, and embrasure form should be an exact prototype of the final prosthesis that is to be constructed. It is the task of clinician performing the surgery to augment the tissues to meet the provisional prosthesis in the most exact manner possible. If a gingival flange of pink-colored acrylic is used around single or multiple pontics on a temporary removable partial denture, the flange must be cut away in order to avoid pressure on the graft and give the tissues room to swell during the immediate post-surgical phase of healing. The soft tissue at the surgically treated recipient site for a graft will undergo considerable swelling during the early phase of healing and the tissues will conform to the tissue-facing surfaces of the bridge or partial denture. The prosthesis is thus used to help in shaping the outline of the augmented ridge to the desired form. The location and shape of interproximal embrasure areas in the provisional bridge will determine

where the "papillae" created in the ridge will be located.

Surgical procedures for ridge augmentation

Numerous surgical graft and implant procedures attempting to reconstruct a partially edentulous ridge or ridge defect have been described in the literature over the years. The procedures may be grouped according to the means used for ridge augmentation as (1) soft tissue augmentation procedures and (2) hard tissue augmentation procedures. In this chapter only soft tissue augmentation procedures will be addressed, while hard tissue augmentation procedures are covered in Chapter 49. To illustrate various approaches for utilization of soft tissues for ridge augmentation, the following procedures will be discussed:

- Pedicle graft procedure:
  - Roll flap procedure
- Free graft procedures:
  - Pouch graft procedure
  - Interpositional graft procedure
  - Onlay graft procedure.

Studer *et al*. (1997) proposed the use of the pedicle graft procedure for correction of a single-tooth ridge defect with minor horizontal and vertical loss, whereas submerged free connective tissue graft procedures should be selected for larger defects. The onlay full-thickness graft procedure is indicated primarily for ridge augmentation in the presence of additional mucogingival problems such as insufficient gingival width, high frenum, gingival scarring, or tattoo. These recommendations were based on short-term evaluation of the obtained volumetric increase of the edentulous ridge following various augmentation procedures, which demonstrated superior results with the use of submerged connective tissue grafts compared to the use of full-thickness grafts (Studer *et al*. 2000).

The "roll flap procedure"

Surgical concept

The "roll flap procedure" (Abrams 1980) involves the preparation of a de-epithelialized connective tissue pedicle graft, which is subsequently placed in a subepithelial pouch (Fig. 44-77). This procedure is used in the treatment of small to moderate class I ridge defects, primarily in cases with a single-tooth space. The technique enables the surgeon to augment tissue apically and labially to the cervical area of a pontic and to give the recipient site the appearance of a normal tooth–gingiva interface. Hence, a buccolingual ridge concavity can be converted into a ridge convexity resembling the eminence produced by the roots of the adjacent teeth (Fig. 44-78).

Technique

A rectangular pedicle of connective tissue is prepared on the palatal side of the defect (Fig. 44-77). The length of the pedicle must match the amount of

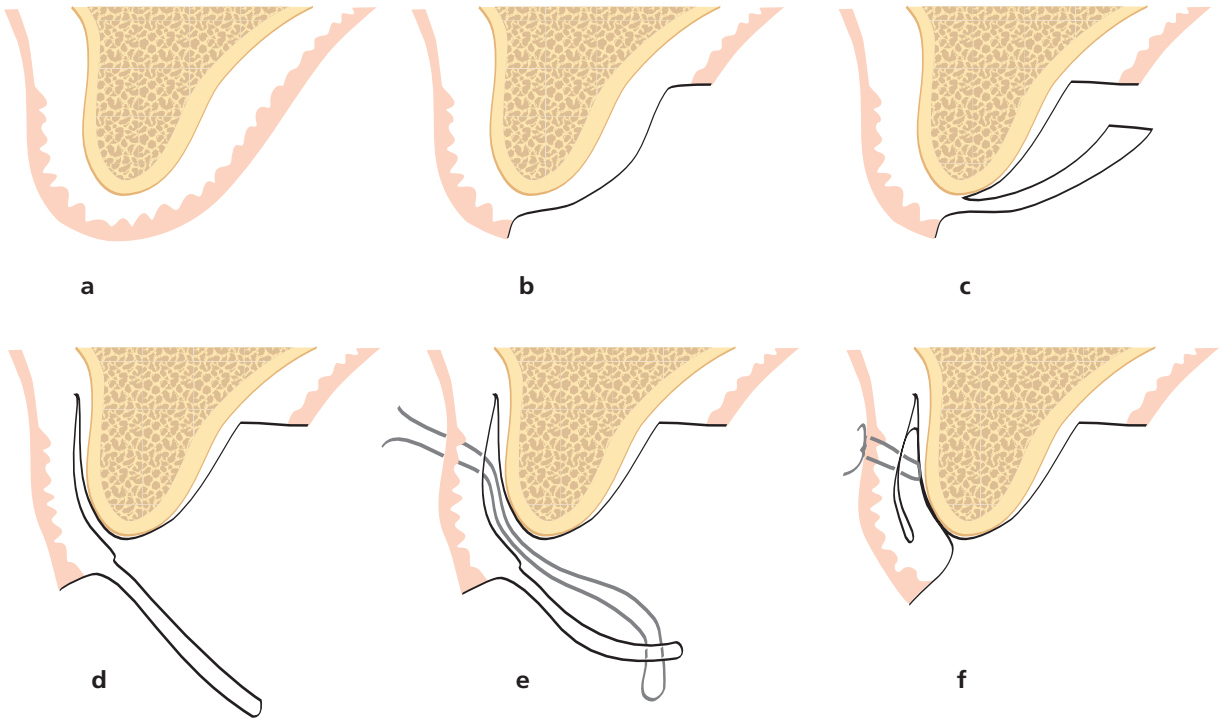


Fig. 44-77 Sequence of steps in the "roll flap procedure". (a) Cross section of the residual edentulous ridge prior to treatment. (b) The removal of the epithelium. (c) The elevation of the pedicle. (d) The pouch is created. (e) Sutures are placed at the mucogingival junction to catch the tip of the pedicle flap and pull it into place in the pouch. (f) The flap is secured. A convexity in the ridge was created.

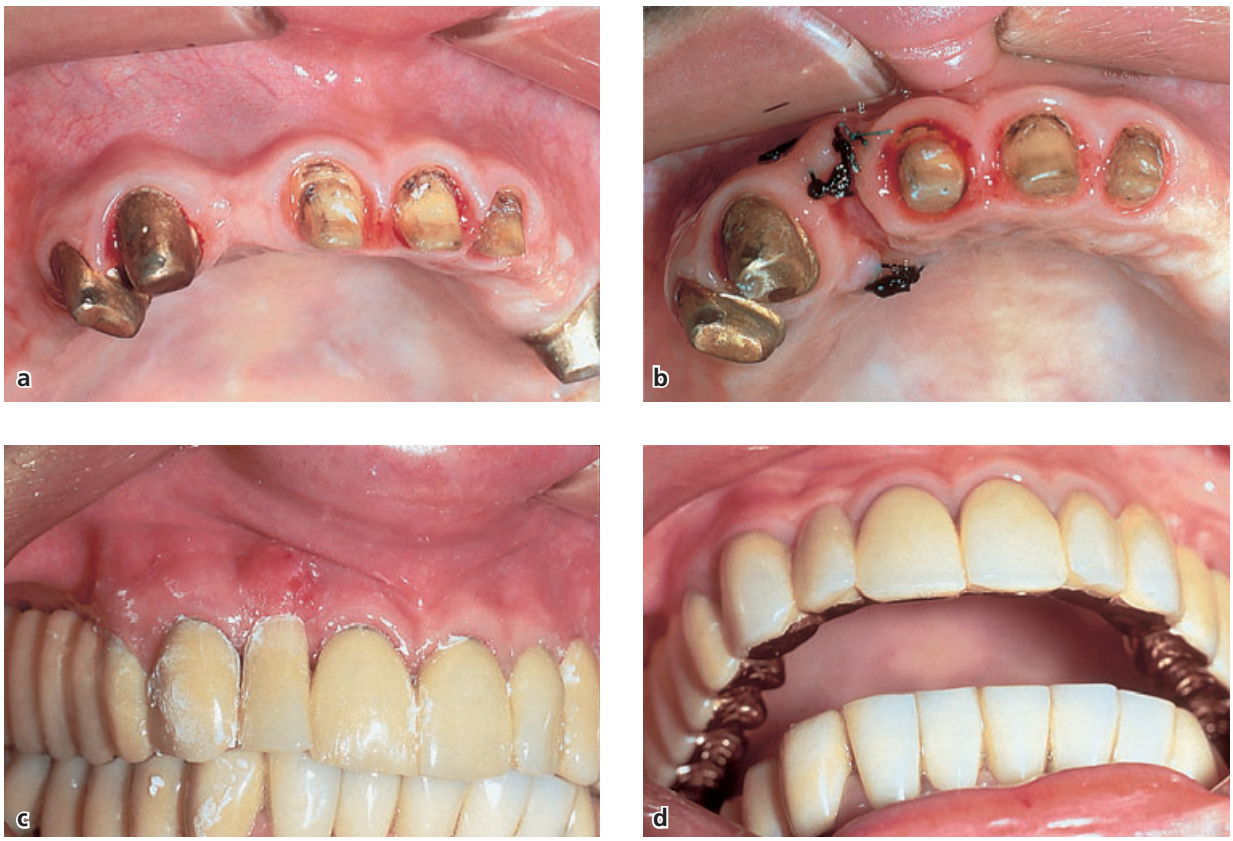


Fig. 44-78 "Roll flap procedure". (a) Pretreatment view of a class I ridge defect in the area of the right lateral incisor. Note the marked concavity in the ridge. (b) This view shows the surgical site 1 week after surgery and prior to the removal of the sutures. (c) The tissue surface of the pontic was relined with autopolymerizing resin. (d) Final prosthesis in place. Note the illusion of a root eminence and a free gingival margin apical to the lateral incisor pontic tooth. (Courtesy of Dr. L. Abrams, Philadelphia, PA, USA.)

apico-coronal augmentation that is planned. This, in turn, is related to the amount of root eminence that exists on either side of the defect. If a two- or three-tooth pontic space is treated with the roll technique, two or three separate pedicles are raised. Each of these pedicles will form a new "root–cervical margin".

The epithelium on the palatal surface of the donor site is first removed. A maximum amount of supraperiosteal connective tissue is raised from the palate using sharp dissection. The void that is produced at the donor site will gradually fill in with granulation tissue. Caution must be exercised in dissection of the pedicle flap so that tissue perforation is avoided when the plane of dissection approaches the facial (labial) surface. A pouch is made in the supraperiosteal connective tissue at the facial (labial) surface of the ridge. In order to preserve as much connective tissue and blood supply as possible at the recipient site, the dissection must be made as close as possible to the periosteum of the facial bone.

The pedicle is tucked into the pouch as a try-in procedure. Adjustment of pedicle size should now be made. Once the pedicle fits as desired, it is made ready for the stabilizing suture. The suturing scheme is illustrated in Fig. 44-77. The suture must be positioned close to the mucobuccal fold. This enables the surgeon to pull the pedicle to the apical portion of the pouch. The suture should not be tied tightly, since it only serves as a positioning and stabilizing device. The use of a resorbable suture material is recommended.

Adjustment of pontic contours

Measures used to adapt the tissue surface of the pontic to the contour of the surgically treated ridge are common to all soft tissue ridge augmentation procedures in patients with fixed bridgework. A light contact is maintained between the pedicle graft and the tissue surface of the pontics. The post-operative swelling will cause the tissue to conform to the shape of the pontic. This enables the clinician to shape the soft tissue into a form that is intended for the augmented site. Autopolymerizing resin is added to the tissue surface of the pontics and is allowed to cure until the resin reaches a dough-like state. The bridge is then seated and pressed into the grafted site. When the resin has set to a firm consistency, the bridge is removed and placed in hot water to complete the process of polymerization (Fig. 44-78). The tissue surface of the pontics and the embrasure areas are then carved to the shape that is intended for the final bridge. The surface of the pontic is polished and the

bridge put in place using appropriate temporary cement.

Post-operative care
A periodontal dressing is placed over the donor site. No dressing should be placed over the facial (labial) surface of the grafted area where swelling will occur. The dressing at the donor site should be changed at weekly intervals and maintained until wound healing has progressed to a point where the tissue is no longer tender to touch.

Pouch graft procedures

Surgical concept
A subepithelial pouch is prepared in the area of the ridge deformity, into which a free graft of connective tissue is placed and molded to create the desired contour of the ridge. The entrance incision and the plane of dissection may be made in different ways (Kaldahl *et al*. 1982; Seibert 1983; Allen *et al*. 1985; Miller 1986; Cohen 1994):

- Coronal–apically: the horizontal incision is made on the palatal or lingual side of the defect and the plane of dissection carried in an apical direction (Fig. 44-79).
- Apical–coronally: the horizontal incision is made high in the vestibule near the mucobuccal fold and the plane of dissection is carried coronally to the crest of the ridge.
- Laterally: one or two vertical entrance incisions are started from either side of the defect (Fig. 44-80). The plane of dissection is made laterally across the span of the deformity.

Indication
The technique is used to correct class I defects. Patients with large-volume defects may have thin palatal tissues, which are insufficient to provide the volume of the donor tissue necessary to fill the deformity. In such cases, various procedures for hard tissue augmentation may be selected (see Chapter 49).

Technique
The pouch is prepared as described above. The mesio-distal entrance incision for the edge of the pouch should be made with a long bevel and must be started well to the palatal (lingual) side of the defect (Fig 44-79). After the pouch has been filled with graft, the facial tissue will be stretched. The long bevel of the entrance incision permits the palatal edge of the flap to slide toward the facial surface

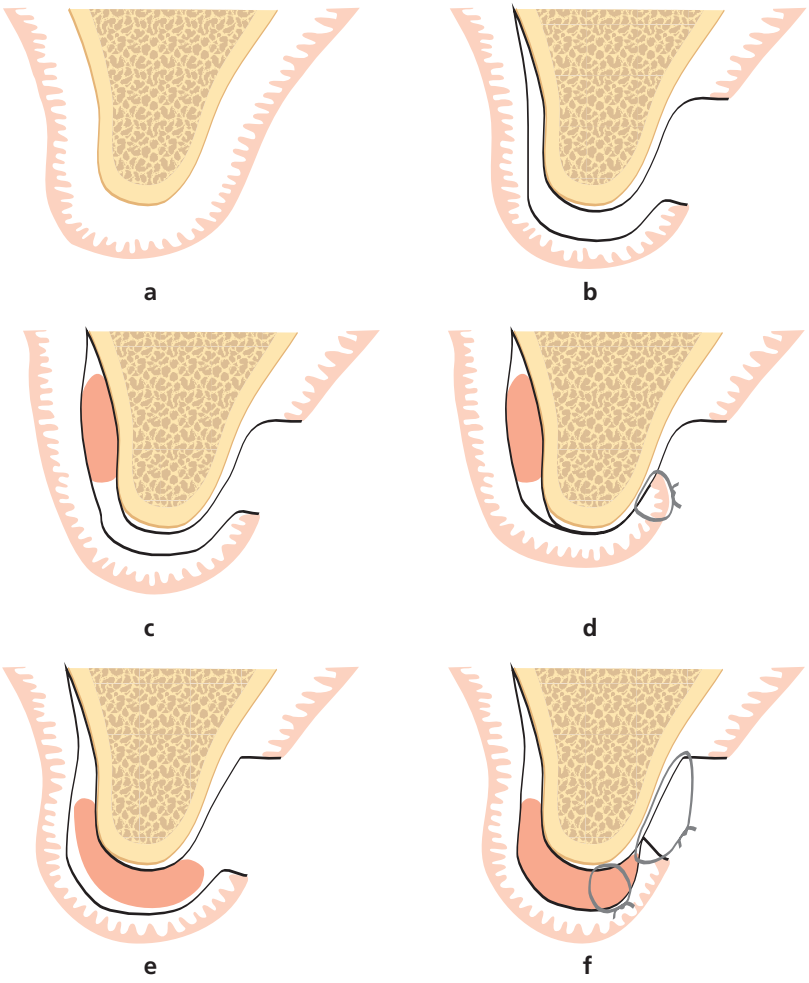


Fig. 44-79 Sequence of steps in the "pouch graft procedure" utilizing a free graft of connective tissue (CT) to expand the ridge. (a) Cross section of the residual edentulous ridge prior to treatment. (b) The horizontal incision to create the pouch is made well to the palatal side of the defect. The incision is started partial-thickness to leave CT to suture to when the flap is closed. The dissection is made supraperiosteal on the labial side of the ridge to (1) ensure an adequate blood supply within the pedicle and (2) permit the flap to expand labially or labially and coronally free of tension. (c,d) The CT graft can be placed as shown for maximal bucco-lingual augmentation. (e,f) If vertical augmentation is desired, the CT implant can be placed closer to the crest of the ridge. As is shown in (d) and (f), the more the flap is stretched or extended to gain augmentation, the more difficult it is to gain primary flap closure.

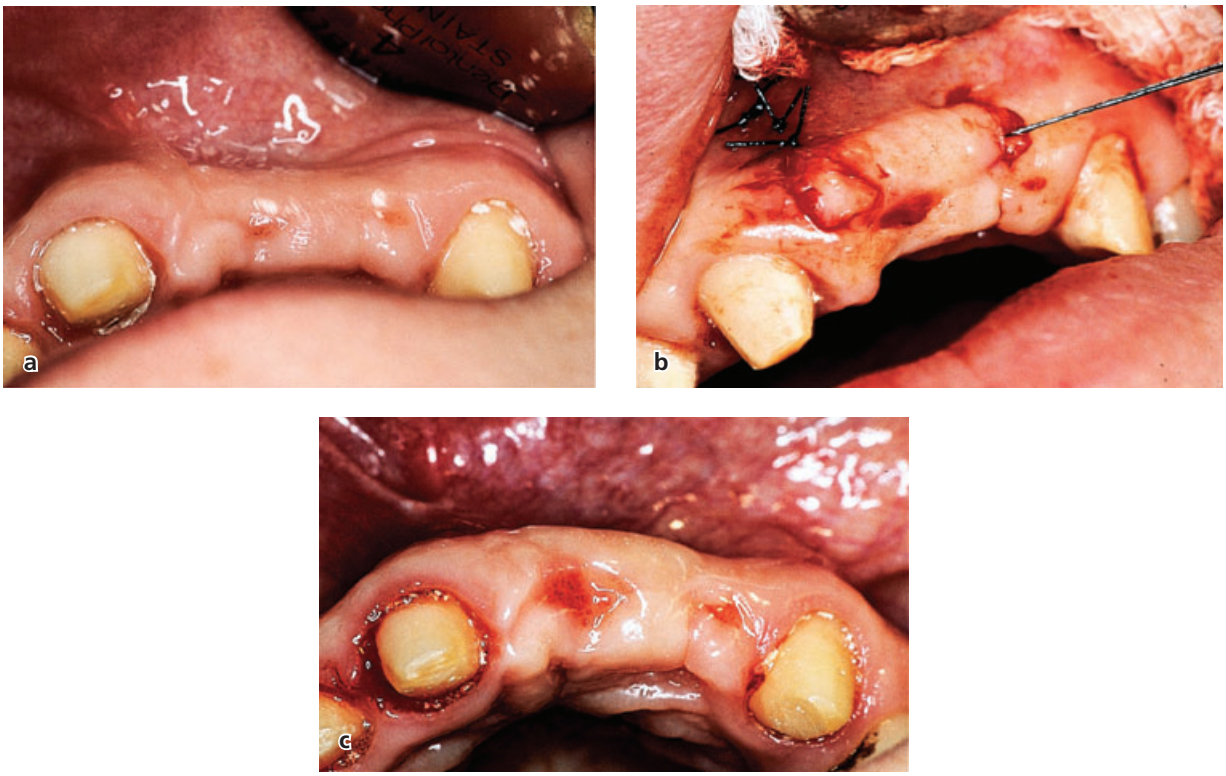


Fig. 44-80 Pouch graft procedure. (a) Pretreatment view of a class I ridge deformity. (b) Placement of the free connective tissue graft in a tunnel prepared by split incision between the two vertical incisions. The graft is brought into position by the use of a suture placed in one end of the free graft. (c) Four months post treatment showing restored facial dimension of the edentulous ridge.

without opening a gap at the incision line. Sometimes vertical releasing incisions have to be made lateral to the border of the defect.

A suitable donor site is selected in the palate, the tuberosity area, or in an edentulous area and a free graft of connective tissue is excised by the use of a "trap-door" approach. The graft is immediately transferred to the recipient site and properly positioned. The palatal entrance incision and the releasing incisions are closed with sutures.

Interpositional graft procedure

Surgical concept

Interpositional grafts are not completely submerged and covered in the manner that a subepithelial connective tissue graft is placed (Fig. 44-81) (Seibert 1991, 1993a,b). Therefore, there is no need to remove the epithelium from the surface of the donor tissue. If augmentation is required not only in the buccolingual but also in the apico-coronal direction, a portion of the graft must be positioned above the surface of the tissue surrounding the recipient site (Fig. 44-82). A certain amount of the grafted connective tissue will thus be exposed in the oral cavity.

Indications

Interpositional graft procedures are used to correct class I as well as small and moderate class II defects.

Technique

An envelope flap, or a split-thickness flap with releasing incisions, is prepared at the facial surface of the defect area. The provisional bridge is placed in position to serve as a reference when estimates are made regarding the amount of tissue that has to be grafted to fill the defect. A periodontal probe may be used to measure the length, width and depth of the void of the pouch. A suitable donor site is selected in the palate or the tuberosity area, and a free graft of epithelium–connective tissue is excised (Fig. 44-81).

The donor tissue is transferred to the recipient site and placed in position. If gain in ridge height is not intended, the epithelial surface for the graft is placed flush with the surrounding epithelium. The graft is sutured along its entire circumference to the tissues of the recipient site. The provisional bridge is placed in position and the pontics are trimmed and adjusted as discussed above. No dressing is used to cover the recipient site.

If gain also in ridge height is intended, a certain portion of the graft has to be kept above the surface of the surrounding tissue (Fig. 44-82d). Granulation tissue formed during healing will eventually make the border between the graft and the adjacent tissue smooth and properly epithelialized. The swelling, which occurs post-operatively, will assist in sculpting the contour of the ridge.

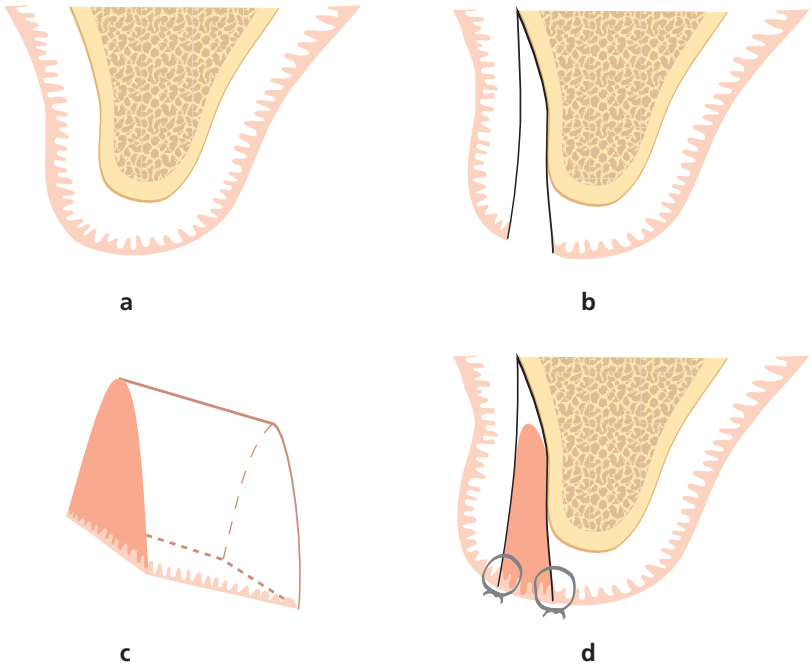


Fig. 44-81 Schematic illustrations of the interpositional graft procedure. (a) Cross section of class I ridge defect. (b) A labial flap (partial-thickness dissection preferred) is used to create the pouch. (c) A wedge-shaped graft is removed from the palate. (d) The epithelial surface of the graft is placed flush with the surface of the tissue surrounding the pouch and sutured around its circumference.

Onlay graft procedures

Surgical concept

The onlay procedure was designed to augment ridge defects in the apico-coronal plane, i.e. to gain ridge height (Meltzer 1979; Seibert 1983). Onlay grafts are epithelialized free grafts which, following placement, receive their nutrition from the de-epithelialized connective tissue of the recipient site. The amount of apico-coronal augmentation that can be obtained is related to the initial thickness of the graft, the events of the wound healing process, and the amount of graft tissue that survives (Figs. 44-82, 44-83, 44-84). If necessary, the grafting procedure can be repeated at 2-month intervals to gradually increase the ridge height.

Indications

Onlay graft procedures are used in the treatment of large class II and III defects. They are not suitable in areas where the blood supply at the recipient site has been compromised by scar tissue formation from previous wound healing.

Technique

An attempt must be made to retain as much of the lamina propria of the recipient site as possible. The anesthetic solution should be placed high in the vestibular fornix and in the palate, thus keeping vasoconstriction in the recipient site to a minimum. A scalpel blade is used to remove the epithelium. The scalpel is moved with short, saw-like strokes across the recipient site at a level approximately 1 mm below the outer surface of the epithelium. The least amount of connective tissue possible should be excised. The margins of the recipient site can be prepared with either a butt joint or a beveled margin. The prepared recipient site should be covered with a surgical gauze moistened with isotonic saline while the donor tissue is dissected (Fig. 44-82g–i).

Selection of donor site

Onlay graft procedures, as well as interpositional graft procedures, require large amounts of donor tissue. As a general rule, the palatal vault region of premolars and first molars, midway between the gingival margin and the midline raphae, is the only area in the maxilla that contains the necessary volume of tissue required to augment large ridge defects. During the presurgical planning phase, the tissue of the palate should be probed with a 30-gauge syringe needle to ensure that an acceptable volume of tissue can be obtained at the time of surgery.

The major palatine artery emerges from the posterior palatine foramen located adjacent to the distal surface of the maxillary second molar, midway between the gingival margin and the midline raphae (Fig. 44-85). The artery passes in an anterior direction close to the surface of the palatal bone. It is important therefore that the second and third molar regions are not used as donor sites for large volume grafts.

Planning in graft preparation

As a rule the graft should be made a few millimeters wider and longer than the dimensions required at the recipient site. The dimensions of the graft are outlined on the palate with the use of a scalpel and light bleeding is provoked to define the surface borders. In order to avoid interference with the palatine artery, the borders of the graft must be planned in such a way that its thinner portions are located high in the palatal vault or in the first molar area. The thicker

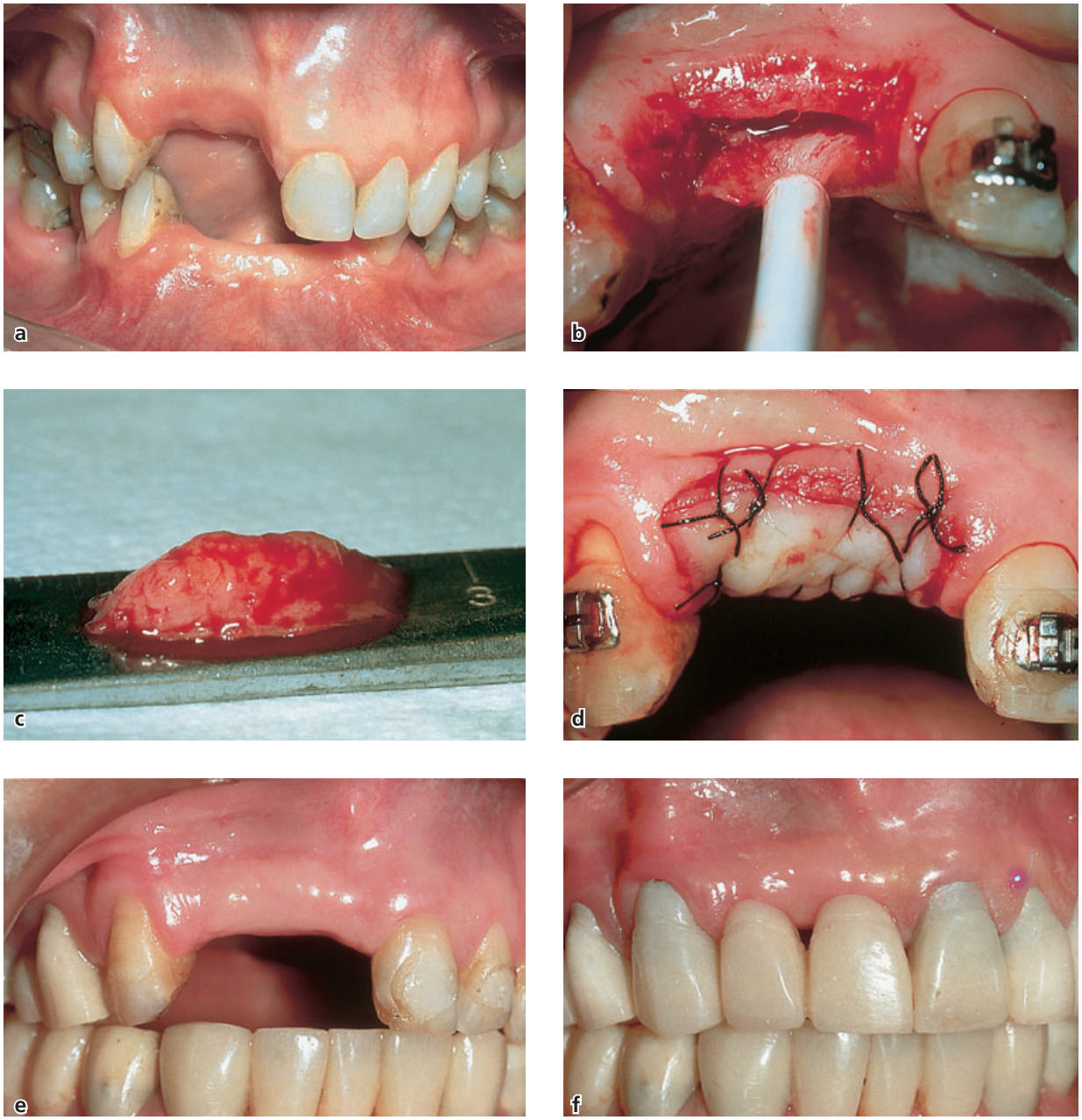


Fig. 44-82 (a) Pretreatment view, class III ridge defect. A two-stage procedure will be used to augment the ridge. (b) A pouch was prepared to receive an interpositional graft. Epithelium was removed from the borders of the recipient site to permit some of the graft to be placed above the level of the surrounding tissue in order to gain apico-coronal augmentation. (c) The wedge-shaped graft was 10 mm thick at its center. (d) The interpositional graft is both displacing the labial surface of the pouch in the labial direction as well as adding height to the ridge. (e) Two months post-treatment. Additional augmentation is needed apico-coronally. (f) A second-stage onlay graft will be used to create a papilla and fill the dark triangle between the pontics. (g) Two months after the first surgical procedure, the ridge was de-epithelialized and cuts were made into the connective tissue prior to placing the second-stage onlay graft into position. (h) The onlay graft was sutured into position. (i) The pontics were adjusted and brought into light contact with the graft. (j) Marked swelling occurred within the graft at 14 days post surgery. (k) Two months following the second surgical procedure, a gingivoplasty was performed to deepen the pontic receptacle sites for the ovate pontics. (l) Post-treatment view 1 year after the final surgical procedure. (Courtesy of Dr. J. Seibert & Dr. P. Malpeso, USA.)

portions should be harvested from the premolar areas.

Dissection of donor tissue

The base of the graft should be V- or U-shaped to match the shape of the defect in the ridge. The different planes of incision prepared in the palate must therefore converge towards an area under the center or toward one edge of the donor site. It is comparatively easy, with the use of a scalpel, to dissect in an antero-posterior or, from an area high in the palate, in a lateral direction towards the teeth. It is, however, difficult to dissect in an anterior direction from the distal edge of the donor site. There is a variety of

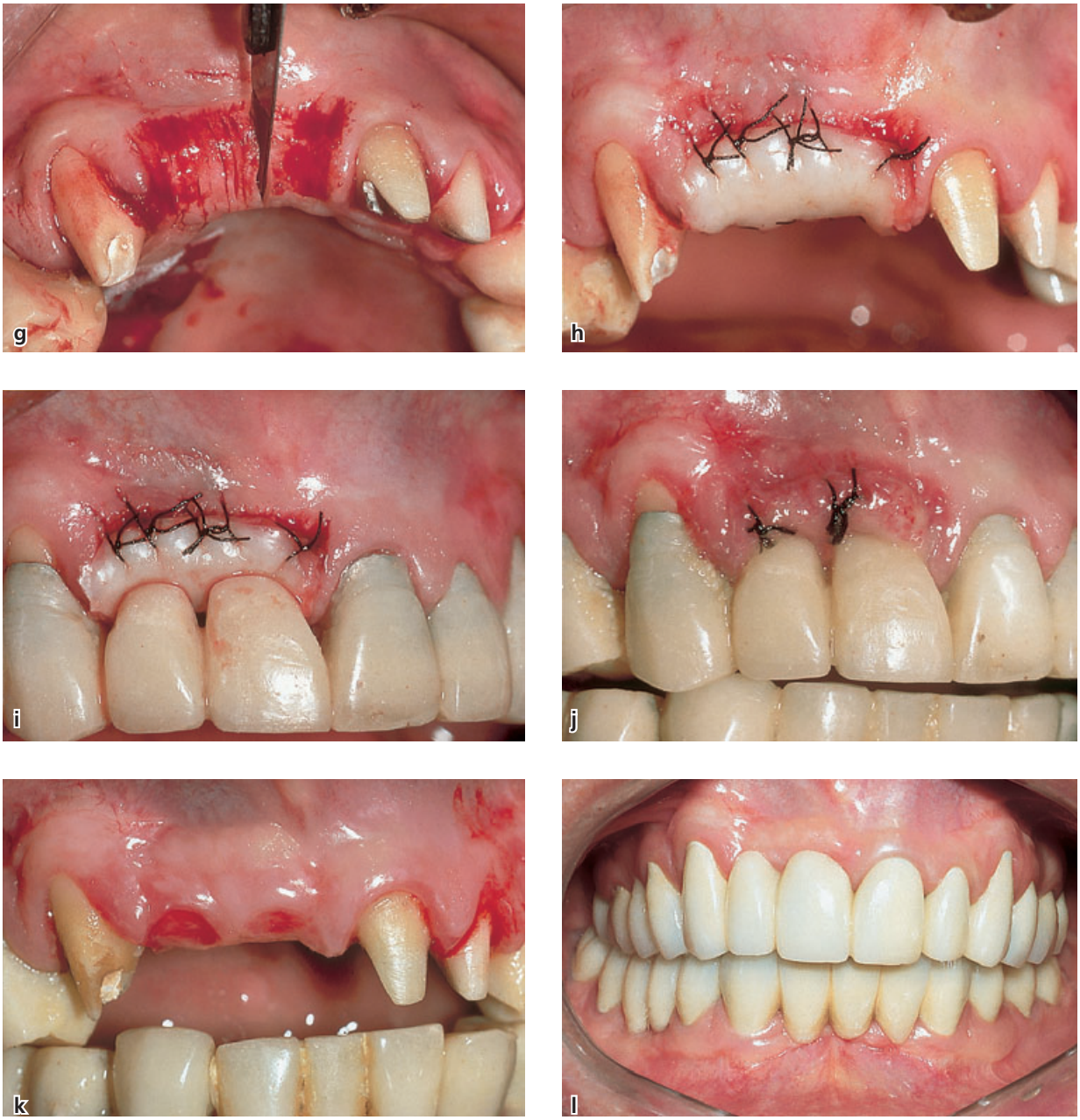


Fig. 44-82 *Continued*

blade holders available which permit the scalpel blade to be positioned at different angles to the holder and which enable the surgeon to cut with a back-action. When the donor tissue has been removed, it must be stored in pieces of surgical gauze moistened in isotonic saline at all times.

Treatment of the donor site

Since it is difficult to anchor and maintain a periodontal dressing at the donor site in the palatal vault, an acrylic stent should be fabricated prior to surgery. The stent should be made with wrought wire clasps on each side to add retention and to aid the patient in removing and inserting the device.

The donor site must be inspected carefully for signs of arterial bleeding. If any small vessel bleeding is observed, a circumferential suture must be placed around the vessel distal to the bleeding point. Immediately thereafter, the void at the donor site should be packed with a suitable hemostatic agent and the edges of the wound be brought closer together with sutures. The stent is then put into position.

Try-in and stabilization of graft

The graft is transferred with tissue forceps to the recipient site for a try-in. The graft is trimmed to the proper shape and adjusted to fit the connective tissue surface of the prepared ridge. A series of parallel cuts may be made deep into the exposed lamina propria of the recipient site to sever large blood vessels (Fig. 44-82g) immediately before suturing. A series of interrupted sutures is placed along the borders of the

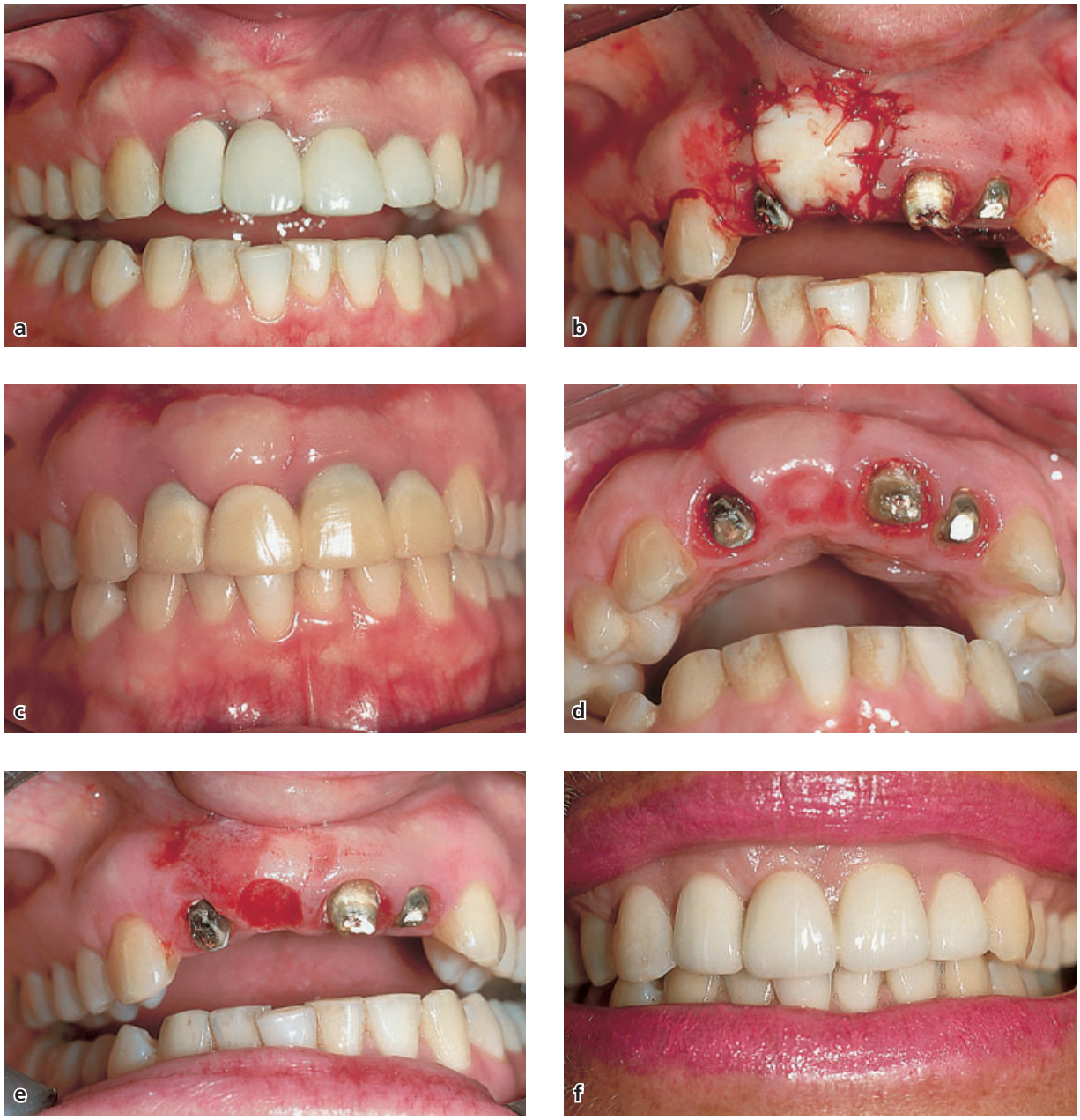
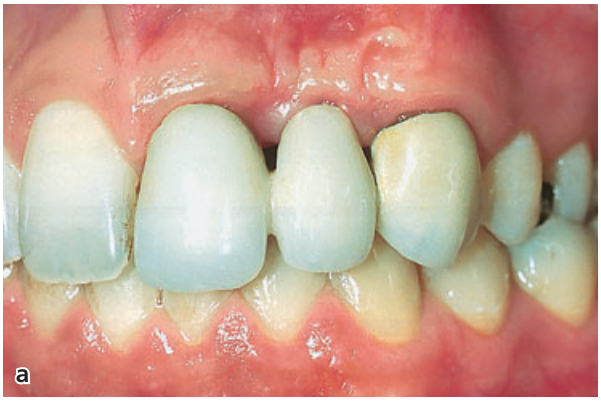


Fig. 44-83 Onlay graft procedure. (a) Pretreatment view. The gingival tissues were distorted from previous attempts at esthetic reconstruction. The patient wished to have a papilla between the right maxillary lateral and central incisor and a natural looking bridge. (b) The pontic area, including the papilla on the mesial of the right lateral incisor, was de-epithelialized and a thick (5 mm) onlay graft was sutured into position. (c) The pontic was shortened at the time of surgery to accommodate the thick graft. At 3 months post surgery the graft had undergone maximum shrinkage and gingivoplasty could now be done. (d) Incisal view at 3 months post surgery. Note the "papilla" that has been created. The indentation in the ridge was naturally created by the tissue swelling against the pontic tooth. (e) Rotary diamond point gingivoplasty was done to reshape the bulky graft to normal contours, deepen the receptacle site for the ovate pontic and level the gingival margins. (f) This view shows the esthetic harmony that was obtained in the soft tissues and tooth form at 2 years post treatment. (Courtesy of Dr. J. Seibert & Dr. C. Williams, USA.)

Fig. 44-84 Onlay graft procedures utilized to augment ridge and create papillae. (a) Pretreatment view. The left lateral incisor was extracted after a traumatic injury. The patient detested the dark triangle on the mesial of the pontic, the poor tooth form in the bridge and the irregular contours in her gingival tissue. (b,c) An onlay graft was used to gain apico-coronal and bucco-lingual ridge augmentation as well as to develop papillae. Note how the graft was extended to the palatal side of the ridge to gain greater blood supply from a larger connective tissue base. (d,e) At 2 months post surgery, a second-stage veneer graft was used to eliminate the surface irregularities on the surface of the gingiva and gain greater bucco-lingual augmentation. (f) At 4 months post second-stage surgery, gingivoplasty was done to prepare the area for an ovate form pontic. (g–h) 1 year post treatment, esthetics have been restored for this patient. (Courtesy of Dr. J. Seibert & Dr. D. Garber, USA.)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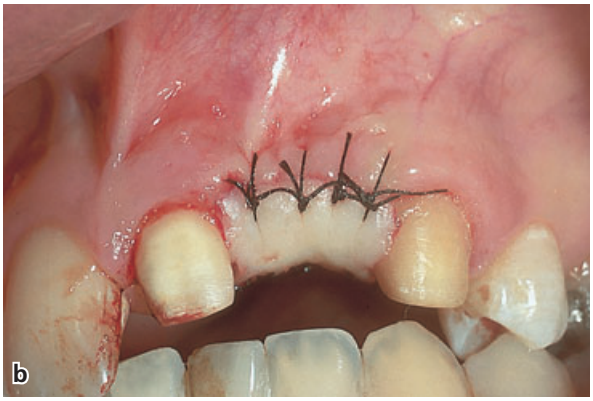
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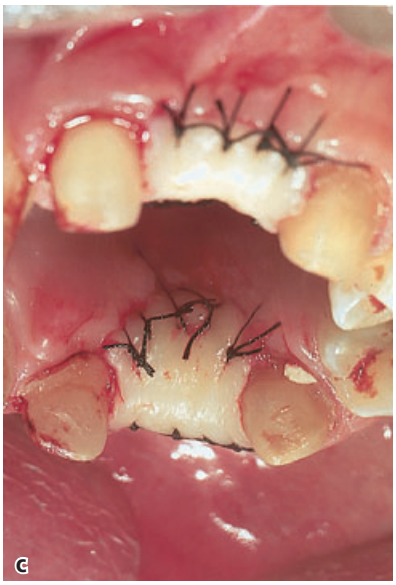
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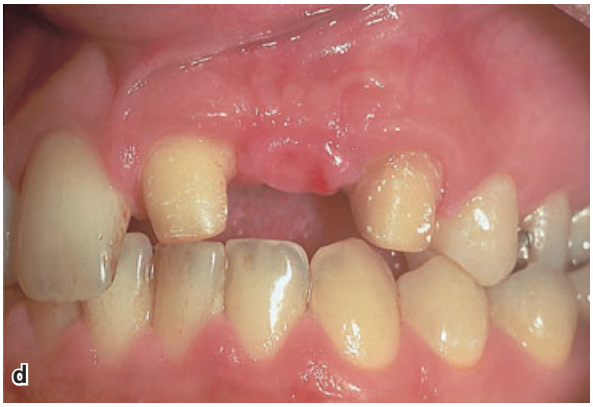
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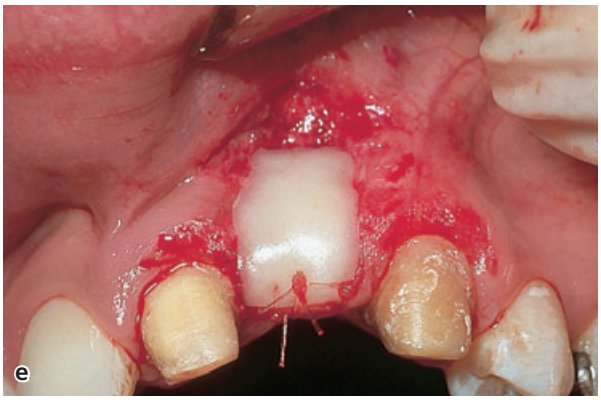
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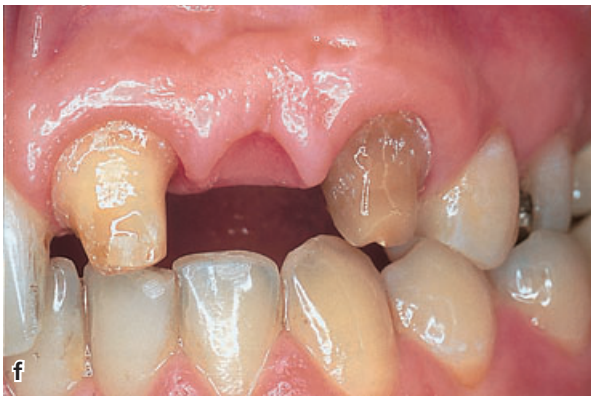
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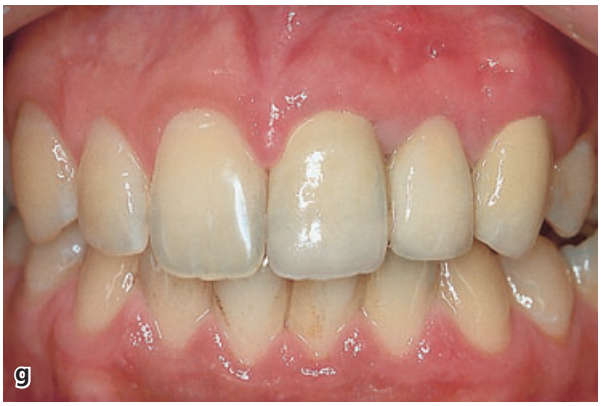
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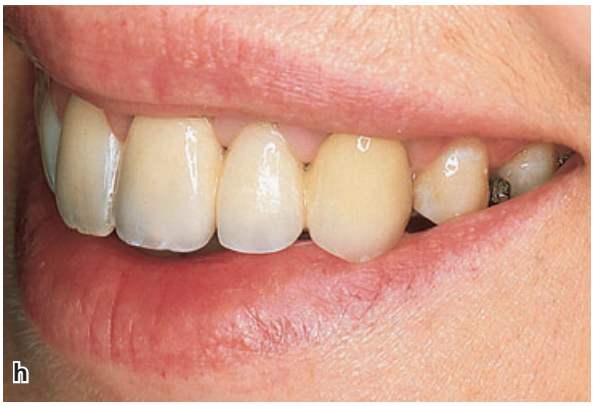
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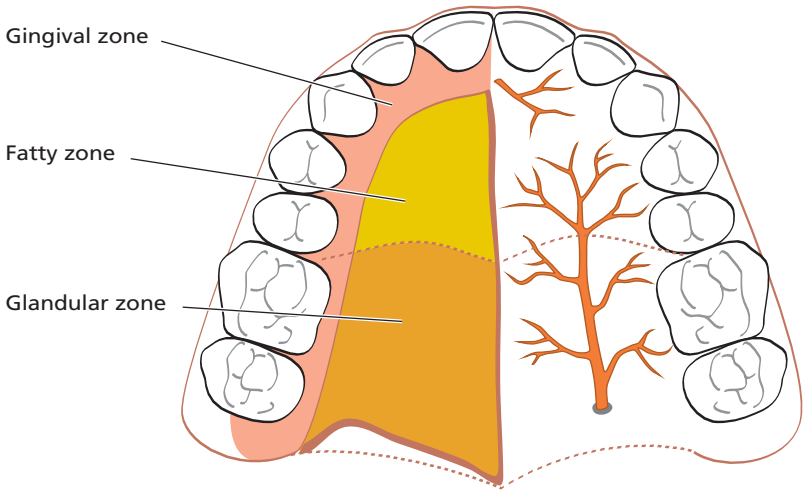


Fig. 44-85 Basic anatomic–histologic zones of the palate. Note the normal location of the greater palatine foramen.

graft. The dental assistant should stabilize the onlay graft against the surface of the recipient site, while the surgeon completes the placement of sutures.

Wound healing in the recipient site

Considerable post-operative swelling often occurs during the first week after pouch and onlay augmentation procedures. The epithelium of the graft will slough to form a white film on the surface of the graft. Patients should rinse two to four times per day with an antimicrobial mouthwash during the first week after surgery and refrain from mechanical cleaning measures in the area until a new epithelial covering has formed over the graft, which will not occur until a functional capillary circulation has been re-established in the graft (4–7 days after the surgery). The grafted tissue will assume a normal color as the epithelium thickens via stratification. Tissue form is usually stable after 3 months, but further shrinkage may occur over a period of several months. Final restorative measures should therefore not be initiated until after 6 months.

Wound healing in the donor site

Granulation tissue will gradually fill the donor site. Initial healing is usually complete within 3–4 weeks after the removal of a 4–5 mm thick graft. Patients should wear the surgical stent for about 2 weeks to protect the healing wound. The palate returns to its presurgical contour after about 3 months.

Combined onlay–interpositional graft procedures

Class III ridge defects pose a major challenge to the clinician since the ridge has to be augmented in both vertical and horizontal dimensions. The combined onlay–interpositional graft procedure (Fig. 44-86 and 44-87) may successfully be used in such a situation (Seibert & Louis 1996). The combined graft procedure may offer the following advantages:

- The submerged connective tissue section of the interpositional graft aids in the revascularization of the onlay section of the graft, thereby gaining a greater percentage of take of the overall graft.
- A smaller post-operative open wound in the palate donor site.
- Faster healing in the palate donor site with less patient discomfort.
- Greater latitude or ability to control the degree of bucco-lingual and apico-coronal augmentation within a single procedure.
- Vestibular depth is not decreased and the muco-gingival junction is not moved coronally, thereby eliminating the need for follow-up corrective procedures.

Refinement of pontic contours and gingivoplasty soft tissue sculpting procedures

It is desirable, when reconstructing defects within a partially edentulous ridge, to moderately over-correct the ridge in the area of the deformity. This will compensate for wound contraction and provide the necessary bulk of tissue within the ridge to sculpt the ridge to its final form. Gingivoplasty techniques using rotary coarse diamond stones in an ultraspeed handpiece with copious water spray are used to smooth out incision lines and perfect the fit and shape of the pontic teeth to the crest of the ridge (Figs. 44-83, 44-87). Adjustments are made to shape the cervical contour and emergence profile of the pontic teeth to match that of the contralateral teeth. The tissue-contacting surfaces of the pontic teeth are immediately rebased with autopolymerizing resin and polished. This final tissue sculpting procedure and reshaping of the provisional prosthesis is minor in nature but aids greatly in defining the shape of the papillae and creating the illusion of the presence of a cuff of free gingiva at the pontic–ridge interface.

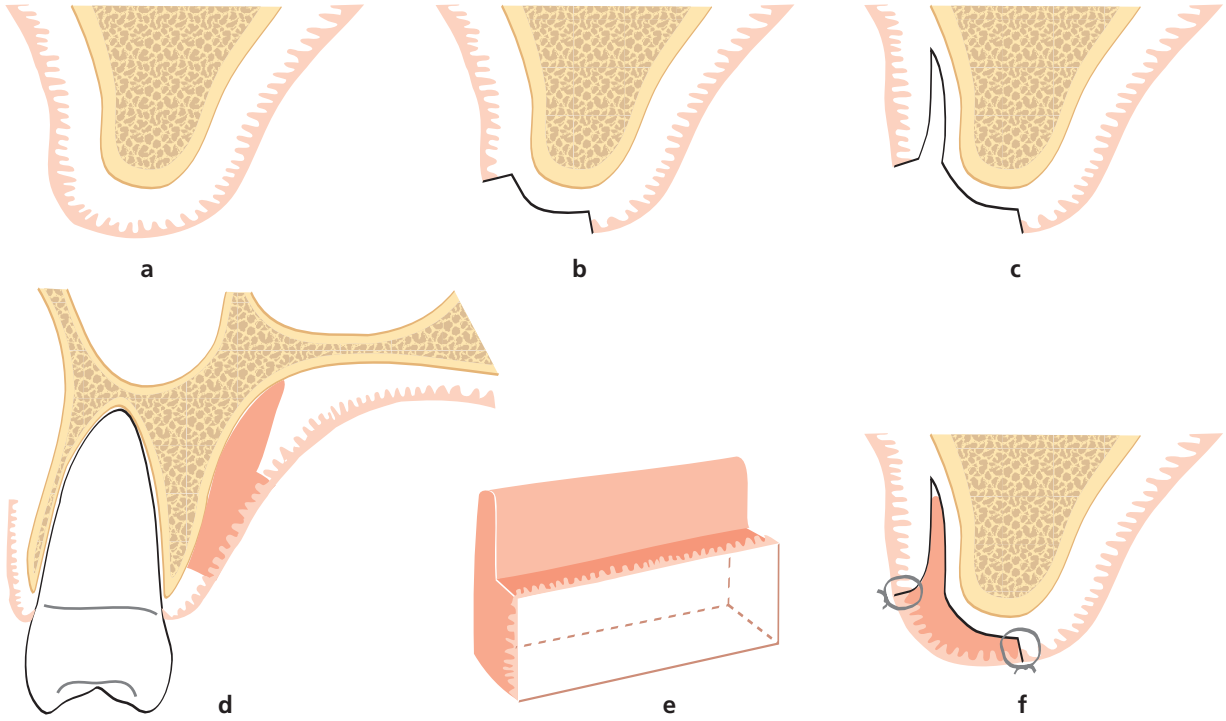


Fig. 44-86 Diagram of the combination onlay-interpositional graft procedure. (a) Cross section of a class III ridge defect. (b) Epithelium is removed on the labial–crestal side of the ridge to prepare the recipient bed for the onlay segment of the graft. (c) Partial-thickness dissection was then used to create a pouch for the interpositional section of the graft. (d) The dissection for the graft is started at right angles to the surface of the palate. The scalpel blade is then angled to remove a long connective tissue segment for the graft. (e) Three-dimensional view of the onlay section of the graft (including epithelium) and the connective tissue segment for buccolingual augmentation. (f) Graft sutured into position. (Reprinted with permission from *The International Journal of Periodontics and Restorative Dentistry*.)

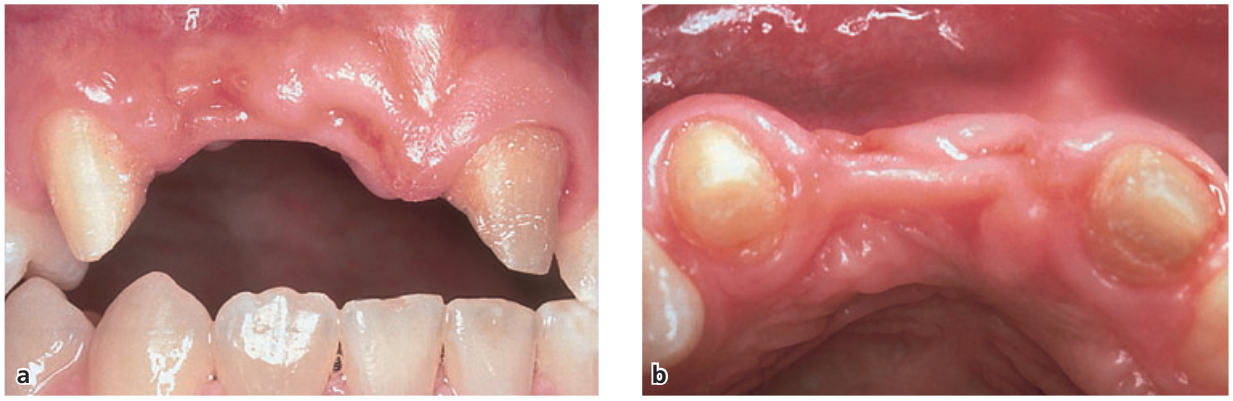
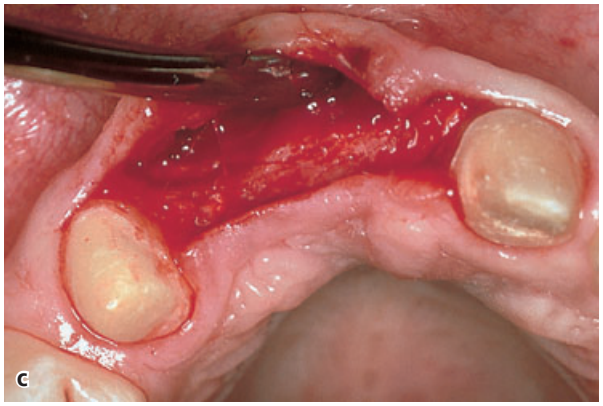
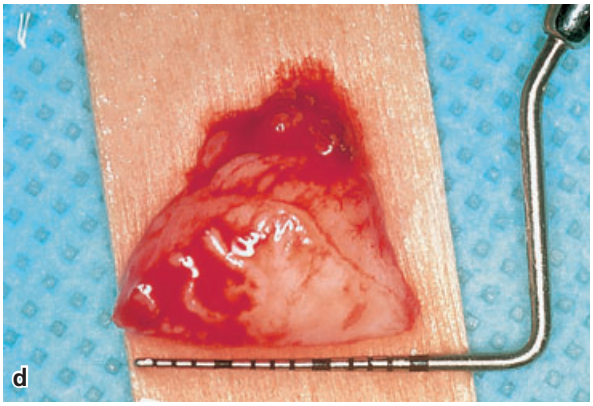
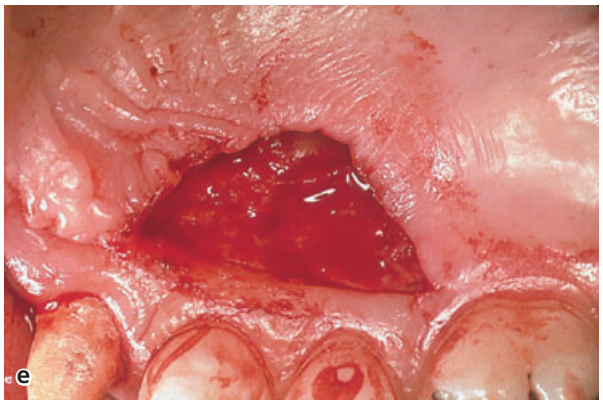
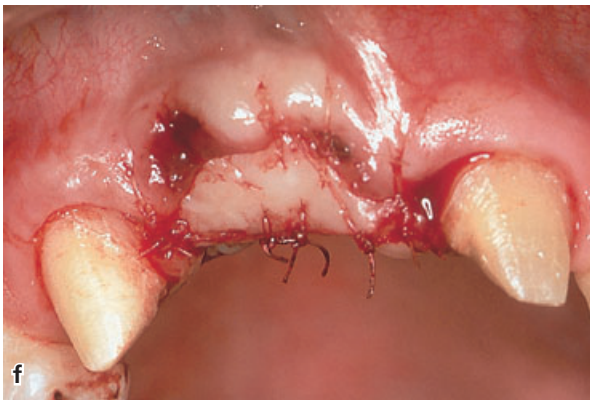


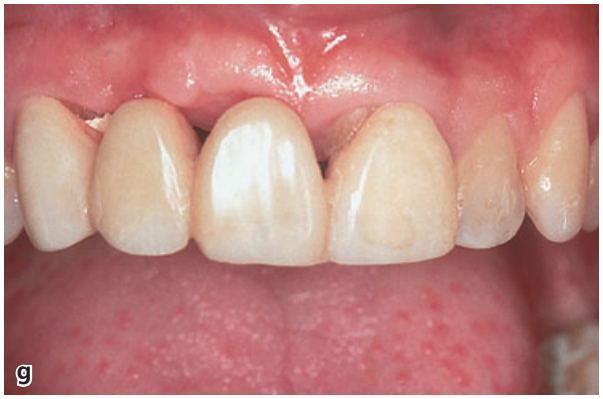
Fig. 44-87 (a,b) The right maxillary lateral and central incisors were lost due to trauma. These views show the horizontal and vertical loss of ridge tissue 10 months after the extractions. (c) A partial-thickness path of incision was extended labially and apically to create a pouch. The amount of space created within the pouch and the degree of relaxation of the flap was then tested with a periosteal elevator. (d) The epithelialized section of the graft can be seen in this view. (e) The premolar area, maxillary right side, was used as a donor area. The area of exposed connective tissue corresponds to the onlay section of the graft. The incisions were extended another 5–7 mm towards the midline on a long bevel to obtain the interpositional segment of the graft. (f) The graft was tucked into the labial pouch and sutured first along its palatal border. The labial flap was then sutured along the epithelial connective border of the graft. The residual labial socket defect in the flap created a soft tissue discontinuity defect along the labial margin of the flap. (g) At 6 weeks post surgery, it can be seen that further augmentation would be required to gain additional soft tissue in both the vertical and horizontal planes. A second-stage procedure was done at this time. (h) An incision 1.5 mm in depth was utilized to de-epithelialize the crestal surface of the ridge. Note that the papillae were not included within the surgical field. The mesial and distal borders of the onlay section of the recipient site were then extended apically to create vertical releasing incisions. The overall recipient site was to be trapezoidal in shape. A labial flap to create the pouch section of the recipient site was made using partial-thickness dissection. (i) The left maxillary premolar area was used as the donor site for the second-stage surgery. (j) This side view clearly shows the epithelialized onlay section of the graft and the de-epithelialized connective tissue section of the graft, as well as tissue thickness. (k) The graft was sutured first along the fixed palatal border to gain initial stabilization. Then the connective tissue interpositional section was sutured along the lateral borders. The flap was then sutured over the interpositional section of the graft at the epithelialized edge of the onlay section of the graft and along the vertical incisions. (l) At 6 weeks post surgery, the provisional prosthesis was modified to bring the tissue surface of the pontics into contact with the healing ridge. (m) At 2 months post surgery, tooth form was further modified on the provisional prosthesis and gingivoplasty was done to sculpt the tissues to final form and smooth out surface irregularities. (n) The final ceramo-metal prosthesis was inserted 4 months later. The life-like reconstruction of the soft tissues and dentition restored dentofacial esthetics for the patient. (Courtesy of Dr. J. Seibert, Dr. J. Louis & Dr. D. Hazzouri, USA. Reprinted with permission from *The International Journal of Periodontics and Restorative Dentistry*.)

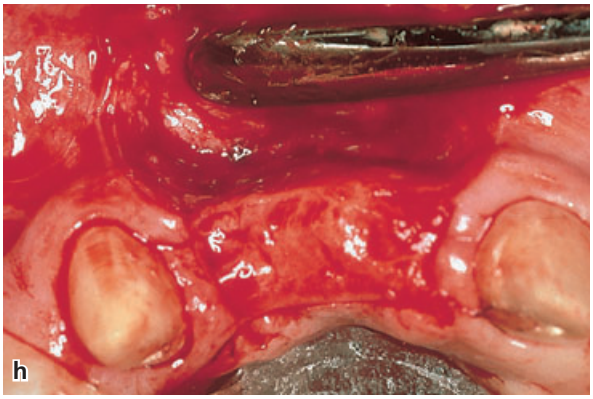


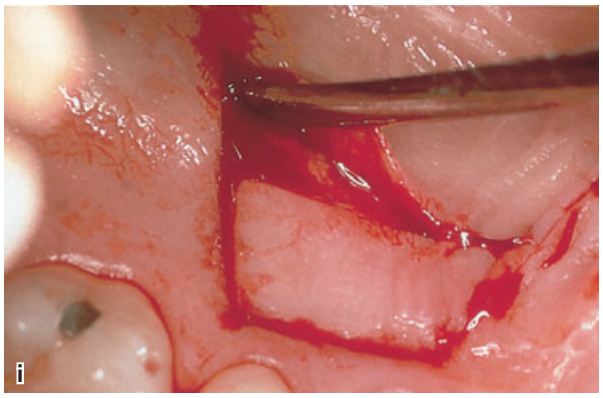












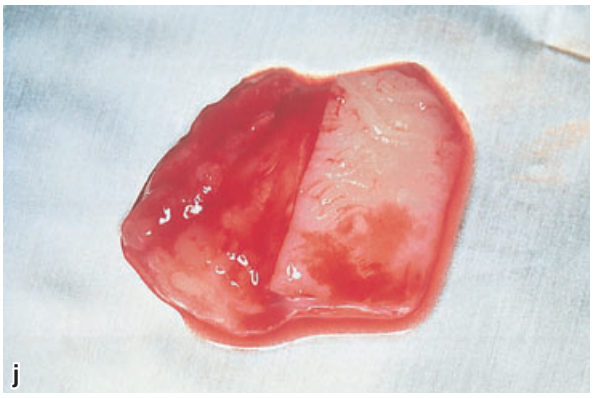


Fig. 44-87 *Continued*

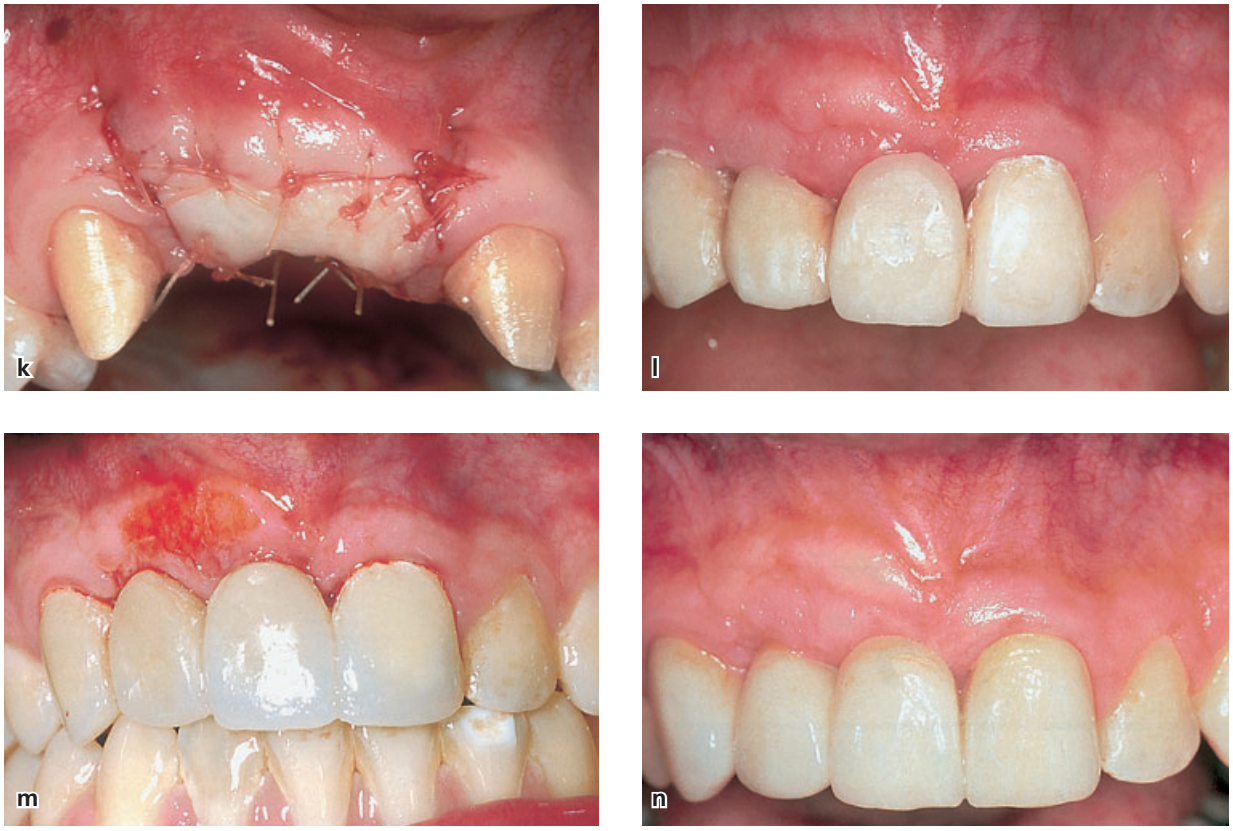


Fig. 44-87 *Continued*

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Chapter 45

Periodontal Plastic Microsurgery

Rino Burkhardt and Niklaus P. Lang

Microsurgical techniques in dentistry (development of concepts)

In general, the main aim of a surgical intervention is no longer only the survival of the patient or one of his organs, but the effort to preserve a maximum amount of function and to improve patient comfort. In many surgical specialties, these demands are met owing to a minimally invasive surgical approach.

Microsurgery in general is not an independent discipline, but is a technique that can be applied to different surgical disciplines. It is based on the fact that the human hand, by appropriate training, is capable of performing finer movements than the naked eye is able to control. First reports on microsurgery go back to the nineteenth century when a microscope was developed for use in ophthalmology (Tamai 1993). Later, the first surgical operation with a microscope was performed in Sweden to correct otosclerotic deafness (Nylén 1924). Microsurgical technique, however, did not attract the interest of surgeons until the 1950s, when the first surgical microscope, OPMI 1, with a coaxial lighting system and the option for stereoscopic view, was invented and commercialized by the Carl Zeiss company.

The micro vessel surgery that later revolutionized plastic and transplantation surgery was mainly developed by neurosurgeons (Jacobsen & Suarez 1960; Donaghy & Yasargil 1967). Applying microsurgically modified techniques, small vessels of a diameter of less than 1 mm could be successfully anastomosed on a routine basis (Smith 1964). As a consequence, a completely amputated thumb was successfully replanted for the first time in 1965 (Komatsu & Tamai 1968). Between 1966 and 1973, a total of 351 fingers were replanted at the Sixth People's Hospital in Shanghai without magnification, resulting in a healing rate of 51% (Zhong-Wei *et al*. 1981). From 1973, the interventions mentioned were solely performed with surgical microscopes and the corresponding success rates of replanted fingers increased to 91.5%. These results documented the importance of a fast and successful restoration of the blood circulation in replanted extremities and free tissue grafts. Further achievements of the microsurgical technique in plastic reconstructive surgery included transplantation of toes to replace missing thumbs (Cobbett 1969), interfascicular nerve transplantation (Millesi 1979), microvascular transplantation of toe joints (Buncke & Rose 1979), micro neurovascular transplantation of the pulp of a toe to restore the sensitivity of the finger tips (Morrison *et al*. 1980), and microvascular transplantation of the nail complex (Foucher 1991). Positive results of microsurgically modified interventions have led to today's clinical routine applications in orthopedics, gynecology, urology, plastic–reconstructive and pediatric surgery.

After a few early single reports (Baumann 1977; Apotheker & Jako 1981), the surgical microscope was introduced in dentistry in the 1990s. Case reports and the applications of the microscope were described in the prosthetic (Leknius & Geissberger 1995; Friedman & Landesman 1997, 1998; Mora 1998), endodontic (Carr 1992; Pecora & Andreana 1993; Ruddle 1994; Mounce 1995; Rubinstein 1997), and periodontal literature (Shanelec 1991; Shanelec & Tibbetts 1994, 1996; Tibbetts & Shanelec 1994; Burkhardt & Hürzeler 2000).

Treatment outcomes have been statistically analyzed in prospective studies in endodontics, since the

introduction of microendodontic techniques (Rubinstein & Kim 1999, 2002). Within 1 year after apical microsurgery, 96.8% of the cases were considered to be healed. At re-evaluation, 5–7 years after the first post-operative year, a success rate of 91.5% measured by clinical and radiographic parameters was still evident (Rubinstein & Kim 2002). The corresponding percentage of healed cases, treated without a surgical microscope, yielded only 44.1%, 6 months to 8 years after conventional apical surgery (Friedman *et al*. 1991).

Despite the positive results in prospective studies (Rubinstein & Kim 2002; Cortellini & Tonetti 2001; Burkhardt & Lang 2005), the surgical microscope experiences a slow acceptance in prosthodontics, endodontics (Seldon 2002), and periodontal surgery. Possible reasons are the long learning curve, the impaired maneuverability of the devices and the high cost of purchasing the instrument.

Concepts in microsurgery

The continuous development of operating microscopes, refinement of surgical instruments, production of improved suture materials and suitable training laboratories have played a decisive role for the worldwide establishment of the microsurgical technique in many specialties. The three elements, i.e. *magnification*, *illumination*, and *instruments* are called the *microsurgical triad* (Kim *et al*. 2001), the improvement of which is a prerequisite for improved accuracy in surgical interventions. Without any one of these, microsurgery is not possible.

Magnification

An optimal vision is a stringent necessity in periodontal practice. More than 90% of the sensations of the human body are perceived by visual impressions. Vision is a complex process that involves the cooperation of multiple links between the eye, the retina, the optic nerve, and the brain. An important element to assess in human eyesight is visual acuity, measured in angular degrees. If necessary, it may be improved by corrective lenses. It is defined by the ability to perceive two objects separately. Visual acuity is influenced by anatomic and physiologic factors, such as the density of cells packed on the retina and the electrophysiologic process of the image on the retina.

Another important factor influencing visual acuity is the lighting. The relation between visual acuity and light density is well established: a low light density decreases visual acuity. The best eyesight can be achieved at a light density of 1000 cd/m^2. At higher densities, visual acuity decreases. This, in turn, means that claims for optimal lighting conditions have to be implemented.

Visualization of fine details is enhanced by increasing the image size of the object. Image size can be increased in two ways: (1) by getting closer to the objects and (2) by magnification. Using the former method, the ability of the lens of the eye to accommodate becomes important and has a relevant influence on the visual capacity. By changing the form of the lens, the refraction of the optical apparatus increases, allowing it to focus on nearer objects. During ageing, the ability to focus at closer distances is compromised because the lens of the eye loses its flexibility (Burton & Bridgeman 1990). This phenomenon is called presbyopia. Presbyopia affects all people in middle age, and becomes especially noticeable when the nearest point at which the eye can focus accurately exceeds ideal working distances (Burton & Bridgeman 1991). To see small objects accurately, the focal length must be increased. As an example, an older individual reading without glasses must hold the reading matter farther from the eyes to see the print. Increasing the distance enables the person to see the words, but the longer working distance results in a smaller size of the written text. This decrease in image size, resulting from the increased working distance, needs to accommodate the limitations of presbyopia and is especially hindering in clinical practice. In periodontal practice, the tissues to manipulate are usually very fine resulting in a situation in which the natural visual capacity reaches its limits. Therefore, the clinical procedure may only be performed successfully with the use of magnification improving precision and, hence, the quality of work.

Optical principles of loupes

In dentistry, two basic types of magnification systems are commonly used: the surgical microscope and loupes. The latter can further be classified as (1) single-lens magnifiers (clip-on, flip-up, jeweller's glasses) and (2) multi-lens telescopic loupes. Single-lens magnifiers produce the described diopter magnification that simply adjust the working distance to a set length. As diopters increase, the working distances decrease. With a set working distance, there is no range and no opportunity for movement; this can create difficulty in maintaining focus and, therefore, may cause neck and back strain from poor posture (Basset 1983; Diakkow 1984; Shugars *et al*. 1987). Additionally, diopter magnifiers also give poor image quality, which restricts the quality of the work (Kanca & Jordan 1995). These types of glasses cannot be considered to be a true means of magnification.

Telescopic loupes (compound or prism loupes), however, offer improved ergonomic posture as well as significant advancements in optical performance (Shanelec 1992). Instead of increasing the thickness of a single lens to increase magnification, compound loupes use multiple lenses with intervening air spaces (Fig. 45-1). These allow an adjustment of magnification, working distance, and depth of the field without excessive increase in size or weight. Prism loupes are

Fig. 45-1 Fixed compound loupe, adjustable only in the interpupilary distance (Galilean principle).

Fig. 45-2 Prism loupe, sealed to avoid leakage of moisture, front frame mounted and fully adjustable (Prism principle).

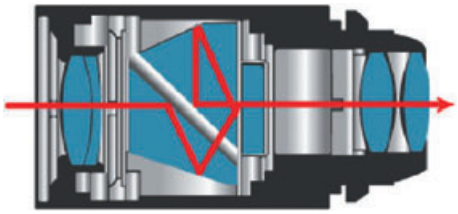

Fig. 45-3 Light path through prism loupe. Even though the distance the light travels has increased, there is no decrease in brightness or image contrast, even at 4× or 5×. This is because the light does not travel through air but instead through the glass of the prism.

the most optically advanced type of loupe magnification available (Fig. 45-2). While compound loupes use multiple refracting surfaces with intervening air spaces to adjust optical properties, prism loupes are actually low-power telescopes. They contain Pechan or Schmidt prisms that lengthen the light path through a series of mirror reflections within the loupes (Fig. 45-3). Prism loupes produce better magnification, larger fields of view, wider depths of field, and longer working distances than do other loupes. To guarantee proper adjustment of loupes, the knowledge of some basic definitions and key optical features of loupes is necessary (Fig. 45-4).

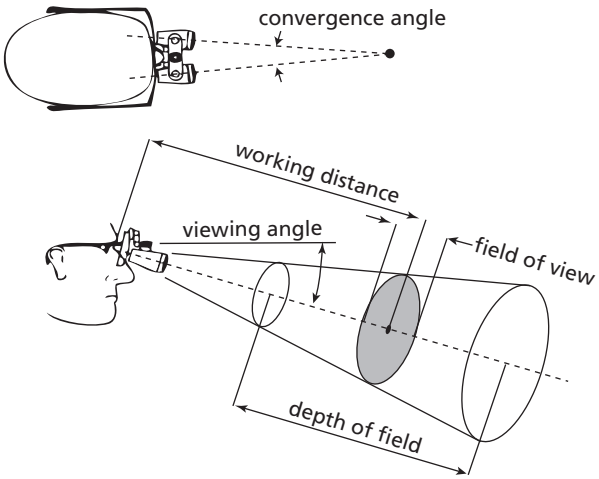

Fig. 45-4 Diagram indicating the principal optical features of loupes.

Working distance

The working distance is the distance measured from the eye lense location to the object in vision. There is no set rule for how much the working distance may be increased. Depending on the height and the resulting length of the arms, the working distance with slightly bended arms usually ranges from 30 to 45 cm. At this distance, postural ergonomics are greatly improved and eye strain reduced due to lessened eye convergence. The multitude of back, neck, shoulder, and eye problems that dentists suffer, working without using loupes, frequently originate from the need to assume a short working distance to increase visual acuity (Coburn 1984; Strassler 1989). By wearing surgical loupes, the head is placed in the centre of its balance over the spine and stabilized against gravity.

Working range

The working range (depth of field) (Fig. 45-4) is the range within which the object remains in focus. The depth of field of normal vision ranges from working distance to infinity. Moving back from a close working distance, the eyes naturally accommodate and refocus to the new distance. Normally, eye position and body posture are not frozen in one place for an extended period, but vary constantly. Wearing loupes changes this geometry. Body posture and position of the extraocular muscles are confined to a range determined by the loupe's characteristics. It is important to understand that each individual's vision is limited to his/her own internal working range, which means that one may only be able to maintain focus on an object within a 15 cm range, even though the loupes have a 23 cm depth of field. With any brand of loupe, the depth of field decreases as the magnification increases.

Convergence angle
The convergence angle (Fig. 45-4) is the pivotal angle aligning the two oculars, such that they are pointing at the identical distance and angle. At a defined working distance, the convergence angle varies with interpupillary distance. Wider-set eyes will have more eye convergence at short working distances. Therefore, the convergence angle defines the position of the extraocular muscles that may result in tension of the internal and external rectus muscles; this may be an important source of eye fatigue.

Field of view
The field of view (Fig. 45-4) is the linear size or angular extent of an object when viewed through the telescopic system. It also varies depending on the design of the optic lens system, the working distance, and the magnification. As with depth of field, when magnification increases, the field of view decreases.

Interpupillary distance
The interpupillary distance (Fig. 45-4) depends on the position of the eyes of each individual and is a key adjustment that allows long-term, routine use of loupes. The ideal setting, as with binoculars, is to create a single image with a slightly oval-shaped viewing area. If the viewing area is adjusted to a full circle, excess eye muscle strain would limit the ability to use loupes for long periods.

Viewing angle
The viewing angle (Fig. 45-4) is the angular position of the optics allowing for comfortable working. The shallower the angle, the greater the need to tilt the neck to view the object being worked at. Therefore, loupes for dental clinicians should have a greater angulation than loupes designed for industrial workers. A slight or no angulation, which results when magnifiers are embedded in the lenses of the eyeglasses, may cause the operator to unduly tilt his or her head to view a particular object. This, again, may lead not only to neck discomfort, but also to pain in the shoulder muscles and possibly to a headache. As the working posture is likely to change over time, the loupes should be adjustable to any posture change.

Illumination
Most of the manufacturers offer collateral lighting systems or suitable fixing options. These systems may be helpful, particularly for higher magnification in the range of 4× and more. Loupes with a large field of view will have better illumination and brighter images than those with narrower fields of view. Important considerations in the selection of an accessory lighting source are total weight, quality, and the brightness of the light, ease of focusing and directing the light within the field of view of the magnifiers, and ease of transport between surgeries (Strassler *et al*. 1998).

It should be realized that each surface refraction in a lens will result in a 4% loss in transmitted light due to reflection. In telescopic loupes, this could amount to as much as 50% reduction in brightness. Anti-reflective coatings have been developed to counteract this effect by allowing lenses to transmit light more efficiently. The quality of lens coatings also varies and should be evaluated when selecting loupes (Shanelec 1992).

Choice of loupes
Before choosing a magnification system, different loupes and appropriate time for a proper adjustment have to be considered. Ill fitting or improperly adjusted loupes and the quality of the optics will influence the performance. For the use in periodontal surgery, an adjustable, sealed prism loupe with high-quality, coated lenses offering a magnification between 4× and 4.5×, either headband- or front frame-mounted, with a suitable working distance and a large field of view, seems to be the instrument of choice. The information in Table 45-1 serves as a basic guide to making an adequate selection.

Optical principles and components of a surgical microscope

The surgical microscope is a complicated system of lenses that allows stereoscopic vision at a magnification of approximately 4–40× with an excellent illumination of the working area. In contrast to loupes, the light beams fall parallel onto the retinas of the observer so that no eye convergence is necessary and the demand on the lateral rectus muscles is minimal (Fig. 45-5). The microscope

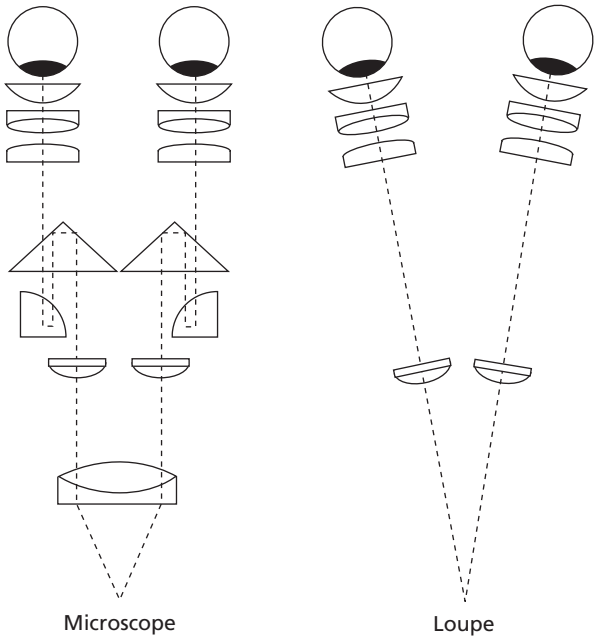

Fig. 45-5 Diagram illustrating the comparison of vision enhancement with loupes and a microscope. The loupes necessitate eye convergence while vision is paralleled through the microscope.

Table 45-1 Features to consider in the selection of a magnifying loupe system

Compound loupes (Galilean)	• Magnification range 2–3.5× • Lighter in weight • Shorter working distance • Shorter loupe barrel
Prism loupes (Keplerian)	• Magnification range 3–5× • Heavier in weight • Longer working distance • Longer loupe barrel
Front-frame mounted	• Allow up to 90% of peripheral vision • No prescription glasses • Require soft and cushioned nose piece • Better weight distribution
Head-band mounted	• Restricted peripheral vision • Allow to use prescription glasses • Better weight distribution • Require adjustment more often
Fixed-lens magnifiers	• No adjustment options when changing posture • Minimum weight
Flip-up capability	• Require removable, sterilizable handle • Allow switch from magnified to regular vision
Quality of the lenses	• Corrected for chromatic and spherical aberration • No drop-off in clarity when approaching the edges • Sealed system to avoid leakage of moisture • Option for disinfection
Adjustment options	• Interpupillary distance • Viewing angle • Vertical adjustment • Lock in adjusted position • Convergence angle (preset angle may be more user-friendly)
Lens coating	• Brighter image • More light
Accessories	• Transportation box • Side and front shields for protection • Mounted light source • Removable cushions

consists of the optical components, the lighting unit, and a mounting system. To avoid an unfavorable vibration of the microscope during use, the latter should be firmly attached to the wall, the ceiling or a floor stand. Mounted on the floor, the position of the microscope in the room must provide quick and easy access.

The optical unit includes the following components (Fig. 45-6): (1) magnification changer, (2) objective lenses, (3) binocular tubes, (4) eyepieces, and (5) lighting unit (Burkhardt & Hürzeler 2000).

Magnification changer

The magnification changer or "Galilean" changer consists of one cylinder, into which two Galilean telescope systems (consisting of a convex and concave lens) with various magnification factors are built. These systems can be used in either direction depending on the position of the magnification changer. A total of four different magnification levels are available. Straight transfer without any optics yields no magnification. The combination of the magnification changer with varying objective lenses and eyepieces yields an increasing magnification line when the control is adjusted.

The stepless motor-driven magnification changer must achieve a magnification of 0.5–2.5× with one optical system, which is operated by either a foot pedal or an electric rotating control, mounted on the microscope. The operator should decide whether to use the manual or motorized magnification changer. If the magnification must be changed frequently, it can be accomplished more quickly with the manual than with the motorized changer, the former not having in-between levels. While the motorized system improves the focus and comfort compared to the manual system, the former is more expensive.

Objective lenses

As processed by a magnification changer, the image is only projected by a single objective. This simultaneously projects light from its source twice for deflection by the prisms into the operation area (i.e. coaxial lighting). The most frequently used objective is 200 mm (f = 200 mm). The focal length of the objective generally corresponds to the working distance of the object.

Binocular tubes

Depending on the area of use, two different binocular tubes are attached (i.e. straight and inclined tubes). With straight tubes, the view direction is parallel to the microscope axis. Using inclined tubes, an angulation to the microscope axis of 45° is achieved. In dentistry, only inclined, swivelling tubes, that permit continuously adjustable viewing, are feasible for ergonomic reasons (Fig. 45-7). The precise adjustment of the interpupillary distance is the basic prerequisite for the stereoscopic view of the operation area.

Eyepieces

The eyepieces magnify the interim image generated in the binocular tubes. Varying magnifications can be achieved (10×, 12.5×, 16×, 20×) using different eyepieces. Eyepiece selection not only determines the magnification, but also the size of the field of view. Corresponding to the loupe spectacles, an indirect relationship exists between the magnification and the field of view. The 10× eyepiece generally provides a sufficient compromise between magnification and field of view. Modern eyepieces allow a correction

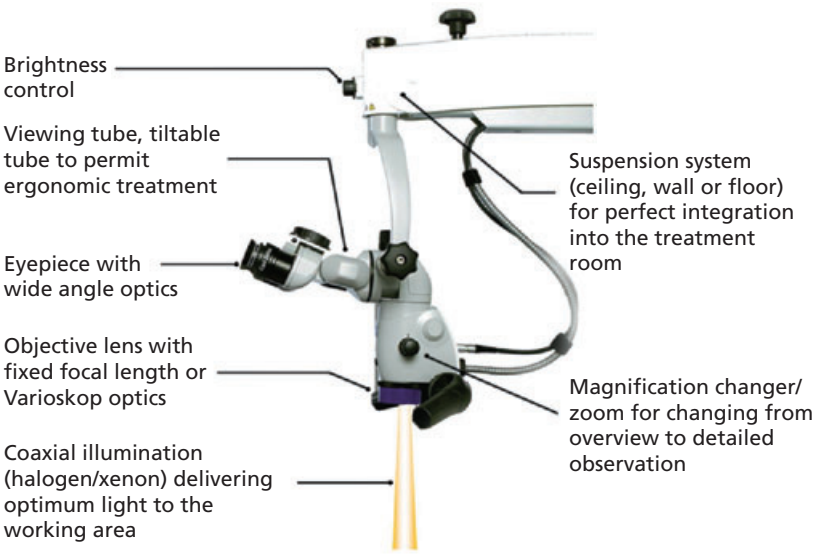

Fig. 45-6 System components of a surgical microscope.

Fig. 45-7 Tiltable viewing tube which provides an ergonomic posture during clinical work, a prerequisite for optimal performance using microsurgical technique.

facility within –8 to +8 diopters that is a purely spherical correction.

The majority of surgical microscopes consist of modules and can be equipped with attachments that include integrated video systems, photographic adapters for cameras, units for image storage, colour printers, and powerful lighting sources. Prior to purchasing accessories, inexperienced clinicians should gather information about the needed equipment. The use of magnifying loupes is recommended prior to purchasing a microscope to accustom oneself to working under magnification.

Lighting unit

Optimal illumination is necessary with high magnifications. In recent years, the use of halogen lamps became popular. These lamps provide a whiter light than do lamps using conventional bulbs due to their higher colour temperature. As halogen lamps emit a considerable portion of their radiation within the infrared part of the spectrum, microscopes are equipped with cold-light mirrors to keep this radiation from the operation area. An alternative to the halogen light is the xenon lamp that functions up to ten times longer than the halogen lamp. The light has daylight characteristics with even a whiter colour and delivers a brighter, more authentic image with more contrast.

Advantages and disadvantages of loupes and surgical microscopes

A substantial number of periodontists have already adopted the use of low magnification in their practices and recognize its great benefits. Most of the present results are based on subjective statements of patients or observations of the attending surgeons. At present, it can only be speculated how significantly the selection of magnification influences the result of the operation. The magnification recommended for surgical interventions ranges from 2.5–20× (Apotheker & Jako 1981; Shanelec 1992). In periodontal surgery, magnifications of 4–5× for loupe spectacles and 10–20× for surgical microscopes appear to be ideal depending on the kind of intervention. As the depth of field decreases with increasing magnification, the maximum magnification for a surgical intervention is limited to about 12–15×, when dealing with a localized problem such as the coverage of a single soft tissue recession or interdental wound closure after guided tissue regeneration of an infrabony defect. A magnification range of 6–8× seems appropriate for clinical inspections or surgical interventions when the entire quadrant is under operation. Higher magnifications such as 15–25× are more likely limited to the visual examination of clinical details only, such as in endodontic interventions.

Loupes have the advantage over the microscope in that they reduce technique sensitivity, expense,

and learning phase. The lighting of the operation field is often insufficient, however, and that may limit magnifications more than 4.5×. The surgical microscope guarantees a more ergonomic working posture (Zaugg *et al*. 2004), optimal lighting of the operation area, and freely selectable magnification levels. These advantages are countered by increased expenses of the equipment and an extended learning phase for the surgeon and his assistant. In order to visualize lingual or palatal sites that are difficult to access, the microscope must have sufficient maneuverability. Recent developments have enabled direct viewing of oral operation aspects. By means of these optical devices, it will be possible to perform all periodontal interventions with the surgical microscope.

Instruments

Proper instrumentation is fundamental for microsurgical intervention. While various manufacturers have sets of microsurgical instruments, they are generally conceived for vascular and nerve surgery and, therefore, inappropriate for the use in plastic periodontal surgery. As the instruments are primarily manipulated by the thumb, index and middle finger, their handles should be round, yet provide traction so that finely controlled rotating movements can be executed. The rotating movement of the hand from two o'clock to seven o'clock (for right-handed persons) is the most precise movement the human body is able to perform. The instruments should be approximately 18 cm long and lie on the saddle between the operator's thumb and the index finger; they should be slightly top-heavy to facilitate accurate handling (Fig. 45-8). In order to avoid an unfavorable metallic glare under the light of the microscope, the instruments often have a coloured coating surface. The weight of each instrument should not exceed 15–20 g (0.15–0.20 N) in order to avoid hand and arm muscle fatigue. The needle holder should be equipped with a precise working lock that should not exceed a locking force of 50 g (0.5–N). High locking forces generate tremor, and low locking forces reduce the feeling for movement.

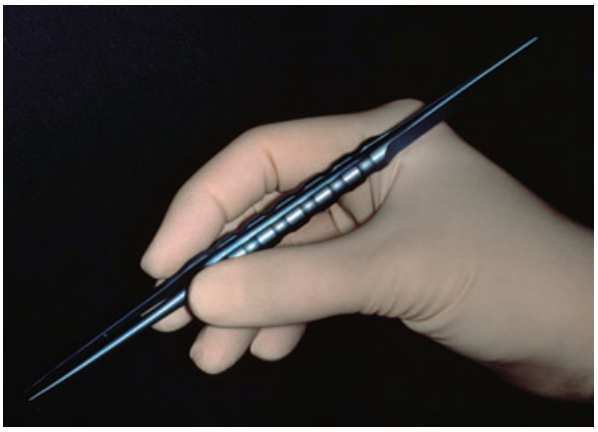

Fig. 45-8 Illustration demonstrating proper hand position for utilization of microsurgical instruments. Fine rotary movements which you get gripping the instrument like a pencil are needed for precise movements.

Appropriate sets of steel or titanium instruments for periodontal surgery are available from different manufacturers. A basic set comprises a needle holder, micro scissors, micro scalpel holder, anatomic and surgical forceps, and a set of various elevators. In order to avoid sliding of the thread when tying the knot, the tips of the forceps have flat surfaces or can be finely coated with a diamond grain that improves the security by which the needle holder holds a surgical needle (Abidin *et al*. 1990). The configuration of the needle holder jaw has considerable influence on needle holding security. The presence of teeth in the tungsten carbide inserts provides the greatest deterrent to either twisting or rotating of the needle between the needle holder jaws. This benefit must be weighed against the potential damaging effects of the teeth on suture material. Smooth jaws without teeth cause no demonstrable damage to 6-0 monofilament nylon sutures, whereas needle holder jaws with teeth ($7000/in^2$) markedly reduce the suture breaking strength (Abidin *et al*. 1990). Additionally, the sharp outer edges of the needle holder jaws must be rounded to avoid breakage of fine suture materials (Abidin *et al*. 1989). When the needle holder jaws are closed, no light must pass through the tips. Locks aid in the execution of controlled rotation movements on the instrument handles without pressure. The tips of the forceps should be approximately 1–2 mm apart, when the instrument lies in the hand idly.

Various shapes and sizes of micro scalpels can be acquired from the discipline of ophthalmology or plastic surgery instrument sets and supplemented with fine instruments (fine chisels, raspatories, elevators, hooks, and suction) from conventional surgery.

In order to prevent damage, micro instruments are stored in a sterile container or tray. The tips of the instruments must not touch each other during sterilization procedures or transportation. The practice staff should be thoroughly instructed about the cleaning and maintenance of such instruments, as cleansing in a thermo disinfector without instrument fixation can irreparably damage the tip of these very expensive micro instruments.

Suture materials

Suture material and technique are essential factors to consider in microsurgery (Mackensen 1968). Wound closure is a key prerequisite for healing following surgical interventions and most important to avoid complications (Schreiber *et al*. 1975; Kamann *et al*. 1997). The most popular technique for wound closure is the use of sutures that stabilize the wound margins sufficiently and ensure proper closure over a defined period of time. However, the penetration of a needle

through the soft tissue in itself causes a trauma, and the presence of foreign materials in a wound may significantly enhance the susceptibility to infection (Blomstedt *et al*. 1977; Österberg & Blomstedt 1979). Hence, it is obvious that needle and thread characteristics influence wound healing and surgical outcome.

Characteristics of the needle

The needle consists of a swage, body, and tip and differs concerning material, length, size, tip configuration, body diameter, and the nature of connection between needle and thread. In *atraumatic* sutures, the thread is firmly connected to the needle through a press-fit swage or stuck in a laser-drilled hole. There is no difference concerning stability between the two attachment modalities (Von Fraunhofer & Johnson 1992). The body of the needle should be flattened to prevent twisting or rotating in the needle holder. The needle tips differ widely depending on the specialty in which they are used. Tips of cutting needles are appropriate for coarse tissues or atraumatic penetration. In order to minimize tissue trauma in periodontal microsurgery, the sharpest needles, reverse cutting needles with precision tips or spatula needle with micro tips (Fig. 45-9), are preferred (Thacker *et al*. 1989).

The shape of the needle can be straight or bent to various degrees. For periodontal microsurgery, the 3/8″ circular needle generally ensures optimum results. There is a wide range of lengths, as measured along the needle curvature from the tip to the proximal end of the needle lock. For papillary sutures in the posterior area, needle lengths of 13–15 mm are appropriate. The same task in the front aspect requires needle lengths of 10–12 mm, and for closing a buccal releasing incision, needle lengths of 5–8 mm are adequate. To guarantee a perpendicular penetration through the soft tissues without tearing, an asymptotic curved needle is advantageous in areas where narrow penetrations are required (e.g. margins of gingivae, bases of papillae). To fulfil these prerequisites for ideal wound closure, at least two different sutures are used in most surgical interventions. Table 45-2 serves as a basic guide to select the appropriate suture material.

Characteristics of the suture material

The suture material may be either *resorbable* or *nonresorbable* material. Within these two categories, the materials can be further divided into *monofilament* and *polyfilament* threads. The bacterial load of the oral cavity demands attention in the choice of the suture material. Generally, in the oral cavity the wound healing process is uneventful, hereby reducing the risk of infection caused by contamination of the thread. As polyfilament threads are characterized by a high capillarity, monofilament materials are to be preferred (Mouzas & Yeadon 1975). *Pseudomonofilaments* are coated polyfilament threads with the aim of reducing mechanical tissue trauma. During suturing the coating will break and the properties of the pseudomonofilament thread then corresponds to that of the polyfilament threads (Macht & Krizek 1978). Additionally, fragments of the coating may invade the surrounding tissues and elicit a foreign body reaction (Chu & Williams 1984).

Resorbable sutures

Resorbable threads may be categorized as *natural* or *synthetic*. Natural threads (i.e. surgical gut) are produced from intestinal mucosa of sheep or cattle. The twisted and polished thread loses its stability within 6–14 days by enzymatic breakdown (Meyer & Antonini 1989). Histologic examinations confirmed the inflammatory tissue reactions with a distinct infiltrate. For that reason, natural resorbable threads are generally obsolete (Bergenholtz & Isaksson 1967; Helpap *et al*. 1973; Levin 1980; Salthouse 1980).

Synthetic materials are advantageous due to their constant physical and biologic properties (Hansen 1986). The materials used belong to the polyamides, the polyolefines or the polyesters and disintegrate by hydration into alcohol and acid. Polyester threads are mechanically stable and, based on their different hydrolytic properties, lose their firmness in different,

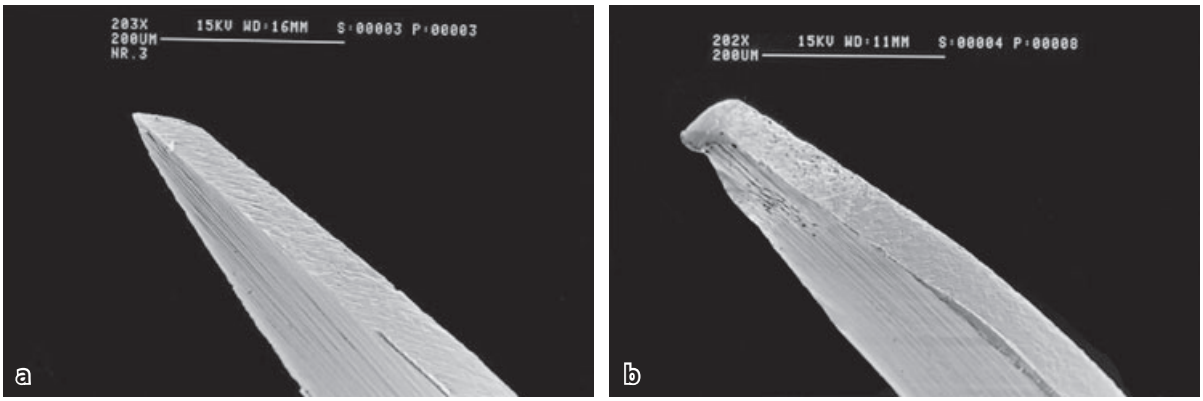

Fig. 45-9 (a) Intact sharp spatula needle. (b) Damaged needle tip after sticking into the enamel surface.

Table 45-2 Ideal needle–thread combinations (non-resorbable) for use in periodontal microsurgery

Indications	Suture gauge	Needle characteristics	Thread materials	Product name
Buccal releasing incisions	7-0 7-0 9-0	3/8 curvature, cutting needle with precision tip, needle length 7.6 mm asymptotic curved needle, cutting needle tip, round body, needle length 8.9 mm 3/8 curvature needle, spatula needle, needle length 5.2 mm	Polypropylene Polypropylene Polyamide	Prolene® Prolene® Ethilon®
Interdental sutures, front area	6-0 7-0	3/8 curvature, cutting needle with precision tip, needle length 11.2 mm 3/8 curvature, cutting needle with precision tip, needle length 11.2 mm	Polypropylene Polyamide	Prolene® Ethilon®
Interdental sutures, premolar area	6-0 6-0	3/8 curvature, cutting needle with precision tip, needle length 12.9 mm 3/8 curvature, cutting needle with precision tip, needle length 12.9 mm	Polyamide Polypropylene	Ethilon® Prolene®
Interdental suture, molar area	6-0	3/8 curvature, cutting needle, needle length 16.2 mm	Polyamide	Ethilon®
Crestal incisions	7-0 6-0	3/8 curvature, cutting needle with precision tip, needle length 11.2 mm 3/8 curvature, cutting needle with precision tip, needle length 12.9 mm	Polyamide Polypropylene	Ethilon® Prolene®
Papilla basis incisions	7-0 9-0	asymptotic curved needle, cutting needle tip, round body, needle length 8.9 mm 1/2 curvature, cutting needle with micro tip, needle length 8.0 mm	Polypropylene Polyamide	Prolene® Ethilon®

but constant times. A 50% reduction of breaking resistance can be expected after 2–3 weeks for polyglycolic acid and polyglactin threads, 4 weeks for polyglyconate, and 5 weeks for polydioxanone threads. The threads are available in twisted, polyfilament forms, and monofilament forms for finer suture materials. The capillary effect is limited and hardly exists for polyglactin sutures (Blomstedt & Österberg 1982).

Non-resorbable sutures

Polyamide is a commonly used material for fine monofilament threads (0.1–0.01 mm) that show adequate tissue properties. Tissue reactions seldom occur except after errors in the polymerization process (Nockemann 1981). Polyolefines, as a variation of choice, are inert materials that remain in the tissues without hydrolytic degradation (Salthouse 1980; Yu & Cavaliere 1983). Polypropylene and its newest development, polyhexafluoropropylene, are materials with excellent tissue properties. After suturing, the thread will be encapsulated in connective tissues and keep its stability for a longer period. In 5-0 and thicker gauges, the monofilament threads are relatively stiff and, for that reason, may impair patient comfort.

A substance with similar biologic, but improved handling properties, is polytetrafluoroethylene. Due to its porous surface structure, the monofilament threads should only be used with restriction in the bacterially loaded oral cavity.

Intraoral tissue reactions around suture materials

The initial tissue reaction after suturing is a result of the penetration trauma, and reaches its culmination at the third post-operative day (Selvig *et al*. 1998). It is quite similar for resorbable and non-resorbable suture threads (Postlethwait & Smith 1975). Histologically, this early response is characterized by three zones of tissue alteration (Selvig *et al*. 1998): (1) an intensive cellular exudation in the immediate vicinity of the entry to the stitch canal, followed by (2) a concentric area, harboring damaged cells as well as intact tissue fragments, and (3) a wide zone of inflammatory cells in the surrounding connective tissues.

If a resorbable suture is left *in situ* for more than 2 weeks after wound closure, an acute inflammatory reaction still exists. This phenomenon is caused by bacteria entering the stitch canal and penetrating along the thread (Chu & Williams 1984; Selvig *et al*. 1998). The bacteriostatic effect of glycolic acid during the resorption process of polyglactin threads (Lilly *et al*. 1972) cannot be established (Thiede *et al*. 1980), and the resorption process of the polyglycolic thread is additionally inhibited by the acid environment caused by the infection (Postlethwait & Smith 1975).

Such studies confirm the increased risk for bacterial migration along the thread in the moist and bacterially loaded oral cavity. Experimental and clinical data indicate that most wound infections begin around suture material left within the wound (Edlich *et al*. 1974; Varma *et al*. 1974). Polyfilament threads additionally facilitate bacterial migration; bacteria can also penetrate into the inner compartment of the thread and evade the immunologic response of the host (Blomstedt *et al*. 1977; Haaf & Breuninger 1988). This is only one reason why monofilament, nonresorbable sutures should be preferred and removed at the earliest biologically acceptable time (Gutmann & Harrison 1991). The infectious potential can be further reduced by using an anti-infective therapy based on a daily rinsing or topical application of chlorhexidine (Leknes *et al*. 2005).

Another promising option to reduce bacterial migration along the suture is coating it with a bacteriostatic substance. Vicryl® Plus (Ethicon®, Norderstedt, Germany) is a resorbable suture material, coated with triclosan that inhibits bacterial growth for up to 6 days by damaging the membrane of the cells (Rothenburger *et al*. 2002; Storch *et al*. 2002).

Training concepts (surgeons and assistants)

The benefits of the operating microscope in periodontal surgery seem to be obvious. What then can be the reasons for the delay in taking advantage of periodontal surgery under the microscope? The main reason is that most surgeons do not adjust to the surgical microscope and those who have been using microscopes successfully, have not made adequate indepth practical recommendations to help other periodontal surgeons overcome their initial problems. Working with magnification changes the clinical settings as the visual direction during the surgical intervention does not meet the working ends of the instruments and the field of view has a smaller diameter. Additionally, the minimal size of tissue structures and suture threads requires a guidance of movement by visual rather than tactile control. This altered clinical situation requires an adjustment of the surgeon.

The three most common errors in the use of the surgical microscope are: (1) using magnification that is too high, (2) inadequate task sharing between surgeon and assistant, and (3) lack of practice.

High magnification

There is a tendency to use magnification which is too high. As described above, this is one of the fundamental optical principles: the higher the magnification, the narrower the field of vision and the smaller its depth. This concept is important because high magnification causes surgery to become more difficult, especially when it involves considerable movement. In these circumstances low magnification of 4–7× should be used. On the other hand, higher magnification of 10–15× may be useful when dissecting within a small area requiring less movement, e.g. in papilla preservation techniques. In general, the magnification should be that which allows the surgeons to operate with ease, and without increasing their usual operating time for a particular surgical procedure. Surgical time does not have to be increased once the surgeon has adapted fully to the microscope. The more experienced and skilled surgeons are with the microscope, the higher the magnification they can use with ease.

It may take 6 months or more for surgeons to be familiar with magnification of 10×, which usually is the maximum used in plastic periodontal surgery. A point of diminishing returns will eventually be reached where the advantages of increased magnification are outweighed by the disadvantages of a narrower field of vision.

Task sharing between surgeon and assistant (teamwork)

In microendodontics, during root canal treatment, the whole procedure is performed with a minimum amount of position changes of the operating persons. Focusing can easily be achieved by moving the mirror towards or away from the objective lenses. In periodontal surgery both hands are used to hold the instruments and position changes are more frequently required which increase the demands on the operating team and require for an ideal cooperation between surgeon and assistant.

In all surgeries at least two operating persons are involved: a surgeon and an assistant, who assists the surgeon in the most rudimentary tasks in the operation. However, the tasks that the assistant constantly repeats in almost all operations with varying levels of skill will be taken into consideration. These tasks include: flap retraction, suction, rinsing, and cutting the sutures. To guarantee a continuous work flow during the surgical intervention, a second assistant who organizes the instruments is frequently desirable.

In periodontal microsurgery, where there is inherently very little access enjoyed by the surgeon, retraction is absolutely vital. Retraction should be done in different positions and must be devoid of all tremor or movement. This is an exceptionally strenuous task as the human assistant is expected to maintain the same posture for up to 1 hour. This is extremely energy consuming and the fatigue experienced by the assistant increases the chances of tremor as time goes by.

For an optimal work flow, magnification is also required for the assistant. An assistant wearing loupes has the advantage of an open peripheral vision to arrange the instruments and to check the patient's facial expression during the operation. On the other hand, co-observer tubes allow the same view for surgeon and assistant, enabling the assistant

to point the suction tube to the right place and keep the view clear. This also becomes an issue during suturing when the air intake of the suction tube can easily suck the fine threads.

Lack of practice

When working with high magnification, the surgeon has to adjust to being a prisoner within a narrow field of view. A new coordination has to be sought between the surgeon's eyes and hands – an adjustment which can come only after much regular practice with simple surgical procedures. The practice unit consists of a microscope, micro instruments, and different suitable models. To start training, a two-dimensional model, such as rubber dam, is appropriate to learn how to manipulate the instruments, how to pick up the needles, and tying knots. After the initial training, working with three-dimensional models (fruits, eggs, chicken) helps the surgeon to get used to the restricted depth of the field.

Another aim of training is the reduction of tremor. Its physiologic basis is uncertain, but it is important to be aware of the causes in order to prevent it. An important factor is the body posture, which must be natural, with the spinal column straight and the forearms and hands fully supported. An adjustable chair, preferably with wheels, is recommended for the surgeon who should place himself in the most comfortable position. Tremor varies with individuals and even in the same individual it varies under different conditions. In some people, intake of coffee, tea or alcohol may increase tremor; in others, emotions, physical exercise, or the carrying of heavy weights can cause it.

After the completion of appropriate training when instrument handling has become automatic, the surgeon has adjusted to the new conditions and can now fully concentrate on the surgical procedure in clinical practice without taking additional time.

Clinical indications and limitations

The clinical benefits of a microsurgical approach in periodontal practice are mainly evaluated by case reports (Shanelec & Tibbetts 1994, 1996; Michaelides 1996; de Campos *et al*. 2006) and case–cohort studies (Cortellini & Tonetti 2001; Wachtel *et al*. 2003; Francetti *et al*. 2004). The different procedures described apply to the surgical coverage of buccal root recessions and flap closure after regenerative interventions. In both interventions, delicate soft tissue structures have to be manipulated during the surgery, which could be refined by selecting a less traumatic surgical approach. All of the studies confirmed the beneficial effects of the microsurgical approach. When covering a root recession, the vascularization of the injured tissues becomes critical as there is no blood supply from the underlying root surface. Frequently, coverage is performed by a connective tissue graft from the palate, which has different vascular characteristics compared to the supracrestal gingiva; supracrestal gingiva is the only tissue, naturally created and specifically designed, to survive and function over avascular root surfaces. As graft survival depends upon early plasmatic diffusion (Oliver *et al*. 1968; Nobutu *et al*. 1988), firm and stable flap or graft adaptation is of crucial importance to minimize the coagulum and facilitate the ingrowth of new vessels. A minimally traumatic approach allows more precise flap preparation and suturing with a reduction in tissue and vessel injuries, resulting in more rapid and more complete anastomosis of new capillary buds from the recipient bed with the existing, but severed, vessels of the graft or the flap.

The interdental gingiva is also a delicate tissue with a limited vascular network. As the gingival plexus does not extend interproximally, the central part of the interdental soft tissue is only supplied by vessels from the periodontal ligament space and arterioles that emerge from the crest of the interdental septa (Folke & Stallard 1967; Nuki & Hock 1974). These anatomic factors influence the wound-healing capacity of the tissues after surgical dissection and the small size of the structures (i.e. papilla or col) complicates a precise adaptation of the flap margins. Wound dehiscences, resulting in healing by secondary intention, are therefore a common finding after suturing the papilla in papilla-preservation techniques (Tonetti *et al*. 2004). Using microsurgery for a modified or simplified papilla preservation flap, primary wound closure could be noted in 92.3% of all treated sites 6 weeks after the intervention (Cortellini & Tonetti 2001).

Historic comparisons with studies performed by the same authors without the use of an operating microscope showed a clear advantage in the use of a microsurgical approach. Complete primary wound closure was observed in only 67% of the cases treated with a simplified (Cortellini *et al*. 1999), and in 73% of the cases treated with a modified papilla preservation flap (Cortellini *et al*. 1995). These results clearly demonstrated the improvement in tissue preservation and handling using a minimally invasive approach in order to achieve primary closure of the interdental space (Fig. 45-10).

A recently published case–cohort study, evaluating a new flap design for regeneration with enamel matrix derivates (MIST, *minimally invasive surgical technique*) combined with microsurgical techniques, confirmed the previous positive results, yielding a primary wound closure of the interdental tissues in all of the treated sites, 6 weeks post-operatively (Cortellini & Tonetti 2007) (Fig. 45-11).

Subjective observations of clinicians have found there is a less traumatic approach in periodontal surgery when magnification aids and fine suture materials are used. This ensures passive wound closure in most surgical interventions. This speculation

was recently substantiated by an *in vitro* experiment, which evaluated the tearing characteristics of mucosal tissue samples for various suture sizes and needle characteristics in relation to the applied tension forces (Burkhardt *et al*. 2006). The pig jaw mucosal tissue samples were attached in a test-tearing apparatus of a Swiss textile company and the tension tearing diagrams were traced for 3-0, 5-0, 6-0, and 7-0 sutures with forces up to 20 N. While the 3-0 sutures almost exclusively led to tissue breakage at an average of 13.4 N, the 7-0 sutures broke before tissues were torn in every instance, at an applied mean force of 3.6 N. With 5-0 and 6-0 sutures both events occured at random, at a mean force of 10 N. This means that a clinician can influence the amount of damage to the tissue by selecting thicker or thinner suture material. Considering this fact, it may be speculated that wound dehiscence can be prevented and passive flap adaptation can be improved by the choice of thinner sutures; this inevitably requires magnification if its benefits are to be fully appreciated.

The opponents of periodontal microsurgery often mention the adverse effect of a prolonged duration of the intervention while working with microscopes. It has been shown that the incidence and severity of complications and pain following periodontal surgery are correlated well with the duration of the surgical procedure (Curtis *et al*. 1985). It may be speculated that an extended operation time may compensate for the beneficial treatment effect of minimally invasive techniques. However, studies comparing micro- and macrosurgical approaches did not support such a hypothesis (Burkhardt & Lang 2005).

Considering all these facts there are no clinical contraindications for the use of magnification in periodontal surgery. From a user's point of view, only few areas in the oral cavity are difficult to access by an operating microscope which may limit its application. In these circumstances and in surgical interventions which require a frequent change of position, the use of loupes may be preferable.

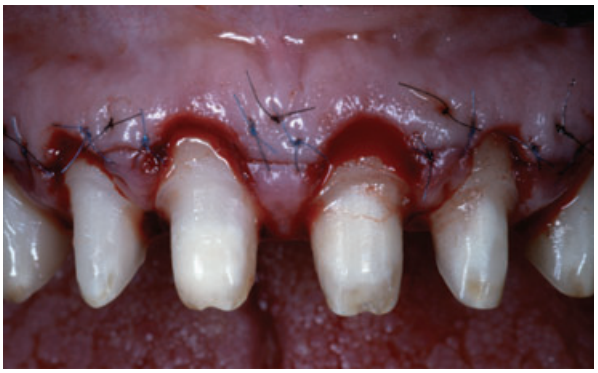

Fig. 45-10 Primary closure of the buccal papillae after a crown-lengthening procedure. Modified mattress sutures (vertically everting) with 7-0 polyamide thread (black) and two single-knot closures with 8-0 polypropylene threads (blue) in each interdental area.

Comparison to conventional mucogingival interventions

Today's *plastic periodontal surgery*, evolving from *mucogingival surgery*, includes all surgical procedures performed to prevent or correct anatomic, developmental, traumatic or disease-induced defects of the gingiva, alveolar mucosa or bone (Proceedings of the World Workshop in Periodontics 1996). To verify the beneficial effects of a microsurgical approach, the results after using a conventional technique in all the different indications have to be evaluated first. The variables to be used as descriptors of the therapeutic end-point of success may vary, depending on the specific goal of the mucogingival therapy. Some results, such as volume changes after ridge augmentation procedures, are clinically difficult to assess due to a lack of a defined end-point and are therefore documented in the literature by qualitative measurements only. Plastic surgical interventions with clearly defined landmarks for measurement, and thus well investigated in the literature, are the guided tissue regeneration procedures (Needleman *et al*. 2006) and the coverage of buccal root recessions (Roccuzzo

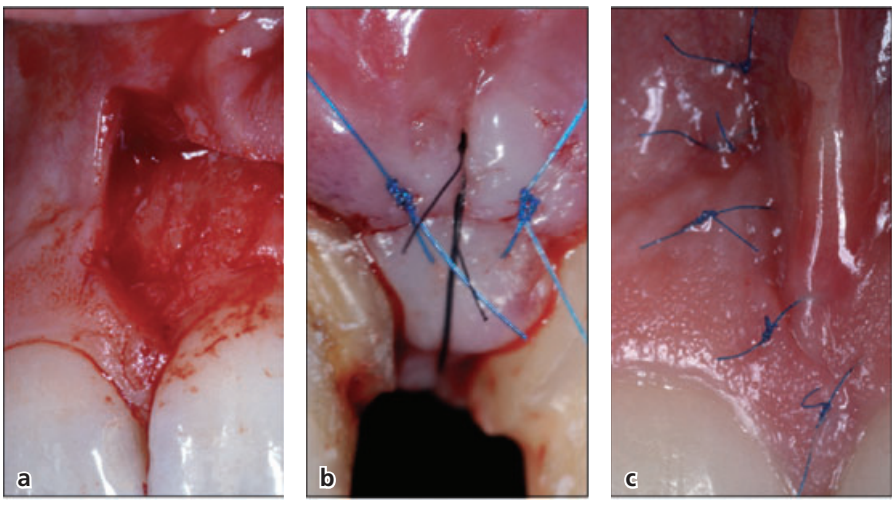

Fig. 45-11 Minimally invasive surgical technique (MIST) (Cortellini & Tonetti 2007). (a) Releasing incision, ending right-angled at the gingival margin. (b) Primary closure of the buccal papilla by a mattress suture (according to Laurell) with 7-0 polyamide thread (black) and two single-knot closures with 8-0 polypropylene threads (blue). (c) Clinical appearance of the releasing incision 4 days post-operatively.

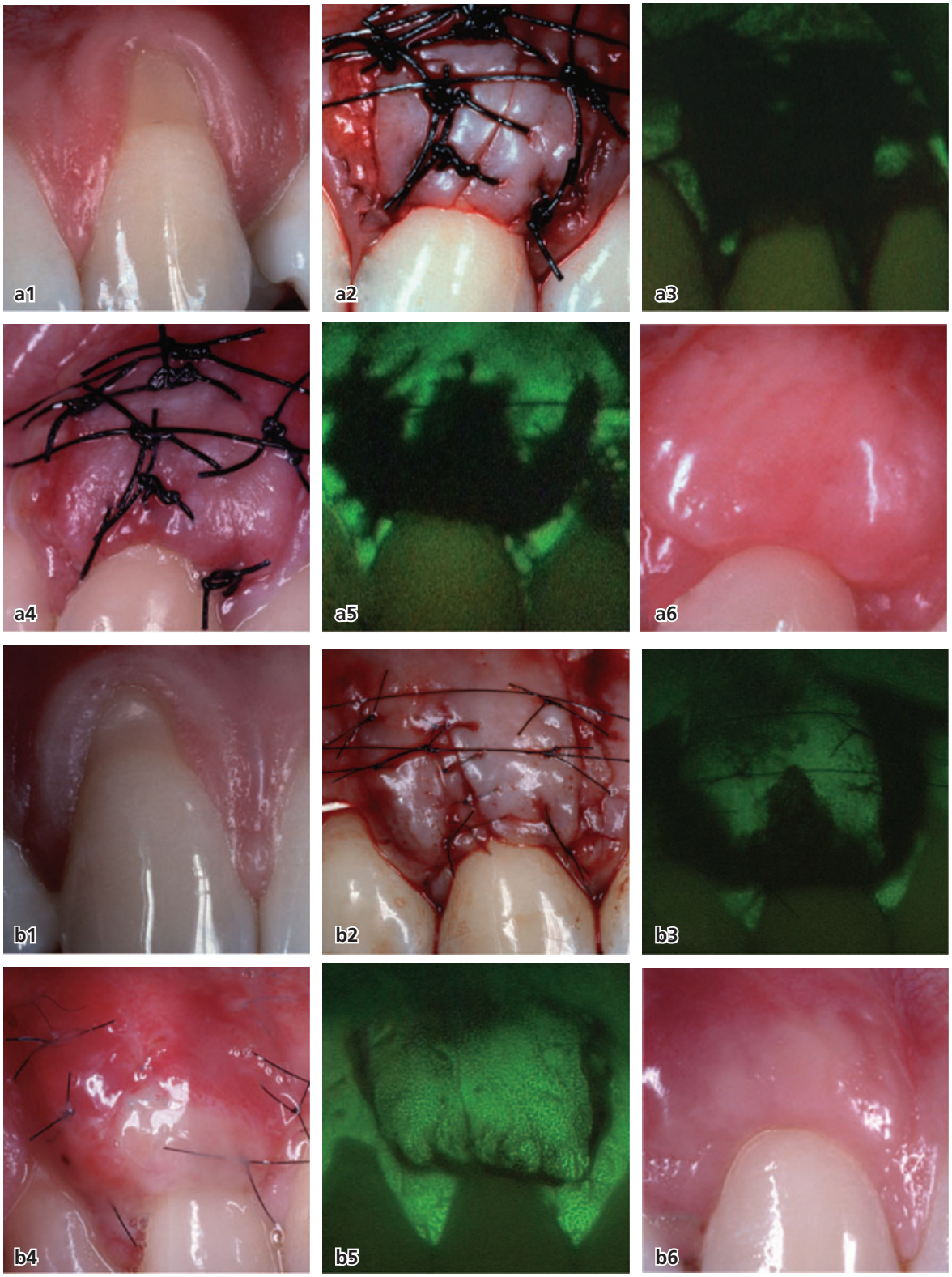

Fig. 45-12 Recession coverage: Macro- and microsurgery in comparison (Burkhardt & Lang 2005). (a) Macrosurgical recession coverage: (a1) pre-operative clinical situation; (a2) immediately after the surgical intervention; (a3) corresponding angiographic evaluation after the intervention; (a4) healing after 7 days; (a5) angiographic evaluation after 7 days; (a6) clinical situation after 3 months (visible contours of incision lines). (b) Microsurgical recession coverage: (b1) pre-operative clinical situation; (b2) immediately after the surgical intervention; (b3) corresponding angiographic evaluation after the intervention; (b4) healing after 7 days; (b5) angiographic evaluation after 7 days; (b6) clinical situation after 3 months (no traces of the intervention visible).

et al. 2002; Oates *et al*. 2003). While the former results in a reduction in probing measures, an improved attachment gain, and less increase in gingival recession compared to open flap debridement, the latter yields a significant reduction in recession depth and also an improvement in clinical attachment level measures. However there is a marked variability between the studies, indicating the influence of case selection, the materials used, the techniques applied, and the surgeons' dexterity. As a result, it is difficult to draw general conclusions because the factors affecting the outcomes are unclear from the literature and these might include study conduct issues such as bias. Among these factors, the dexterity of the surgeon ranks high and seems to influence the results strongly. It is a complicated, proprioceptive reflex involving eye, hand, and brain, and is therefore difficult to assess in clinical settings. To eliminate its influence and to estimate the magnitude of the real benefits of a microsurgical approach, micro- and macrosurgical techniques should be compared in controlled studies.

Concerning the coverage of mucosal recessions, a comparison between the two approaches (micro- and macrosurgery) has been performed in a randomized controlled clinical trial (Burkhardt & Lang 2005). The study population consisted of ten patients with bilateral class I and class II recessions at maxillary canines. In split-mouth design, the defects were randomly selected for recession coverage either by a microsurgical (test) or macrosurgical (control) approach. Immediately after the surgical procedures and after 3 and 7 days of healing, fluorescent angiograms were performed to evaluate graft vascularization. The results at test sites revealed a vascularization of 8.9 ± 1.9% immediately after the procedure. After 3 days and after 7 days, the vascularization rose to 53.3 ± 10.5% and 84.8 ± 13.5%, respectively. The corresponding vascularization at control sites were 7.95 ± 1.8%, 44. 5 ± 5.7%, and 64.0 ± 12.3%, respectively (Fig. 45-12). All the differences between test and control sites were statistically significant.

In addition, the clinical parameters were assessed before the surgical intervention, and 1, 3, 6, and 12 months post-operatively. The clinical measurement revealed a mean recession coverage of 99.4 ± 1.7% for the test and 90.8 ± 12.1% for the control sites after the first month of healing. Again, this difference was statistically significant. The percentage of root coverage in both test and control sites remained stable during the first year, at 98% and 90%, respectively.

The present clinical experiment has clearly demonstrated that mucogingival surgical procedures designed for the coverage of exposed root surfaces, performed using a microsurgical approach, improved the treatment outcomes substantially and to a clinically relevant level when compared with the clinical performance under routine macroscopic conditions. However, the choice of micro- and macrosurgical approaches must be seen in different lights, including treatment outcomes, logistics, cost, and patient-centered parameters. Future comparative studies will produce the evidence whether the use of the surgical microscope will further increase surgical effectiveness and thus become an indispensable part of periodontal surgical practice.

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Chapter 46

Re-osseointegration

Tord Berglundh and Jan Lindhe

Introduction

In Chapter 24 (Peri-implant Mucositis and Peri-implantitis) important features of inflammatory lesions in the peri-implant tissues were described. Peri-implantitis is defined as a progressive inflammatory process that involves the mucosa and the bone tissue at an osseointegrated implant in function, and that this process results in loss of osseointegration and supporting bone (Fig. 46-1).

In Chapter 41 (Treatment of Peri-implant Lesions) it is emphasized that peri-implantitis is associated with the presence of submarginal deposits of plaque and calculus and that the successful treatment of the condition must include (1) comprehensive debridement of the implant surface and (2) subsequent interceptive supportive therapy including professional and self-performed plaque removal measures.

An obvious, additional goal in the treatment of peri-implantitis is the regeneration and *de novo* bone formation, i.e. "re-osseointegration", at the portion of the implant that lost its "osseointegration" in the inflammatory process. Furthermore, since the level of the peri-implant mucosa is dependent on the level of the marginal bone, an increase of the height of the osseous tissue will result in a marginal shift of the mucosa. Soft tissue esthetics may also be enhanced, therefore, through re-osseointegration.

Is it possible to resolve a marginal hard tissue defect adjacent to an oral implant?

Non-contaminated, pristine implants at sites with a wide marginal gap (crater)

Peri-implantitis lesions are per definition associated with bone loss and loss of osseointegration. The pattern of bone loss is angular and the ensuing defect often has the shape of a marginally open crater.

Findings from animal experiments and fracture healing suggested that hard tissue bridging, through woven bone formation, may occur in a bone defect provided that the distance between the fracture lines was ≤1 mm (Schenk & Willenegger 1977). This concept was translated to implant dentistry. Thus, it was implied that if a large (>1 mm) marginal defect were present between a newly installed oral implant and the host bone of the alveolar process, osseointegration would become compromised (Wilson *et al.* 1998, 2003).

Results presented by Botticelli *et al.* (2004) challenged this hypothesis. In a human study that included implant placement in fresh extraction sockets, they were able to demonstrate that a large void (gap) between the newly installed implant and the socket walls could become completely resolved

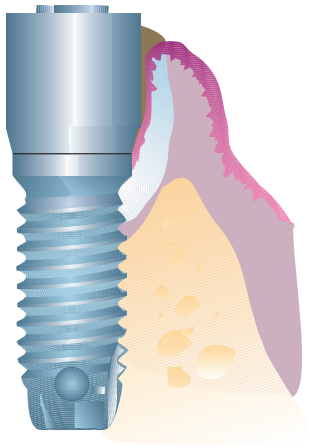

Fig. 46-1 Schematic drawing illustrating characteristics of peri-implantitis including the inflammatory lesion and the associated bone defect.

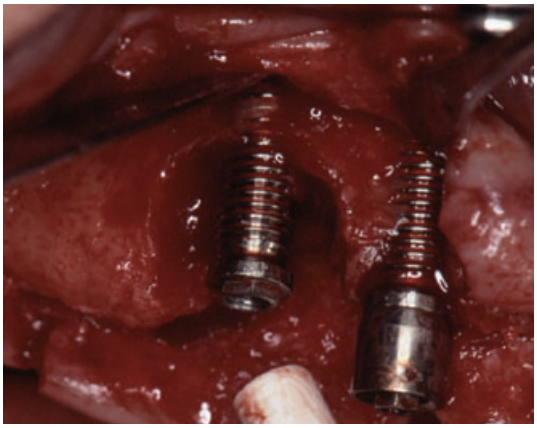

Fig. 46-2 Clinical photograph from a peri-implantitis site following flap elevation. Granulation tissue was removed and the implant surface was cleaned. The decision on whether a regenerative procedure may be considered is based on the morphology of the crater-like bone defect.

within a 4-month period. Furthermore, in animal experiments Botticelli *et al*. (2003a,b, 2005, 2006) produced – by mechanical means – large hard tissue defects in the marginal portion of edentulous sites prior to implant installation. The authors reported that (1) the presence of the wide marginal defect *per se* was not an impediment for osseointegration, (2) depending on the surface characteristics of the implant, complete resolution of the defect occurred within a 4-month period, and (3) bone fill in the defect was always the result of appositional osteogenesis.

Contaminated implants and crater-shaped bone defects

Experimental model

In order to study the ability of the tissues in the peri-implant defect to regenerate and to establish *de novo* bone tissue deposition on the contaminated implant surface, a research model was developed. The model was used to induce well defined peri-implantitis lesions in the dog (Lindhe *et al*. 1992) or in the monkey (Lang *et al*. 1993; Schou *et al*. 1993) and is described in detail in Chapter 24.

Re-osseointegration

"Re-osseointegration" can be defined as the establishment of *de novo* bone formation and *de novo* osseointegration to a portion of an implant that during the development of peri-implantitis suffered loss of bone-to-implant contact and became exposed to microbial colonization (alt. the oral environment) (Fig. 46-2). A treatment procedure that aims at re-osseointgration must (1) ensure that substantial regeneration of bone from the walls of the defect can occur and (2) "re-juvenate" the contaminated (exposed) implant surface.

Is re-osseointegration a feasible outcome of regenerative therapy?

Regeneration of bone from the walls of the defect

Persson *et al*. (1999) induced peri-implant tissue breakdown in beagle dogs according to the Lindhe model referred to above (Lindhe *et al*. 1992). Mandibular premolars were extracted, socket healing allowed, and fixtures (Brånemark System®) with a turned surface were placed and submerged. Abutment connection was performed after 3 months. When the mucosa surrounding all implants had attained a clinically normal appearance, plaque accumulation was allowed and ligatures (cotton floss) were placed around the neck of the implants and retained in a position close to the abutment/fixture junction. After 3 months when the soft tissue exhibited signs of severe inflammation and deep crater-like defects had formed in the peri-implant bone compartments, the ligatures were removed (Fig. 46-3a). Treatment was performed and included (1) systemic administration of antibiotics (amoxicillin and metronidazole for 3 weeks), (2) elevation of full-thickness flaps at the experimental sites and curettage of the hard tissue defect, (3) mechanical debridement of the exposed portion of the implants, (4) removal of the abutment portions of the implants and placement of pristine cover screws, and finally (5) flap management and closure of the soft tissue wound. Radiographs and biopsies were obtained after 7 months of submerged healing. The analysis of the radiographs indicated a complete bone fill in the hard tissue defects (Fig. 46-3b). The histologic analysis of the biopsy sections revealed that treatment had resulted in (1) a complete resolution of the soft tissue inflammation and (2) the formation of substantial

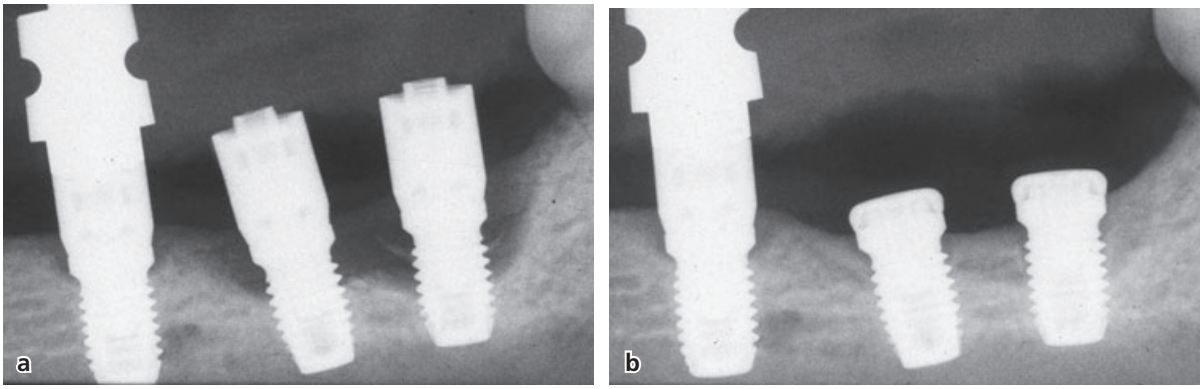

Fig. 46-3 (a) Radiographs obtained from two sites exposed to experimental peri-implantitis. (b) The sites in (a) at 7 months of submerged healing after treatment of peri-implantitis. Note the bone fill in the previous osseous defects.

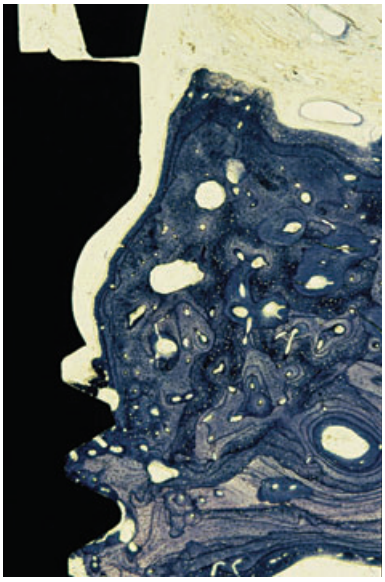

Fig. 46-4 Ground section representing 7 months of submerged healing after treatment of peri-implantitis. Note the newly formed bone in the hard tissue defects.

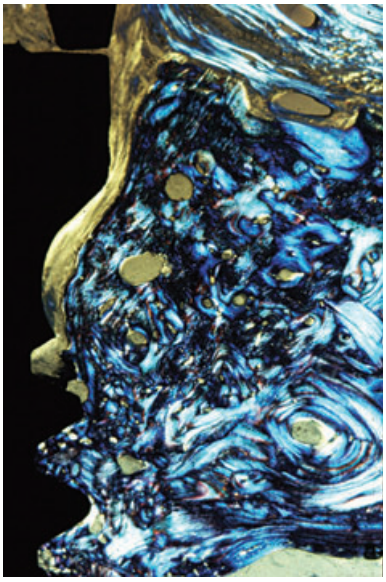

Fig. 46-5 The ground section in Fig. 46-4 in polarized light. Note the connective tissue capsule located between the newly formed bone and the implant surface.

amounts of new bone (appositional osteogenesis) in the previous hard tissue defects (Fig. 46-4). However, only small amounts of "re-osseointegration" to the decontaminated titanium surface could be observed and consistently only at the apical base of the defects. In most sites a thin connective tissue capsule separated the "exposed" implant surface from the newly formed bone (Fig. 46-5). Similar findings were reported by Wetzel *et al*. (1999) from another study in the beagle dog and the use of implants with various surface characteristics (turned, plasma sprayed, and sandblasted–etched surfaces).

Conclusion: Based on the outcome of the above studies it was concluded (1) that the inflammatory lesions in experimentally induced peri-implantitis can be resolved, (2) that *de novo* bone formation (appositional growth) predictably will occur from the hard tissue walls of the defect, and (3) that often the large defects may become more or less completely filled with new bone following a treatment that is based on antimicrobial measures. Hence, the problem inherent in re-osseointegration appears to be the implant surface rather than the host tissues at the site.

"Rejuvenate" the contaminated implant surface

Different techniques have been proposed for a local therapy aimed at "rejuvenating" the once contaminated implant surface. Such techniques have included mechanical brushing of the surface, the use of air–powder abrasives, and the application of chemicals such as citric acid, hydrogen peroxide, chlorhexidine, and delmopinol (Persson *et al*. 1999; Wetzel *et al*. 1999; Kolonidis *et al*. 2003). These local therapies were effective in cleaning the titanium surface and allowing soft tissue healing and bone fill in the bone craters, but only limited amounts of re-osseointegration occurred.

Is the quality of the implant surface important in a healing process that may lead to re-osseointegration?

The surface of the metal device in the compromised implant site

It is well known that pristine implants made of commercially pure titanium are covered with a thin layer of titanium dioxide (Kasemo & Lausmaa 1985, 1986). This dioxide layer gives the implant a high surface energy that facilitates the interaction between the implant and the cells of the host tissues. Contamination of a titanium surface, however, alters its quality and an implant with a low surface energy results. Such a surface may not allow tissue integration to occur but may instead provoke a foreign body reaction (Baier & Meyer 1988; Sennerby & Lekholm 1993).

The problem regarding the implant surface was addressed a dog study (Persson *et al*. 2001a) in which pristine implant parts were placed in crater-like bone defects that had developed during "experimental peri-implantitis" (a.m. Lindhe *et al*. 1992). The test implants used were comprised of two separate parts, one 6 mm long apical and one 4 mm long marginal part, that were joined together via a connector. During surgical therapy following experimental peri-implantitis, the marginal portions of the implants were removed and replaced with pristine analogues. In biopsies obtained after 4 months of healing it was observed that new bone had formed in the crater-like defects and that "re-osseointegration" had occurred to a large area of the pristine implant components.

In an experiment in the dog, Persson *et al*. (2001b) evaluated the potential for "re-osseointegration" to implants designed with either smooth (polished) or roughened (SLA; sandblasted, large grit acid etched) surfaces. Custom-made solid screw implants were placed in the edentulous mandible; in the right side implants with a rough, SLA surface (Fig. 46-6) and in the left side implants with a smooth surface (Fig. 46-7). "Experimental peri-implantitis" was induced and then blocked when about 50% of the peri-implant bone support was lost (Fig. 46-8a). Treatment included (1) systemic antibiotics (amoxicillin and metronidazole for 17 days), (2) flap elevation and curettage of the bone defect, and (3) mechanical debridement of the implant surface (cotton pellets soaked in saline). The implants were submerged and biopsies obtained after 6 months of healing. In all implant sites most of the crater-like defects had been filled with newly formed bone (Fig. 46-9b). However, at sites with smooth surface implants only small amounts of "re-osseointegration" (Fig. 46-10) had occurred. Examination of the histologic sections from sites with rough surface implants, however, revealed that >80% of the previously exposed rough surface exhibited "re-osseointegration" (Fig. 46-11).

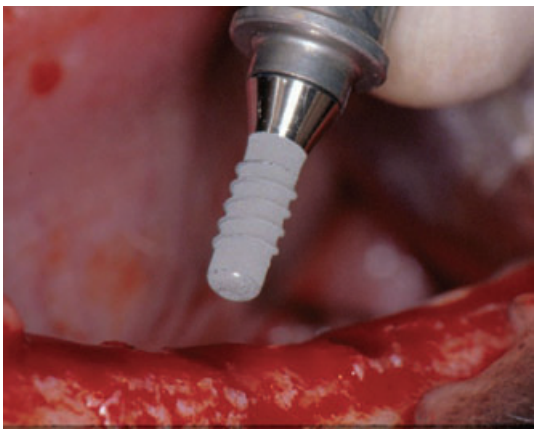

Fig. 46-6 Custom-made implant with a roughened (SLA) surface.

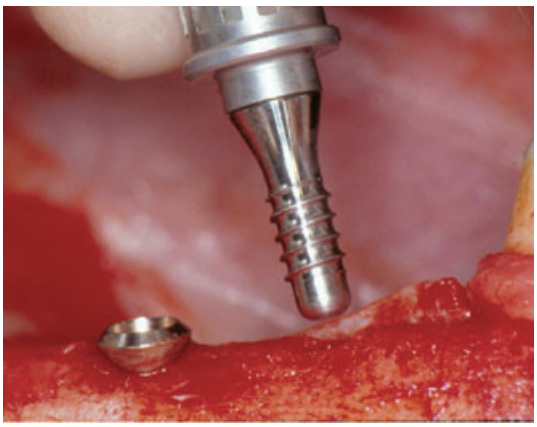

Fig. 46-7 Custom-made implant with a smooth (polished) surface.

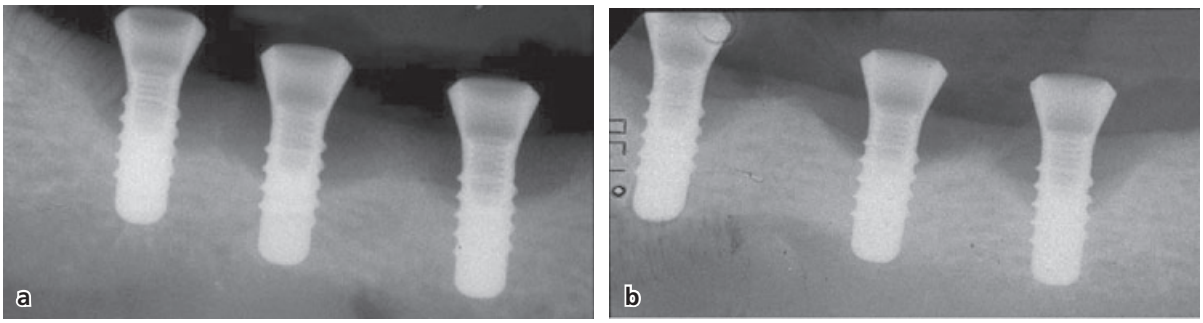

Fig. 46-8 Radiographs illustrating crater-like bone defects following experimental peri-implantitis at implants with a rough (a) and smooth (b) surface.

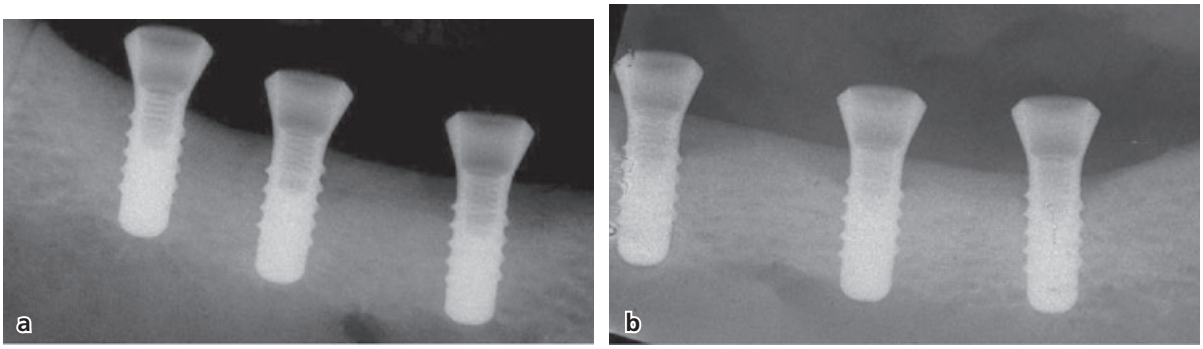

Fig. 46-9 Radiographs illustrating substantial bone-fill in bone defects at 6 months of healing after treatment of experimental peri-implantitis at implants with a rough (a) and smooth (b) surface.

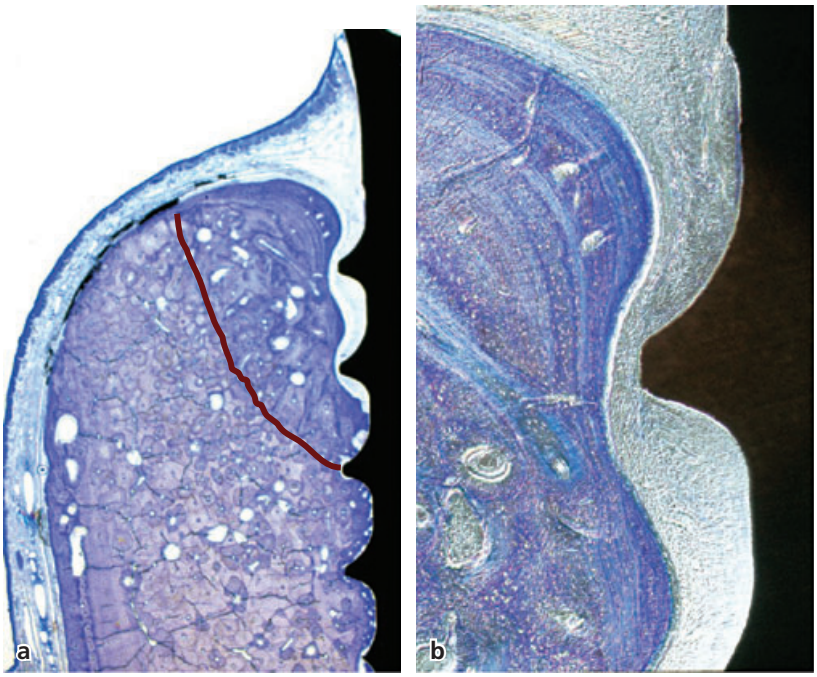

Fig. 46-10 (a) Ground section representing 6 months of healing after treatment of peri-implantitis at sites with smooth surface implants. The red line indicates the outline of the previous hard tissue defect. (b) Note the connective tissue capsule between the newly formed bone and the implant surface.

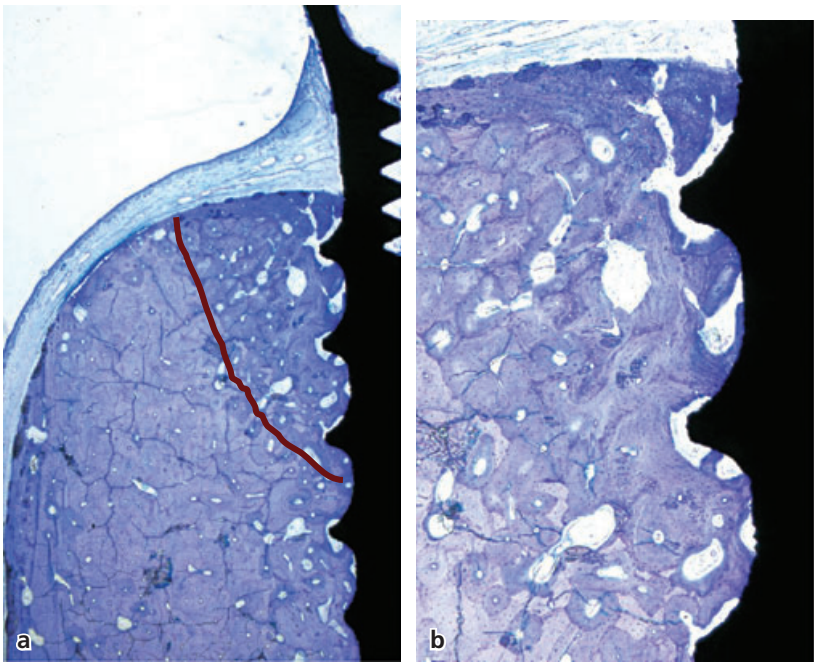

Fig. 46-11 (a) Ground section representing 6 months of healing after treatment of peri-implantitis at sites with rough surface implants. The red line indicates the outline of the previous hard tissue defect. (b) Note the high degree of re-osseointegration to the previously exposed rough implant surface.

Conclusion: Based on the above documentation it is proposed that the rough implant surface may have contributed to a better stability of the blood clot in the bone crater. In addition, during the phase of contraction of the coagulum and formation of granulation tissue, the rough surface may have ensured a continued contact between the newly formed immature tissue and the implant. This upheld contact relationship may, in turn, have facilitated the subsequent formation of a provisional matrix, an osteoid, and eventually woven bone (see Chapter 4). The maintained contact may thus have made possible the bridging of the gap between the walls of the hard tissue crater and the previously exposed implant surface.

In this context it is important to point out that the surface characteristics (smooth vs. rough) of the implant may also influence the risk for a rapid progression of peri-implantitis once initiated (see Chapter 24). Thus, in an experimental study in dogs Berglundh *et al*. (2007) demonstrated that progression of peri-implantitis was more pronounced at implants with a rough (SLA) than with a smooth (polished) surface.

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Part 14: Surgery for Implant Installation

Chapter 47

Timing of Implant Placement

Christoph H.F. Hämmerle, Maurício Araújo, and Jan Lindhe

Introduction

Restorative therapy performed on implant(s) placed in a fully healed and non-compromized alveolar ridge, has high clinical success and survival rates (Pjetursson *et al*. 2004). Currently, however, implants are also being placed in (1) sites with ridge defects of various dimensions, (2) fresh extraction sockets, (3) the area of the maxillary sinus, etc. Although some of these clinical procedures were first described many years ago, their application has only recently become common. Accordingly one issue of primary interest in current clinical and animal research in implant dentistry includes the study of tissue alterations that occur following tooth loss and the proper timing thereafter for implant placement.

In the optimal case, the clinician will have time to plan for the restorative therapy (including the use of implants) prior to the extraction of one or several teeth. In this planning, a decision must be made whether the implant(s) should be placed immediately after the tooth extraction(s) or if a certain number of weeks (or months) of healing of the soft and hard tissues of the alveolar ridge should be allowed prior to implant installation. The decision regarding the timing for implant placement, in relation to tooth extraction, must be based on a proper understanding of the structural changes that occur in the alveolar process following the loss of the tooth (teeth). Such adaptive processes were described in Chapter 2.

The removal of single or multiple teeth will result in a series of alterations within the edentulous segment of the alveolar ridge. Hence during socket healing the hard tissue walls of the alveolus will resorb, the center of the socket will become filled with cancellous bone and the overall volume of the site will become markedly reduced. In particular, the buccal wall of the edentulous site will be diminished not only in the bucco-lingual/palatal direction but also with respect to its apico-coronal dimension (Pietrokovski & Massler 1967; Schropp *et al*. 2003). In addition to hard tissue alterations, the soft tissue in the extraction site will undergo marked adaptive changes. Immediately following tooth extraction, there is a lack of mucosa and the socket entrance is thus open. During the first weeks following the removal of a tooth, cell proliferation within the mucosa will result in an increase of its connective tissue volume. Eventually the soft tissue wound will become epithelialized and a keratinized mucosa will cover the extraction site. The contour of the mucosa will subsequently adapt to follow the changes that occur in the external profile of the hard tissue of the alveolar process. Thus, the contraction of the ridge is the net result of bone loss as well as loss of connective tissue. Figure 47-1 presents a schematic drawing illustrating the tissue alterations described above. It is obvious that no ideal time point exists following the removal of a tooth, at which the extraction site presents with (1) maximum bone fill in the socket and (2) voluminous mature covering mucosa.

A consensus report was published in 2004, describing issues related to the timing of implant placement in extraction (Hammerle *et al*. 2004). Attempts had previously been made to identify advantages and disadvantages with early, delayed, and late implant placements. Hämmerle and coworkers considered it

necessary, however, to develop a new concept (classification) that incorporated the growing knowledge in this field of implant dentistry. This new classification took into consideration data describing structural alterations that occur following tooth extraction as well as knowledge derived from clinical observations.

The classification presented in Table 47-1 was introduced in the consensus report. Important aspects of this new classification included the following:

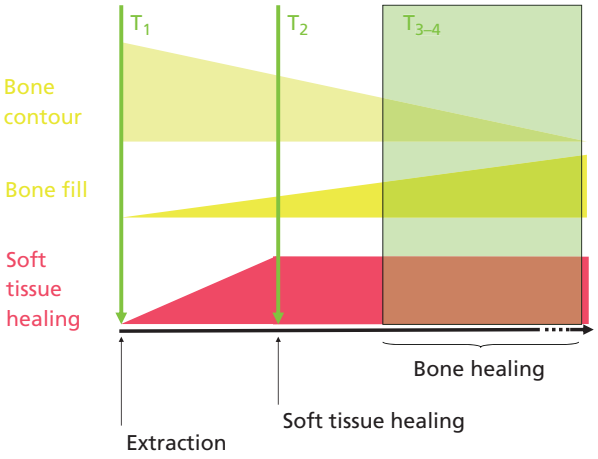

Fig. 47-1 Schematic drawing depicting the changes in the soft and hard tissues following tooth extraction over time. $T_{1–4}$ represent the four different time points regarding timing for implant placement.

- In clinical practice the decision to place an implant following tooth extraction is usually determined by some soft and hard tissue characteristics of the healing socket. Healing does not necessarily follow rigid time frames, and may vary according to site and patient factors.
- To avoid temporal-based descriptions, this new classification used numerical descriptors – types 1, 2, 3, and 4 – that reflect the conditions of the hard and soft tissues:
  - Type 1 placement: the implant is placed immediately following the extraction of a tooth
  - Type 2 placement: the implant is placed in a site where the soft tissues have healed and a mucosa is covering the socket entrance
  - Type 3 placement: the implant is placed in an extraction site at which substantial amounts of new bone have formed in the socket
  - Type 4 placement: the implant is placed in a fully healed ridge
- It was further recognized that there is a clear separation between hard tissue healing and soft tissue healing within and around the extraction socket.

Advantages and disadvantages with the various timings are presented in Table 47-1.

Two methods for flap closure have been described at implant sites. One approach requires primary would closure, whereas the other one allows for a

Table 47-1 Classification types 1–4, descriptive definition as well as advantages and disadvantages of each type

Classification	Definition	Advantages	Disadvantages
Type 1	Implant placement as part of the same surgical procedure and immediately following tooth extraction	Reduced number of surgical procedures Reduce overall treatment time Optimal availability of existing bone	Site morphology may complicate optimal placement and anchorage Thin tissue biotype may compromise optimal outcome Potential lack of keratinized mucosa for flap adaptation Adjunctive surgical procedures may be required Technique-sensitive procedure
Type 2	Complete soft tissue coverage of the socket (typically 4–8 weeks)	Increased soft tissue area and volume facilitates soft tissue flap management Allows resolution of local pathology to be assessed	Site morphology may complicate optimal placement and anchorage Increased treatment time Varying amounts of resorption of the socket walls Adjunctive surgical procedures may be required Technique-sensitive procedure
Type 3	Substantial clinical and/or radiographic bone fill of the socket (typically 12–16 weeks)	Substantial bone fill of the socket facilitates implant placement Mature soft tissues facilitate flap management	Increased treatment time Adjunctive surgical procedures may be required Varying amounts of resorption of the socket walls
Type 4	Healed site (typically >16 weeks)	Clinically healed ridge Mature soft tissues facilitate flap management	Increased treatment time Adjunctive surgical procedures may be required Large variation in available bone volume

transmucosal position of the implant or the healing cap. No differences regarding survival rates and interproximal bone levels were found when these two methods were compared in a split-mouth design (Ericsson *et al*. 1997; Astrand *et al*. 2002; Cecchinato *et al*. 2004). These studies did, however, not analyze in detail the differences between submerged or transmucosal healing in sites of high esthetic importance. Hence, not only the width of the gap but also the width of the alveolar ridge are parameters to be considered during treatment planning.

Type 1: placement of an implant as part of the same surgical procedure and immediately following tooth extraction

Ridge corrections in conjunction with implant placement

It has become common to insert implants immediately after the removal of teeth that were scheduled for extraction for various reasons. Over the years, many claims have been made regarding advantages of immediate implant placement (Chen *et al*. 2004). These advantages include easier definition of the implant position, reduced number of visits in the dental office, reduced overall treatment time and costs, preservation of bone at the site of implantation, optimal soft tissue esthetics, and enhanced patient acceptance (Werbitt & Goldberg 1992; Barzilay 1993; Schwartz-Arad & Chaushu 1997a; Mayfield 1999; Hammerle *et al*. 2004).

It was proposed that placement of an implant in a fresh extraction socket may stimulate bone tissue formation and osseointegration and hence counteract the adaptive alterations that occur following tooth extraction. In other words, type 1 implant installation may allow the preservation of bone tissue of the socket and the surrounding jaw. It was in fact recommended (e.g. Denissen *et al*. 1993; Watzek *et al*. 1995; for review see Chen *et al*. 2004) that implant installation should be performed directly following tooth extraction as a means to avoid bone atrophy.

Clinical studies in man (Botticelli *et al*. 2004; Covani *et al*. 2004) and experiments in dogs (Araujo & Lindhe 2005; Araujo *et al*. 2006a,b) have examined the influence of implant installation in the fresh extraction socket on bone modeling and remodeling in the surgical site.

Botticelli *et al*. (2004) examined hard tissue alterations that occurred in the alveolar ridge during a 4-month period of healing following implant placement in fresh extraction sockets. Eighteen subjects (21 extraction sites) with moderate chronic periodontitis were studied. The treatment planning of all 18 subjects called for extraction of single teeth, and restoration by means of implants in the incisor, canine, and premolar regions of the dentition.

Following sulcus incisions, full-thickness mucosal flaps were raised and the tooth was carefully mobilized and removed with forceps. The site was prepared for implant installation with the use of pilot and twist drills. The apical portion of the socket was pre-tapped. A non-cutting solid screw implant (Straumann®; Basel, Switzerland) with a rough surface topography was installed. The implant was positioned in such a way that the marginal level of its rough surface portion was located apical of the marginal level of the buccal and lingual/palatal walls of the socket (Fig. 47-2a). After implant installation (1) the distance between the implant and the inner and outer surface of the buccal and/or lingual bone plates, and (2) the width of the marginal gap that was present between the implant and the buccal, lingual, mesial, and distal bone walls were determined with the use of sliding calipers.

The soft tissue flaps were replaced and the implants were "semi-submerged" during healing (Fig. 47-2b). After 4 months of healing a surgical re-entry procedure was performed (Fig. 47-2c). The clinical measurements were repeated so that alterations that had occurred during healing regarding (1) the thickness and height of the buccal and lingual/palatal socket walls and (2) the width of the marginal gap could be calculated.

Figure 47-3a presents a photograph of an extraction socket immediately after the removal of a maxillary canine tooth. At re-entry it was realized that the

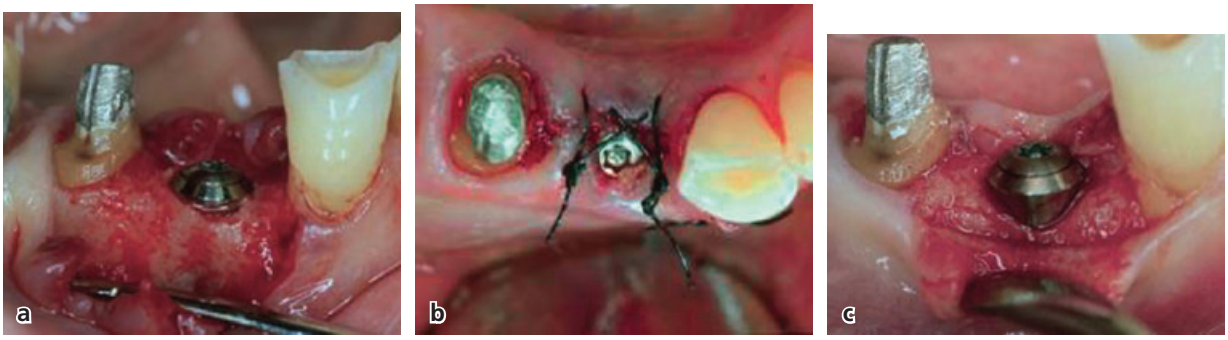

Fig. 47-2 (a) Clinical view of the implant position in the fresh extraction socket. (b) Clinical view of the flaps replaced and sutured. (c) Clinical buccal view of the implant site after 4 months of healing.

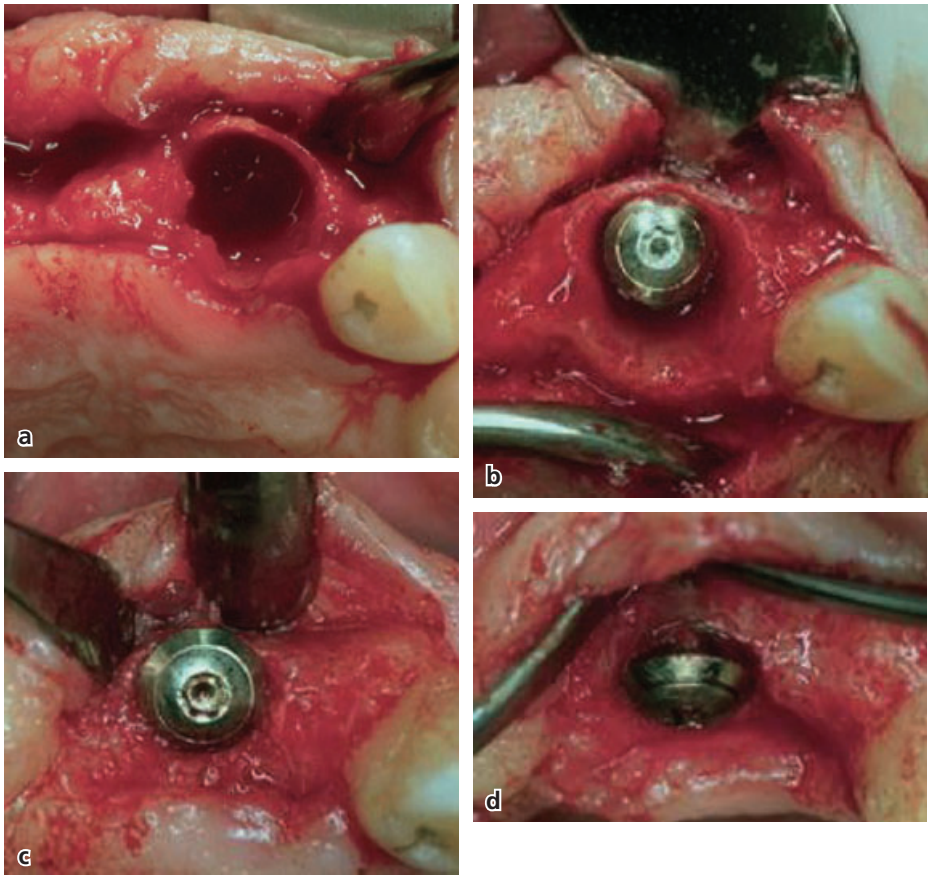

Fig. 47-3 (a) Clinical view of the alveolar socket of a maxillary canine. (b) Clinical view of the implant position in the fresh extraction socket. (c) Clinical occlusal view of the implant site after 4 months of healing. (d) Clinical buccal view of the implant site after 4 months of healing. Note the very thin bone covering the buccal aspect.

marginal gap had completely resolved. Furthermore, the thickness of the buccal as well as the palatal bone walls had become markedly reduced (Fig. 47-3c,d). In Fig. 47-3d the implant surface can be seen through the very thin remaining buccal bone wall.

Another site from this clinical study is presented in Fig. 47-4. The first maxillary premolar (tooth 14) was removed (Fig. 47-4a) and one implant was placed in the palatal socket of the fresh extraction site. A second implant was placed in the healed edentulous ridge and in position 25 (Fig. 47-4b). At re-entry, it was observed that (1) the marginal gap had been entirely resolved and (2) the distance between the implant and the outer surface of the buccal bone plate had become markedly reduced (Fig. 47-4c).

Botticelli *et al*. (2004) reported that during the 4 months of healing following tooth extraction and implant installation practically all marginal gaps had become resolved. At the time of implant placement, the mean distance (18 subjects, 21 sites) between the implant and the outer surface of the buccal bone wall was 3.4 mm while the matching dimension on the lingual/palatal aspect was 3.0 mm. At re-entry after 4 months, the corresponding dimensions were 1.5 mm (buccal) and 2.2 mm (lingual). In other words, the reduction of the buccal dimension was 1.9 mm (or 56%) while the equivalent reduction of the lingual dimension was 0.8 mm (or 27%).

The findings by Botticelli *et al*. (2004) strongly indicate that implant placement in a fresh extraction socket may, in fact, not prevent the physiologic modeling/remodeling that occurs in the ridge following tooth removal.

In order to study bone modeling/remodeling that occurs in the fresh extraction site following implant placement in more detail, Araújo and Lindhe (2005) performed an experiment in the dog. In this study the authors used histologic means to determine the magnitude of the dimensional alterations that occurred in the alveolar ridge following the placement of implants in fresh extraction sockets. Buccal and lingual full-thickness flaps were elevated in both quadrants of the mandible of beagle dogs. The distal roots of the 3rd and 4th premolars were removed (Fig. 47-5a). In the right jaw quadrants, implants (solid screw, Straumann®, Basel) with a rough surface were placed in the sockets so that the marginal border of the rough surface was below the buccal and lingual bone margin (Fig. 47-5b). The flaps were replaced to allow a "semi-submerged" healing (Fig. 47-5c). In the left jaws the corresponding sockets were left without implantation and the extraction sockets were fully submerged under the mobilized flaps (Fig. 47-5d).

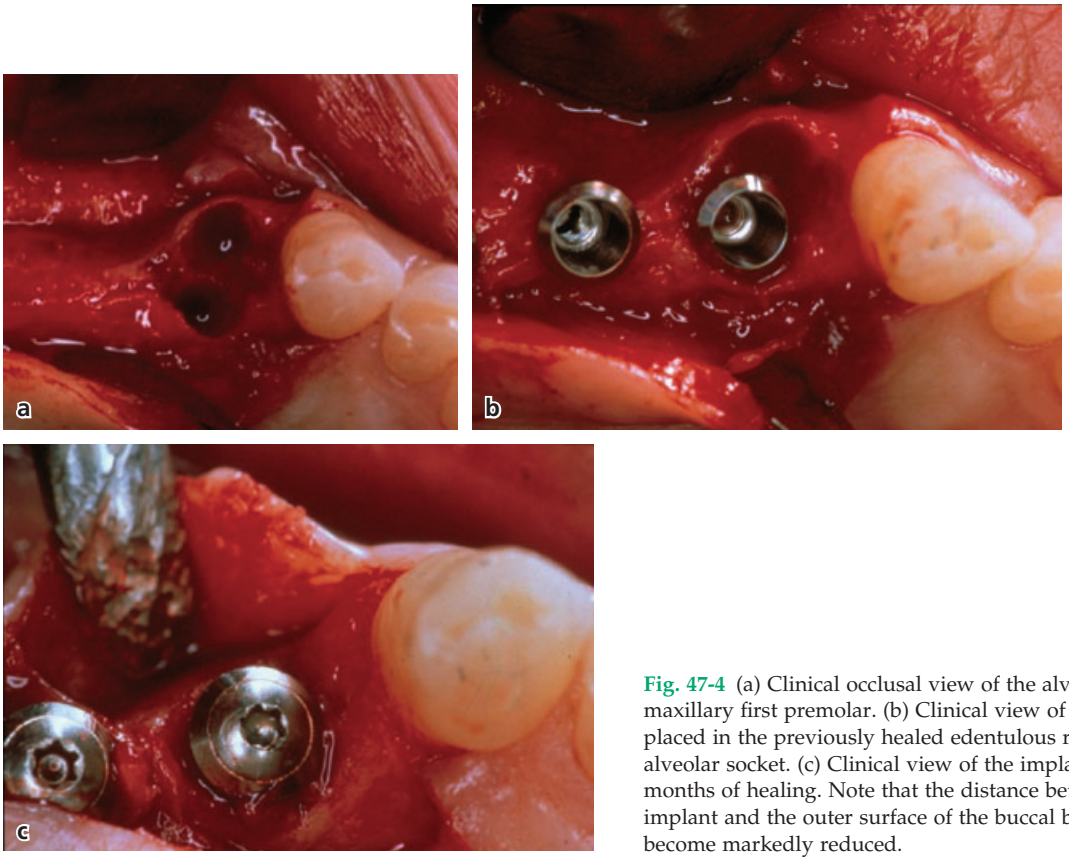

Fig. 47-4 (a) Clinical occlusal view of the alveolar socket of a maxillary first premolar. (b) Clinical view of the implants placed in the previously healed edentulous ridge and in the alveolar socket. (c) Clinical view of the implant sites after 4 months of healing. Note that the distance between the implant and the outer surface of the buccal bone plate had become markedly reduced.

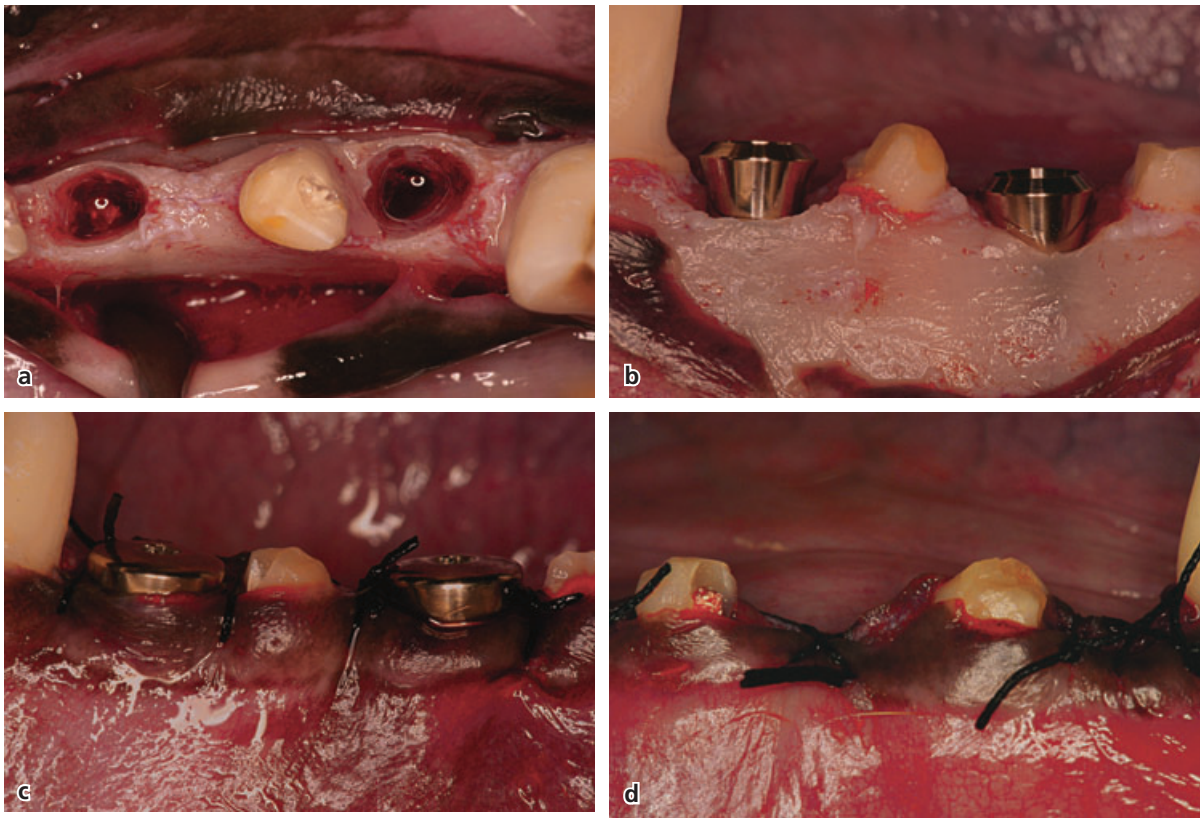

Fig. 47-5 (a) Photograph illustrating a mandibular premolar site (from a dog experiment) from which the distal root of the 4th premolar was removed. (b) In the test side of the mandible, the implant was placed in the socket in such way that the rough surface marginal limit was flush with the bone crest. (c) The mucosal, full-thickness flaps were replaced and sutured to allow a "semi-submerged" healing. (d) In the contralateral side of the mandible, the sockets were left without implantation.

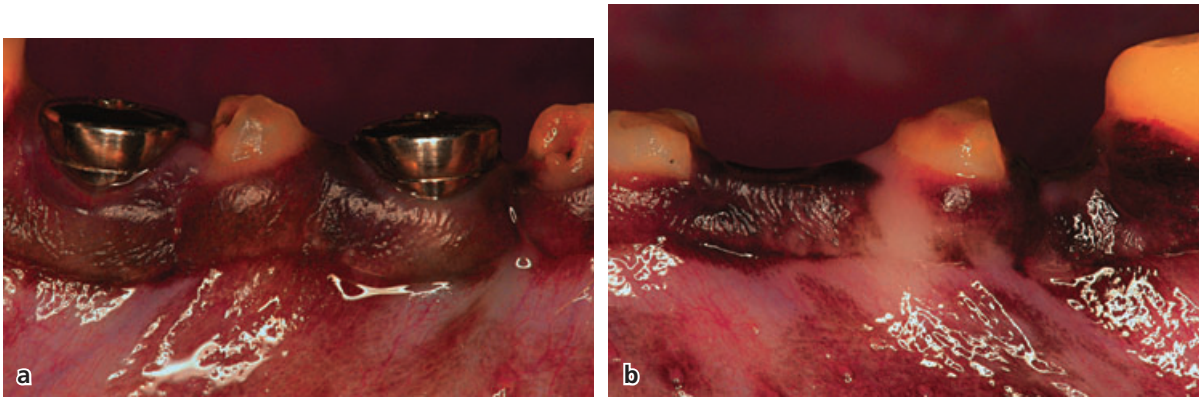

Fig. 47-6 Photograph illustrating the implant (a) and edentulous (b) sites after 6 months of healing.

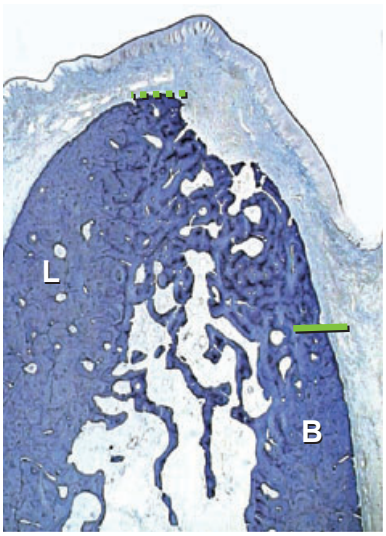

Fig. 47-7 Buccal–lingual section of the edentulous site. Note that the remaining buccal crest (continuous line) is located far below the lingual counterpart (dotted line). B = buccal aspect; L = lingual aspect.

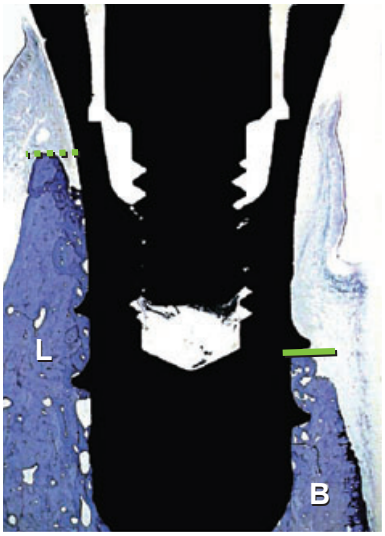

Fig. 47-8 Buccal–lingual section of the implant site. Note that the remaining buccal crest (continuous line) is located far below the lingual counterpart (dotted line). B = buccal aspect; L = lingual aspect.

After 3 months, the mucosa at the experimental sites in the right and left jaw quadrants appeared properly healed (Fig. 47-6). The animals were sacrificed and tissue blocks containing the implant sites and the edentulous socket sites were dissected and prepared for histologic examination.

Figure 47-7 presents a buccal–lingual section of one edentulous site after 3 months of healing. Newly formed bone is covering the entrance of the socket. The lamellar bone of the buccal, cortical plate is located about 2.2 mm apical of its lingual counterpart. Figure 47-8a presents a similar section from an implant site in the same dog. The marginal termination of the buccal bone plate is located about 2.4 mm apical to the lingual crest. In other words, the placement of an implant in the fresh extraction socket failed to influence the process of modeling that occurred in the hard tissue walls of the socket following tooth removal. Thus, after 3 months of healing the amount of reduction of the height of the buccal bone wall (in comparison to lingual bone alteration) was similar at the implant sites and the edentulous sites. At 3 months, the vertical discrepancy between the buccal and lingual bone margins was >2 mm in both categories of sites; edentulous sites = 2.2 mm and implant sites = 2.4 mm.

In a follow-up experiment in the dog, Araújo *et al*. (2006a,b) studied whether osseointegration, once established following implant placement in a fresh extraction socket, could be lost as a result of continued tissue modeling of the bone walls during healing. As was the case in their previous study the distal roots of the 3rd and 4th premolars in both quadrants of the mandible were removed following flap elevation. Implants were installed in the fresh extraction sockets, and initial stability of all implants was secured. The flaps were replaced and "semi-submerged" healing of the implant sites was allowed. Immediately following flap closure, biopsies were obtained from two dogs, while in five dogs healing periods of 1 month and 3 months were permitted prior to biopsy.

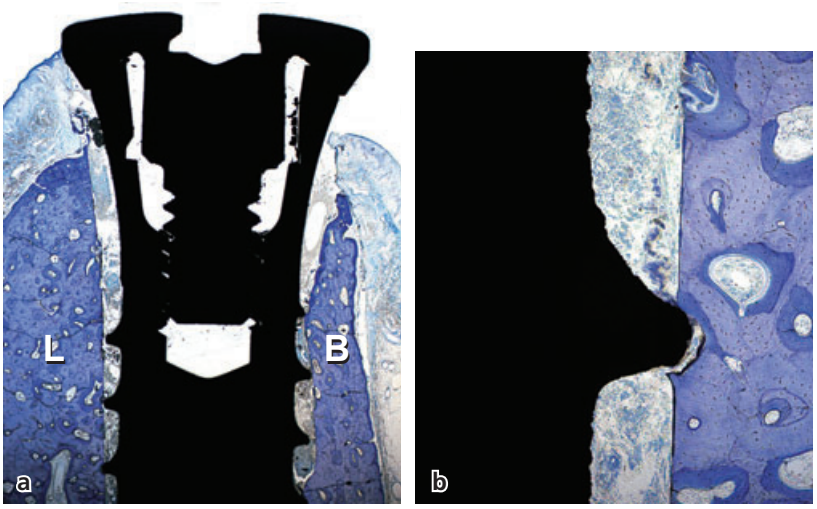

Fig. 47-9 (a) Buccal–lingual section of an extraction site immediately after implant installation. (b) Contact was established between the pitch on the surface of the implant body and the walls of the socket. B = buccal aspect; L = lingual aspect.

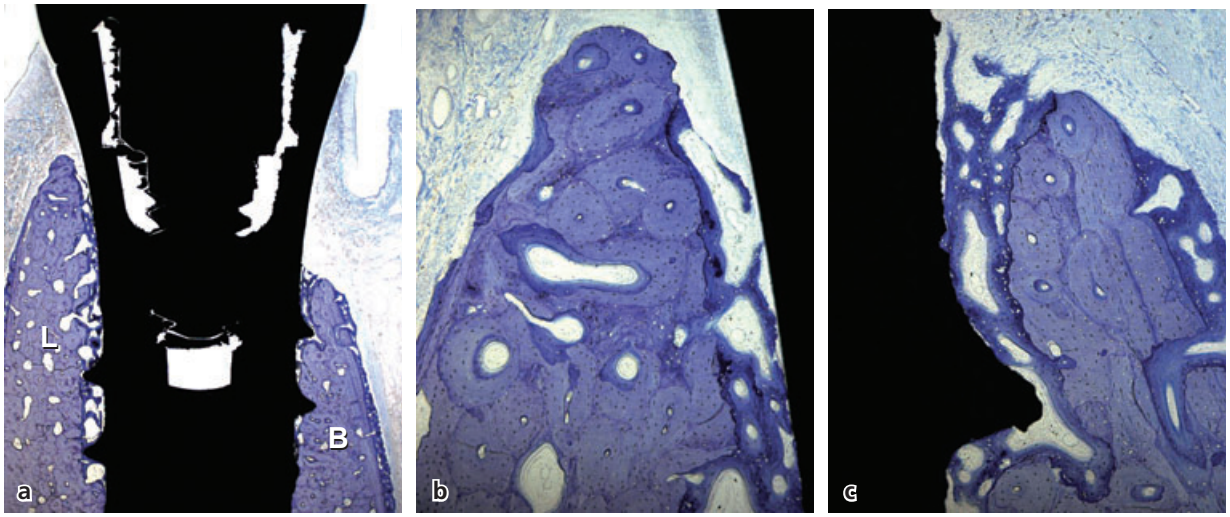

Fig. 47-10 (a) Buccal–lingual section 4 weeks after implant installation. The void between the implant surface and the bone wall was completely filled with newly formed bone in both lingual (b) and buccal (c) aspects. B = buccal aspect; L = lingual aspect.

Figure 47-9a presents a buccal–lingual aspect of an extraction site immediately after implant installation. Contact was established between the pitch on the surface of the implant body and the walls of the socket. A coagulum resided in the void between the contact regions (Fig. 47-9b) and also in the marginal gap. In sections representing 4 weeks of healing, it was observed that this void had become filled with woven bone that made contact with the rough surface part of the implant (Figs. Fig 47-10). In this 4-week interval, (1) the buccal and lingual bone walls had undergone marked surface resorption, and (2) the height of the thin buccal hard tissue wall had been reduced.

In the interval between 4 weeks and 12 weeks of healing the buccal bone crest shifted further in an apical direction (Fig. 47-11). The woven bone at the buccal aspect that in the 4-week sample made contact with the implant in the marginal gap region had modeled and only fragments of this bone remained (Fig. 47-11c). At the end of the study, the buccal bone crest was located >2 mm apical to the marginal border of the rough implant surface.

These findings demonstrate that the bone (woven bone)-to-implant contact that was established during the early phase of socket healing following implant installation, was in part lost when the buccal bone wall underwent continued atrophy.

It is obvious, therefore, that the alveolar process following tooth extraction (loss) will adapt to the altered functional demands by atrophy and that an implant, in this respect is unable to substitute for the tooth. The clinical problem with type 1 placement is that the bone loss will frequently cause the buccal portion of the implant to gradually lose its hard tissue coverage, and that the metal surface may become visible through a thin peri-implant mucosa and cause esthetic concerns (Fig. 47-12).

The question now arises whether it is possible to overcome this problem. This issue was studied in a beagle dog experiment by Araújo *et al*. (2006b). The distal root of the 3rd mandibular premolar and the

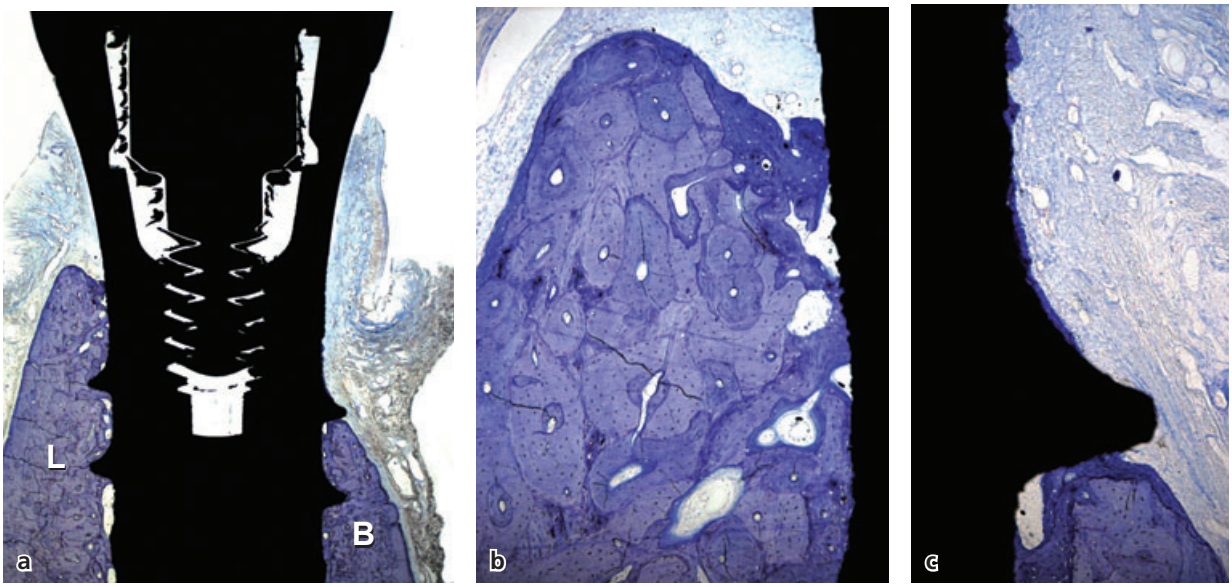

Fig. 47-11 (a) Buccal–lingual section 12 weeks after implant installation. Note that buccal bone crest shifted in an apical direction and fragments of it could be seen on the denuded implant surface (c). The lingual bone crest, however, remained stable (b). B = buccal aspect; L = lingual aspect.

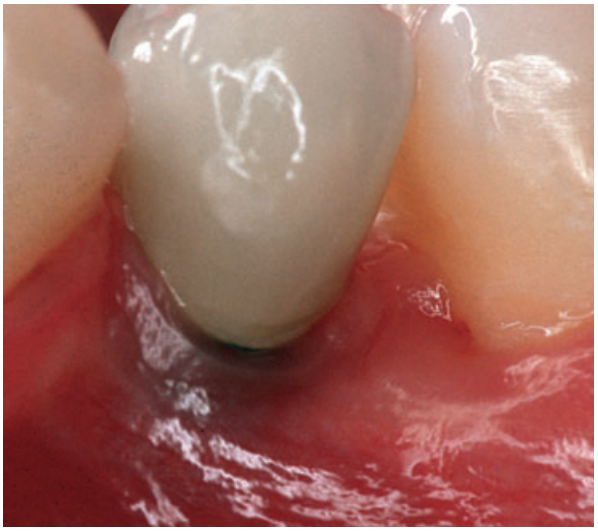

Fig. 47-12 Clincal view of an implant lacking the buccal bone. Note that the metal surface had become visible through the thin mucosa.

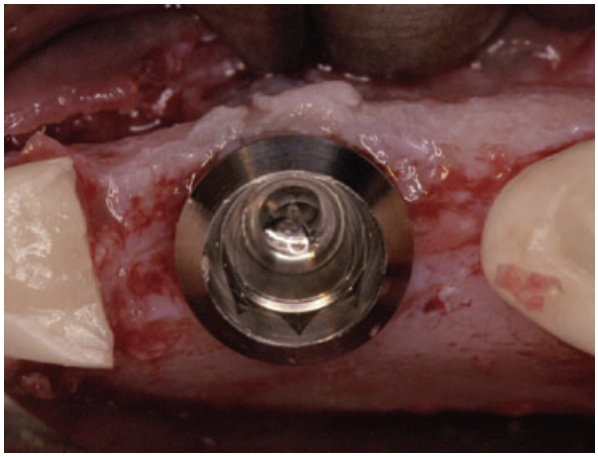

Fig. 47-13 Photograph illustrating implant installation in the narrow, 3rd premolar alveolar socket.

distal root of the 1st mandibular molar were removed and implants placed in the fresh extraction sockets. The 3rd premolar socket in this dog model is comparatively small, and hence the implant inserted (Straumann® Standard Implant, diameter 4.1 mm) occupied most of the hard tissue wound (Fig. 47-13). During healing resorption of the buccal bone wall occurred (Fig. 47-14) and >2 mm of the marginal portion of the implant became exposed to peri-implant mucosa.

The molar socket, on the other hand is very large (Fig. 47-15) and hence after implant (Straumann® Standard Implant, diameter 4.1 mm) placement a >1 mm wide marginal gap occurred between the metal body and the bone walls (Fig. 47-16b). Primary stability of the implant was achieved through contacts between the metal body and the bone in the apical (periapical) portions of the socket. During the early phase of healing this gap in the molar site became filled with woven bone. In the interval when the buccal bone wall underwent programmed atrophy, the newly formed bone in the gap region maintained osseointegration and continued to cover all surfaces of the implant (Fig. 47-16a,b).

Conclusion: The data reported illustrate an important biologic principle. Atrophy of the edentulous ridge will occur following tooth loss. This contraction of the ridge cannot be prevented by placing an implant in the fresh extraction socket. The atrophy includes a marked reduction of the width and the height of both the buccal and lingual bone plates; in particular the buccal bone plate will undergo marked change. To some extent the problem with buccal bone

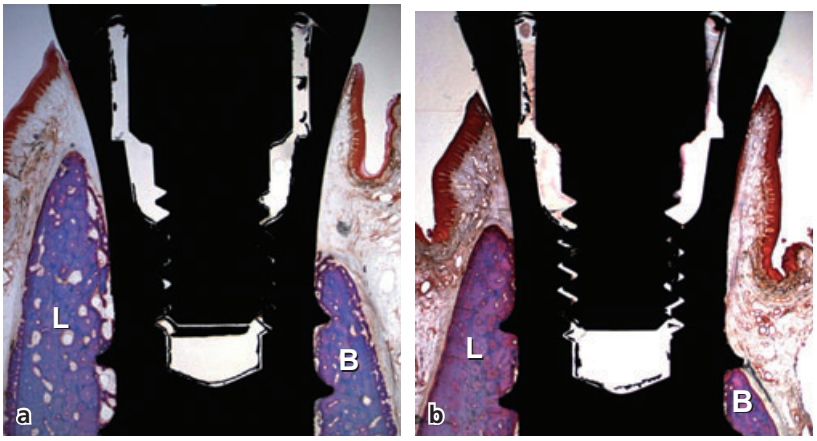

Fig. 47-14 Buccal–lingual section of the healed premolars sites representing (a) 4 and (b) 12 weeks after implant installation. B = buccal aspect; L = lingual aspect.

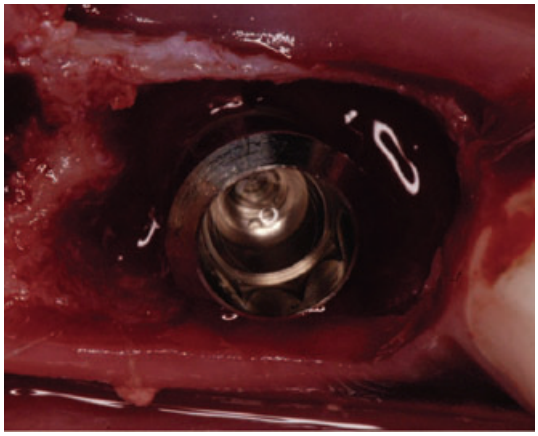

Fig. 47-15 Photograph illustrating implant installation in the wide, 1st molar alveolar socket.

resorption can be overcome by placing the implant deeper into the fresh socket and in the lingual/palatal portion of the socket.

As a consequence of the above described healing, bone regeneration procedures may be required to improve or retain bone volume and the buccal contour at a fresh extraction site. Such bone augmentation is sometimes mandatory in the esthetic area.

Stability of implant

Another issue with type 1 (and also type 2) placement is the anchorage of the implant to obtain primary stability in a position in the jaw that will enable the subsequent restoration to meet high demands regarding esthetics and function. In most cases of type 1 placement, the implants are fixed in native bone apical to the alveolus (Fig. 47-17). Additional retention may be achieved by anchoring the implant in the bony structures of the alveolar walls or inter-radicular septa.

In a recently presented controlled clinical trial (Siegenthaler *et al*. 2007) it was observed that primary stability for some implants in a type 1 procedure could not always be achieved. In this study implants were inserted to replace teeth either exhibiting periapical pathology (test) or presenting healthy periapical conditions (control). In four implant sites in the test group and one in the control group no implants could be placed due to an unfavorable bone morphology, which precluded primary implant stability.

Type 2: completed soft tissue coverage of the tooth socket

There are several reasons why the type 2 approach is often recommended. At this stage of healing the socket entrance is covered with a mucosa. The soft tissue is (1) comparatively mature, (2) has proper volume, and (3) can be easily managed during flap elevation and replacement procedures. Furthermore, the type 2 timing permits an assessment of the resolution of periapical lesions that may have been associated with the extracted tooth. The disadvantages inherent in the type 2 approach include (1) resorption of the socket walls and (2) an extended treatment time (Table 47-1).

Following tooth extraction, the socket becomes filled with a coagulum that is replaced with granulation tissue within a few weeks. In the normal case it takes about 4–8 weeks before the soft tissue (granulation tissue, provisional connective tissue; see Chapter 2) fills the socket and its surface becomes covered with epithelium (Amler 1969; Zitzmann *et al*. 1999; Hämmerle & Lang 2001; Nemcovsky & Artzi 2002). The maturation of the soft tissue (further deposition and orientation of collagen fibers) that may facilitate flap management may require an even longer healing time.

The larger amount of soft tissue that is present at the site of implant placement when the type 2 approach is used will allow for precise management of the mucosal flap and hence optimal soft tissue healing (Fig. 47-18). This advantage with the type 2 timing must be matched against the hard tissue reduction and the change of the ridge contour that results from the resorption of the socket walls and of the buccal bone plate. It must be observed that at

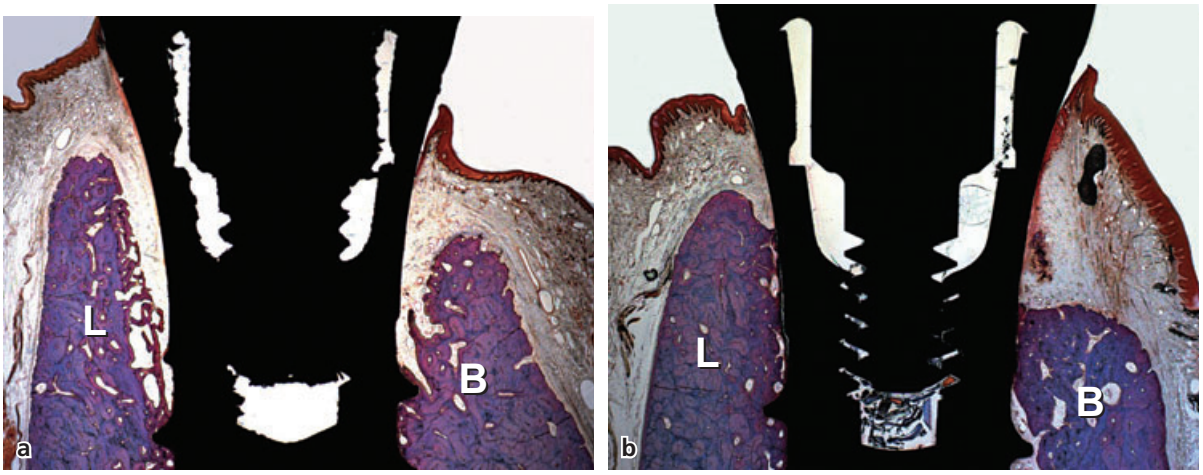

Fig. 47-16 Buccal–lingual section of the healed molars sites representing (a) 4 and (b) 12 weeks after implant installation. B = buccal aspect; L = lingual aspect.

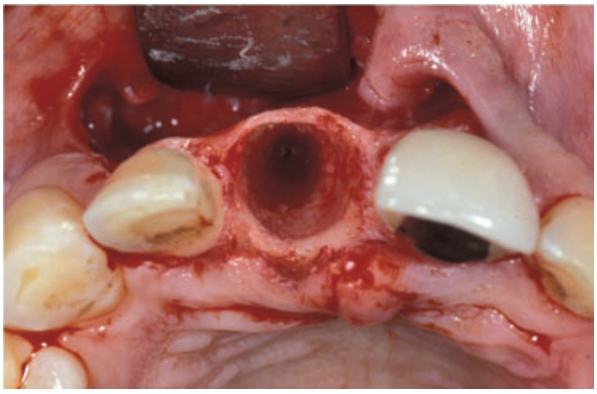

Fig. 47-17 Type 1 implant placement provides optimal availability of existing bone contours. Note the presence of a thin buccal bone plate. Anchorage of an implant can be achieved by engaging the bone apical to the apex of the extracted tooth and the palatal wall of the socket.

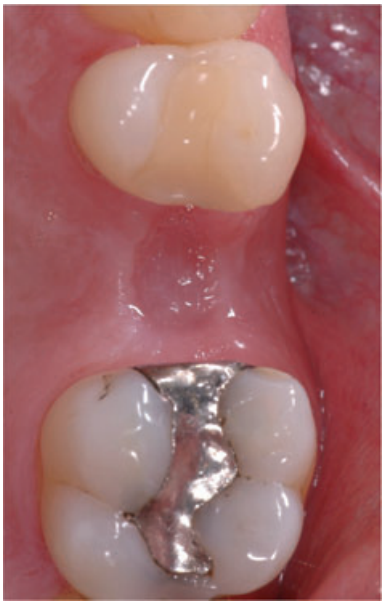

Fig. 47-18 The soft tissues have completely healed over the extraction socket 8 weeks after tooth removal (type 2).

some extraction sites the mucosa may remain adherent via scar tissue to the underlying bone or to the provisional connective tissue of the socket. In such cases it may be difficult to separate the soft tissue from the bone and to mobilize the flap. In such a situation, the trauma caused in conjunction with flap elevation may rupture the soft tissue and compromise healing. This in turn may result in soft tissue dehiscence, local infection, and inflammation (Zitzmann *et al*. 1997).

As described in the schematic drawing in Fig. 47-1 the initial gain in mucosa (area and volume) is later followed by an overall loss of soft tissue volume. This is evidenced by the fact that the volume of alveolar ridge – including the bone as well as the mucosal compartments – markedly decreased during the first 12 months following tooth extraction (Schropp *et al*. 2003).

During the 4–8 weeks between tooth extraction and type 2 implant placement only small amounts of new bone (woven bone) will form in the socket. This means that the risk of not achieving primary implant stability is similar in type 1 and type 2 approaches. Thus, in sites where the available bone height apical to the tip of the root is less than 3 mm, it is frequently impossible to obtain primary implant stability in the bone beyond the apex of the extracted tooth. When, in addition, a wide alveolus is precluding the engagement of its bony walls, the type 3 approach may be favored.

Type 3: substantial bone fill has occurred in the extraction socket

The type 3 time frame is chosen for implant installation at sites where, for various reasons, bone fill is required within the extraction socket. Newly formed woven bone will occupy the socket area after healing periods extending from 10–16 weeks (Evian *et al*. 1982). In this period, however, the walls of the socket are frequently completely resorbed and replaced

with woven bone. The entrance to the socket is closed with a cap of woven bone that is in the process of remodeling. The mucosa that covers the extraction site is (1) residing on a mineralized ridge, and (2) mature and more easy to manage during surgical flap elevation and replacement procedures.

The type 3 approach often allows the clinician to place the implant in a position that facilitates the prosthetic phase of the treatment. The disadvantages with the type 3 approach encompass (1) a prolonged treatment time, (2) additional resorption and diminuton of the ridge including a substantial change of its contour, and (3) a concomitant loss of soft tissue volume.

Type 4: the alveolar ridge is healed following tooth loss

In the type 4 approach the implant is placed in a fully healed ridge. Such a ridge can be found after 4 but more likely after 6–12 months of healing following tooth extraction (loss). After 6–12 months of healing following tooth extraction, the clinician will find a ridge that is lined by a mature, often well keratinized mucosa that resides on dense cortical bone. Beneath the cortical bone plate, cancellous bone occupies a varying portion of the alveolar process (for detail see Chapter 2).

In a study including human volunteers it was observed that the rate of formation of new bone within the extraction site started to decrease after 3–4 months of healing. At this stage the newly formed bone and the remaining bone of the socket walls entered into a phase of remodeling (Evian *et al*. 1982). Concomitant with the remodeling of this centrally located bone tissue, extra-alveolar resorptive processes leading to a further contraction of the ridge and change of its contour continued for at least 12 months (Schropp *et al*. 2003).

The advantage of type 4 installation is that healing is more or less complete and that only minor additional change of the ridge may occur. The disadvantages include (1) increased treatment time and (2) further reduction of the overall volume of the ridge and change of its external contour. This pronounced additional loss of ridge volume may at times require complicated bone augmentation procedures (Fig. 47-19). As a consequence type 4 placement is avoided in most cases when the tooth (teeth) to be replaced is (are) present at the time of examination and treatment planning.

Clinical concepts

When implants are to be placed in the edentulous portion of the ridge, factors other than the tissue changes over time must be considered. Thus, in the treatment planning phase aspects, such as (1) the overall objective of the treatment, (2) the location of the tooth within the oral cavity – in the esthetic or non-esthetic zone – and (3) the anatomy of the bone and the soft tissue at the site(s) to be treated, must be evaluated.

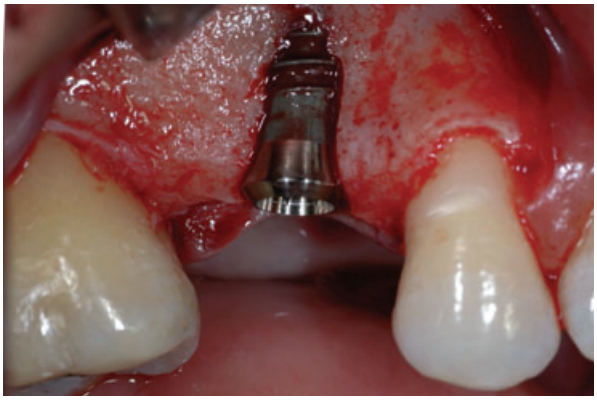

Fig. 47-19 A buccal dehiscence defect is present at an implant placed into a ridge, which has undergone substantial buccal bone resorption since tooth extraction several months ago (type 4).

Aim of therapy

Dental implants are most often used to restore health and function. During the surgical phase of therapy, therefore, ideal conditions must be established for successful bone and soft tissue integration to the implant. In a growing number of cases, however, treatment must also satisfy demands regarding the esthetic outcome. In such cases, the overall surgical and prosthetic treatment protocol may become more demanding, since factors other than osseointegration and soft tissue integration may play an important role.

Restoration of health and function

In cases where the restoration of health and function constitutes the primary goal of the treatment, the location and volume of available hard and soft tissues are the important factors to consider. In such cases the type 1 approach is usually selected (Wichmann 1990).

The replacement of a single-rooted tooth with an implant in a fully healed ridge will, in most cases, ensure proper primary stability with the implant in a correct position (Fig. 47-20). In addition, the soft tissues are sufficient in volume and area. The mucosal flap can be adapted to the neck (or the healing cap) of the implant (one-stage protocol). When primary wound closure is intended (two-stage protocol), mobilization of the soft tissue will allow tension-free adaptation and connection of the flap margins.

When an implant is placed in the fully healed site of a multi-rooted tooth, the surgical procedure becomes more demanding. Often the ideal position for the implant is in the area of the inter-radicular septum. If the septa are delicate, anchorage for

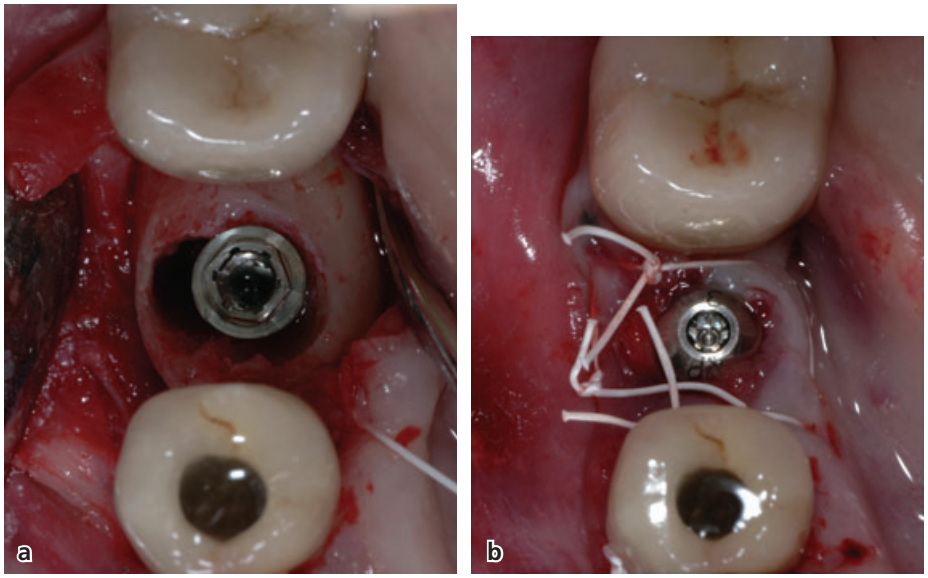

Fig. 47-20 (a) Immediate implant placement (type 1) in a mandibular premolar extraction socket. Note the buccal bone deficiency, where bone will be augmented by guided bone regeneration (GBR). (b) The same site as in (a) following adaptation of the flap around the neck of the implant obtaining a transmucosal mode of healing.

primary implant stability may become difficult to achieve. In addition, in molar sites there is often only a small amount of soft tissue present. This may create a problem with respect to wound closure with a mobilized, tension-free flap. In some molar sites, primary wound closure may not be possible at times following implant installation.

The presence of marginal defects (gaps) between the implant and the fully healed ridge following type 4 placement was regarded in the past as a significant problem that could compromise osseointegration. Recent studies in man and animals have demonstrated, however, that in such a horizontal marginal defect (gap) of ≤2 mm, new bone formation as well as defect resolution and osseointegration of the implant (with a rough titanium surface) will occur (Wilson *et al*. 1998; Botticelli *et al*. 2004; Cornelini *et al*. 2005).

Esthetic importance and tissue biotype

The replacement of missing teeth with implants in the esthetic zone is a demanding procedure. Deficiencies in the bone architecture and in the soft tissue volume and architecture may compromise the esthetic outcome of treatment (Grunder 2000). Hence, when an implant is to be placed in the esthetic zone, not only the anatomy of the hard tissues but also the texture and the appearance of the soft tissues must be considered.

Type 2 installation is often to be preferred when implants are placed in the esthetic zone (Fig. 47-21). The key advantage in type 2 (as opposed to type 1) is the increased amount of soft tissue that has formed during the first weeks of healing following tooth extraction. It must be emphasized, however, that comparative studies analyzing the treatment outcomes in randomly selecting type 1 or type 2 placements have so far not been reported.

In a recent clinical study, implants were placed in fresh extraction sockets (Botticelli *et al*. 2004). During healing, the implants became clinically osseointegrated within the borders of the previous extraction socket. Significant loss of buccal bone height (contour) however also occurred. In esthetically critical situations this loss of contour may lead to a compromised outcome. Hence not infrequently, tissue augmentation procedures must be performed in the esthetic zone.

In this context it is important to realize that when a two-stage implant placement protocol is used, the labial mucosa will recede following abutment connection surgery. Mean values of recession between 0.5 mm and 1.5 mm with large variations have been reported in several clinical studies (Grunder 2000; Oates *et al*. 2002; Ekfeldt *et al*. 2003). These findings additionally stress the necessity for a careful treatment approach when implants are placed in the esthetic zone.

The biotype (see Chapter 3) of the soft and hard tissue tissues may play a role regarding the esthetic outcome of implant therapy. Characteristics of soft and hard tissues at teeth were described and classified into two biotypes: the flat thick or the pronounced scalloped thin biotype (Weisgold *et al*. 1997; Olsson & Lindhe 1991; Olsson *et al*. 1993). The thin tissues in the pronounced scalloped biotype include a thin free gingiva, a narrow zone of attached mucosa, and a pronounced "scalloped" contour of the gingival margin. In addition, the scalloped thin biotype is associated with a delicate bone housing. In a recent study it was found that buccal tissue recession at single-tooth implants was more pronounced in patients exhibiting a thin biotype compared to

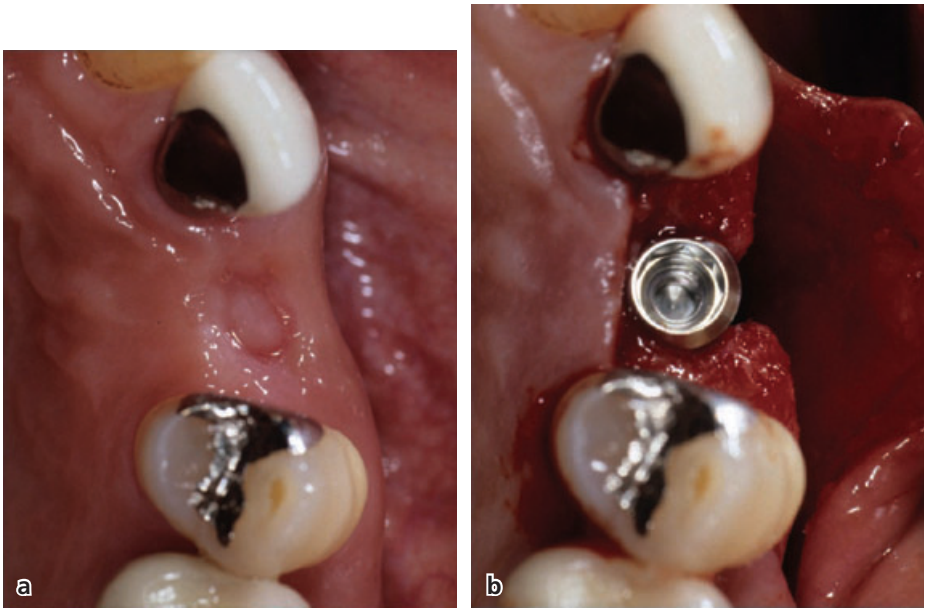

Fig. 47-21 (a) A single tooth gap 8 weeks following tooth extraction. The soft tissues have completely healed over the extraction socket. (b) The same site as in (a). An implant has been placed in the edentulous gap. The resulting buccal dehiscence defect will be augmented with bone by applying GBR.

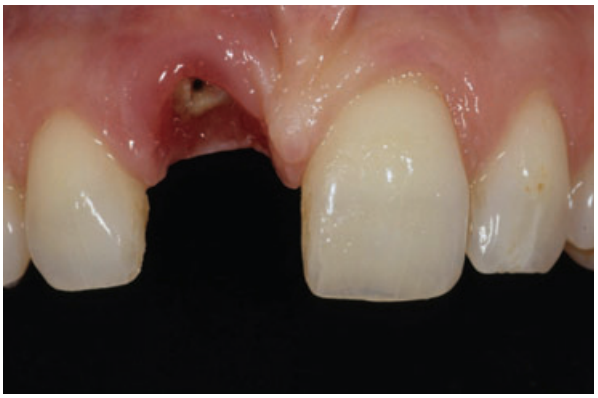

Fig. 47-22 A patient exhibiting a thin tissue biotype as characterized by a thin free gingiva, a narrow zone of keratinized and of attached mucosa, shallow probing depths, and a pronounced "scalloped" contour of the gingival margin including recessions at some maxillary anterior teeth. Tooth 11 is scheduled for extraction and replacement by an implant using a type 2 or 3 approach.

patients with a thick biotype (Evans & Chen 2007). Based on these findings and on clinical experience it was proposed that patients exhibiting a pronounced scalloped biotype should be treated with a type 2, 3, or 4 rather than with a type 1 implant installation approach (Fig. 47-22). Data collected from properly designed clinical studies regarding this issue are presently lacking.

Success of treatment and long-term outcomes

Numerous clinical studies have demonstrated that type 1 implant placement is a successful and predictable clinical method (Lang *et al*. 1994; Schwartz-Arad & Chaushu 1997b; Hämmerle *et al*. 1998; Covani *et al*. 2004). In addition, success and survival rates for type 1 implants have been reported to be of the same magnitude as implants placed in healed ridges (Gelb 1993; Grunder 2000; Gomez-Roman *et al*. 2001; Gotfredsen 2004; Schwartz-Arad *et al*. 2004). Histologic studies in animals confirmed the viability of type 1 placement. Unloaded titanium implants placed in extraction sockets showed a high degree of osseointegration (Anneroth *et al*. 1985), i.e. similar to the one at implants placed in healed sites. Furthermore, a few studies analyzing survival rates of type 2 and 3 placements have shown similar survival rates as the ones reported for types 1 and 4 (Watzek *et al*. 1995; Nir-Hadar *et al*. 1998; Polizzi *et al*. 2000).

Conclusions

In situations where teeth are to be replaced with implants, various factors govern the decision regarding the optimal time point for implantation following tooth extraction. Of special importance are the overall objective of the treatment, the location of the tooth within the oral cavity, the anatomy of the bone and the soft tissue at the site, and the adaptive changes of the alveolar ridge following tooth extraction. The decision regarding the timing for implant placement needs to be based on a thorough understanding of the structural changes that occur in the alveolar process following tooth extraction, with and without implant placement as presented in this chapter.

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Chapter 48

The Surgical Site

Marc Quirynen and Ulf Lekholm

Bone: shape and quality

It is imperative that the conditions of the soft and hard tissues as well as of the shape of the bone in the recipient sites intended for implants are carefully examined. Both clinical and radiographic parameters must be used in this examination.

Clinical examination

The clinical examination should include assessment of (1) colour and texture alterations of the mucosa (indicative of a lesion) and (2) the thickness of the soft tissues. The recipient site should also be palpated in order to estimate the volume of the tissues available in the edentulous region of the jaw. It must be realized, however, that both the mucosa and the bone of the edentulous region are included in this clinical measure. Hence, the clinician must realize that palpation may overestimate the volume of hard tissue present at the site.

The clinical examination must also determine the inter-arch gap and the dimensions of the edentulous area to ascertain that enough space is present (1) to allow optimal maneuvering (access of the hand piece together with the preparation drills) during surgical procedures, (2) to avoid damage of the periodontium of teeth adjacent to the edentulous area during implant insertion, and (3) to allow placement of the prosthetic device. As a rule of thumb, the inter-arch distance should be ≥5 mm, and the distance between a tooth and an implant should be ≥3 mm. If the size of the edentulous region is diminutive, implants with a small diameter must be selected, and eventually a surgical guide (stent) used to assist the surgeon during implant installation. This might help to avoid contact with the neighboring teeth.

The jaw relation (angle class) must also be determined, as this will have an influence on the direction of insertion of the implants (further discussed below). In the final step of the clinical examination impressions of the jaws (dentition) are obtained and stone cast models prepared. Such models can later be used during treatment planning and for the preparation of surgical position and direction stents.

Radiographic examination

The radiographic examination (see Chapter 28) will provide more detailed information on the amount and quality of the bone available at the recipient site. Lekholm and Zarb (1985) proposed that the edentulous jaw (segment of the jaw) should be classified regarding its shape and quality. Thus a grading into five groups was used to describe the shape of the jaw (Fig. 48-1a) while four groups were used to describe the quality of the bone tissue (Fig. 48-1b).

Panoramic and intraoral apical radiographic images give a first impression of the bone, as well as of important anatomic landmarks such as: the floor of sinusal and nasal cavities; the incisive nerve; the inferior alveolar nerve; the roots and apices of neighboring teeth; and the crest of the alveolar ridge. From the two-dimensional images it is also possible to obtain some information about the available height of the bone at the recipient site, while three-dimensional radiographs are essential to determine the width of the alveolar crest. It is important to realize that the definitive evaluation of the dimension

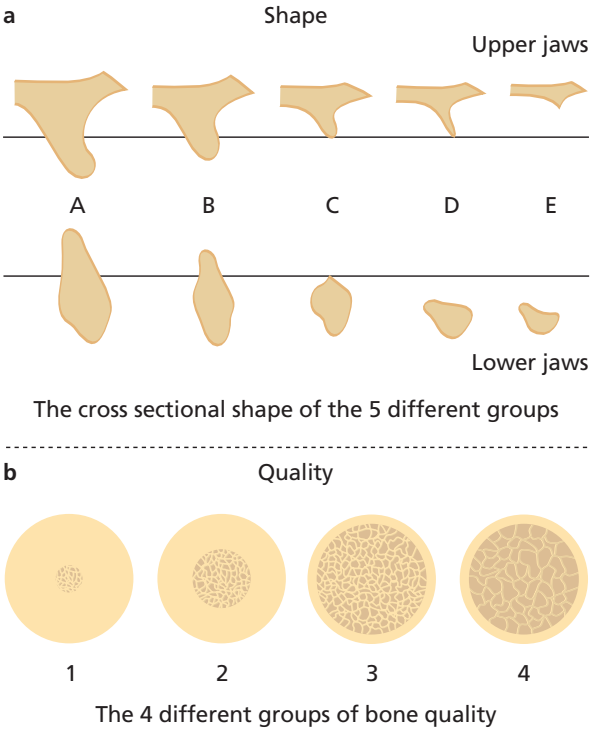

Fig. 48-1 Schematic drawings showing (a) residual jaw shape classification, and (b) jaw bone quality classification, according to Lekholm and Zarb (1985).

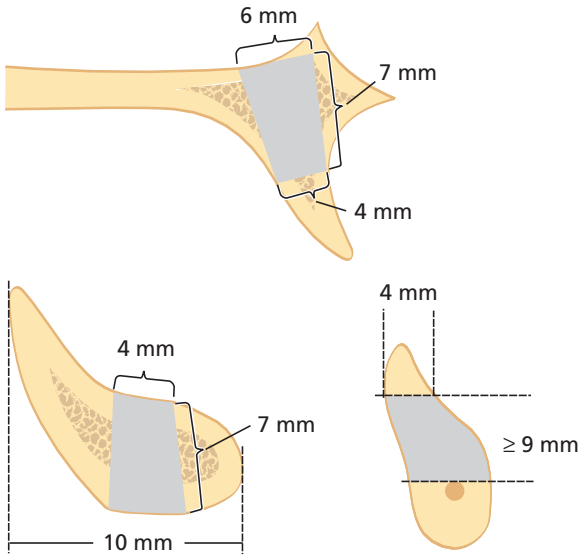

Fig. 48-2 Schematic drawings showing minimum bone volume needed for standard implants of the Brånemark System.

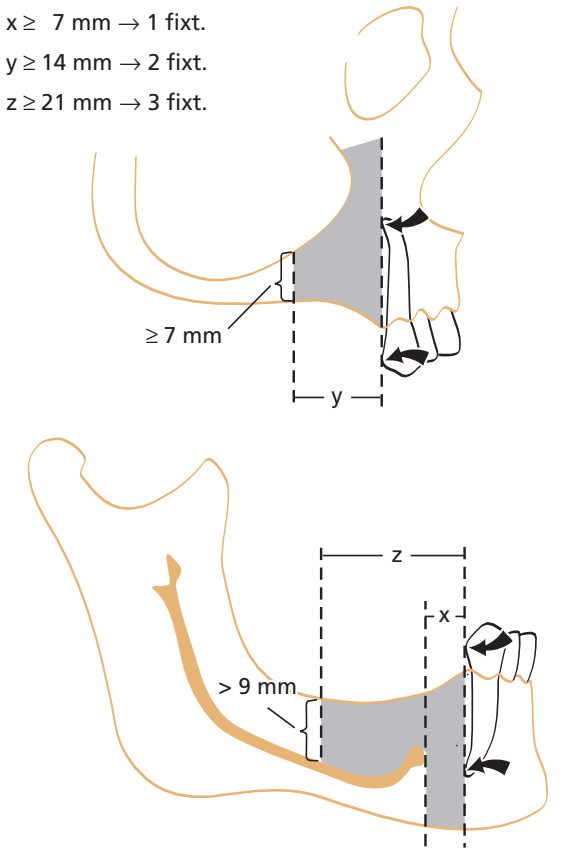

Fig. 48-3 Schematic drawings indicating location of minimum bone volume areas in distal directions, and giving distances needed for various numbers of implants. Arrows indicate prominence and apex of the nearest tooth.

of the recipient site should not be based on observations made in intraoral radiographs or in orthopantomograms. This is especially true in cases where intraoral palpation indicated the presence of a narrow ridge (jaw). Indeed, the precise location of the inferior alveolar nerve must be identified via measurements made in images from conventional or computer-assisted tomography (CT). Correct identification of the mandibular canal may assist the clinician to avoid damaging the nerve during surgery and thereby preventing the occurrence of complications such as impaired sensory function and paresthesia of the lower lip and neighbouring soft tissues (Abarca *et al*. 2006).

The cylinder-shaped cavity prepared in the recipient site to house the endosseous part of the implant is, as a rule, 1–2 mm longer than the titanium device *per se*. Thus, for a 7-mm long implant, the required minimum height of the bone of the recipient site is 8–9 mm (Fig. 48-2). In cases where implants are to be installed in positions above the inferior alveolar nerve, a minimum height of 9–10 mm of bone is required for a 7-mm long implant.

Planning for implant placement

Radiographs are used to make preliminary decisions regarding the position(s) as well as the number and dimensions of implants to be used. The location of the most distal implant is determined first (Fig. 48-3). The number and the position of more mesially located implants are identified thereafter. In this treatment planning process it must be recognized that the inter-implant distance must be ≥3 mm.

The final decision regarding the number and dimension of implants to be inserted, however, is most often made during surgery, i.e. after the soft

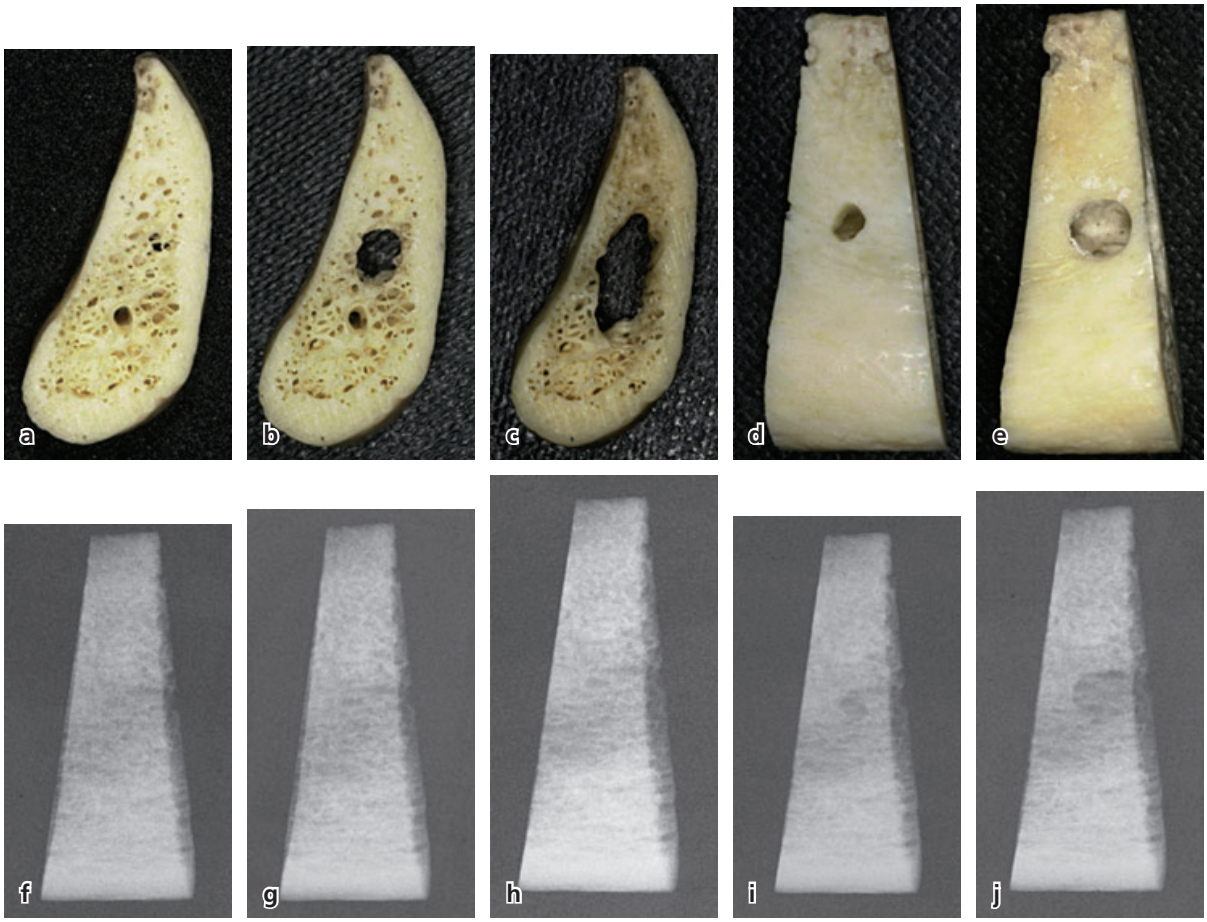

Fig. 48-4 An example (for this illustration without soft tissues) of part of a jawbone in which a progressively larger defect has been created, initially within the spongious bone (a–c), later (d,e) also perforating the cortex. The images (f–j) represent the corresponding radiographs.

tissue flaps have been elevated and the bone of the recipient sites has been exposed.

Defects in the jaw bone

Intraoral (conventional or digital) as well as extraoral radiographic images (conventional tomography, spiral CT) may not necessarily reveal all lesions and defects in the jawbone. In a recent *ex vivo* study (Van Assche *et al*. 2007), intraoral radiographs were taken of progressively larger, artificially created, defects in both the mandible and the maxilla. As illustrated in Fig. 48-4, a defect first became visible in the radiograph when the area (junction) including the cortical plate and cancellous bone was involved. This indicates that the clinician may overlook such intra-ridge lesions (Quirynen *et al*. 2005).

During implant installation surgery, minor fenestrations or marginal dehiscences sometimes occur. Hence some threads of the implants may be exposed (not covered by bone). In most cases such uncovered threads may be left unattended since no adverse reactions have been observed in the mucosa at such locations (Lekholm *et al*. 1996). On the other hand, if the jaws contain defects of such a magnitude that the implants cannot be placed in proper positions without having major parts of their surfaces exposed, ridge augmentation is often recommended. This may include guided bone regeneration (Molly *et al*. 2006) and/or bone grafting (Buser *et al*. 1994; Deporter 2001). A recent systematic review on augmentation techniques (Chiapasco *et al*. 2006) indicated that several different procedures may enhance the bone volume in a predictable manner and establish better conditions for implant insertion. For further details regarding ridge augmentation see Chapter 49.

Summary: the local condition of edentulous areas considered for implants must be properly evaluated, and no pathology in the soft and/or hard tissues of the jaws should be accepted at the time of implant placement. Radiographic evaluations are necessary in order to identify important landmarks in the jaws as well as to study the shape and the quality of the bone tissue in areas considered for implants. Tomography is used when implants are to be placed above the inferior alveolar nerve, and/or when the clinical examination indicates that the recipient site harbors minute amounts of bone. The minimum amount of bone required for implant surgery is related to the size and surface of the implants to be used.

Implant placement

Guiding concept

The main purpose for the use of implants in dentistry is to establish a stable anchorage for a fixed or removable prosthesis (Brånemark *et al*. 1985). In order to allow osseointegration to occur and be maintained, the handling of the bone tissue during surgery must be diligent. It is important to recognize that bone is a living tissue that must not be exposed to undue trauma. The surgical procedure must be performed according to carefully established guidelines (e.g. Adell *et al*. 1985; Lekholm & Jemt 1989). Furthermore, the surgeon must pay maximum attention to basic rules of sterility and asepsis. It is often noticed that sterile drapes are used while the nose, the most infected site of the entire facial area, is left uncovered. The use of a sterile nose cap that allows the patient to breath freely but prevents the contamination of the sterile gloves and instruments (van Steenberghe *et al*. 1997) is recommended.

Flap elevation

The mucosa of the ridge can be incised using either a crestal or a vestibular approach. At present there is no information available to indicate that one of the two approaches is more advantageous than the other. Consequently, the clinician can select the method best suited for the individual situation. Crestal incisions may be preferred at sites where the crest of the ridge is wide. If the crest is high but narrow, a buccal approach might be preferred. Moreover, when ridge augmentation is to become part of the surgical procedure, incisions on top of the area to be augmented should be avoided (to prevent early exposure of bone substitute or membrane). In cases of so-called one-stage installation surgery, a crestal incision is, of course, mandatory.

Implants are often placed in edentulous sites that are bordered by teeth. Whenever possible, and in particular in the "esthetic zones", the gingiva (papillae) of the neighboring teeth should not be included in the flap. Shrinkage of the papillae during healing is therefore avoided and the occurrence of black triangles in the "tooth–implant" region prevented.

At narrow edentulous sites where implants must be placed close to teeth, it is often necessary to include the gingiva in the flap. In such cases, the crestal incision made in the edentulous area is continued mesially and/or distally into the pocket of the adjacent teeth and is sometimes combined with vertical releasing incisions in the gingiva. The flap is hereby increased in dimension, will receive a more adequate vascular support, and may be managed to allow full soft tissue coverage of the bone and the implant(s).

It is important to make sure that, during the soft tissue elevation procedure, the entire periosteum is properly released from the walls of the jaw and included in the flap (full-thickness flap). This is particularly important when a flap is released from the lingual side of the mandible. The exposure of the lingual hard tissue wall of the mandible allows the surgeon to detect an accidental perforation of the lingual cortex during drilling and implant installation. It is also important to release a full-thickness flap on the buccal side of both the maxilla and the mandible. This will make it possible to observe the presence of cavities and/or protrusions of the jaws, contours of tooth roots, and nerve entrances, i.e. structures that may influence the positioning of the implants. Finally flap elevation and exposure of the osseous tissue will facilitate irrigation (cooling) of the site during drilling.

Flapless implant insertion

Implant installation without flap elevation and exposure of the bone tissue was recently introduced. This approach is obviously supported by commercial pressure. Flapless surgery no doubt may offer some advantages including (1) reduction in complications for the patient (less pain and swelling), (2) reduced surgical time and no suturing, and (3) good fit between implant and soft tissues that facilitates the restorative phase of treatment. The success of this implant installation approach depends to a large extent on the quality of the surgical template (stent) that must be used.

The scientific data on flapless implant surgery is sparse (Becker *et al*. 2005; van Steenberghe *et al*. 2005; Fortin *et al*. 2006). Hence, the use of flapless implant insertion as "routine" procedure in daily practice is questioned, due to the absence of long-term data.

Model-based guided surgery

With the use of a plaster model that presents the edentulous area and with additional information on the thickness of the soft tissues, the dental technician can replicate the underlying jaw bone. The implant insertion can be planned and performed on the plaster model and the most convenient position for the permanent restoration can also be determined. In a next step, the model can be used to prepare a surgical template. The template can be fitted with sleeves (canals) to guide the drilling procedure. Since the model also reproduces the soft tissues of the recipient site, fabrication of a provisional restoration can be made even before the implants are actually inserted in the jaw of the patient.

Bone preparation

Bone tissue must not be exposed to adverse heat. Drilling in bone tissue may increase the temperature at the recipient site (Brånemark *et al*. 1985). The threshold level for osteocyte damage lies around 47°C, only about 10°C above body temperature

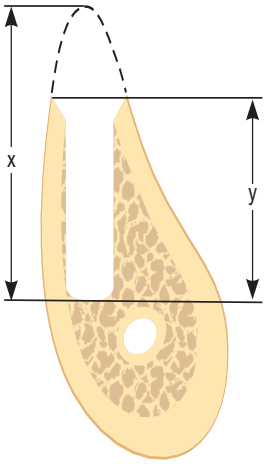

Fig. 48-5 Schematic drawing showing maximum drilling depth (x) without reaching the nerve, as measured from the top of the crest, and implant site length (y), as measured from the lowest bone level in the canal entrance.

(Eriksson & Adell 1986). Consequently, all mechanical preparation of the jaw must be performed with a minimum rise in temperature. This can be achieved via the use of an intermittent drilling technique, together with the use of sharp burs. The preparation of the implant bed should be performed in a sequence of steps, and consistently with profuse saline irrigation (Adell *et al*. 1985). In the presence of particularly dense bone, e.g. in the symphysis region of the mandible, it is also recommended to use an extra wide twist drill, prior to the pretapping procedure and/or insertion the implants (Friberg 1994). When implants are to be placed in soft bone, drilling must be performed with the greatest care, as there is a risk that the entrance of the implant site may be widened too much, and the inserted implant may become unstable. To minimize the risk of initial implant instability, an adjusted surgical technique using either thinner drills or wider diameter implants was recommended (Bahat 1993; Friberg 1994; Watzek & Ulm 2001).

The only structure that can clearly be identified both in radiographs and clinically is the top of the alveolar crest. Consequently, this configuration has to be used as reference for all measurements, both in radiographs and during surgery. During the preparation of the site it is also of particular importance to keep an eye on the depth indicators of the drills and how they relate to the top of the crest. It must be pointed out that during the preparation of the site, the reference point on the crest for the depth measurements may move in an apical direction, particularly if a narrow and drop-shaped alveolar crest is present in the recipient site (Fig. 48-5).

Anatomic landmarks with potential risk

Implant surgery is often regarded/promoted, especially by implant companies, as a safe and minimally invasive procedure. This is not the case, however, especially when implants are placed in the lower jaw (Mraiwa *et al*. 2003a,b). Mechanical compression and/or direct injury during implant insertion may (1) disturb the nerve and initiate a neural degenerative process, or (2) disturb the microcirculation and cause edema and/or a local hematoma.

Neurosensory disorders of the inferior alveolar, mental, or incisive nerves have been reported to occur after implant surgery. Usually the resulting anesthesia, paresthesia, or even dysesthesia are transient phenomena, but certain long-lasting/permanent neuropathies have been reported. An optimal radiographic analysis of the lower jaw is mandatory when planning for implant placement in the neighborhood of the mental foramen or above the inferior alveolar nerve. It still remains a matter of discussion whether injury to the incisive canal in the lower jaw can cause neuropathy.

Several cases of severe hemorrhage in the floor of the mouth, with subsequent life-threatening upper airway obstruction, have been recorded in association with implant placement in both the anterior and posterior portions of the mandible (for review see Kalpidis & Setayesh 2004). Two arteries are responsible for the vascular supply to the mandible (Fig. 48-6a). At the anterior border of the hypoglossus muscle, the lingual artery gives rise to the sublingual artery. This important artery (2 mm in diameter) traverses the floor of the mouth in a frontal direction, near the medial and superior surface of the mylohyoid muscle, medially to the sublingual gland, and inferio-medially to the submandibular duct and the lingual nerve. The sublingual artery gives off several alveolar branches for complementary blood supply to the lingual anterior cortical plate of the mandible. A second small artery, the submental artery (2 mm in diameter), a branch of the facial artery, runs along the inferior plane of the mylohyoid muscle lateral to the anterior belly of the digastric muscle. As illustrated in Fig. 48–6b, the submental artery runs close to the lingual lower border of the mandible. The largest branches of this artery may be seen on a cone-beam or dental CT as they extend into the bone (Fig. 48-6c–e).

The intimate proximity of these arteries, or their vascular plexa, to the lingual cortical plate explains why a lingual perforation in the lower third of the mandible can result in a massive hematoma in the floor of the mouth. Due to the presence of the strong cervical fasciae in the neck region (the *superficial layer*, the *fasciae of the infra-hyoid muscles*, the *pretracheal layer*), the hematoma will displace the tongue and floor of the mouth superiorly and posteriorly, posing a potentially serious threat of obstruction of the upper airway (for review see Kalpidis & Setayesh 2004). Several reports have appeared in the literature describing massive hematoma in the floor of the mouth, where unfortunately a tracheostomy or

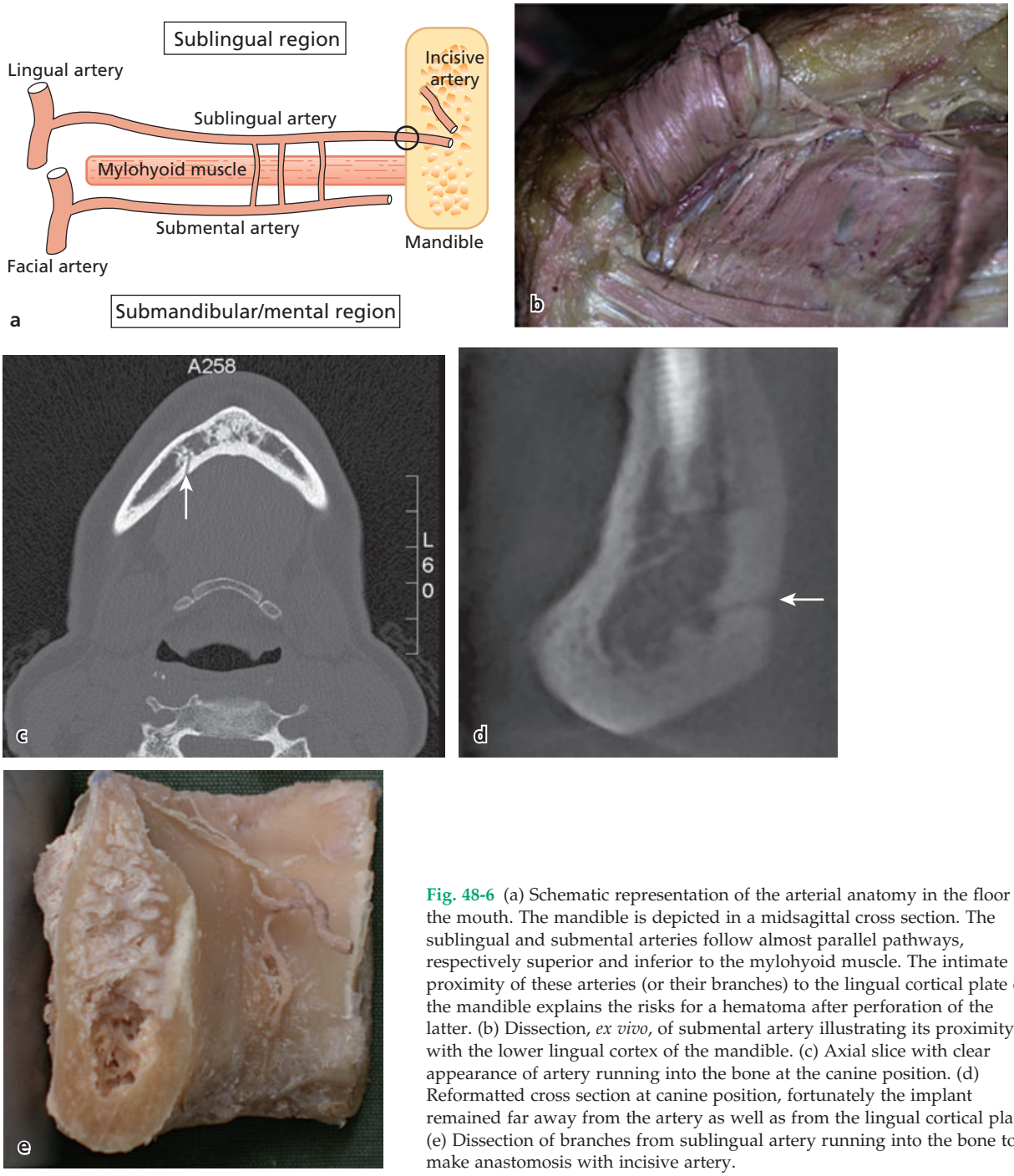

Fig. 48-6 (a) Schematic representation of the arterial anatomy in the floor of the mouth. The mandible is depicted in a midsagittal cross section. The sublingual and submental arteries follow almost parallel pathways, respectively superior and inferior to the mylohyoid muscle. The intimate proximity of these arteries (or their branches) to the lingual cortical plate of the mandible explains the risks for a hematoma after perforation of the latter. (b) Dissection, *ex vivo*, of submental artery illustrating its proximity with the lower lingual cortex of the mandible. (c) Axial slice with clear appearance of artery running into the bone at the canine position. (d) Reformatted cross section at canine position, fortunately the implant remained far away from the artery as well as from the lingual cortical plate. (e) Dissection of branches from sublingual artery running into the bone to make anastomosis with incisive artery.

intubation was the only option to save the life of the patient.

The shape of the lower jaw exhibits large individual variation. A small proportion of jaws (3%) (Quirynen *et al*. 2003) has a distinct lingual depression between lateral incisor and second premolar, superior to the mylohyoid muscle, to house the lingual gland (called the sublingual fovea). Perforation of the bone with a drill in this region must be avoided. As stated previously, deep dissection of the mucoperiosteal flap lingually is strongly recommended in implant installation surgery to expose the cortical plate of the mandible.

Implant position

If possible an implant should be placed in tooth position (Fig. 48-7), both in a mesio-distal and in a bucco-lingual direction. To achieve this, the starting point for the insertion in the bone must, in most instances, be located towards the buccal side of the crest in the mandible, and towards the palate in the maxilla. This is due to the presence of concavities that often exist in the jaws. Depending on the size of such concavities, the starting point (for the instertion) will be located either close to the top of the crest, as in the case of a wide alveolar process, or deeper down

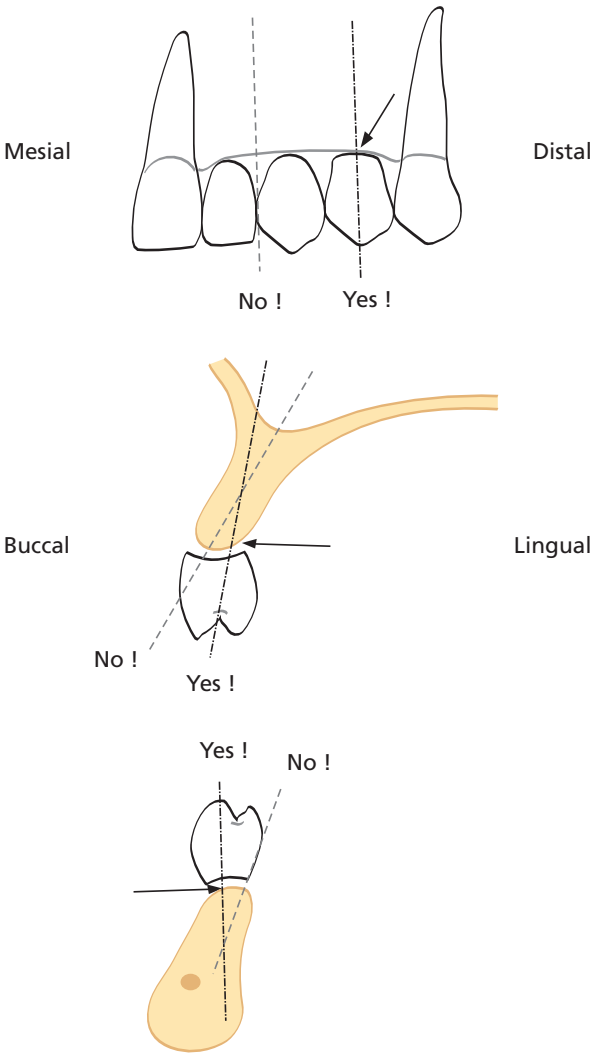

Fig. 48-7 Schematic drawings showing implant positions in mesial–distal and buccal–lingual dimensions. Indicated starting points for drilling are marked with black arrows.

palatally or buccally (Fig. 48-7), if the jaw is thin in its coronal portion.

In cases of partial edentulism, the recipient site closest to a tooth must first be identified. The cylindrical canal in the recipient site is prepared approximately 3.5–4 mm away from the prominence of the tooth. The subsequent implant positions, in a distal direction, are then identified. The minimum amount of bone that must be present in a recipient site is dependent on the dimension of the implants used; as a rule of thumb: the bone tissue of the site should be about 4(5) mm (in a horizontal direction) and about 7(9) mm (in a vertical direction) (Figs. 48-2, 48-3).

In a fully edentulous jaw, it might be preferable to start by placing the most distal implants, so that the position of other implants can be selected accordingly. The longest distance that can be accepted between two implants has not yet been properly defined. As an alternative to a reduced inter-implant distance, and an increased number of implants, it is sometimes possible to use wider diameter implants, as discussed below.

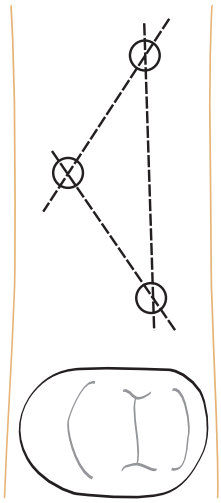

Fig. 48-8 Schematic drawing indicating a tripod placement of the implants in order to minimize individual load distribution onto each implant by creating several rotational axes.

Number of implants

In partially edentulous jaws preferably three implants should be inserted in order to avoid overloading of the anchorage units (Rangert *et al*. 1989). The failure rate has been reported to be higher for reconstorations placed on two than for those on three or more implants (Jemt & Lekholm 1993). Furthermore, the implants should be placed in a tripod position (Fig. 48-8) instead of being inserted in a straight line, thereby minimizing the transmission of bending forces on to each individual implant (Rangert *et al*. 1989). If only one implant can be inserted, then in most cases this anchorage should be used to support a single crown restoration. Implants should never be placed in the midline of the maxilla, not only because they might eventually expand the suture between the two maxillae, but such implants may eventually compromise the esthetics and phonetics after the prosthetic device has been inserted.

Implant direction

After the position of the implant has been identified, the direction/inclination of the implant in the jaw (bucco-lingual and mesio-distal) must be determined. If possible the implants should be placed in tooth position. This means that in the normal case the long axis of the implant should be directed through the occlusal surface of the final restoration. Regarding the bucco-lingual dimension (Fig. 48-9), the long axis of mandibular implants will mainly be directed towards the limbus part of the incisors or the palatal cusps of the teeth in the maxilla. For implants placed in the maxilla, the corresponding inclination should be towards the incisal edges of the frontal teeth or the buccal cusps of the premolars or molars of the mandible. If the starting point of the implant sites in the maxilla is located close to the top of the crest, and if

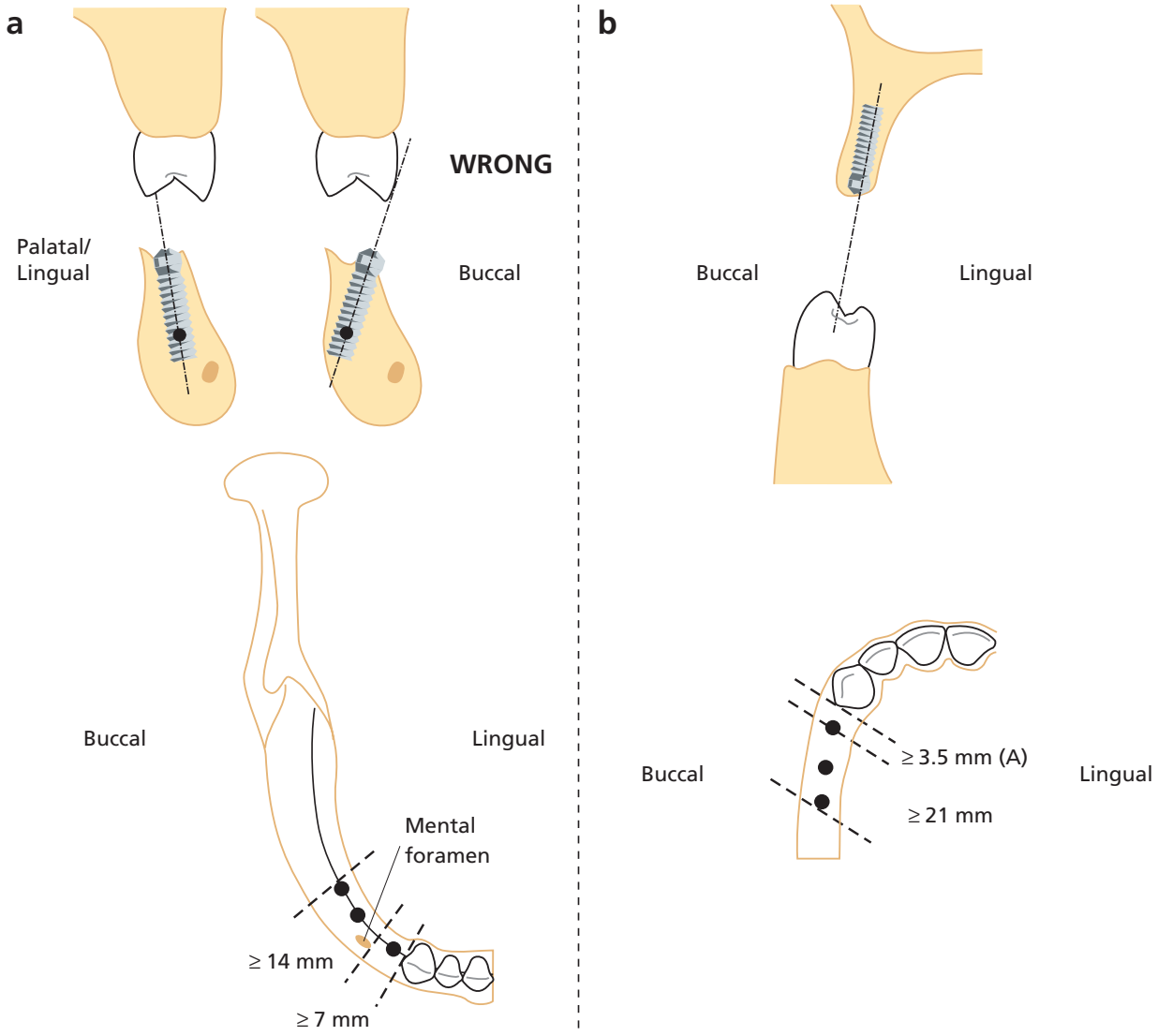

Fig. 48-9 Schematic drawings showing the most favorable starting points and implant directions in a buccal–lingual dimension within (a) the mandible and (b) the maxilla. A = closest distance of a site to a tooth.

a concavity on the buccal side of the ridge is present, there is a risk that the surgeon leans the long axis of the implants too far buccally. The equivalent for the mandible is an implant directed too far lingually owing to the presence of lingual concavities. Such adverse directions can impair the esthetics and function of the future restoration (Fig. 48-7), even though angulated abutments may to some extent compensate for such a surgical shortcoming.

In addition, the inclination of the implants to be inserted will depend on the existing jaw relation. In the case of angle class I jaw relation, the implants should be placed rather vertically in both jaws. In angle class II, the implants should often be placed vertically in the maxilla and slightly buccally in the mandible. In angle class III relations, the implants are inclined buccally in the maxilla and more lingually in the mandible. If the relation between the jaws is markedly adverse, orthognatic surgery may be considered (Clokie 2001) to correct the abnormal jaw relation. Another treatment option in such cases is an overdenture, retained by a bar construction on two implants in the mandible and/or on four implants in the maxilla. The overdenture often offers a favorable outcome to the patient with respect to esthetics, speech, lip and facial support, and function (Naert *et al*. 1998; van Steenberghe *et al*. 2001; Mericske-Stern *et al*. 2002; Eckert & Carr 2004; Kronstrom *et al*. 2006), even though the success rates of the supporting implants might be slightly lower than for implants that support fixed full bridges (Schwartz-Arad *et al*. 2005).

For the mesio-distal orientation of the implant (Fig. 48-10), the rule is that the implant closest to the last tooth is placed parallel with the long axis of the root of this tooth. The further distally the site is located into the molar region, on the other hand, the more inclined are the positions of the implants. In the mandible, for example, it is recommended that the most distal implants be placed in a slightly mesial direction to facilitate the connection of the abutments with the fixed bridge restoration.

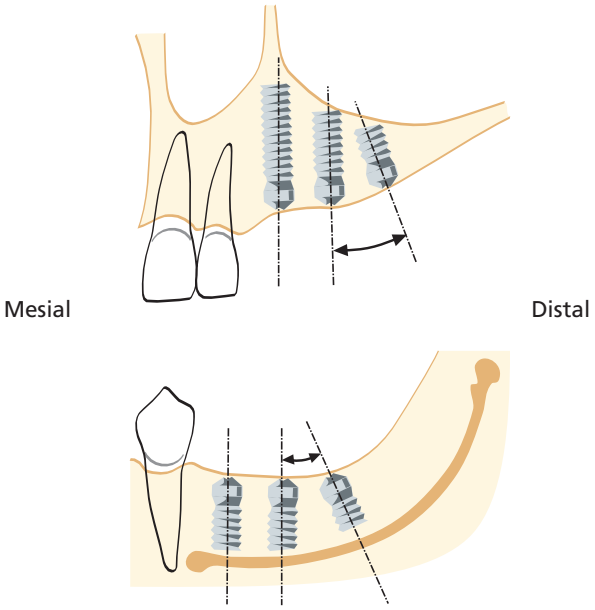

Fig. 48-10 Drawings showing implant directions in the mesial–distal dimension of posterior parts of the jaws. In the maxilla, the most distal implant is directed distally due to the orientation of the sinus wall to engage more bone. In the mandible, the implant is tilted mesially to provide better access for instruments during abutment and prosthetic procedures.

In extremely resorbed mandibles, the most distal implant that is placed immediately in front of the mental foramen, can be tilted distally in order to achieve optimal spreading of the supporting units (Maló *et al*. 2005). Correspondingly, in the resorbed maxilla, the canal prepared for the most distal implant (lateral to the canine) can be directed slightly distally and follow the mesial wall of the maxillary sinus, thereby allowing a longer implant to be placed (Maló *et al*. 2005). An alternative to this procedure would be to use of sinus elevation and grafting techniques (Hochwald & Davis 1992; Neukam & Kloss 2001).

Healing time

According to early protocols the healing time following installation of implants with a turned surface was 3–4 months (Lekholm & Zarb 1985). For the maxilla and occasionally in the posterior areas of the mandible the healing time was 5–6 months, as the bone is normally more cancellous in these portions of the jaws (Adell *et al*. 1985; Watzek & Ulm 2001). Furthermore, for implants placed in quality 4 bone (Lekholm & Zarb 1985), it was recommended that the healing time in the mandible was also extended another 1 or 2 months (Friberg 1994). As variations may exist between different regions of the same jaw, e.g. between frontal and distal segments or even between different sites within the same region (Watzek & Ulm 2001), it is also important to individualize the healing time and to allow the softest bone site to decide the timing.

For implants with a (mechanically or chemically) modified surface, reduced healing times (6 weeks) have been advocated. Such implants have also been recommended for early or even immediate loading protocols (see also Chapter 47). Immediate loading of implants, both with the use of provisional (Balshi & Wolfinger 1997; Schnitman *et al*. 1997) and/or definite reconstructions has been proposed (Brånemark *et al*. 1999; Randow *et al*. 1995; Ericsson *et al*. 2000a; van Steenberghe *et al*. 2005). The current experience with immediate occlusal loading of oral implants was summarized in several consensus reports and systematic reviews (Aparicio *et al*. 2003; Cochran *et al*. 2004; Misch *et al*. 2004a,b; Nkenke & Fenner 2006). Thus, the outcomes of short-term randomized controlled trials have shown that survival and success rates of immediately loaded implants in fully edentulous jaws may be similar to those of conventionally loaded implants (Chiapasco *et al*. 2001; Romeo *et al*. 2002).

The survival rate of immediately restored single-tooth implants was similar to or slightly lower than that of conventionally loaded single-tooth implants (Ericsson *et al*. 2000b; Cannizzaro & Leone 2003). Ericsson *et al*. (2000b) had a restoration placed immediately on the implant, but occlusal contacts were avoided. Some clinicians try to protect "immediately loaded" implants from forces exerted by the tongue or during chewing by using occlusal splints (Lorenzoni *et al*. 2003). To date, there are no controlled studies that enable evidence-based decisions to be made as to whether single-tooth implants can be loaded immediately or should only be restored without occlusal contacts (Nkenke & Fenner 2006).

Currently, it is not possible to draw conclusions concerning exclusion and inclusion criteria for immediate loading, threshold values for implant stability that allow immediate loading, bone quality needed for immediate loading, and the relevance of immediate functional loading and immediate non-functional loading (Nkenke & Fenner 2006). In most of the studies on immediate loading, good bone quality has been mentioned as an important prognostic factor for the success of the procedure (Chiapasco *et al*. 2001; Romeo *et al*. 2002). Although this conclusion seems reasonable, the level of evidence that supports the assumption is low (Nkenke & Fenner 2006). There are, in fact, no controlled studies that have been especially designed to compare immediate loading of oral implants placed in bone of varying density (soft/hard). The same is true for the lengths and diameters of implants that should be used for immediate loading. In one controlled study, moderately rough implant surfaces appeared to improve the survival rate of immediately loaded implants (Rocci *et al*. 2003a,b). In this study, however, the difference between the moderately rough as opposed to the machined-surface implants was not significant.

Review papers on immediate loading have also addressed additional biomechanical aspects of this

procedure (Szmukler-Moncler *et al*. 2000; Gapski *et al*. 2003; Chiapasco 2004; Nkenke & Fenner 2006). Based on different experimental studies, it was stated that a micromotion threshold should not be exceeded; otherwise, osseointegration would be hindered. The critical threshold seems to be 50–150 µm (Pilliar *et al*. 1986; Szmukler-Moncler *et al*. 1998). Therefore, it has been claimed that a high initial stability is necessary for immediate loading of dental implants (Chaushu *et al*. 2001; Calandriello & Tomatis 2005). For this purpose, these authors used modified drilling protocols combined with bone compaction with osteotomes to achieve increased primary stability. Some authors have chosen insertion torque as a measure of implant stability, and arbitrarily selected torque values of ≥32–40 Ncm as thresholds to allow immediate loading (Wöhrle 1998; Hui *et al*. 2001; Lorenzoni *et al*. 2003). With resonance frequency analysis (Meredith *et al*. 1996) it has become possible to measure initial implant stability, i.e. the density of the bone surrounding the implant. The bone quality can thereby be analyzed repeatedly over time and the healing period individualized without using any invasive technique for the tests. An implant stability quotient (ISQ) value of >60 was recommended (Sennerby & Meredith 2002) to allow oral implants to be loaded directly after their insertion. Until now, controlled studies that have compared the relationship between different levels of implant stability and implant survival rate have been lacking. Consequently, there is currently no proven threshold value that indicates that immediate loading will be successful. Besides high initial stability, it has been stressed that immediately loaded implants in multi-unit situations should be rigidly splinted by the use of superstructures (Nikellis *et al*. 2004; van Steenberghe *et al*. 2004). In order to optimize splinting, the use of metal-reinforced superstructures was advocated. High success rates have also been reported for immediate loading of implants connected with superstructures that were not reinforced with metal (Nikellis *et al*. 2004).

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Part 15: Reconstructive Ridge Therapy

Chapter 49

Ridge Augmentation Procedures

Christoph H.F. Hämmerle and Ronald E. Jung

Introduction

Successful implant therapy is dependent upon an adequate volume of bone at the site of implant placement, since the long-term prognosis of dental implants is adversely affected by inadequate bone volume (Lekholm *et al*. 1986).

In principle, four methods have been described to increase the rate of bone formation and to augment bone volume: osteoinduction by the use of appropriate growth factors (Reddi 1981; Urist 1965); osteoconduction, where a grafting material serves as a scaffold for new bone growth (Buch *et al*. 1986; Reddi *et al*. 1987); distraction osteogenesis, by which a fracture is surgically induced and the two fragments are then slowly pulled apart (e.g. Ilizarov 1989a,b); and finally, guided tissue regeneration (GTR), which allows spaces maintained by barrier membranes to be filled with new bone (Dahlin *et al*. 1988, 1991a; Kostopoulos & Karring 1994; Nyman & Lang 1994).

Among these methods, guided bone regeneration (GBR) is the best documented for the treatment of localized bone defects in the jaws. GBR has allowed the use of endosseous implants in areas of the jaw with insufficient bone volume. Lack of bone volume may be due to congenital, post-traumatic, or post-surgical defects or result from disease processes. The predictability and success which can now be achieved with GBR procedures enable the clinician to obtain similar rates of treatment success at sites with bone defects compared to sites without defects (Hammerle *et al*. 2002).

Although bone augmentation procedures are an important part of contemporary implant therapy, other factors are also critical in order to obtain treatment success. In this respect a systematic approach to a given patient situation is key to achieving the desired aim. In complex cases with a multitude of problems, several aspects have to be taken into consideration. These include the patient's general health status, behavior of the patient, environmental factors, the presence of any oral diseases, and the situation at the site planned for implantation as well as the regions of the dentition adjacent to and opposing this site.

GBR is frequently part of complex treatments, but this chapter will focus only on the aspects of bone augmentation at localized defects in the alveolar process.

More than two decades have passed since the introduction of GBR into clinical practice. Today, general understanding of the mechanisms leading to regeneration of desired tissues still agrees with the initially published statements (Karring *et al*. 1980; Nyman *et al*. 1980, 1989). In brief, when a space is formed, cells from the adjacent tissues will grow into this space to form their parent tissue, i.e. the tissue they migrated in from. In order to give preference to

cells from desired tissues, membranes are placed to prevent cells from undesired tissues having access to the space.

Patient situation

It is generally agreed that certain general health conditions represent a risk for successful GBR procedures. In a recent consensus conference one group examined the effect of systemic diseases on implant success (Mombelli & Cionca 2006). It was found that the scientific literature is inconclusive on these issues due to a lack of well performed clinical studies. Hence, it was concluded that neither the same rate of success nor an increased rate of failures have been documented in the presence of the specific systemic conditions under investigation. Furthermore, no conclusive data are available with respect to bone augmentation procedures in patients suffering from systemic diseases which cause impaired tissue healing. The same was found for patients who show behaviors (e.g. smoking, poor compliance) which lead to impaired tissue healing or to a higher susceptibility for disease development. Risk–benefit analysis should be performed with these uncertainties in mind, when planning implant therapy in the presence of bone defects.

It has been demonstrated that implant therapy in patients who have lost their teeth due to periodontal disease will be subject to more implant failures and complications regarding the supporting tissues than in patients who have lost their teeth due to other reasons (Mengel *et al*. 2001; Hardt *et al*. 2002; Karoussis *et al*. 2003; Wennstrom *et al*. 2004). Although, there are few well controlled studies available, it may be expected that these problems also exist when implants are supported by regenerated bone.

Bone morphology

Bone defects may be classified into intra-alveolar, horizontal, and vertical defects. Intra-alveolar defects are dealt with in Chapter 43.

When examining a clinical situation regarding bone morphology, the following aspects are of therapeutic importance: the presence of a bone defect; the size of the edentulous gap (single-tooth, double-tooth or multiple-tooth); and the bone level at the teeth adjacent to the defect.

Horizontal bone defects

Horizontal bone defects are the ones most frequently encountered. They include dehiscences and fenestrations.

The treatment of these types of defects has been shown to be highly successful in numerous studies (Balshi *et al*. 1991; Jung *et al*. 2003; Lundgren *et al*. 1994b; Mayfield *et al*. 1997; Simion *et al*. 1997). In addition, both bioresorbable and non-resorbable membranes have been successfully employed (Sandberg *et al*. 1993; Sevor *et al*. 1993; Schliephake *et al*. 1994; Crump *et al*. 1996; Chung *et al*. 1997; Hammerle *et al*. 1997, 1998; Lundgren *et al*. 1997). In a controlled clinical trial 18 implants with exposed surfaces were treated in nine patients (Simion *et al*. 1997). In the test sites bioresorbable membranes of polylactic and polyglycolic acid (PLA/PGA) were used, whereas non-resorbable membranes of expanded polytetrafluoroethylene (e-PTFE) were applied in the control sites. Autogenic bone was additionally placed to cover the exposed implant threads prior to membrane adaptation. The results at re-entry, 6–7 months later, revealed favorable healing and bone regeneration in both test and control sites, with the control sites demonstrating slightly higher amounts of bone regeneration.

In situations with a bone defect at a site where primary stability of an implant cannot be achieved, or when implant placement is not possible in the ideal location for subsequent prosthetic therapy, GBR prior to implantation represents the method of choice.

Experimental research on ridge augmentation using GBR was presented in the early 1990s (Seibert & Nyman 1990). In a dog model, large defects of the alveolar ridge were surgically prepared both in the mandible and in the maxilla. Morphologic and histologic analysis revealed that, in sites treated with membranes, with or without the addition of grafts, the entire space between the membrane and the jawbone was filled with bone. In the absence of membranes, bone formation was lacking.

The conclusions drawn from these and other pioneering experiments were that the method of GBR can indeed be successfully employed in the regeneration of alveolar ridge defects (Seibert & Nyman 1990; Schenk *et al*. 1994; Smukler *et al*. 1995).

Ridge augmentation in a lateral direction has been shown to be a method with predictable success (Nyman *et al*. 1990; Dahlin *et al*. 1991b; Becker *et al*. 1994b; Nevins & Mellonig 1994; Buser *et al*. 1996; von Arx *et al*. 1996). Successful methods regarding augmentation of the alveolar ridge in a vertical direction, however, are not well established.

Vertical bone defects

Data from animal experiments have clearly demonstrated that gain of bone above the external borders of the skeleton were possible using GBR (Lundgren *et al*. 1995; Hämmerle *et al*. 1996, 1997; Schliephake & Kracht 1997; Schmid *et al*. 1997; Lorenzoni *et al*. 1998).

Vertical ridge augmentation represents the most demanding indication in GBR therapy. Established techniques involve the placement of autogenous, particulated or block bone grafts, or bone substitute materials in combination with e-PTFE membranes of various configurations (Simion *et al*. 1994b, 1998;

Tinti *et al*. 1996; Tinti & Parma-Benfenati 1998; Chiapasco *et al*. 2004). The membranes were either supported by the graft alone or additionally supported by the implant protruding vertically from the host bone for various lengths. The results after submerged healing consistently showed bone formation reaching above the previous border of the alveolar crest. In some situations vertical bone formation reached up to 4 mm above the previous border of the alveolar crest. Within the area of the newly formed bone, osseointegration of the implants had occurred as demonstrated by histologic analysis of experimentally retrieved test implants. The amount of vertical bone formation, however, was not predictable and bone growth to the top of the membrane was not consistently reached when several millimeters of new bone formation were attempted. The remainder of the space between the newly formed bone and the membrane was occupied by non-mineralized tissue (Simion *et al*. 1994a).

Soft tissue morphology

The morphology of the soft tissues at the site of bone regeneration has a significant impact on the result of treatment. On the one hand, soft tissue coverage is a prerequisite for successful bone augmentation. On the other hand, in situations with high esthetic importance the soft tissues and the reconstruction determine whether or not a result is esthetically pleasing.

In many situations the availability of the soft tissues will limit the amount of bone formation possible. In other words a lack of soft tissues may prevent large amounts of bone volume gain because it is impossible to cover the area intended for regeneration. In such situations it may be advisable first to augment the volume of the soft tissues and then perform the bone augmentation procedure as a second step.

Critical aspects regarding the soft tissues include: vertical or horizontal soft tissue defects; level of the soft tissues at the teeth neighboring the gap; gingival biotype; and scars, pathologies or discolorations in the soft tissues lining the area of the bone defect.

Augmentation materials

Membranes

A wide range of membrane materials has been used in experimental and clinical studies to achieve GBR, including polytetrafluoroethylene (PTFE), expanded PTFE (e-PTFE), collagen, freeze-dried fascia lata, freeze-dried dura mater allografts, polyglactin 910, polylactic acid, polyglycolic acid, polyorthoester, polyurethane, polyhydroxybutyrate, calcium sulfate, micro titanium mesh, and titanium foils. Devices used for GBR in conjunction with endosseous implants should be safe and effective. Since no life-threatening diseases or deficiencies are treated, possible adverse effects emerging from the implanted devices should be kept to a minimum. At the same time, documentation of the effectiveness of the procedures and materials should be available. Certain critical criteria regarding membranes used for GTR have been formulated (Hardwick *et al*. 1994): biocompatibility, cell occlusiveness, integration by the host tissues, clinical manageability, and the space making function. For bioresorbable and biodegradable membranes additional criteria need to be fulfilled. Tissue reactions resulting from the resorption of the membrane should be minimal, these reactions should be reversible, and they should not negatively influence regeneration of the desired tissues (Gottlow 1993).

Although GBR is quite a successful procedure, a better understanding of the factors critical for success or failure is mandatory. This understanding will lead to more refined clinical protocols and will allow for the manufacturing of membrane materials with improved performance for a given indication. Some of these factors include membrane stability, duration of barrier function, enhanced access of bone and bone marrow-derived cells to the area for regeneration, ample blood fill of the space, prevention of soft tissue dehiscence, *in situ* forming, and delivery of factors influencing tissue formation beneficially.

Non-resorbable membranes

With the presentation of the first successful GBR procedures and the subsequent wide and successful application of e-PTFE membranes, this material soon became a standard for bone regeneration. Expanded PTFE is characterized as a polymer with high stability in biologic systems. It resists breakdown by host tissues and by microbes and does not elicit immunologic reactions.

A frequent complication with membrane application in conjunction with implants is membrane exposure and infection. Wound dehiscence and membrane exposure have been reported to impair the amount of bone regenerated in a number of experimental animal (Gotfredsen *et al*. 1993; Kohal *et al*. 1999a) and clinical investigations (Gher *et al*. 1994; Simion *et al*. 1994a; Hämmerle *et al*. 1998).

In situations where bone formation is desired in large defects or in supracrestal areas, conventional e-PTFE membranes do not adequately maintain space unless supported by grafting materials. The alternative approach involves the use of membranes with a stable form, such as titanium-reinforced membranes. Recent research has demonstrated the successful use of these membranes in vertical ridge augmentation and in the treatment of large defects in the alveolar process (Jovanovic & Nevins 1995; Tinti *et al*. 1996; Simion *et al*. 1998).

Many of the factors critical for successful bone formation were identified in experimental studies

applying e-PTFE membranes. Furthermore, clinical protocols regarding surgical procedures, postoperative care, and healing times required were established using non-resorbable membranes. Today, as evidence of the effectiveness of bioresorbable membranes increases, non-resorbable membranes are losing importance in clinical practice and their use is increasingly limited to specific indications. Since e-PTFE membranes have been documented to allow successful GBR therapy, results obtained using new materials should always be compared with results of e-PTFE membranes.

Bioresorbable membranes

Non-resorbable membranes have to be removed during a second surgical intervention. The removal surgery will impose morbidity and psychologic stress on the patient and represents a risk for tissue damage. Since these disadvantages do not occur when working with bioresorbable membranes, they are increasingly applied in the clinic.

Apart from the fact that there is no need for surgical intervention for removal of the membrane, bioresorbable membranes offer some additional advantages. These include improved soft tissue healing (Lekovic *et al*. 1997, 1998; Zitzmann *et al*. 1997), the incorporation of the membranes by the host tissues (depending on material properties), and quick resorption in case of exposure, thus eliminating open microstructures prone to bacterial contamination (Zitzmann *et al*. 1997; Lorenzoni *et al*. 1998).

Bioresorbable materials that may be used for the fabrication of membranes all belong to the groups of natural or synthetic polymers. The best known groups of polymers used for medical purposes are collagen and aliphatic polyesters. Currently tested and used membranes are made of collagen, or of polyglycolide and/or polylactide or copolymers thereof (Hutmacher & Hürzeler 1995).

A wide range of bioresorbable membranes made of either collagen or polyglycolide and/or polylactic acid has been investigated in experimental and clinical studies (Lundgren *et al*. 1994a; Mayfield *et al*. 1997; Simion *et al*. 1997; Zitzmann *et al*. 1997). Results have generally been good, partly because of the low rate of complications, so bioresorbable membranes have become the standard for most clinical situations and have, thus, largely replaced the non-resorbable e-PTFE membranes.

It should be realized, however, that in a recent systematic review a reasonable comparison between bioresorbable and non-resorbable membranes could not be drawn due to a lack of well designed studies (Chiapasco *et al*. 2006). Only a few studies could be identified which compared the results of bioresorbable and non-resorbable membranes (Zitzmann *et al*. 1997, 2001b; Christensen *et al*. 2003). These studies did not find any difference between the two treatment modalities.

Obviously, choice of material is critical when it comes to bioresorbable membranes for GBR. Inflammatory reactions have been documented in the tissues adjacent to some bioresorbable membranes, ranging from mild (Sandberg *et al*. 1993; Piatelli *et al*. 1995; Aaboe *et al*. 1998; Kohal *et al*. 1999a,b) to severe (Gotfredsen *et al*. 1994). Another study reported on therapeutic failures using polylactic membranes for bone regeneration at peri-implant defects in dogs (Schliephake *et al*. 1997). Soft tissue complications were frequent, and the results did not reveal any improvement over control sites without the use of membranes.

Convincing results of bone regeneration in animal experiments have been reported for collagen membranes (Hürzeler *et al*. 1998; Zahedi *et al*. 1998). Furthermore, reports of human cases or case series (Hämmerle & Lang 2001) as well as controlled clinical studies (Zitzmann *et al*. 1997) have been presented describing the successful use of collagen membranes for GBR at exposed implant surfaces.

Bioresorbable membranes that are commercially available at present are not capable of maintaining adequate space unless the defect morphology is very favorable (Oh *et al*. 2003; Lundgren *et al*. 1994b). Even if the membranes seem able to maintain space initially, they generally lose their mechanical strength soon after implantation into the tissues. Favorable results have been reported only in situations where the bony borders of the defects adequately support the membrane. When defects do not maintain the space by themselves, failure of bone regeneration results (Zellin *et al*. 1995; Mellonig *et al*. 1998). Therefore, they need to be supported in some way.

In summary, animal experiments, human case reports, and initial controlled clinical studies demonstrate that bioresorbable and non-resorbable membranes can successfully be used for bone regeneration at implants with exposed surface areas. It appears, however, that bioresorbable membranes generally show better clinical performance compared with non-resorbable membranes. Hence, unless the defect morphology or other factors prevent the application of bioresorbable membranes their use is to be preferred. The choice of the best material has to be based on the individual patient situation.

Bone grafts and bone graft substitutes

Bone grafts have long been used in reconstructive surgery with the aim of increasing the bone volume in the previous defect area. Bone grafts and bone substitute materials may be classified into two main groups: autogenic and xenogenic materials. The term autogenic graft refers to tissues that are transplanted within one and the same organism. Xenogenic grafts encompass all materials of an origin other than the recipient organism and may further be divided into materials from the same species but different individuals, materials from other species, and finally products of non-organic origin.

Bone grafts or bone graft substitutes in conjunction with GBR need to fulfill a number of requirements. They should adequately support the membrane to provide a predefined volume of the regenerated bone. In addition, they should serve as a guiding structure into which the bone can grow or is even encouraged to grow. As a result capillaries and perivascular cells can easily form and migrate, respectively, within the voids provided by the supporting material. Later bone-forming cells can populate the spaces and produce new bone. Finally, the supporting material should be resorbed and replaced by the patient's own bone (Jensen *et al*. 1996; Fugazzotto 2003a,b).

The successful combination of autogenic corticocancellous bone grafts and GBR has been shown in a clinical study (Buser *et al*. 1990). A group of 40 patients, who had been treated with this method, demonstrated very low frequency of soft tissue complications and successful ridge augmentation in 66 sites. A mean gain in crest width of 3.5 mm was measured allowing implant placement in a proper position in all 66 sites. More recently, studies in humans and animals have lead to further development and refinement of this method with very good clinical success (Buser *et al*. 1996).

The necessity for membranes in conjunction with block grafts was tested in a prospective randomized clinical study involving 13 patients (Antoun *et al*. 2001). Patients were either treated with onlay bone grafts alone or additionally covered by e-PTFE membranes. The width of the ridges was evaluated clinically immediately following graft placement and at the time of membrane removal 6 months later. In the group with membranes significantly less resorption had occurred. This controlled clinical study confirms animal experimental data and is in accordance with case series reporting the occurrence of pronounced resorption of bone grafts (Jensen *et al*. 1995; Widmark *et al*. 1997; von Arx *et al*. 2001; Cochran *et al*. 2002).

Xenogenic bone substitutes have been developed and applied to GBR. Experimental studies have dealt with materials manufactured synthetically, derived from corals or algae, or originated from natural bone mineral (for review see Hammerle & Jung 2003). These materials are regarded to be biocompatible and osteoconductive. Nevertheless, considerable differences have been reported in their behavior based on material properties.

In a recent systematic review it was concluded that the paucity of available scientific data precludes clear recommendations regarding the choice of a specific supporting material for GBR procedures (Chiapasco *et al*. 2006). Comparative data were rarely found (Christensen *et al*. 2003) and no randomized controlled clinical trials were available as a basis for decision making.

The studies evaluating clinical outcomes of lateral ridge augmentation with GBR procedures in staged implantation commonly used autogenous bone as filler materials in combination with non-resorbable membranes (Nevins & Mellonig 1994; Buser *et al*. 1996). Limited data are available reporting on the application of bone substitutes in combination with bioresorbable membranes for ridge augmentation prior to implant placement (Zitzmann *et al*. 2001a; Friedmann *et al*. 2002; Hammerle *et al*. 2008).

In one of these studies 12 patients with 15 sites exhibiting lateral bone defects were treated using blocks of deproteinized bovine bone mineral and bioresorbable collagen membranes (Hammerle *et al*. 2008). The size of the defects precluded implant placement without prior bone augmentation. Initially the average ridge width amounted to 3.2 mm. At the re-entry operation 9–10 months later, the mean crestal bone width had increased to 6.9 mm. In all of the cases but one, the resulting bone volume was adequate to place the implant in a prosthetically optimal position. In one case, no gain of bone volume had occurred during the phase of regeneration for unknown reasons. While in previous clinical studies, small bone defects at implant sites had been augmented by use of DBBM (Hämmerle & Lang 2001; Zitzmann *et al*. 2001a; Friedmann *et al*. 2002; Hellem *et al*. 2003), larger bone defects were predictably augmented in this case series (Hammerle *et al*. 2008).

The technique of applying biomaterials to support bioresorbable membranes avoids the risks associated with harvesting autogenic bone (Nkenke *et al*. 2001; von Arx *et al*. 2005). This is a significant benefit to the patient and represents an important step in the development of GBR procedures. Future research should be focused on such patient-centered outcomes. The development of biomaterials, ideally coupled with the incorporation of bone growth factors and bioactive peptides, represents an important line of research in this direction (Jung *et al*. 2003).

Long-term results

Recent systematic reviews have compiled the literature regarding survival and success rates of implants partly or fully placed into regenerated bone (Hammerle *et al*. 2002; Fiorellini & Nevins 2003; Chiapasco *et al*. 2006). The survival rate of implants placed into sites with regenerated/augmented bone using barrier membranes varied between 79% and 100% with the majority of studies indicating more than 90% after at least 1 year of function. The survival rates obtained in the studies identified by these systematic reviews were similar to those generally reported for implants placed conventionally into sites without the need for bone augmentation. Two studies were identified that provided internal control data (Mayfield *et al*. 1998; Zitzmann *et al*. 2001b). In particular, the data from these two studies provided survival and success rates with no significant differences for implants in regenerated compared to non-regenerated bone. In addition, the loss of crestal bone

was not different between test and control implants in one of these studies (Mayfield *et al*. 1998).

The long-term stability of vertically augmented bone was assessed in a multi-center study involving 123 patients (Simion *et al*. 2001). The results demonstrated marginal bone level changes to be within the range of variations reported for implants placed into intact bony beds.

Long-term analysis of the stability of the regenerated bone is almost exclusively focused on radiographic assessments of the interproximal bone and on implant survival. There is a need for studies to evaluate the fate of the buccal bone plate, regenerated or not, over time. As has been suggested in previous studies, the stability of the regenerated bone may be assessed using various clinical or radiographic measures (Chiapasco *et al*. 1999).

Clinical concepts

Analysis of the bony defect morphology is the basis for deciding which treatment strategy to follow and which materials to apply for GBR. Basically there are two procedures: a one-step (combined approach) and a two-step (staged approach) procedure. Whenever the bone morphology allows anchorage of the implant with primary stability in prosthetically correct position the one-step approach is preferred. In situations where the defect morphology precludes primary implant stability, the two-step procedure is performed, i.e. the bone volume is first augmented to a degree allowing implant placement in a second intervention. The classification of bone defects is intended as a guideline for choosing the best techniques and materials for GBR at implant sites (Fig. 49-1).

Ridge preservation

In situations where there is a substantial lack of soft and/or hard tissues it may be advisable to apply methods for improving hard tissue as well as soft tissue healing. Attempts have been made to maintain the contour of the ridge by placing non-resorbable materials into the fresh extraction socket. Cones of hydroxyapatite were placed into the socket (Denissen & de Groot 1979; Quinn & Kent 1984). Whereas the resorption of the ridge could be somewhat reduced the overall result was not satisfactory. A large number of soft tissue dehiscences occurred and in some situations the cones had to be removed (Kwon *et al*. 1986).

GBR has been used to preserve or augment the alveolar ridge at the time of tooth removal. Supporting materials were placed into fresh extraction sockets and subsequently covered by non-resorbable membranes (Nemcovsky & Serfaty 1996; Lekovic *et al*. 1997; Fowler *et al*. 2000). One of the problems encountered, as described above, is the lack of soft tissue to cover the GBR site completely. In order to solve this problem coronal and lateral sliding flaps or soft tissue grafts were employed. In some studies no attempt was made to contain the filler material with membranes nor was the soft tissue manipulated to allow for primary closure. In these situations and when necrosis of the covering soft tissues occurred, loss of grafting particles was a common finding (Nemcovsky & Serfaty 1996).

Histomorphometric analysis of biopsies revealed that more vital bone had formed at sites treated with GBR compared to sites that were left to spontaneous healing. The investigators attributed this positive finding to the characteristics of the filler materials.

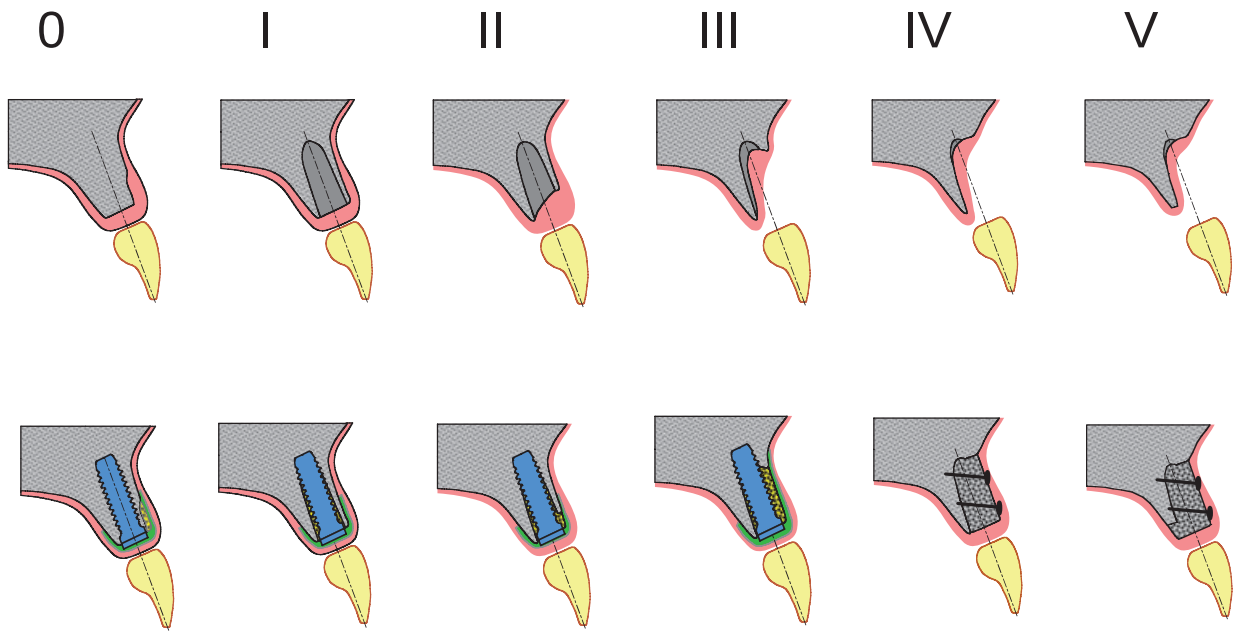

Fig. 49-1 Schematic drawing depicting the defect classification with classes 0–V.

Both osteoconductivity and resorbability of the materials apparently influenced new bone formation in a positive manner (Smukler *et al*. 1999; Artzi *et al*. 2000; Bolouri *et al*. 2001; Froum *et al*. 2002).

When applying GBR procedures it was clinically observed that the rate of resorption of the alveolar process could be reduced compared to untreated control sites (Lekovic *et al*. 1997, 1998; Yilmaz *et al*. 1998; Camargo *et al*. 2000). Complications with soft tissue dehiscences, however, frequently occurred in GBR-treated sites (Fowler *et al*. 2000; Yang *et al*. 2000). Although, the method of using GBR to reduce the loss of ridge volume has been well documented, it is not practical in many clinical situations due to the following shortcomings: it requires a long healing period before the implant therapy can be continued; the method is invasive and technique sensitive; soft tissue coverage is difficult to achieve and may lead a compromized esthetic result; and it is costly.

A different approach to provide optimal conditions for implant therapy regarding the profile of the alveolar ridge has led to the development of techniques aimed at improving the soft tissue conditions. Previous case reports described the use of autogenous soft tissue grafts to seal extraction sites before (Landsberg & Bichacho 1994) or at the time of implant placement (Evian & Cutler 1994; Landsberg 1997; Chen & Dahlin 1996; Tal 1999). Several problems exist with these procedures, including necrosis of the transplanted mucosa and poor color integration at the recipient site. In order to address this issue in a systematic way 20 patients in need of tooth extraction received soft tissue grafts to seal the entrance to the alveolus of the freshly extracted tooth (Jung *et al*. 2004) (Fig. 49-2a). First a grafting material was placed into the socket with the aim of maintaining the contour of the ridge. Subsequently, a soft tissue graft harvested from the palate was carefully sutured to cover the grafting material and thus seal off the alveolus from the oral cavity (Fig. 49-2b). Six weeks later, the vitality of the graft and the color match with respect to the surrounding mucosa were assessed. More than 99% of the grafted tissue area appeared vital. Digital measurement of the color difference between the grafted and the neighboring host tissues generated values below thresholds for normally detectable values in such situations (Fig. 49-2c). This technique, therefore, beneficially influenced the conditions at extraction sites for subsequent implant placement and soft tissue management in comparison to spontaneous healing (Fig. 49-3). Due to the effort and expense necessary to perform this treatment approach, it is primarily recommended for situations with high esthetic priority.

At times the implant is completely inserted into native bone but the buccal contour of the hard and soft tissues is insufficient for an optimal treatment outcome. This may be the case in esthetically highly demanding situations. In order to improve the esthetic result an augmentation procedure is conducted (class 0). A membrane-supporting material and a membrane are placed to promote labial bone formation in order to obtain the desired tissue contours.

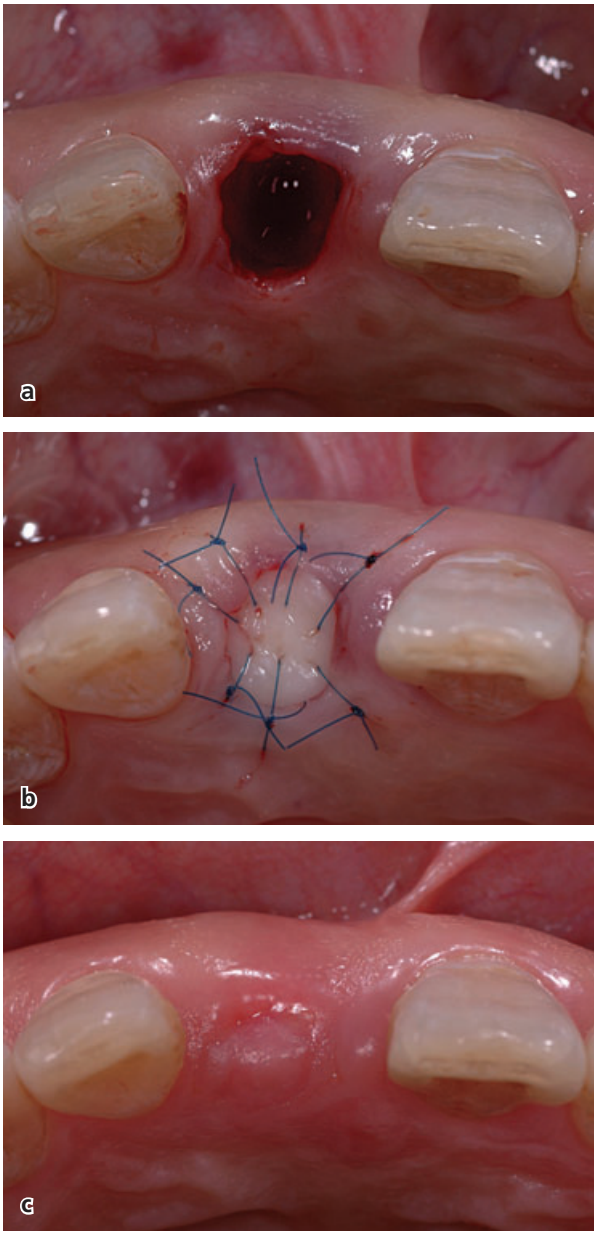

Fig. 49-2 (a) Occlusal view of an extraction site 11 immediately following removal of the tooth. Note the normal appearance of the external ridge contour and the soft tissue deficit over the extraction socket. (b) A soft tissue graft taken from the palate has been placed and sutured to seal the entrance of the alveolus. (c) After 6 weeks of healing, the soft tissue graft is completely integrated at the recipient site and a healthy soft tissue cover of the former entrance of the alveolus is present.

Extraction sockets (class I)

Currently implants are often placed in fresh extraction sockets. Although some of these clinical procedures were first described many years ago, their application has become more common in recent years.

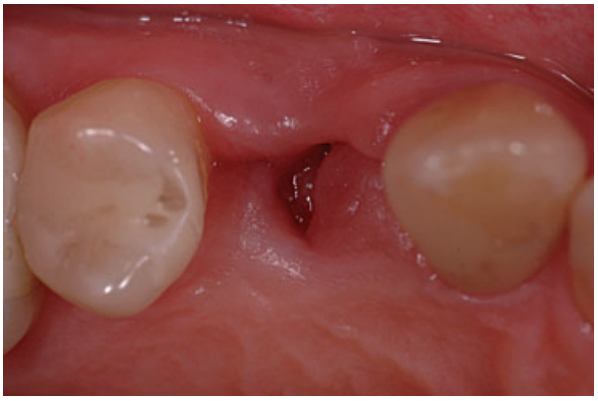

Fig. 49-3 An extraction site after 6 weeks of spontaneous healing. Note the incomplete healing rendering soft tissue management difficult.

In situations where teeth are to be replaced with implants, a decision must be taken during treatment planning whether the implant should be placed immediately after tooth extraction or if a certain number of weeks of healing of the soft and hard tissues of the alveolar ridge should be allowed prior to implant placement. For details regarding timing of implant placement into extraction sockets see Chapter 47.

If bone augmentation is required at implants immediately placed into extraction sockets, the following procedure is recommended. A flap is raised to allow easy access to the site and the implant is inserted. A membrane-supporting material is adapted to support the membrane. Depending on the defect morphology (for details see Chapter 47) this material is placed into the space between the walls of the socket and the implant surface. In addition, in some situations, especially in the esthetic zone, it may be necessary to augment the bone beyond the labial wall of the socket. Thus, the membrane-supporting material is also applied in order to correct the ridge profile to obtain a more prominent labial tissue contour. Subsequently, the membrane is adapted to cover the supporting material and a narrow zone of the adjacent bone and the flap is adapted and sutured. Whenever a partial or complete loss of the buccal wall of the socket is encountered the procedure described for dehiscence defects is applied.

Dehiscence defects (classes II and III)

Dehiscence defects may range from a very small lack of marginal bone to large areas of denuded implant surfaces. As long as the implant can be securely anchored in the existing bone, concomitant implantation and bone regeneration may be performed. When the defect is quite small, it may be questionable whether or not a regeneration procedure will improve the treatment outcome and its long-term stability (Hämmerle 1999). Often the esthetic result, as well as aspects of health and function, is important. In esthetically demanding situations it is generally recommended to perform an augmentation procedure, whereas in other areas of the mouth recommendations are not as strict. It needs to be understood, however, that the presently available scientific data do not allow an evidence-based statement to be made regarding the borderline between a situation requiring bone augmentation and a situation without this requirement (Chiapasco *et al*. 2006).

In situations where it is decided to carry out a GBR procedure, the material of choice should fulfill the following requirements: it should have proven efficacy; be thoroughly researched and scientifically documented; and be re-evaluated at regular intervals. In recent clinical studies, it has been demonstrated that the application of bone substitutes in conjunction with the placement of implants lead to successful coverage of the previously exposed implant surfaces (Zitzmann *et al*. 1997; Hämmerle *et al*. 1998; Moses *et al*. 2005). Hence, harvesting of autogenous bone for the treatment of dehiscence defects may not always be necessary for a successful treatment outcome.

The grafting material should reliably support the area intended for bone augmentation, allow or preferably promote in-growth of bone forming cells, and support bone–implant contact formation. Among other materials deproteinized bovine bone mineral is very well researched and has consistently demonstrated excellent clinical results (Esposito *et al*. 2006).

When choosing an appropriate membrane the same basic documentation as required for the supporting materials needs to be available: i.e. it should have proven efficacy; be thoroughly researched and scientifically documented; and be re-evaluated at regular intervals. Additional parameters regarding selection of a suitable membrane include the mechanical properties, the risk for soft tissue dehiscence, and the ease of clinical handling. In most situations with dehiscence defects a bioresorbable collagen membrane will be optimal regarding the scientifically and clinically required characteristics. In contrast, in situations, where the defect morphology requires improved stability of the area to be regenerated, e-PTFE membranes are most suitable. Apart from the substantial risk for soft tissue dehiscence and subsequent infection of the area, the need for membrane-removal surgery represents the major disadvantage of non-resorbable membranes. As a consequence, bioresorbable membranes are preferred whenever possible for the treatment of small and larger dehiscence defects.

The clinical protocol to promote bone formation for successful coverage of exposed implant surfaces includes the following steps. After a flap is raised, the implant is inserted (Fig. 49-4a). A membrane-supporting material is placed in the area of the buccal dehiscence defect with the aim of promoting bone formation for bone integration of the implant and

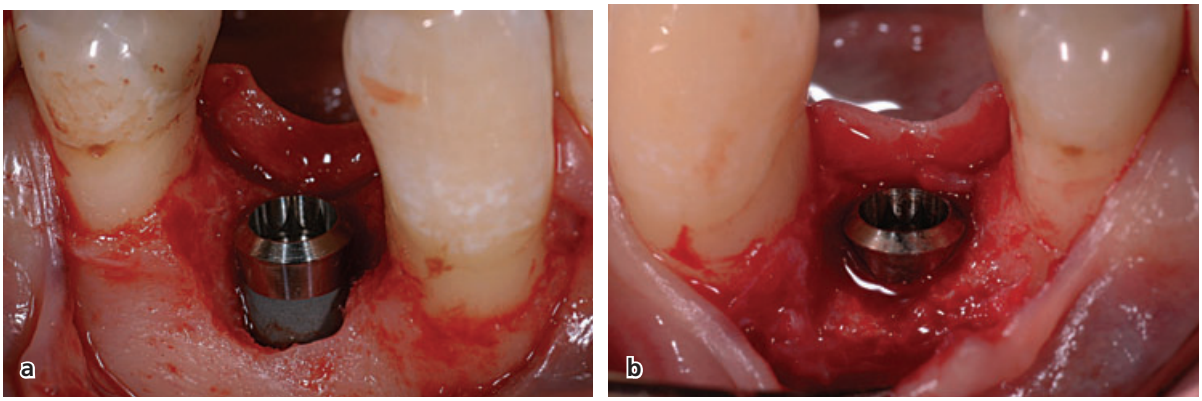

Fig. 49-4 (a) A small labial dehiscence defect at an implant in position of tooth 44. The defect is treated by GBR applying a bioresorbable membrane and a deproteinized bovine bone mineral for membrane support. (b) The same case as in (a) at re-entry surgery. New bone has formed within the previous defect area. A thin layer of non-mineralized tissue covers the regenerated bone.

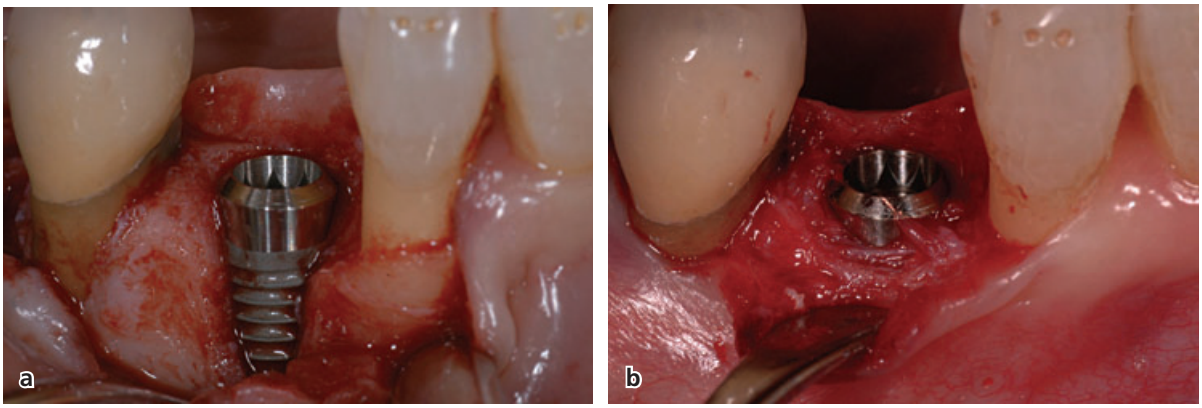

Fig. 49-5 (a) A large labial dehiscence defect at an implant in position of tooth 43. The defect is also treated by GBR applying a bioresorbable membrane and a deproteinized bovine bone mineral for membrane support. (b) The same case as in (a) at re-entry surgery. The dehiscence defect has been augmented with bone, which is covered by a thin layer of non-mineralized tissue.

obtaining a natural appearance of the bone and soft tissue contours of the alveolar ridge. Subsequently a membrane is adapted and placed to cover the supporting material and the defect. A decision has to be taken on how the membrane is fixed in place to provide the stability necessary for bone to form. This fixation may be obtained by simply adapting the membrane to the intact walls of the bone defect, by tacking it with pins, by suturing it to the soft tissues, or by adapting it to the implant. Thereafter, the flap is adapted and sutured to allow for submerged or transmucosal healing of the implant site. Following 4–6 months of healing the former defect is filled with new bone (Fig. 49-4b). The same clinical protocol is applied for the treatment of larger dehiscence defects (Fig. 49-5).

Horizontal defects (class IV)

The autogenous block transplant represents the gold standard for treatment of horizontal ridge defects (Becker *et al*. 1994a; Buser *et al*. 1996; von Arx *et al*. 2001). Both intraoral and extraoral harvesting procedures have been described. Intraoral sites have been preferred, especially for the treatment of localized bone defects in partially edentulous jaws (Joshi & Kostakis 2004). Intraorally, common donor sites include the chin and the area of the retromolar region in the mandible. Intraoral harvesting procedures also have disadvantages, such as limited availability of bone graft volume, complications including altered sensation of teeth, neurosensory disturbances, wound dehiscence, and infection (Nkenke *et al*. 2001; von Arx *et al*. 2005).

The advantages of autogenic block grafts include the large scientific and clinical documentation, handling properties, stabilization of the area intended for regeneration due to the possibility of securing the grafts in place by metal screws, and the optimal biologic properties. The disadvantages include donor site morbidity, technically difficult harvesting procedures, and the impossibility of using the graft as a carrier for growth factors.

Clinical procedures require harvesting of the graft, adaptation to the defect area, fixation by screws, coverage with a membrane, and primary closure with the soft tissue flap. During a second surgical intervention after 4–9 months of healing, the result of the

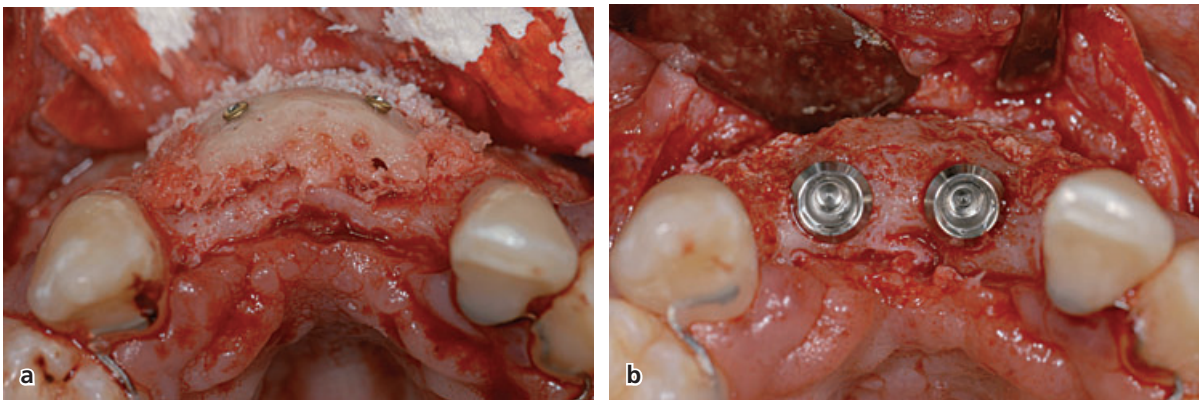

Fig. 49-6 (a) An extensive bone defect in the anterior maxilla. A bone graft harvested from the chin is adapted and secured in place by titanium screws. In the periphery bone chips and deproteinized bovine bone mineral are added to improve contouring of the area. Subsequently, a bioresorbable collagen membrane is placed to cover the area intended for bone augmentation and the flap is closed. (b) The same case as in (a) at the time of implant placement. Note the large volume of bone available for implant placement and as a basis for achieving an optimal esthetic result.

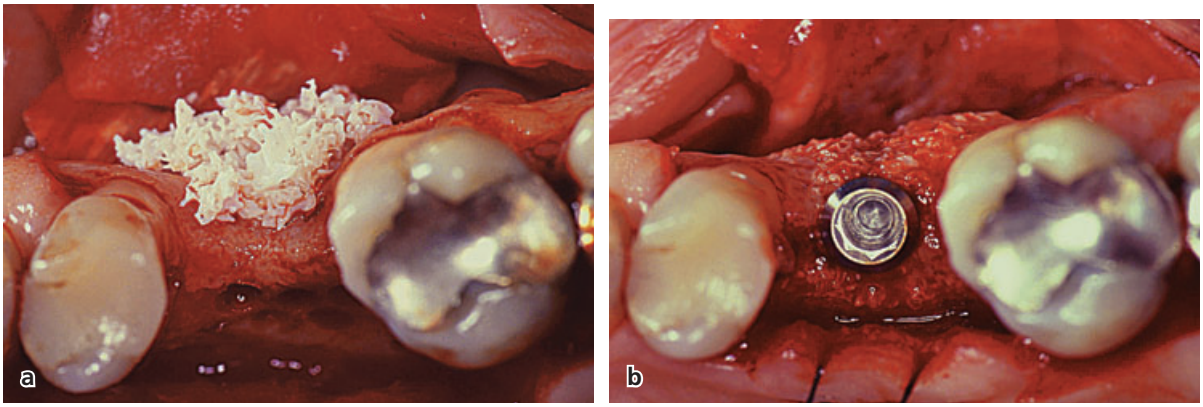

Fig. 49-7 (a) A lateral bone defect at a single tooth gap. A block of deproteinized bovine bone mineral and chips generated from this block are placed to support a bioresorbable collagen membrane before the flap is closed. (b) The same case as in (a) at the time of implant placement. Note the substantial volume of bone available for implant placement as a basis for achieving an optimal result.

augmentation procedure can be seen and implants can be placed (Fig. 49-6).

As described above recent case reports and case series have described the use of deproteinized bovine bone mineral in conjunction with bioresorbable collagen membranes and found successful bone augmentation at lateral ridge defects (Zitzmann *et al*. 2001a; Friedmann *et al*. 2002; Hammerle *et al*. 2008). During the second surgical intervention implants could be placed in a prosthetically optimal position in most situations (Fig. 49-7).

These newer studies indicate that, provided the appropriate protocols are developed, ridge augmentation without the use of autogenous block grafts could become a standard procedure.

Vertical defects (class V)

The indications for vertical ridge augmentation include situations where the remaining bone height is too small for proper anchorage of oral implants, where unfavorable crown:implant ratios will result, and where unfavorable esthetic outcomes are expected from the lack of remaining hard and soft tissues.

The same procedures are recommended for patient treatment as described for the class IV defects with the exception that the bone block is partially or fully placed on to the ridge in order to gain bone in a vertical direction. Other than that the materials and the techniques applied are identical to the ones for lateral bone augmentation using bone grafts. Obviously, flap adaptation is more difficult due to the increased volume intended for regeneration, which needs to be covered by the flap.

It appears that varying amounts of bone height may be gained, depending on the clinical treatment protocol. The factors critical for success or failure have not been elucidated. In addition, no data is presently available indicating whether there is a biologically limited maximum of bone gain, and if so, what parameters influence this maximum.

Future developments

Progress in every medical discipline is largely based on better understanding of the physiologic and pathologic mechanisms governing health, disease, and healing. This understanding is a key step to the development of new strategies and materials in medicine. The aim is to develop more effective techniques that predictably promote the body's natural ability to regenerate lost tissue instead of using external materials to repair lost tissue. The most intriguing method currently being investigated is the application of polypeptide or natural proteins that regulate wound and tissue regeneration.

Growth and differentiation factors

In the past decade a number of basic science experiments and clinical studies have clarified biologic mechanisms of several growth and differentiation factors on the regeneration of oral soft and hard tissue (Howell *et al*. 1997a). Growth and differentiation factors currently believed to contribute to periodontal and alveolar ridge augmentation include platelet-derived growth factor (PDGF), insulin-like growth factor (IGF-I and IGF-II), transforming growth factor beta (TGF-β), fibroblast growth factor (a-FGF and b-FGF), and bone morphogenetic proteins (BMPs 1–15). Among these bone morphogenetic protein is the most widely studied in the dental literature. BMP, by chemotaxis, triggers proliferation and differentiation of mesenchymal progenitor cells (Wozney *et al*. 1988). Recombinant biotechnology has enabled characterization of at least 15 BMPs and production of quantities of purified recombinant protein for therapeutic application (Groeneveld & Burger 2000). Recombinant human BMP-2 (rhBMP-2) has been found to exhibit very high osteogenic activity in experimental (Sigurdsson *et al*. 1996; Hanisch *et al*. 1997; Cochran *et al*. 1999; Higuchi *et al*. 1999; Jung *et al*. 2005) and in clinical studies (Boyne *et al*. 1997; Howell *et al*. 1997a; Jung *et al*. 2003, 2005).

Delivery systems for growth and differentiation factors

The regenerative potential of growth and differentiation factors depends upon the carrier material (Sigurdsson *et al*. 1996; Hunt *et al*. 2001). The effect of such proteins is dependent upon a carrier material, which serves as a delivery system and as a scaffold for cellular in-growth (Ripamonti & Reddi 1994).

Collagen has extensively been studied as a carrier material for growth factors applied to promote bone formation in different kinds of indications (Nevins *et al*. 1996; Boyne *et al*. 1997; Howell *et al*. 1997b). Different studies (Barboza *et al*. 2000) using rhBMP-2 in an absorbable collagen sponge (ACS) for alveolar ridge augmentation gained only small amounts of bone. The investigators concluded that the compromised results were due to the failure of the ACS to adequately support the supra-alveolar wound space. In order to overcome this lack of structural strength rh-BMP-2/ACS has been combined with hydroxyapatite (HA) in an experiment attempting lateral ridge augmentation (Barboza *et al*. 2000). In contrast to rhBMP-2/ACS alone, a significant clinical improvement in ridge width was observed with the addition of HA to rhBMP-2/ACS. However, the HA particles were largely encapsulated by fibrous tissue and they appeared partially to obstruct bone formation. The investigators concluded that space maintenance in BMP-induced bone formation is an important factor (Barboza *et al*. 2000). A recent study demonstrated that the results of GBR procedures in humans could be improved by the addition of rhBMP-2 to a xenogenic bone substitute mineral. This improvement was documented by a higher degree of bone maturation and an increased graft–bone contact fraction at the BMP-treated sites (Jung *et al*. 2003). Synthetic polymers, on the other hand, can reproducibly be fabricated and the growth factors can be incorporated under controlled manufacturing conditions (Weber *et al*. 2002).

In a recent study in dogs implants were placed in the mandible and peri-implant infra-osseous defects were prepared (Jung *et al*. 2007). The defects were grafted with a synthetic polyethylene glycol (PEG) matrix, which was either empty or contained a 35 amino acid peptide of parathyroid hormone (cys-$PTH_{1–34}$). Control defects were grafted with autogenous bone or left empty. One and three months later, the sites with PEG and PTH showed similar amounts of bone formation compared with the sites grafted with autogenous bone. In the two other groups less bone formation was observed. It was concluded that the synthetic PEG hydrogel containing $PTH_{1–34}$ was a suitable matrix-differentiation factor system to obtain bone regeneration.

However, the ideal carrier material, which is easy to apply, able to provide space for regeneration, bioresorbable, and allows controlled release of the bioactive molecules, has not yet been discovered. Further research is needed to determine the ideal combination of factors for regeneration, the best delivery system, and the optimum doses.

Membrane developments

The benefit of using both barrier membranes and BMP for bone augmentation remains controversial (Linde & Hedner 1995; Howell *et al*. 1997b; Cochran *et al*. 1999; Jung *et al*. 2003). It was found that the presence of a non-resorbable e-PTFE membrane initially (4 weeks) inhibited bone formation with rhBMP-2 but did no longer do so at later time points (12 weeks) (Cochran *et al*. 1999). It has been shown that bone induction by rhBMP-2 occurs at early time points and that rhBMP-2 undergoes rapid clearance. Hence, the use of a membrane may potentially reduce

the bone-forming effect of rhBMP-2 due to limited availability of inducible cells. Another animal study in rats reported no difference in bone healing with the combination of rhBMP-2 and an e-PTFE membrane compared to rhBMP-2 alone (Linde & Hedner 1995). From a clinical point of view, the use of a membrane simplifies the handling and stabilization of the bone substitute mineral at the time of bone augmentation, but from a biologic point of view the use of a membrane may block the recruitment of cells from the environment.

The question whether or not bioactive molecules are best used in conjunction with membranes or in the absence of membranes has not yet been answered conclusively. On the one hand, it is reasonable to apply them as adjunctive agents to GBR therapy in order to accelerate membrane-guided bone regeneration. On the other hand, it may be hypothesized that their mode of action is best taken advantage of when membranes are not applied simultaneously, thus allowing all inducible cells from the wound environment access to the area to be regenerated.

Common to all presently used membranes is the fact that their fabrication is completed before they are delivered for patient use. Consequently, they are made available in standard sizes and forms and need to be adapted to the patient's individual situation. Alternatively, a membrane could be custom made directly for an individual defect intra-operatively, using a material different from the ones mentioned above.

Hydrogels made of PEG fulfill a number of criteria required to serve as synthetic membranes which form *in situ*. Polyethylene glycol has been shown to be highly biocompatible (Pang 1993; Working *et al*. 1997). It is presently approved for several pharmaceutical applications (Zalipsky & Harris 1997) and as medical devices, e.g. a sprayable adhesion barrier.

In a recent study in rabbits, four evenly distributed craniotomy defects, 6 mm in diameter, were prepared in the area of the right and left parietal and frontal bones (Jung *et al*. 2006). All sites were grafted with highly porous hydroxyapatite (HA)/tricalciumphosphate (TCP) granules. The sites were covered towards both the internal and external soft tissue either with e-PTFE or PEG membranes or left uncovered as control sites. A similar amount of newly formed bone was observed within the former defect space at e-PTFE- and PEG-treated sites. These findings demonstrated that the PEG membrane formed *in situ* could be successfully applied for bone regeneration.

Future outlook

Further developments in bone augmentation procedures can be related to either the simplification of clinical handling or influencing of biologic processes. In order to simplify clinical handling new materials should be comprised of a matrix with optimal cell in-growth capacities and with good mechanical properties providing space for tissue regeneration. No membrane and no specific procedures for mechanical fixation should be necessary. This would reduce the technique sensitivity and therefore increase the predictability of bone augmentation.

From a biologic point of view the growth and differentiation factors may induce earlier bone growth into the area to be regenerated. Thus, the area of regeneration would be stabilized earlier. Furthermore, the use of such materials would allow treatment of extensive bone defects. At present, large bone defects are regularly augmented with autogenous block grafts and membranes. The use of synthetic materials would result in lower surgical risks and lower morbidity in the augmentation procedure and would represent an important step forward in simplifying bone regeneration techniques.

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Chapter 50

Elevation of the Maxillary Sinus Floor

Bjarni E. Pjetursson and Niklaus P. Lang

Introduction

Elevation of the maxillary sinus floor was first reported by Boyne in the 1960s. Fifteen years later, Boyne and James (1980) reported on elevation of the maxillary sinus floor in patients with large, pneumatized sinus cavities as a preparation for the placement of blade implants. The authors described a two-stage procedure, where the maxillary sinus was grafted using autogenous particulate iliac bone at the first stage of surgery. In the second stage of surgery after approximately 3 months, the blade implants were placed and later used to support fixed or removable reconstructions (Boyne & James 1980).

As implant dentistry developed, it became more evident that the posterior maxillary region was often limited for standard implant placement, since the residual vertical bone height was reduced (Fig. 50-1). An elevation of the maxillary sinus floor was an option in solving this problem. Several surgical techniques have been presented for entering the sinus cavity, elevating the sinus membrane, and placing bone grafts.

A crestal approach for sinus floor elevation with subsequent placement of implants was first suggested (Tatum 1986). Utilizing this crestal approach, a "socket former" for the selected implant size was used to prepare the implant site. A "green-stick fracture" of the sinus floor was accomplished by hand tapping the "socket former" in a vertical direction. After preparation of the implant site, a root- formed implant was placed and allowed to heal in a submerged way.

Summers (1994) later described another crestal approach, using tapered osteotomes with increasing diameters (Fig. 50-2). Bone was conserved by this osteotome technique because drilling was not performed. Adjacent bone was compressed by pushing and tapping as the sinus membrane was elevated. Then, autogenous, allogenic or xenogenic bone grafts were added to increase the volume below the elevated sinus membrane. A follow-up of 173 press-fit submerged implants, placed using this technique, reported a success rate of 96% at 18 months after loading (Rosen *et al*. 1999).

Today, two main procedures of sinus floor elevation for dental implant placement are in use: a two-stage technique using the lateral window approach, and a one-stage technique using a lateral or a crestal approach. The decision to use the one- or the two-stage technique is based on the amount of residual bone available and the possibility of achieving primary stability for the inserted implants.

Treatment options in the posterior maxilla

Implant placement in the posterior maxilla remains a challenge. Reduced bone volume due to alveolar

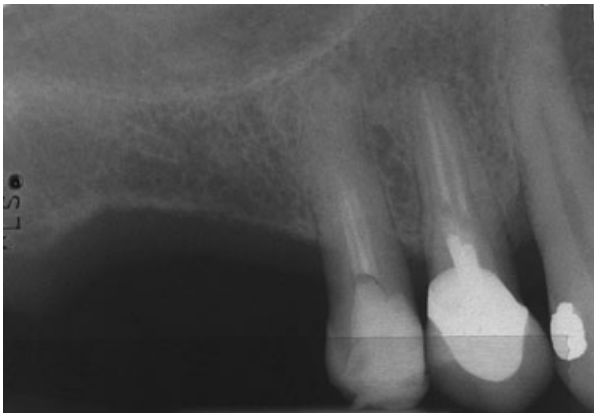

Fig. 50-1 Radiograph of a posterior maxilla, showing reduced residual bone height which will not allow standard implant placement.

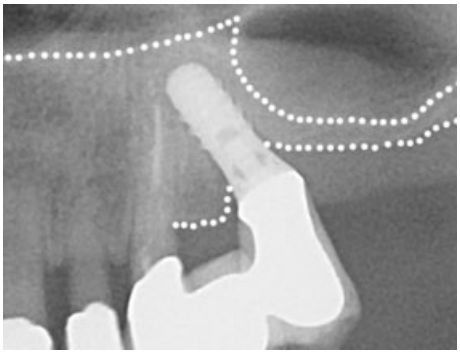

Fig. 50-3 Radiograph showing a tilted implant placed in the position of 25 to avoid entering the sinus cavity. After remodeling, the bone level on the distal aspect of the implant is more apical than at the time of implant placement. This may lead to increased probing pockets depths around tilted implants. (The dotted lines represent the outlines of the residual bone.)

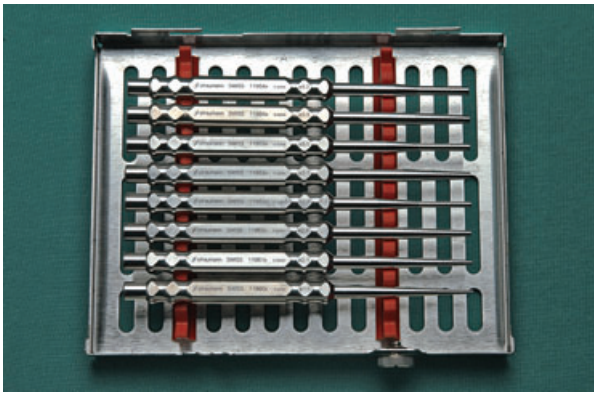

Fig. 50-2 In 1994, Summers introduced a set of tapered osteotomes with different diameters to compress and push the residual bone from the implant preparation into the sinus cavity and to elevate the sinus membrane.

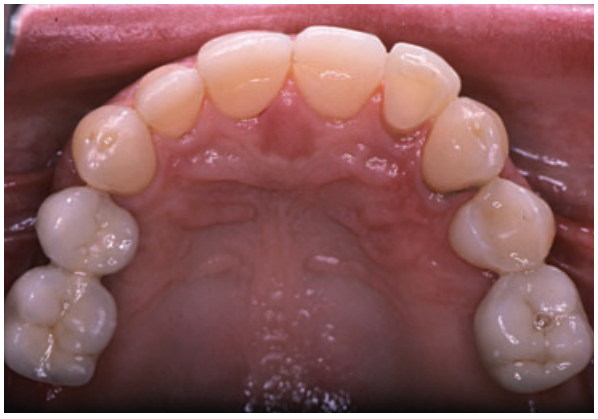

Fig. 50-4 Patient with a shortened dental arch. Three implants were placed in the positions of 15, 14, and 25 without elevating the maxillary sinus floor and, consequently, the patient was restored to the second premolar.

bone resorption and pneumatization of the sinus cavity makes it more difficult to place implants to support a dental prosthesis.

Several treatment options have been used in the posterior maxilla to overcome the problem of inadequate bone quantity. The most conservative treatment option would be to place short implants to avoid entering the sinus cavity. For placement of short implants, there is still a need for at least 6 mm of residual bone height, however. Another way of avoiding grafting the maxillary sinus would be to place tilted implants in a position mesial or distal to the sinus cavity if these areas have adequate bone (Fig. 50-3). Furthermore, extra-long zygomatic implants can be placed in the lateral part of the zygomatic bone.

However, in patients with appropriate residual bone height, minor augmentation of the sinus floor can be accomplished via the crestal approach using the osteotome technique (Summers 1994; Rosen *et al*. 1999; Ferrigno *et al*. 2006). The problem of inadequate bone height may be overcome by elevating the maxillary sinus floor via the closed technique to provide sufficient quantity of bone for dental implant placement.

The most invasive treatment option in the posterior maxilla is the one- or two-stage sinus floor elevation with a lateral approach. By mastering these different methods, most edentulous areas in the maxilla can by restored with implant-supported reconstructions. The concept of a shortened dental arch must also be kept in mind. The work of Käyser (1981) has shown that patients maintained adequate (50–80%) chewing capacity with a premolar occlusion (Fig. 50-4).

Sinus floor elevation with a lateral approach

Anatomy of the maxillary sinus

The maxilla consists of a variety of anatomic structures, including the maxillary sinus, the lateral nasal

walls, the pterygoid plates, associated vasculature structures, and teeth.

The maxillary sinus is pyramidal in shape. The base of the pyramid is the medial wall of the sinus that is also the lateral wall of the nasal cavity, and its apex is pointed towards the zygomatic bone. The roof of the sinus is also the floor of the orbit. The sinus has a non-physiologic drainage port high on the medial wall (maxillary ostium) that opens into the nasal cavity between the middle and lower nasal conchae.

The maxillary sinus maintains its overall size while the posterior teeth remain in function. It is, however, well known, that the sinus expands with age, and especially when posterior teeth are lost. The average volume of a fully developed sinus is about 15 ml but may range between 4.5 and 35.2 ml. The sinus cavity expands both inferiorly and laterally, potentially invading the canine region. This phenomenon is possibly the result of atrophy caused by reduced strain from occlusal function. One or more septa termed "Underwood's septa" may divide the maxillary sinus into several recesses.

The overall prevalence of one or more sinus septa is between 26.5% and 31% (Ulm *et al*. 1995; Kim *et al*. 2006) and is most common in the area between the second premolar and first molar. Edentulous segments have a higher prevalence of sinus septa than dentate maxillary segments.

The sinus is lined with respiratory epithelium (pseudo-stratified ciliated columnar epithelium) that covers a loose, highly vascular connective tissue (Fig. 50-5). Underneath the connective tissue, immediately next to the bony walls of the sinus, is the periosteum. These structures (epithelium, connective tissue, and periosteum) are collectively referred to as the Schneiderian membrane.

The blood supply to the maxillary sinus is derived primarily from the maxillary artery and, to a lesser degree, from the anterior ethmoidal and superior labial arteries. The sinus floor receives blood supply from the greater/lesser palatine and sphenopalatine arteries. These vessels penetrate the bony palate and ramify within the medial, lateral, and inferior walls of the sinus. The posterior superior alveolar artery has tributaries that perfuse the posterior and lateral walls. The posterior superior alveolar and infraorbital arteries anastomose in the bony lateral wall, on average 19 mm from the alveolar bone crest (Solar *et al*. 1999). The dense vascular network of the maxilla reduces after tooth loss and with increased age. The vast majority of the blood vessels in the maxilla (70–100%) come from the periosteum (Chanavaz 1990, 1995). Venous drainage is into the sphenopalatine vein and pterygomaxillary plexus. Neural supply comes from branches of the maxillary nerve.

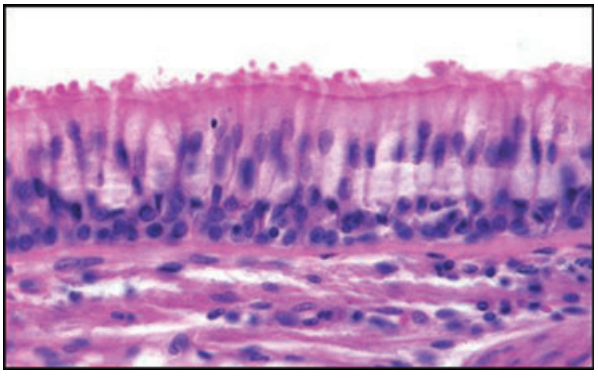

Fig. 50-5 Pseudostratified, ciliated columnar epithelium.

Non-hemolytic and alpha-hemolytic streptococci and *Neisseria* spp. are the normal commensal microbiota of the maxillary sinus. Staphylococci, diphtheroids, *Hemophilus* spp., pneumococci, *Mycoplasma* spp., and *Bacteroides* spp. are also found in varying amounts (Timmenga *et al*. 2003).

The healthy maxillary sinus is self-maintaining by postural drainage and actions of the ciliated epithelial lining, which propels bacteria toward the ostium. The maxillary sinus also produces mucus containing lysozymes and immunoglobulins. The significant vascularity of the Schneiderian membrane helps maintain its healthy state by allowing lymphocytic and immunoglobulin access to both the membrane and the sinus cavity.

The fact that the maxillary sinus opening to the nasal cavity is not in the lower part of the sinus (where a graft may be placed) is important and provides an anatomic rationale to sinus floor elevation, as the grafting procedure does not interfere with normal sinus function. In fact, a maxillary sinus floor elevation may improve symptoms of sinusitis/congestion by bringing the floor of the sinus closer to the drainage port.

Pre-surgical examination

Prior to planning complicated surgical procedures like elevation of the maxillary sinus floor, a thorough examination, including medical and dental history, should be obtained (see Chapters 27, 30, and 33).

The dental and periodontal status are evaluated using clinical and radiologic examination methods. The vitality of the neighbouring teeth has to be tested. The infraorbital, lateral nasal, and superior labial areas of the face must be examined regarding tenderness to palpation, swelling or asymmetry. The patient's history along with findings made during the clinical examination should provide sufficient information for diagnosing acute, allergic, and chronic sinusitis.

Pre-operative screening to assess a potential pathologic condition in the maxillary sinus should include radiographic examination, such as e.g. orthopantomography (OPT), tomography, computerized tomography (CT) scans or aquitomo-scans (see Chapter 28).

Before performing the sinus floor elevation surgery, all dentate patients should receive cause-related therapy (see Chapters 34–37).

Medical or surgical therapy of sinusitis, and removal of polyps and tumors must be completed prior to sinus floor elevation.

Indications and contraindications

The main indication for maxillary sinus floor elevation utilizing a lateral approach is reduced residual bone height, which does not allow standard implant placement or placement of implants in combination with minor sinus floor elevation using the osteotome technique. In cases of reduced bone height due to alveolar bone resorption and pneumatization of the sinus cavity the so-called lateral approach, with or without horizontal bone augmentation, is indicated.

Contraindications for sinus floor elevation can by divided into three groups: intraoral contraindications, medical conditions, and local contraindications.

The *medical* contraindications include: chemotherapy or radiotherapy of the head and neck area at the time of sinus floor elevation or in the preceding 6 months depending on the field of radiation; immunocompromised patients; medical conditions affecting bone metabolism; uncontrolled diabetes; drug or alcohol abuse; patient non-compliance; and psychiatric conditions.

Whether or not smoking is an absolute contraindication for maxillary sinus floor elevation remains controversial. In a case series, Mayfield and coworkers (2001) evaluated survival of implants placed in combination with bone augmentations (horizontal, vertical, and sinus elevations). The survival rate of these implants was 100% for non-smokers compared to only 43% for smokers after 4–6.5 years of functional loading (Mayfield *et al*. 2001). This reduced survival rate has been corroborated by several other authors (Bain & Moy 1993; Jensen *et al*. 1996; Gruica *et al*. 2004). However, a large study evaluating 2132 implants after sinus floor elevation with simultaneous implant placement found conflicting results (Peleg *et al*. 2006). Two hundred and twenty-six sinus floor elevations (627 implants) were performed on smokers, and 505 sinus floor elevations (1505 implants) on non-smokers. After a follow-up time of up to 9 years, the survival rate of the implants was 97.9%, and there were no statistically significant differences between survival rates in smokers and in non-smokers.

Alteration of the nasal–maxillary complex that interferes with normal ventilation as well as the mucociliary clearance of the maxillary sinus, may be a contraindication for sinus floor elevation. However, such abnormal conditions may be clinically asymptomatic or only present with mild clinical symptoms. These conditions include viral, bacterial, and mycotic rhinosinusitis, allergic sinusitis, sinusitis caused by intra-sinus foreign bodies, and odontogenic sinusitis resulting from necrotic pulp tissue. All odontogenic, periapical, and radicular cysts of the maxillary sinus should be treated prior to sinus floor elevation.

A sinus floor elevation under any of the above conditions may disturb the fine mucociliary balance, resulting in mucus stasis, suprainfection or a subacute sinusitis.

Absolute local contraindications for sinus floor elevation are: acute sinusitis; allergic rhinitis and chronic recurrent sinusitis; scarred and hypofunctional mucosae; local aggressive benign tumors; and malignant tumors.

Surgical techniques

The original Caldwell-Luc technique, commonly referred to as the lateral window or lateral approach, describes an osteotomy prepared in a superior position just anterior to the zygomatic buttress. Two other positions have also been described: a mid-maxillary position between the alveolar crest and zygomatic buttress area, and a low anterior position near the level of the existing alveolar ridge (Lazzara 1996; Zitzmann & Scharer 1998). The technique described in this chapter is a modification of these techniques:

- A presurgical rinse with chlorhexidine 0.1% is performed for a period of 1 minute.
- Local anesthesia is delivered buccal and palatal to the surgical area.
- The initial incision is midcrestal extending well beyond the planned extension of the osteotomy. The incision is carried on forward beyond the anterior border of the maxillary sinus. Releasing incisions are made anteriorly extending into the buccal vestibulum to facilitate reflection of a full-thickness mucoperiosteal flap.
- A mucoperiosteal flap is raised slightly superior to the anticipated height of the lateral window.
- After the lateral sinus wall has been exposed, a round carbide bur in a straight hand piece is used to mark the outline of the osteotomy (Fig. 50-6).

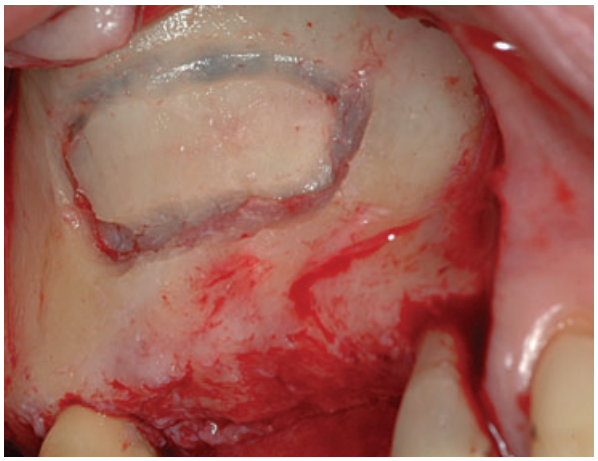

Fig. 50-6 The outline of the lateral window has been marked with a round bur.

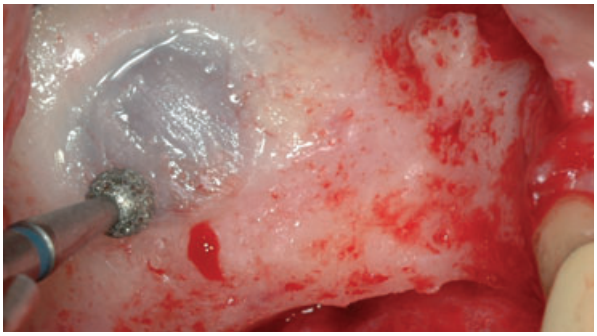

Fig. 50-7 The buccal bony plate is trimmed to a paper-thin lamella with a fine grit round diamond bur, avoiding the perforation of the sinus membrane.

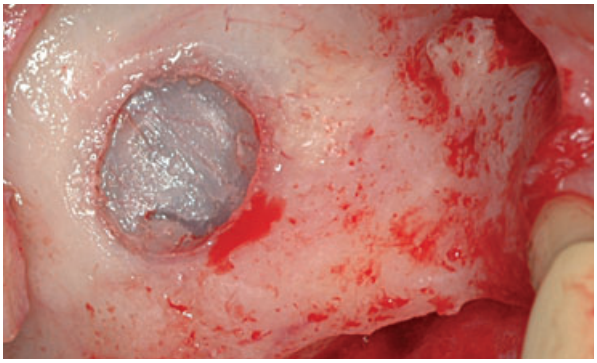

Fig. 50-9 Before elevating the sinus membrane the entire buccal bone is removed to gain access to the membrane.

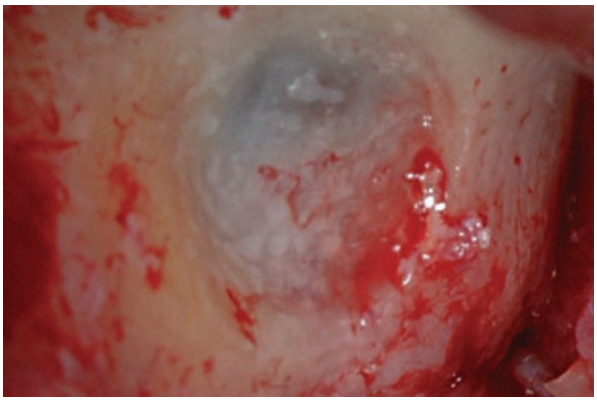

Fig. 50-8 After removing the buccal bony plate, the bluish hue of the sinus membrane becomes clearly visible.

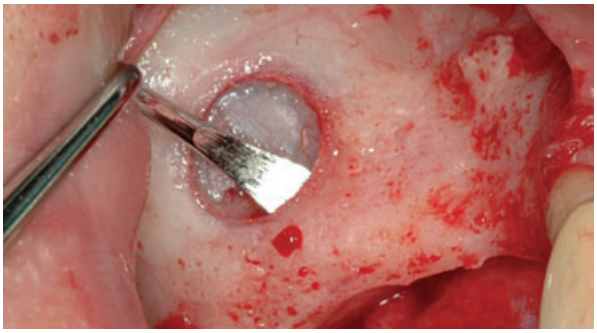

Fig. 50-10 The sinus membrane is carefully elevated using a blunt instrument. To avoid penetration, it is essential to keep contact with the underlying bone at all time during this procedure.

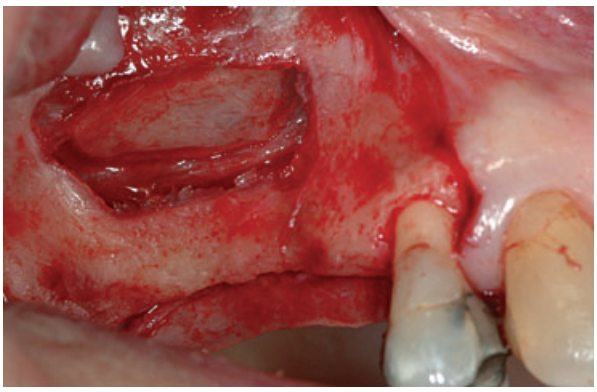

Fig. 50-11 The buccal cortical bony plate was fractured and moved upwards and inwards like a "trap-door". The cortical bony plate is delineating the superior border of the maxillary sinus compartment.

When the bone has been trimmed down to a thin bony plate, the preparation is continued with a round diamond bur (Fig. 50-7) in a straight hand piece until a bluish hue of the sinus membrane is observed (Fig. 50-8). Three methods for handling the buccal cortical bone plate have been proposed. The most common one is the thinning of the buccal bone to a paper-thin bone lamella using a round bur, and removing it prior to the elevation of the sinus membrane (Fig. 50-9). The second method is to fracture the cortical bony plate like a trap-door and use it as the superior border to the sinus compartment, leaving it attached to the underlying mucosa. Since the cortical bony plate is resistant to bone resorption this may protect the graft. The third method proposed is to remove the cortical bony plate during sinus floor elevation and replace it on the lateral aspect of the graft at the end of the grafting procedure. The rationale for this method was the notion that the lateral window would not completely heal without replacement of its cortical plate. However, healing of the lateral window by bone apposition has been demonstrated to occur without replacing the cortical bony plate (Boyne 1993).

- The next step will be chosen according to the technique used. If the buccal wall is eliminated, the sinus membrane is elevated directly with blunt instruments (Fig. 50-10). On the other hand, gentle tapping is continued until movement of the bony plate is observed if the "trap-door" technique is used. Then, in combination with the elevation of the sinus membrane in the inferior part of the sinus, the bony plate is rotated inwards and upwards to provide adequate space for grafting material (Fig. 50-11). Care should be taken not to perforate the sinus membrane.

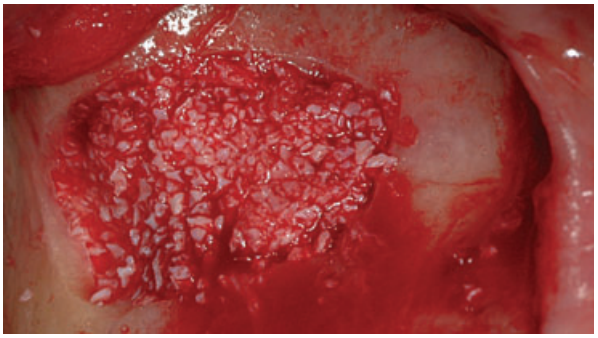

Fig. 50-12 The sinus compartment has been filled with a loosely packed 1 : 1 mixture of particulate autogenous bone and a xenograft.

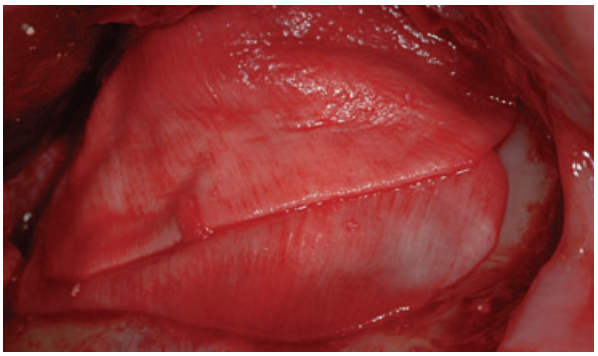

Fig. 50-13 The lateral window has been covered with single or double layer of resorbable barrier membrane.

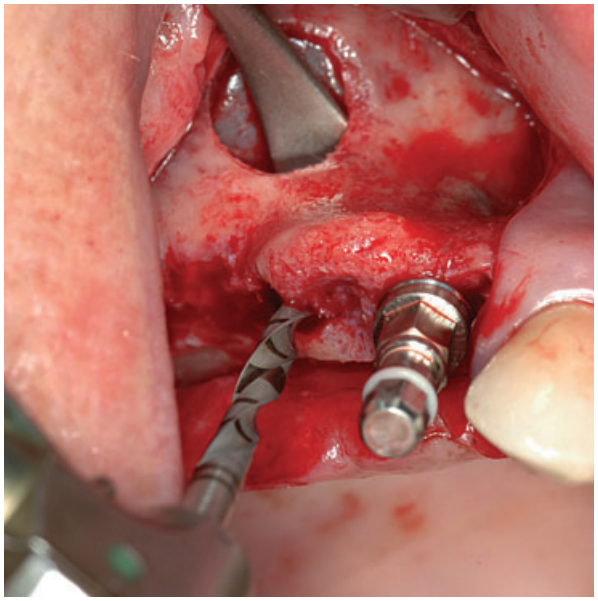

Fig. 50-14 If rotary instruments are used to prepare the implant site, the sinus membrane has to be protected with a periosteal elevator that is placed into the sinus compartment.

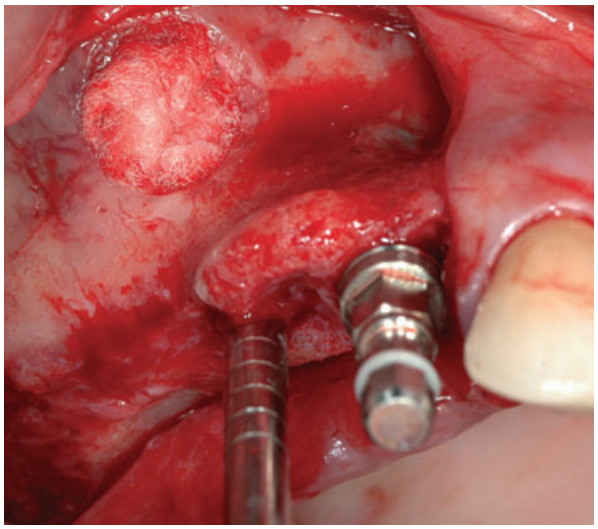

Fig. 50-15 If osteotomes are utilized to prepare the implant site, the sinus membrane can be protected by inserting sterile gauze into the sinus compartment.

Depending on the clinical condition and the surgeon's preference, a delayed (two-stage) or a one-stage sinus floor elevation simultaneously with the implant installation is chosen.

- Two-stage sinus elevation (delayed installation of the implant):
  - Grafting material is placed in the compartment made by the elevation of the sinus membrane. The grafting material should not be densely packed, because this reduces the space needed for ingrowth of newly forming bone. In addition, pressurizing the thin sinus membrane may result in a late perforation.
  - After the compartment has been filled with grafting material (Fig. 50-12), the lateral window is closed by covering it with a resorbable or a non-resorbable barrier membrane (Fig. 50-13). Subsequently, the flap is closed free of tension. In most conditions, there is a need for deep periosteal incisions to achieve tension-free closure.
- One-stage sinus floor elevation with simultaneous implant placement:
  - After the sinus membrane has been elevated, the implant sites are prepared. If rotary instruments are used, the sinus membrane has to be protected using a periosteal elevator (Fig. 50-14). Osteotomes of different diameters may be used to prepare the implant site, and then the membrane can be protected by inserting sterile gauze into the sinus compartment (Fig. 50-15).
  - The appropriate implant length is measured with a blunt depth gauge (Fig. 50-16). Before placing the implant, the grafting material is inserted into the medial part of the sinus compartment (Fig. 50-17). After implant placement (Fig. 50-18), the lateral part of the compartment is filled with grafting material (Fig. 50-19).
  - The subsequent steps coincide with those described for the two-stage procedure.

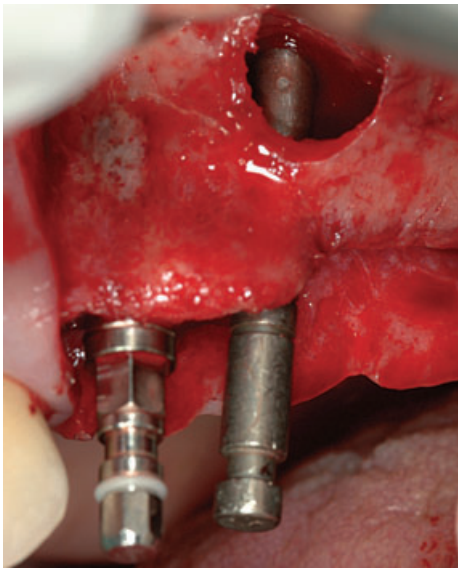

Fig. 50-16 If sinus floor elevation and simultaneous implant placement are performed, the height of the sinus compartment and implant length may be determined by inserting a blunt depth gauge into the implant site. Care must be taken not to apply too much pressure on the sinus membrane.

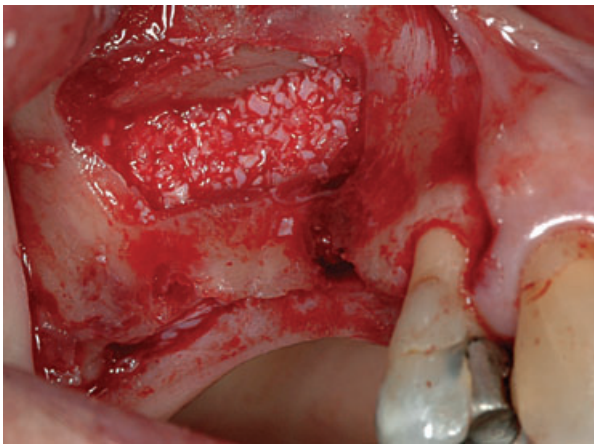

Fig. 50-17 Before placing the implants, grafting material has to be inserted into the medial part of the sinus compartment, because access to the medial part of the sinus compartment is restricted after implant installation.

The main differences between the methods used presently are the position and technique used to prepare the lateral window, the amount of sinus membrane elevation, the type of graft utilized, and the choice of one-stage or two-stage approaches.

Histomorphometric evidence of enhanced bone formation following membrane placement over the lateral window is available. In a randomized controlled clinical trial (Tarnow *et al*. 2000), a split mouth design with bilateral sinus grafts was performed for 12 patients with or without covering the lateral window using a membrane. After 12 months, histologic samples were taken through the lateral window. The mean percentage of vital bone formation was 25.5% with and 11.9% without a covering barrier.

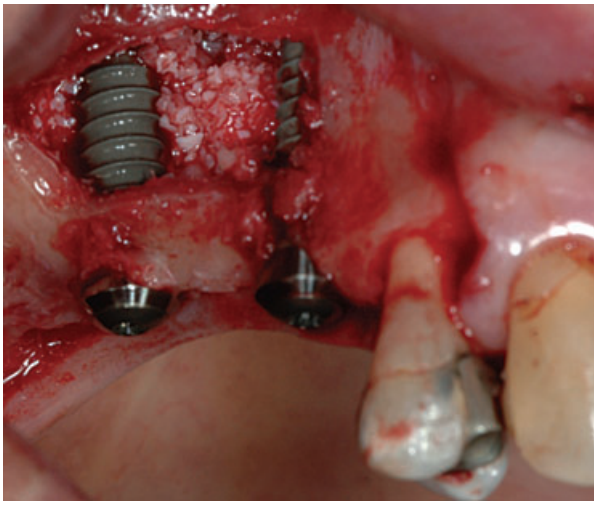

Fig. 50-18 Two implants have been installed after filling the medial part of the sinus compartment.

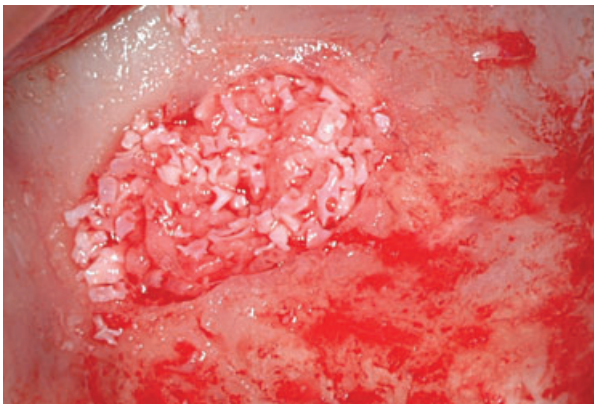

Fig. 50-19 After implant installation the lateral part of the sinus compartment is filled up with loosely packed grafting material.

Similar results were obtained in a controlled clinical trial (Froum *et al*. 1998) measuring bone formation in 113 sinuses grafted either with xenograft alone or a composite of xenograft and autograft. The mean vital bone formation was 27.6% when a membrane was used compared to 16% without.

Post-surgical care

In order to minimize post-operative pain and discomfort for the patient, surgical handling should be as atraumatic as possible. Precautions must be taken to avoid perforation of the flap and the sinus membrane. The bone should be kept moist during the surgery, and a tension-free primary flap closure is essential. The pain experienced by patients is mostly limited to the first days after surgery. Swelling and bruising of the area are usually the chief post-operative sequelae. Often, swelling and bruising extend from the inferior border of the orbit to the lower border of the mandible or even to the neck. In order to reduce swelling, it is important to cool the area

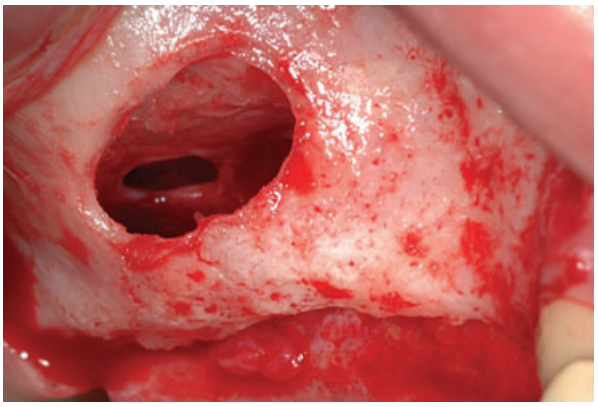

Fig. 50-20 The most frequent complication during maxillary sinus floor elevation is perforation of the sinus membrane. A medium-sized perforation can be detected after elevation of the membrane.

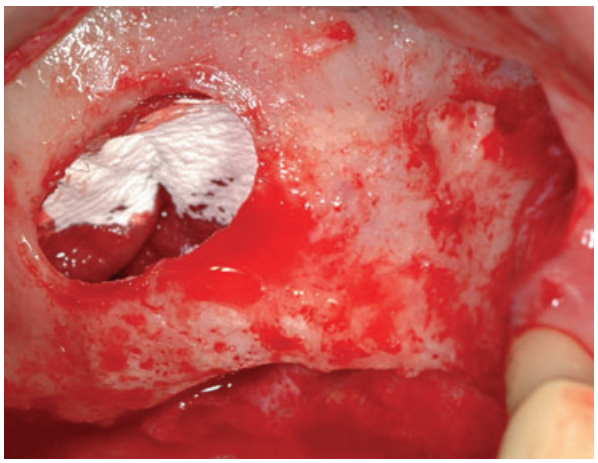

Fig. 50-21 Small- to medium-sized sinus membrane perforations may be closed by applying a resorbable barrier membrane.

with cooling pads at least for the first post-operative hours. Occasionally, minor bleeding may arise from the nose. It is important to inform the patients that some irritation in the nasal area may be expected. In the event of the need for sneezing, the nose should not be covered so that air pressure is allowed to escape. After the surgery, patients are placed on antibiotic therapy. Furthermore, antiseptic rinses with 0.1–0.2% chlorhexidine twice daily are indicated for the first 3 weeks after surgery.

Complications

When performing sinus floor elevation, the risk of complications must be considered and the appropriate treatment foreseen. The most common intra-operative complication is perforation of the sinus membrane (Fig. 50-20). Presence of maxillary sinus septa and root apices penetrating into the sinus may increase the risk of membrane perforation. The risk of perforation has been reported to be between 10 and 40% during surgery (Block & Kent 1997; Timmenga *et al*. 1997; Pikos 1999). In the event of a membrane perforation, it is recommended to elevate the membrane in the opposite direction to prevent further enlargement of the perforation. Smaller perforations (<5 mm) may be closed by using tissue fibrin glue, suturing or by covering them with a resorbable barrier membrane (Fig. 50-21). In cases of larger perforations, larger barrier membranes, lamellar bone plates or suturing may be used either alone or in combination with tissue fibrin glue to provide a superior border for the grafting material. In instances of larger perforations, where a stable superior border cannot be achieved the grafting of the maxillary sinus must by aborted and a second attempt at sinus floor elevation may be performed 6–9 months later (Tatum *et al*. 1993; van den Bergh *et al*. 2000).

Other complications that were reported during surgery included excessive bleeding from the bony window or the sinus membrane, and wound dehiscences. Iatrogenic complications include injury of the infraorbital neurovascular bundle from deep dissection to free the flap from tension or blunt trauma due to the compression of the neurovascular bundle during retraction. Implant migration, hematoma, and adjacent tooth sensitivity have also been reported.

Infection of the grafted sinuses is a rare complication. However, the risk for infection increases with a membrane perforation. Hence, it is recommended to avoid sinus grafting and simultaneous implant placement in situations of membrane perforation (Jensen *et al*. 1996). Infection of the grafted sinuses is usually seen 3–7 days post surgically and may lead to a failure of the graft. Possible complication secondary to infection may involve a parasinusitis with the spread of the infection to the orbita or even to the brain. For these reasons, infected sinus grafts must be treated immediately and aggressively. Surgical removal of the entire graft from the sinus cavity and administration of high doses of antibiotics are essential.

Sinusitis is another complication that may occur after sinus grafting. In a study (Timmenga *et al*. 1997) evaluating the function of the maxillary sinus after sinus floor elevation, 45 patients who had received 85 sinus grafts underwent endoscopic examination. Of these, five were diagnosed with sinusitis. In these five patients, the endoscopic examination revealed oversized turbinates and septal deviation. Hence, the result of this study showed that the incidence of sinusitis was low and mainly found in patients with an anatomic or functional disorder prior to the sinus grafting.

Late failure reports include chronic infection, graft exposure, loss of the entire bone graft, oro-antral fistula, ingrowth of soft tissue through the lateral window, granulation tissue replacing the graft, and sinus cysts.

Grafting materials

There are differences in opinion on the necessity of grafting material when elevating the maxillary sinus floor.

Sinus floor elevation without grafting material

Studies in monkeys (Boyne 1993) showed that implants protruding into the maxillary sinus following elevation of the sinus membrane without grafting material, exhibited spontaneous bone formation over more than half of the implant's height. Hence, protrusion of an implant into the maxillary sinus does not appear to be an indication for bone grafting. In the same study, it was also seen that the design of the implant influenced the amount of spontaneous bone formation. Implants with open apices or deep-threaded configurations did not reveal substantial amounts of new bone formation. On the other hand, implants with rounded apices tended to show spontaneous bone formation extending all around the implants if they only penetrated 2–3 mm into the maxillary sinus. However, when the same implants penetrated 5 mm into the maxillary sinus, only a partial (50%) growth of new bone was seen towards the apex of the implant.

In a clinical study (Ellegaard *et al*. 2006), 131 implants were placed using the lateral approach. The sinus membrane was elevated, implants were inserted and left to protrude into the sinus cavity. The sinus membrane was allowed to settle on to the apex of the implants, thus creating a space to be filled with a blood coagulum. After a mean follow-up time of 5 years, the survival rate of these implants was 90%. It must be kept in mind, however, that the residual bone height in this study was at least 3 mm.

Autogenous bone

Autogenous bone grafts are considered the gold standard for grafting due to their maintenance of cellular viability and presumptive osteogenic capacity. The use of autogenous grafts in sinus floor elevation was first reported by Boyne and James (1980) and Tatum (1986).

Grafts may be harvested intraorally or extraorally. Common intraoral donor sites are the maxillary tuberosity, the zygomatico-maxillary buttress, the zygoma, the mandibular symphysis and the mandibular body and ramus (Fig. 50-22). Bone may be harvested in block section or in particulate form. The extraoral donor sites that have been utilized are the anterior and posterior iliac crest, the tibial plateau, the rib, and the calvaria.

Autologous bone grafts contain bone morphogenic proteins (BMPs) that are capable of inducing osteogenic cells in the surrounding tissues. They also contain other growth factors essential for the process of graft incorporation. Processing of autograft, with grinding or morselizing, does not seem to disturb the viability of the osteogenic cells (Springer *et al*. 2004). The main source of osteogenic cells during graft consolidation is the periosteum that includes mesenchymal progenitor cells and provides a rich source of blood vessels. Osteoclasts are then required for remodeling of the graft–woven bone complex. The consolidation of the graft depends on the properties of the graft material and the osteogenic potential of the recipient bed. Initially, cortical bone grafts act as weight-bearing space fillers and remain a mixture of necrotic and viable bone for a prolonged period of time. The ideal graft material has to allow ingrowth of blood vessels and formation of bone on its surfaces for integration into the recipient bed (osteoconductivity).

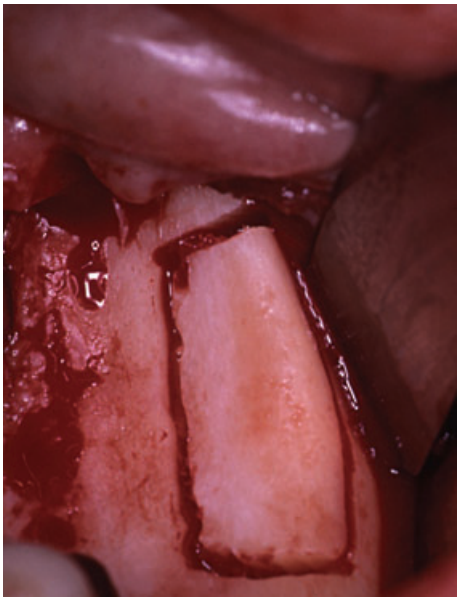

Fig. 50-22 The most suitable sites used to harvest block or particulate bone grafts intraorally are the mandibular body and the mandibular ramus.

In situations of sinus floor elevations that do not eventually receive dental implants, the bone grafts may resorb due to the lack of functional load and strain.

Bone substitutes

Loss of autografts during healing occurs when resorption of the autograft exceeds new bone formation during the consolidation phase. Thus, to overcome excessive resorption of autografts, bone substitutes that are known for their slow resorption process, are added to autografts to increase the stability of grafts during the consolidation phase.

Tricalcium phosphate was the first bone substitute to be applied successfully for sinus floor elevation (Tatum 1986). Over the years, allografts, alloplasts, and xenografts of various types have been used alone or in combination with autografts. Studies in animal models showed that the use of bone substitutes, such

Fig. 50-23 A 1 : 1 mixture of particulate autologous bone and bone substitute. The autologous bone particles include viable osteogenic cells, bone morphogenic proteins, and other growth factors. The bone substitute is supposed to decrease the resorption of the grafting material.

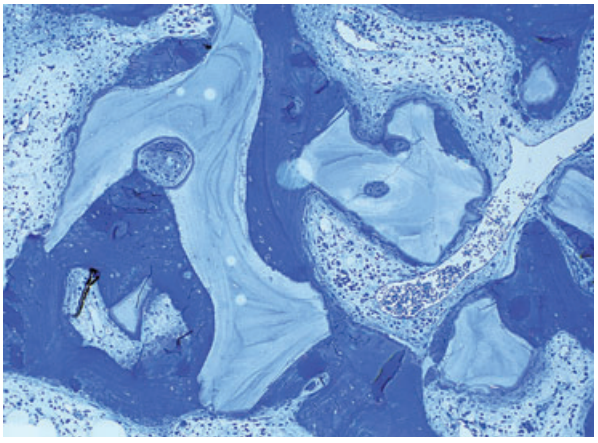

Fig. 50-24 The bovine bone mineral particles (xenograft) are mostly surrounded by new mature compact bone. No gaps can be seen at the interface between the xenograft particles and the newly formed bone. (Courtesy of Dr. Dieter D. Bosshardt, Berne.)

as bovine bone mineral, either alone or in combination with autografts, preserved the vertical height of the graft over time (Fig. 50-23). In a human study, sinus grafts consisting of autografts and demineralized allografts, were observed over a period of time. A graft resorption of up to 25% was seen. Furthermore, a more recent human study (Hatano *et al*. 2004) showed also significant reduction in graft volume, when either autogenous bone alone or a mixture of autogenous bone and xenografts were used. There is a definitive need for good long-term studies that address the stability of the different types of grafting materials in the maxillary sinuses over time.

Histologic analysis of human biopsy specimens from sinuses augmented with xenografts revealed that xenograft particles were mostly surrounded by mature compact bone (Fig. 50-24). In some Haversian canals, it was possible to observe small capillaries, mesenchymal cells, and osteoblasts in conjunction with new bone. No gaps were noted at the interface between the xenograft particles and the newly formed bone (Piattelli *et al*. 1999).

A human study (Froum *et al*. 1998) evaluating bone formation after sinus floor elevation using xenografts alone or in combination with autogenous bone and/or demineralized freeze-dried bone allografts reported statistically significant increase in vital bone formation, when as little as 20% of autologous bone was added to the bone substitutes. The mean vital bone formation was 27.1% after a healing period of 6–9 months. However, comparative studies (Hising *et al*. 2001; Hallman *et al*. 2002a,b; Valentini & Abensur 2003) reported higher survival rates for implants placed into sinuses grafted with 100% xenograft as compared to those placed in sinuses grafted with 100% autogenous bone or composite graft of xenograft and autogenous bone.

Another indication for using bone substitutes is to reduce the volume of bone that must be harvested. When a large sinus cavity is grafted with autologous bone alone, 5–6 ml of bone may be necessary. Using bone substitutes alone or in combination with autografts, the amount of autogenous bone to be harvested is greatly reduced.

Success and implant survival

Jensen and co-workers (1996) published the findings from the Consensus Conference of the Academy of Osseointegration. Retrospective data was collected from 38 clinicians who collectively performed 1007 sinus floor elevations and placed 2997 implants over a 10-year period. The majority of the implants had been followed for 3 years or more. Two hundred and twenty-nine implants were lost resulting in a overall survival rate of 90.0%. However, the database was so variable that no definitive conclusions regarding the grafting material, the type of implants, and the timing for implant placement could be drawn.

Survival of implants cannot be the sole criterion for success of maxillary sinus floor elevation. Factors, such as the pre-operative residual bone height, the long-term stability of the bone graft, and the incidence of failing two-stage sinus grafting due to graft resorption must also be considered.

Of the 900 patient records that were screened for the Consensus Conference in 1996, only 100 had radiographs of adequate quality for analysis of the residual bone height. In total, only 145 sinus grafts in 100 patients, with 349 implants, were analyzed. After a mean follow-up period of 3.2 years, 20 implants were lost. Of the implants lost, 13 were initially placed in residual bone with a height ≤4 mm, seven were placed in residual bone with a height of 5–8 mm. None of the implants placed in residual bone height of more than 8 mm was lost. There was a statistically significant difference in implant loss when residual bone height was 4 mm or less as compared to 5 mm or greater (Jensen *et al*. 1996).

A critical appraisal of the dental literature on maxillary sinus floor elevation shows that the two-stage approach (delayed implant installation) is more likely

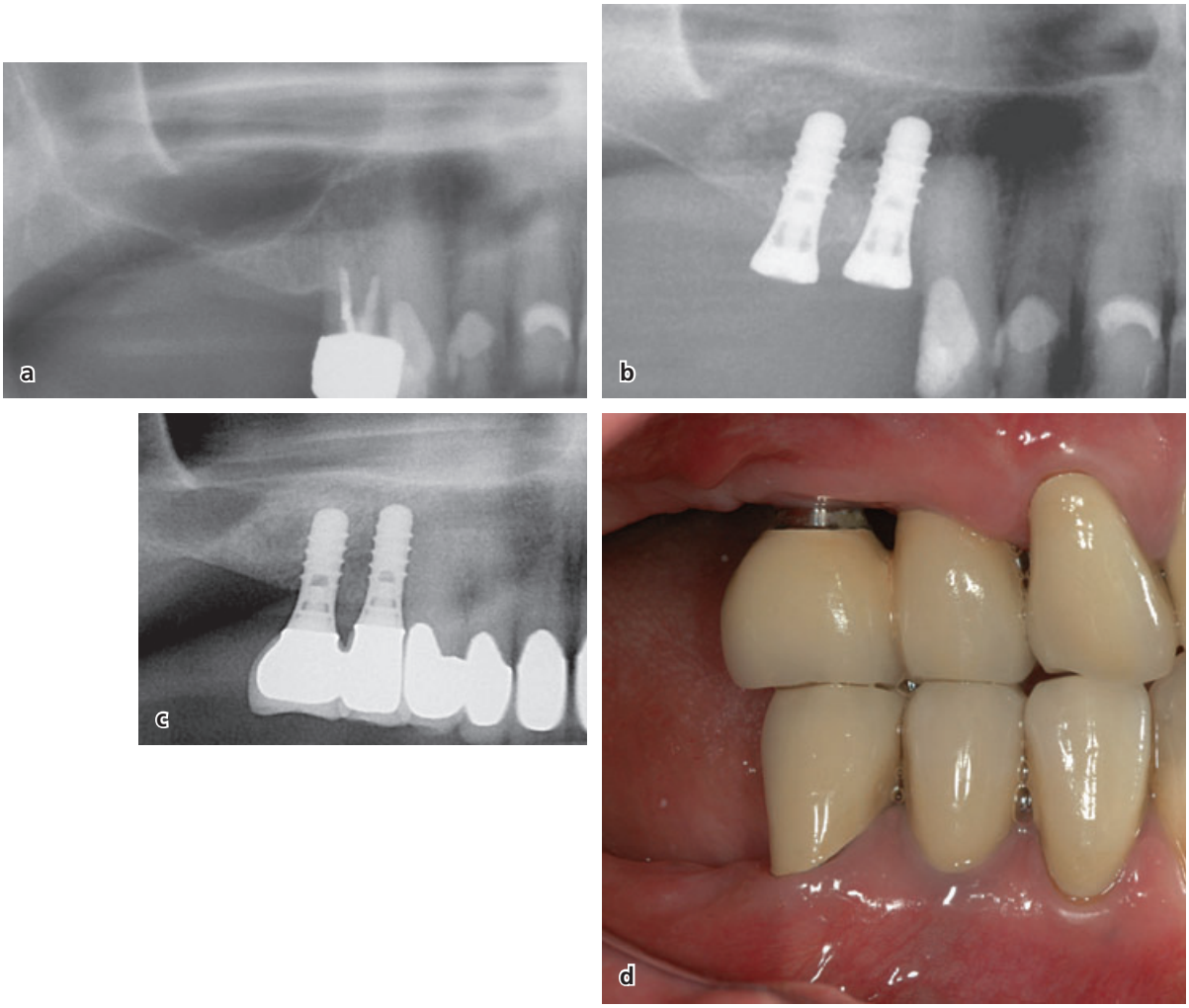

Fig. 50-25 One-stage sinus floor elevation. (a) A panoramic radiograph showing oblique inferior sinus borders and a residual bone height between 2 and 6 mm in the position of 25. (b) Two implants were placed, a standard implant placement in the position of 24 and an implant installed in combination with sinus floor elevation in the position of 25. A 1 : 1 mixture of particulate autologous bone harvested from the maxillary tuberosities and the zygomatic bone combined with bovine bone mineral was used as the grafting material. (c) OPT taken 1 year after functional loading. A new inferior border of the maxillary sinus and a stable graft volume was evident. (d) The clinical situation at the 1-year follow-up visit.

to be used in situations with less residual bone height compared to the one-stage approach (simultaneous implant placement).

The efficacy of performing a one-stage sinus floor elevation in patients whose residual alveolar bone height in the posterior maxilla was between 3 and 5 mm was assessed (Peleg *et al*. 1999). Using the modified Caldwell-Luc technique, the maxillary sinus was elevated with composite grafts of symphysal autograft and demineralized freeze-dried bone allograft in a 1 : 1 ratio. One hundred and sixty implants were placed in 63 elevated sinuses. A 100% survival rate of the implants was reported after 4 years. In a second study (Peleg *et al*. 1998) using a similar protocol on 55 implants placed into 20 elevated sinuses, the residual alveolar bone height was only 1–2 mm. All implants osseointegrated successfully, and no implants were lost after 2 years of functional loading.

Only one randomized controlled clinical trial (Wannfors *et al*. 2000) compared one- and two-stage sinus floor elevation, in 40 patients divided into groups. The residual bone height ranged from 2 to 7 mm. The one-stage protocol (Fig. 50-25) with 75 implants placed reported a survival rate of 85.5% as compared to the two-stage protocol (Fig. 50-26) with 90.5% survival rate for 74 implants placed after 1 year in function. Apparently, the risk of implant failure in grafted areas for the one-stage procedure was greater than for two-stage procedure, although the results did not reach statistical significance.

The stability of the sinus graft height was evaluated on panoramic radiographs for 349 implants. After a mean follow-up period of 3.2 years, the reduction of the graft height varied between 0.8 mm (autograft and alloplast) and 2.1 mm (autograft). This indicated that all of the graft materials appeared to be stable, with only 1–2 mm of the graft height being lost over the 3-year period (Jensen *et al*. 1996). Further studies evaluating the long-term stability of sinus grafts (Block *et al*. 1998; Hatano *et al*. 2004) yielded similar results.

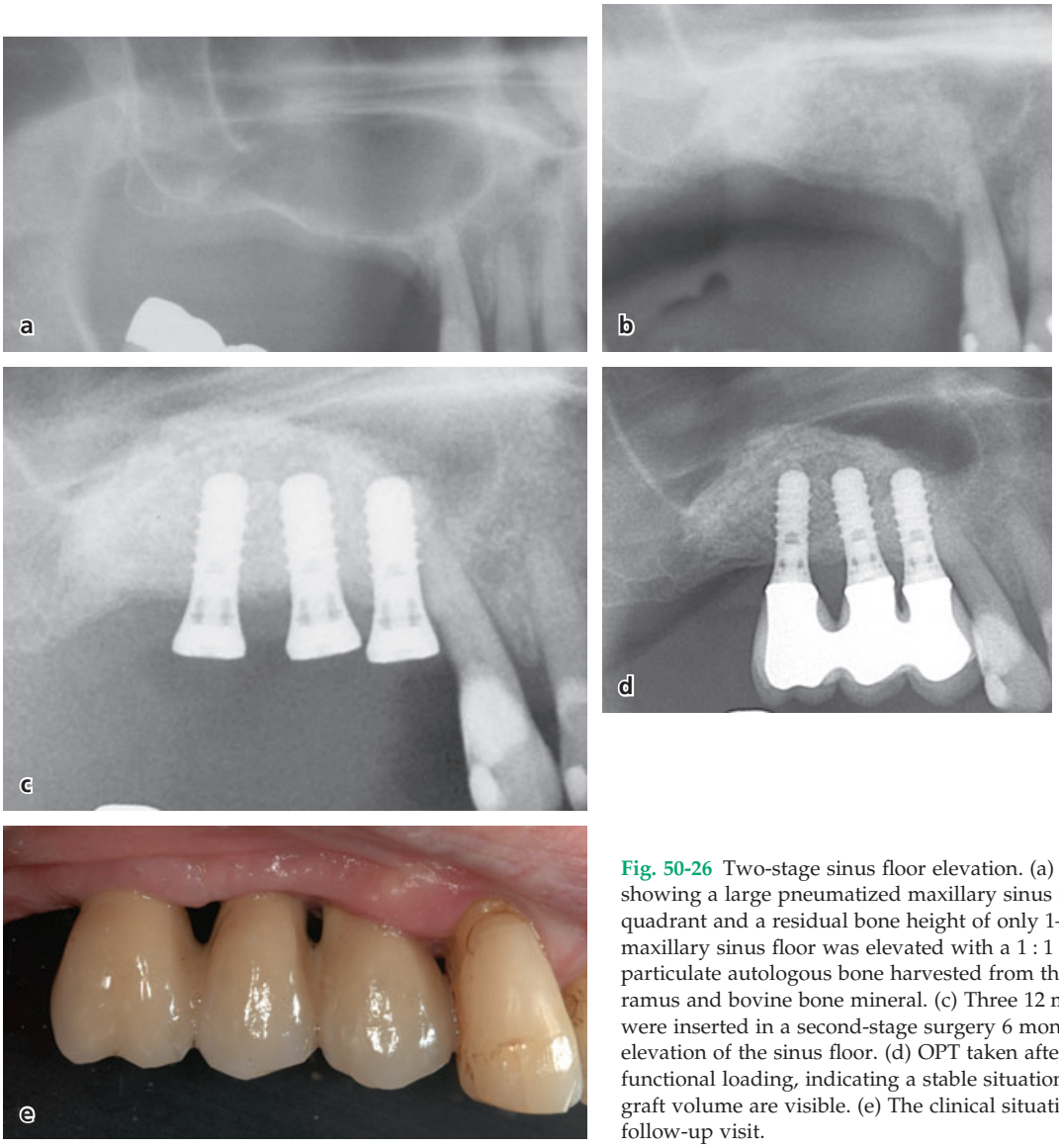

Fig. 50-26 Two-stage sinus floor elevation. (a) An OPT showing a large pneumatized maxillary sinus in the 1st quadrant and a residual bone height of only 1–2 mm. (b) The maxillary sinus floor was elevated with a 1 : 1 mixture of particulate autologous bone harvested from the mandibular ramus and bovine bone mineral. (c) Three 12 mm implants were inserted in a second-stage surgery 6 months after the elevation of the sinus floor. (d) OPT taken after 1 year of functional loading, indicating a stable situation. No changes in graft volume are visible. (e) The clinical situation at the 1-year follow-up visit.

In 2003, Wallace and Froum published a systematic review on the effect of maxillary sinus floor elevation on the survival of dental implants. The inclusion criteria were human studies with a minimum of 20 interventions, a follow-up time of 1 year of functional loading and with an outcome varied of implant survival. The main results indicated:

1. A survival rate of implants placed in conjunction with sinus floor elevation with the lateral approach varied between 61.7 and 100%, with an average of 91.8%.
2. Implant survival rates compared favorably to reported survival rates for implants placed in the non-grafted maxilla.
3. Rough-surfaced implants yielded higher survival rate than machined-surface implants when placed in grafted sinuses.
4. Implants placed into sinuses augmented with particulate autografts showed higher survival rates than those placed in sinuses that had been augmented with block grafts.
5. Implant survival rates were higher when barrier membranes were placed over the lateral window.
6. The utilization of grafts consisting of 100% autogenous bone or the inclusion of autogenous bone as a component of composite grafts did not affect implant survival.

Sinus floor elevation with the crestal approach (osteotome technique)

The osteotome technique was first developed to compress soft, type III and IV maxillary bone. The concept is intended to increase the density of bone in the maxilla leading to better primary stability of inserted dental implants.

In the maxilla, the bone crest in edentulous ridges is often narrow in the bucco-palatal dimension. This

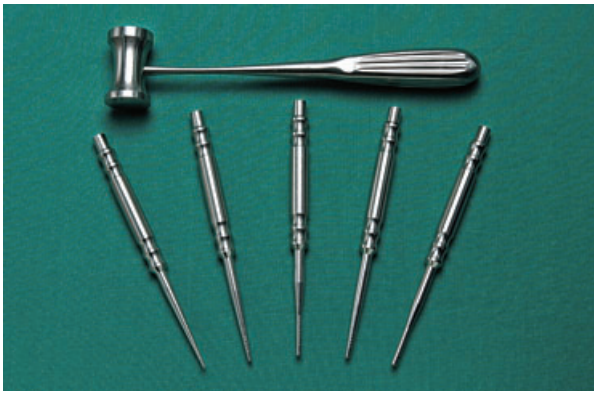

Fig. 50-27 Set of straight and tapered osteotomes used to prepare the implant site and to elevate the maxillary sinus floor.

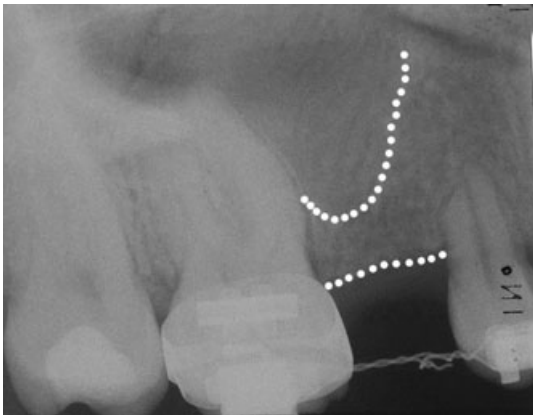

Fig. 50-28 Edentulous space in position 15. The oblique inferior border of the maxillary sinus lies at approximately 60° to the inferior border of the alveolar crest (the dotted lines represent the outlines of the residual bone). In a clinical situation like this, it is difficult to elevate the maxillary sinus floor with osteotomes. The osteotomes will first enter the sinus cavity distally at the lowest level of oblique sinus floor while still having bone resistance on the cranial level of the sinus floor. Hence, the risk of the sharp margin perforating the sinus membrane is high.

limits the possibility of standard drilling in preparing an implant site. Thus, to address this difficult situation, tapered round osteotomes of increasing diameters have been used to expand the compactible cancellous maxillary bone and gently move it in a lateral direction to increase crestal width. This procedure is known as "ridge expansion osteotome technique" and will not be addressed further in this chapter.

Tatum (1986) described the crestal approach to elevate the sinus floor. The osteotome technique for sinus floor elevation, using a set of osteotomes of varying diameters (Fig. 50-27) to prepare the implant site, was first presented by Summers (1994). The bone-added osteotome sinus floor elevation (BAOSFE), today referred to as the *Summers technique*, may be considered to be a more conservative and less invasive approach than the conventional lateral approach of sinus floor elevation. A small osteotomy is made through the crest of the edentulous ridge, at the inferior region of the maxillary sinus. This intrusion osteotomy procedure elevates the sinus membrane, thus creating a "tent". This creates space for bone graft placement. It should be noted that the bone grafts are placed blindly into the space below the sinus membrane. Hence, the main disadvantage of this technique is the uncertainty of possible perforation of the sinus membrane. However, an endoscopic study has shown that the sinus floor can be elevated up to 5 mm without perforating the membrane (Engelke & Deckwer 1997).

Indications and contraindications

Indications for the transalveolar osteotome technique (crestal approach) include a flat sinus floor with a residual bone height of at least 5 mm and adequate crestal bone width for implant installation.

The contraindications for the osteotome technique are similar to those previously described for the lateral approach. In addition, however, patients with a history of inner ear complications and positional vertigo are not suitable for the osteotome technique. As for the local contraindications, an oblique sinus floor (>45° inclination) is not suitable for the osteotome technique either (Fig. 50-28). The reason is the fact that the osteotomes first enter the sinus cavity at the lower level of an oblique sinus floor, while still having bone resistance on the higher level. In this situation, there is a high risk of perforating the sinus membrane with the sharp margin of the osteotome (Fig. 50-29).

Surgical technique

Apart from the original technique (Summers 1994), only minor modifications have been presented (Rosen *et al*. 1999; Fugazotto 2001; Chen & Cha 2005). The technique described in this chapter represents a modification of the original technique:

- Pre-surgical patient preparation includes oral rinsing with 0.1% chlorhexidine for a period of 1 minute.
- Local anesthesia is administered into the buccal and palatal regions of the surgical area.
- A mid-crestal incision with or without releasing incision is made and a full-thickness mucoperiosteal flap is raised.
- With a surgical stent or a distance indicator, the implant positions are marked on the alveolar crest with a small round bur (#1). After exactly locating the implant positions, the opening of the preparations are widened with two sizes of round burs (#2 and #3) to a diameter about half a millimeter smaller than the implant diameter that is chosen (Fig. 50-30).

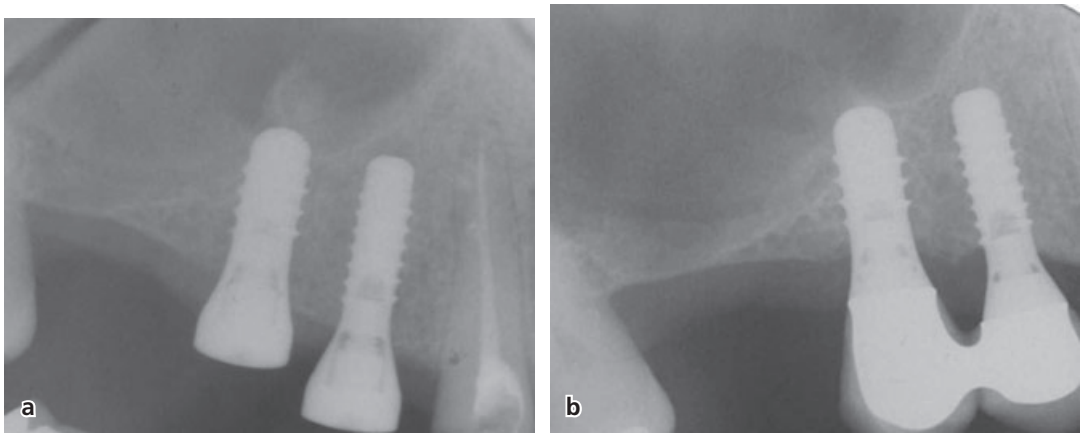

Fig. 50-29 (a) A sinus floor elevation was performed with the osteotome technique in a situation of an oblique sinus floor. The cortical bone of the sinus floor was in-fractured and rolled-up causing a perforation of the sinus membrane. Due to the membrane perforation no grafting material was utilized. (b) The same patient at the 5-year follow-up visit. The implant was stable, but only minor new bone formation is visible at the distal aspect of the implant.

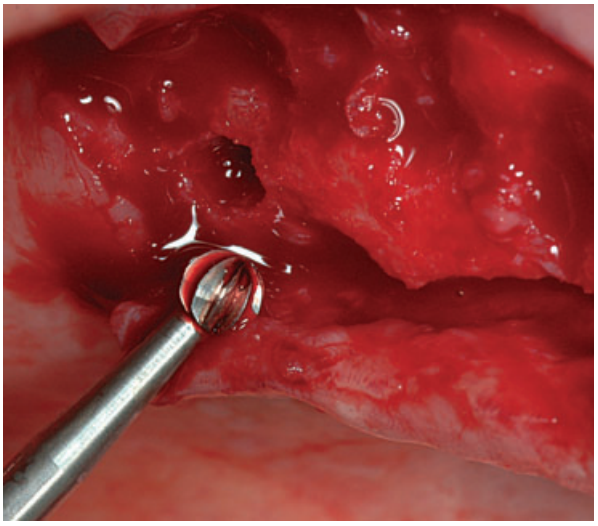

Fig. 50-30 The exact position of the implant site is first marked with a small round bur (#1) and then extended with two sizes of round burs (#2 and #3) to a diameter about 0.5–1 mm smaller than that of the implant to be installed.

- The distance from the crestal floor of the ridge to the floor of the maxillary sinus, measured prior to implant site preparation on the pre-operative radiograph, can in most cases, be confirmed at surgery by penetrating the opening of the preparation with a blunt periodontal probe through the soft trabecular bone (type III or IV bone) to the floor of the maxillary sinus.
- After confirming the distance to the sinus floor, pilot drills with small diameters (1–1.5 mm smaller than the implant diameter) are used to prepare the implant site to a distance of approximately 2 mm below from the sinus floor (Fig. 50-31a). In conditions of soft type IV bone and a residual bone height of 5–6 mm, there is usually no necessity to use the pilot drills. It is sufficient to perforate the cortical bone at the alveolar crest with the round burs.
- The first osteotome used in the implant site is a small diameter tapered osteotome (Fig. 50-32). With light malleting, the osteotome is pushed towards the compact bone of the sinus floor (Fig. 50-31b). After reaching the sinus floor, the osteotome is pushed about 1 mm further with light malleting in order to create a "greenstick" fracture on the compact bone of the sinus floor. A tapered osteotome with small diameter is chosen to minimize the force needed to fracture the compact bone.
- The second tapered osteotome, with a diameter slightly larger then the first one, is used to increase the fracture area of the sinus floor (Fig. 50-33). The second osteotome is applied to the same length as the first one.
- The third osteotome used is a straight osteotome with a diameter about 1–1.5 mm smaller than the implant to be placed (Fig. 50-34).

From this point onwards, the technique utilized in the surgical procedure depends on whether or not bone grafts or bone substitutes will be placed.

Implant placement without grafting material

- Without applying grafting material, the straight osteotome with a diameter about 1–1.5 mm smaller than that of the implant will be pushed further until it penetrates the sinus floor.
- The last osteotome to be used must have a form and diameter suitable for the implant to be placed. For example, for a cylindrical implant with a diameter of 4.1 mm, the last osteotome should be a straight osteotome with a diameter about 0.5 mm smaller than the implant diameter (3.5 mm). It is important that last osteotome only enters the preparation site once (Fig. 50-35). If several attempts have to be made in sites with soft bone (type III or IV), there is a risk of increasing the diameter of the

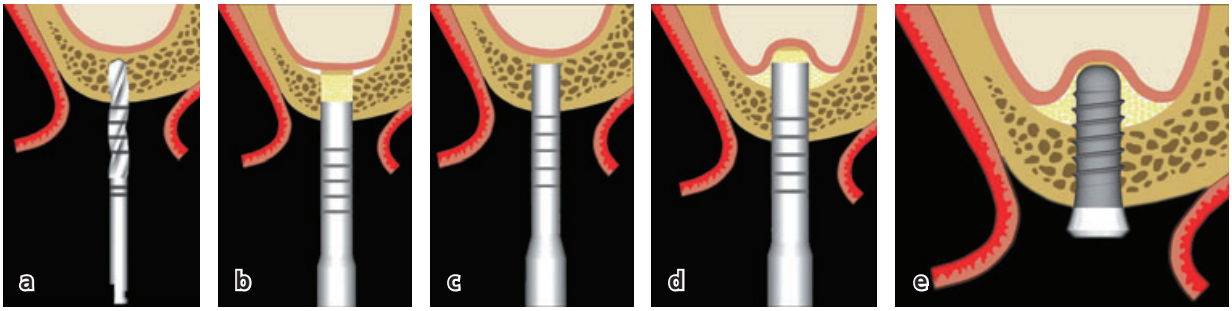

Fig. 50-31 (a) The implant site is prepared to a distance of approximately 2 mm below the sinus floor with a small diameter pilot drill. (b) After reaching the sinus floor, the osteotome is pushed approximately 1 mm further with light malleting in order to create a "greenstick" fracture on the compact bone of the sinus floor. (c) Grafting material is slowly pushed into the sinus cavity with a straight osteotome. This procedure is repeated several times. (d) The tip of the osteotome is only supposed to enter the sinus cavity after some grafting material has been pushed through the preparation site to elevate the sinus membrane. (e) The inserted implant and the grafting material maintain space below the sinus membrane.

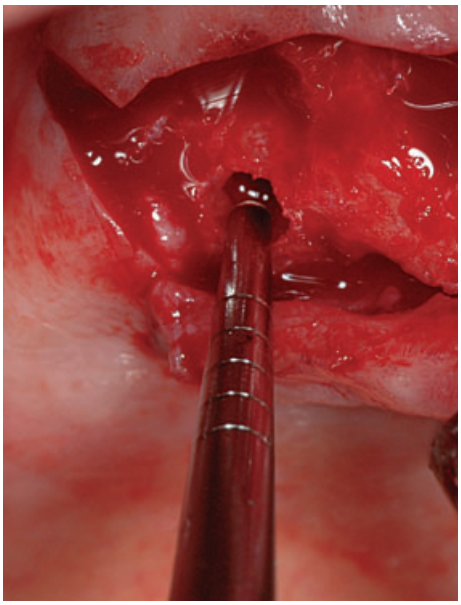

Fig. 50-32 The first osteotome used in the implant site is a small-diameter tapered osteotome. Such an osteotome is chosen to minimize the force needed to fracture the compact bone.

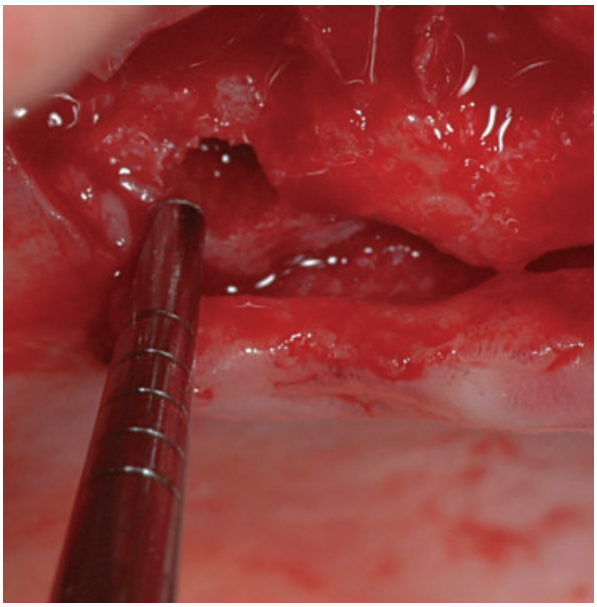

Fig. 50-33 A second osteotome, which is also tapered, but with a diameter slightly larger then the first one, is used to increase the fractured area of the sinus floor.

preparation that might jeopardize achieving good primary stability. On the other hand, if the last osteotome diameter is too small compared to the implant diameter, too much force must be used to insert the implant. By squeezing the bone, more bone trauma and, hence, greater bone resorption will occur, delaying the osseointegration process (Abrahamsson *et al*. 2004). It is thus important, especially when placing implants in sites with reduced bone volume, that the fine balance between good primary stability and traumatizing the bone is respected.

- During the entire preparation, it is crucial to maintain precise control of the penetration length. Regular osteotomes have sharp cutting edges, thus entry into the sinus cavity increases the risk of membrane perforation. The final step before placing the implant is to check that the preparation

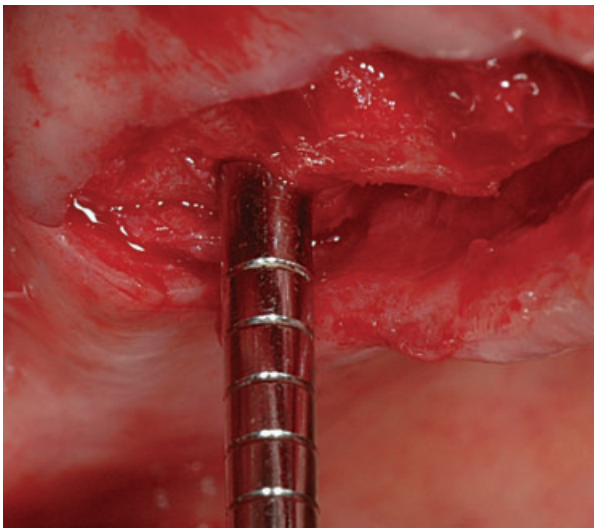

Fig. 50-34 The third osteotome utilized is a straight osteotome with a diameter about 1–1.5 mm smaller than that of the implant to be placed.

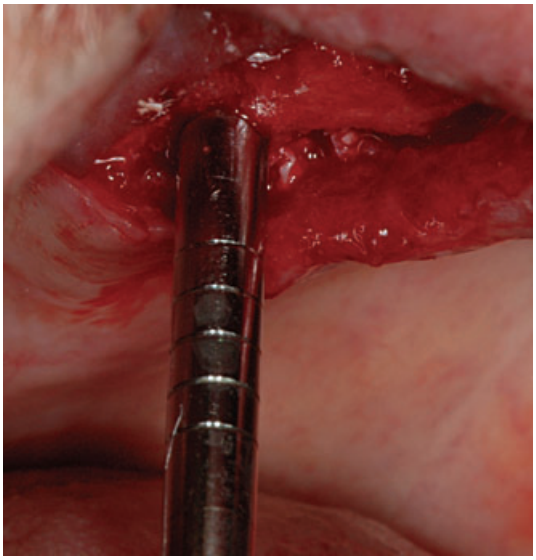

Fig. 50-35 The last osteotome to be used must have a form and diameter suitable for the implant to be placed. For example, for a cylindrical implant with a diameter of 4.1 mm, the last osteotome should be straight with a diameter approximately 0.5 mm smaller than that of the implant (3.5 mm). It is important that the last osteotome is allowed to enter the preparation site only once.

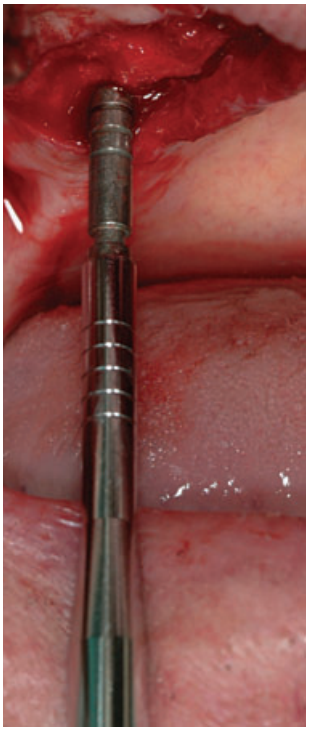

Fig. 50-36 The final step before placing the implant is to check that the preparation is patent to the planned insertion depth. An osteotome with a rounded tip or a depth gauge, for the relevant implant diameter, is pushed to the decided length.

is patent to the planned insertion depth. An osteotome with a rounded tip or a depth gauge, for the relevant implant diameter, is pushed to the decided length (Fig. 50-36).

Implant placement with grafting materials

- When performing the osteotome technique with grafting materials, the osteotomes are not supposed to enter the sinus cavity *per se*. Repositioned bone particles, grafting materials, and the trapped fluid will create a hydraulic effect moving the fractured sinus floor and the sinus membrane upwards. The sinus membrane is less likely to tear under this kind of pressure that has a fluid consistency.
- After pushing the third osteotome up to the sinus floor and before placement of any grafting material, the sinus membrane must by tested for any perforations. This is tested with the Valsalva maneuver (nose blowing). The nostrils of the patients are compressed (Fig. 50-37), and the patient blows against the resistance. If air leaks out of the implant site, the sinus membrane is perforated, and no grafting material should be placed into the sinus cavity.
- If the sinus membrane is judged to be intact, the preparation is filled with grafting material (Fig. 50-38). The grafting material is then slowly pushed into the sinus cavity with the same straight third osteotome (Fig. 50-39). This procedure is repeated four to five times (Fig. 50-31c) until about 0.2–0.3 g of grafting material has been pushed into the sinus cavity below the sinus membrane (Fig. 50-40). In the fourth and fifth time of applying grafting material, the tip of the osteotome may enter about 1 mm into the maxillary sinus cavity to test if there is resistance in the preparation site (Fig. 50-31d).
- Finally, before implant placement (Fig. 50-41), the preparation is checked for patency, as mentioned before, and the Valsalva maneuver is repeated.

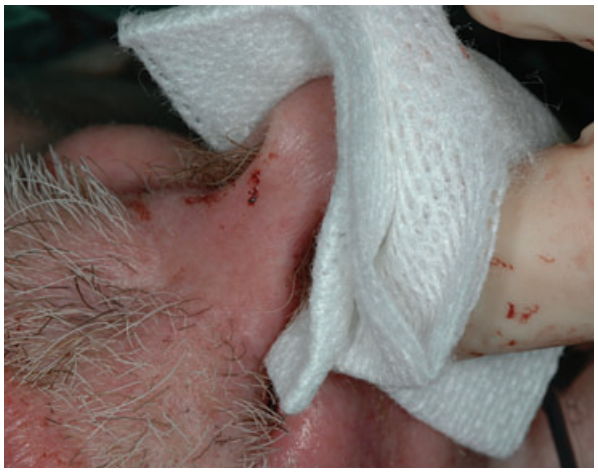

Fig. 50-37 To test the sinus membrane, the nostrils of the patients are compressed and the patient is asked to blow against the resistance. If air leaks out of the implant site, the sinus membrane is perforated, and no grafting material should be placed into the sinus cavity.

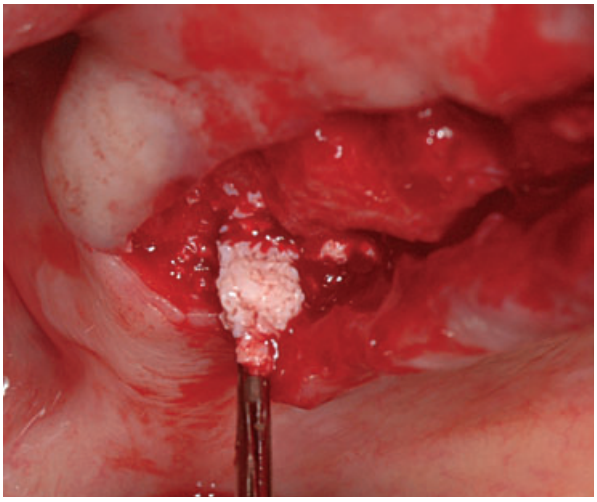

Fig. 50-38 If the sinus membrane is intact, the preparation site is filled four to five times with grafting material.

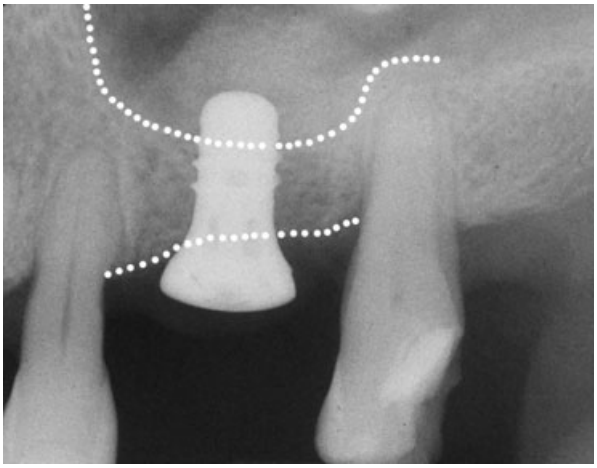

Fig. 50-40 A radiograph, taken after implant placement, showing a dome-shape configuration of the graft. In this instance, 0.25 g of grafting material (xenograft) was used to elevate the sinus membrane (the dotted lines represent the outlines of the residual bone).

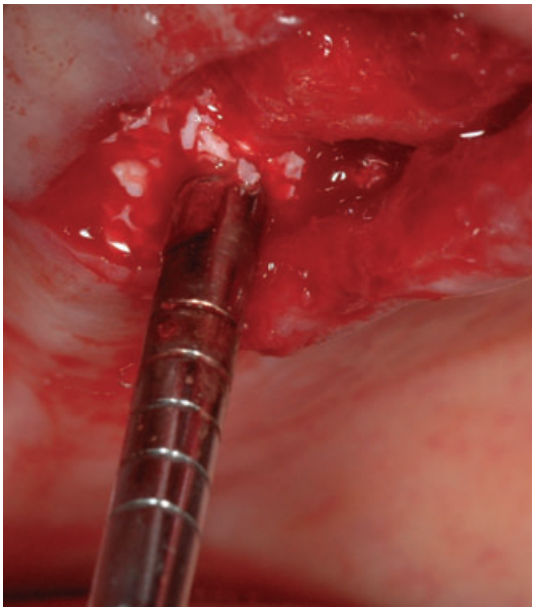

Fig. 50-39 The grafting material is then slowly pushed into the sinus cavity with a straight osteotome with a diameter about 1–1.5 mm smaller than that of the intended implant.

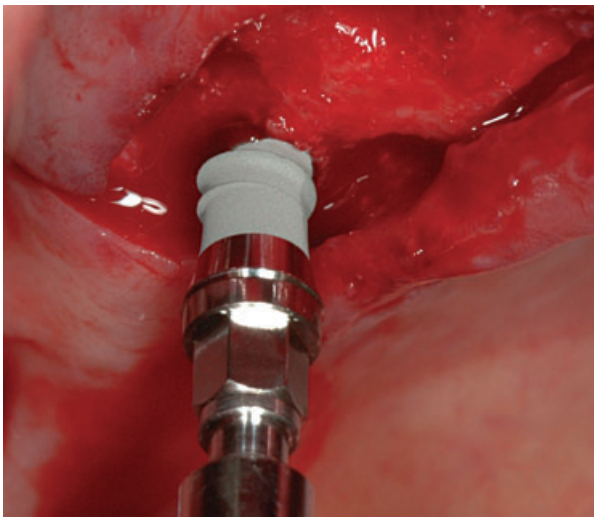

Fig. 50-41 A rough-textured implant was installed after preparing the implant site with the osteotome technique. Good primary stability was achieved.

Post-surgical care

The post-surgical care after placing implants with the osteotome technique is similar to that after standard implant placement. In addition to the standard oral home care, antiseptic rinsing with 0.1–0.2% chlorhexidine twice daily for the first 3 weeks after surgery is highly recommended. However, if bone substitutes were used, the patients are placed on antibiotic prophylaxis for a period of 1 week.

Grafting material

There is still controversy with regards to the necessity of a grafting material to maintain the space for new bone formation after elevating the sinus membrane utilizing the osteotome technique. Shortly after Summers introduced the BAOSFE, a multi-center retrospective study of eight centers was performed. Evaluation was carried out with 174 implants placed in 101 patients. The use of grafting material was decided by the individual clinician. Autografts, allografts, and xenografts were used, alone or in combinations. The authors concluded that the type of grafting material did not influence implant survival (Rosen *et al*. 1999).

When no grafting material is used, some dense structure is often visible apical to the implant, immediately after implant placement. However, after at least 1 year of remodeling, this structure may no longer be detectable and only a moderate amount of bone gain mesially and distally may persist

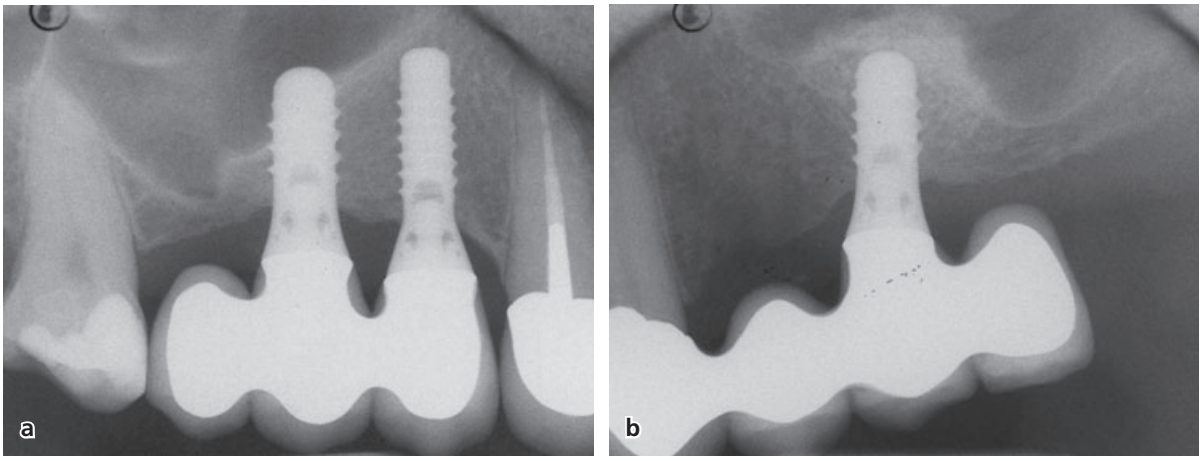

Fig. 50-42 (a) A radiograph, taken at the 5-year follow-up visit, of an implant placed in the 1st quadrant utilizing the osteotome technique without grafting material. A new cortical bony plate at the inferior border of the maxillary sinus is clearly visible, but no bony structure can be detected apical to the implant. (b) A radiograph (same patient) of an implant placed in the 2nd quadrant utilizing the osteotome technique with xenograft grafting material, taken after 5 years in function. A dome-shaped structure is clearly visible documenting a definite increase in bone volume compared to the initial situation. The "dome" is surrounded with a new cortical bony plate.

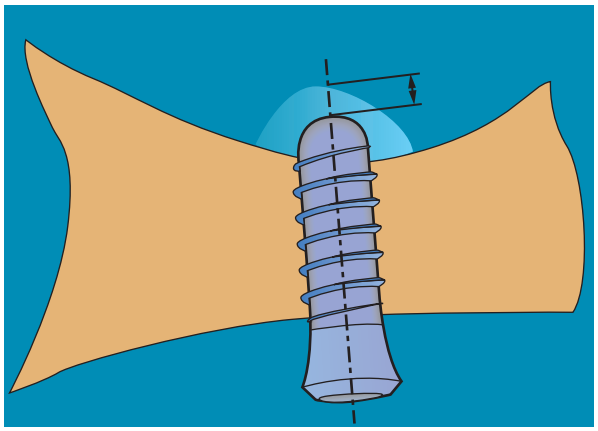

Fig. 50-43 Grafted area apical to the implants undergoes shrinkage and remodeling and the original border of the sinus is eventually consolidated and replaced by a new cortical plate (Brägger *et al*. 2004).

(Pjetursson *et al*. 2008a,b). When grafting material is used, a cloudy dome-shaped structure with a hazy demarcation may be visible after implant placement. The size of this dome is usually reduced after remodeling but still gives a definite increase in bone volume compared to the pre-operative situation (Pjetursson *et al*. 2008a,b) (Fig. 50-42).

Brägger and co-workers (2004) investigated the patterns of tissue remodeling after placement of 25 implants in 19 patients using the osteotome technique with composite xenografts and autografts. Intraoral radiographs were obtained pre-surgically and post-surgically at 3 and 12 months. The mean height of the new bone reaching apical and mesial to the implants was 1.52 mm at surgery, but was reduced significantly to 1.24 mm at 3 months and 0.29 mm after 12 months (Fig. 50-43). It was concluded that the grafted area apical to the implants underwent shrinkage and remodeling (Fig. 50-44) and the original outline of the sinus was eventually consolidated and replaced by a new cortical plate.

Implants installed into the sinuses of 40 patients using an osteotome technique with no graft or cushion materials were recently evaluated (Leblebicioglu *et al*. 2005). The authors reported a mean gain of alveolar bone height in scanned panoramic radiographs of 3.9 ± 1.9 mm.

Success and implant survival

In a multi-center retrospective study (Rosen *et al*. 1999) evaluating the Summers technique applied to the placement of 174 implants in 101 patients, the survival rate was 96%, when residual bone height was 5 mm or more, but dropped down to 85.7% when residual bone height was 4 mm or less (Fig. 50-45).

Survival and success rates of 588 implants placed in 323 consecutive patients with a residual bone height ranging from 6–9 mm after a mean observation period of 5 years were 94.8% and 90.8%, respectively (Ferrigno *et al*. 2006). During the study period, only 13 perforations of the sinus membrane were detected, giving a perforation rate of only 2.2%. The authors also concluded that the installation of short implants in conjunction with osteotome sinus floor elevation is predictable and may reduce the indications for more invasive and complex procedures, such as the sinus floor elevation by the lateral approach.

Moreover, a systematic review (Emmerich *et al*. 2005) evaluated the effectiveness of sinus floor elevation using osteotomes. The inclusion criteria considered studies that had more than ten patients and at least 6 months of functional loading. Eight studies met these inclusion criteria. Within the limits of the small amount of long-term data, the reviewers con-

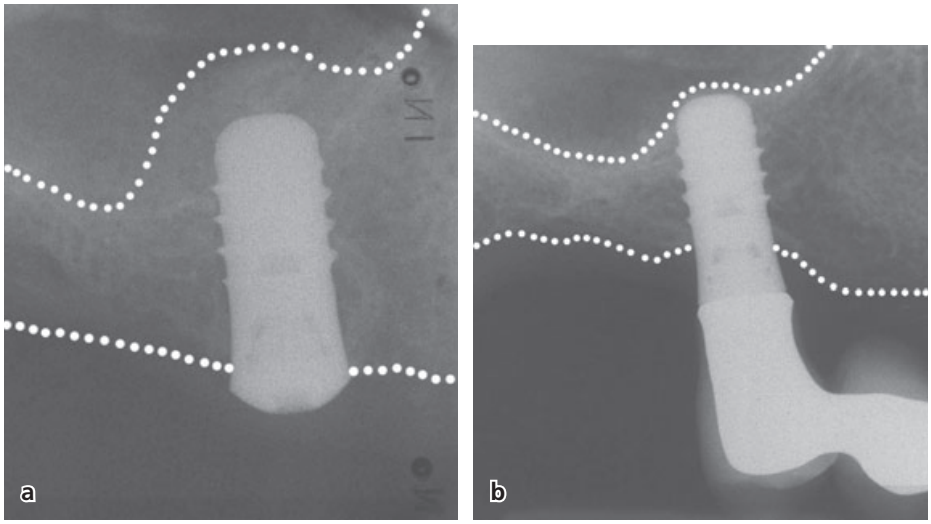

Fig. 50-44 (a) Radiograph taken immediately after implant insertion with the osteotome technique and grafting material, showing a cloudy dome-shaped structure extending 2–3 mm apical to the implant. (b) Radiograph of the same implant taken 1 year later showing significant reduction of the size of the "dome", but the new bony structure is clearly visible apical to the implant (the dotted lines represent the outlines of the grafting material and the residual bone).

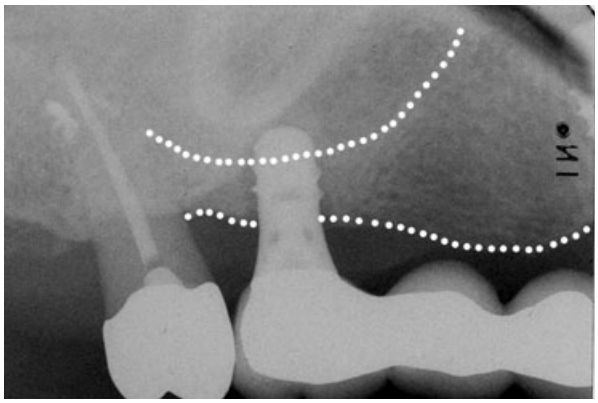

Fig. 50-45 Radiograph of a 6 mm implant that was inserted utilizing the osteotome technique without grafting material. The residual bone height was only 3 mm. After 6 months of functional loading, the implant became loose and had to be removed. After a healing time of 2 months, the maxillary sinus floor was elevated with the lateral approach and two new implants were placed simultaneously (the dotted lines represent the outlines of the residual bone).

cluded that the short-term success rates were similar to success rates of implants conventionally placed in partially edentulous patients (96.0% after 36 months). Long-term outcomes (>5 years) of implants placed with the osteotome technique are still scarse. The database was heterogenous regarding different surgical techniques, implant types, and grafting materials. Hence, no statistical analysis was performed on these parameters.

Short implants

In the light of sinus floor elevation techniques being indicated to facilitate the installation of dental implants in the maxillary posterior region without adequate bone volume, treatment alternatives have to be discussed (see Chapter 31). Since patient-centered outcomes and morbidity associated with these procedures have not been addressed so far, it has to be anticipated that a great number of patients may not choose sinus floor elevation for their treatment. Hence, shortened dental arches (Käyser 1981) may have to be considered in treatment planning.

Another variation to conventional implant installation in the posterior maxilla is the choice of short implants to avoid penetration into the sinus cavity. Jemt and Lekholm (1995) reported that implant failure in edentulous maxilla correlated significantly with bone quality especially for short (7 mm) implants. Other studies (Friberg *et al*. 1991; Jaffin & Berman 1991) had also reported low survival rates of short implants. However, it must be kept in mind that all these studies reported on implants with machined surface geometries. Based on these studies and others, the clinical "dogma" has been followed, that generally only long implants should be inserted in type IV "poor-quality" bone in the posterior maxilla.

A targeted review (Hagi *et al*. 2004) of study outcomes with short (≤7 mm) implants placed in partially edentulous patients, concluded that machined-surface implants experienced greater failure rates than rough-textured implants. The implant surface geometry appeared to be a major determinant in the performance of these short implants.

In a multi-center study (ten Bruggenkate *et al*. 1998) evaluating 6-mm non-submerged rough-surface dental implants, only one of 208 short implants placed in the mandible was lost compared to six of 45 implants placed in the maxilla. Four of these implants were lost during the healing phase

with three remaining in function. The survival rates were 99.5% and 86.7% respectively, after a follow-up time up to 7 years.

In contrast, recent clinical studies (Fugazotto *et al*. 2004; Renouard & Nisand 2005) on short implants with rough surfaces, designed for high initial stability, reported survival rates of about 95% which correlates with the survival rate reported for implants after 5 years in a systematic review (Berglundh *et al*. 2002). Two multi-center studies on rough-surface implants (Buser *et al*. 1997; Brocard *et al*. 2000) analyzed the survival and success rates of implants of different lengths. No significant difference was found between 8, 10, and 12 mm implants with rough-surface geometry after up to 8 years follow-up time.

The most recent review prepared for the Consensus Meeting of the European Association of Osseointegration (EAO) (Renouard & Nisand 2006) concluded on the basis of 12 studies on machined-surface implants meeting the inclusion criteria and 22 studies on rough-textured implants that the survival and success rates of short (<10 mm) implants was comparable to those obtained with longer implants, provided that surgical preparation was related to bone density, rough-textured implants were employed and operators' surgical skills were developed.

The use of short implants may be considered in sites thought unfavorable for implant placement, such as those associated with bone resorption or previous injury and trauma. While in these situations implant failure rates may be increased, outcomes should be compared with those associated with advanced surgical procedures such as bone grafting and sinus floor elevation.

Conclusions and clinical suggestions

In the posterior maxilla, implants with morphometry designed to achieve high initial stability and with rough surface geometry giving high percentage of bone-to-implant contact during initial healing phase (Abrahamsson *et al*. 2004), are to be preferred. Implants with slightly conical morphometry or implants with wider implant neck tend to give better primary stability in cases of reduced residual bone height and soft bone geometry.

The clinical decision on which method (short implants, osteotome technique or lateral approach) should be chosen, depends on the residual bone height of the alveolar crest and surgeons' preferences. The following recommendations are suggested:

1. Residual bone height of 8 mm or more and flat sinus floor: standard implant placement (Fig. 50-46).
2. Residual bone height of 8 mm or more and oblique sinus floor: standard implant placement using short implant or elevation of the maxillary sinus floor using the osteotome technique without grafting material (Fig. 50-47).

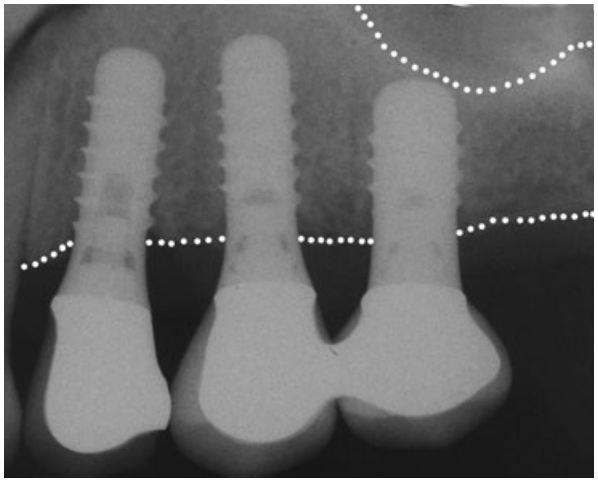

Fig. 50-46 Radiograph of a short (8 mm) implant in the posterior maxilla (the dotted lines represent the outlines of the residual bone).

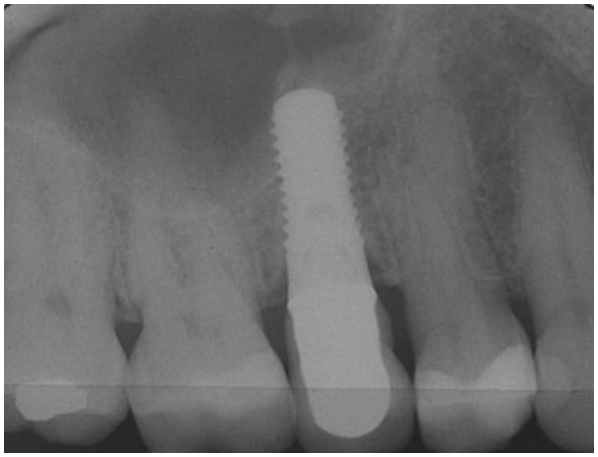

Fig. 50-47 Radiograph of an implant inserted in the posterior maxilla with an oblique sinus floor and a residual bone height of 8–10 mm. The osteotome technique without grafting material was used. The distal aspect of the apex of the implant extends into the sinus cavity, but the mesial aspect is covered with residual bone.

3. Residual bone height of 5–7 mm and flat sinus floor: elevation of the maxillary sinus floor using the osteotome technique with grafting material that is resistant to resorption (Fig. 50-48).
4. Residual bone height of 5–7 mm and oblique sinus floor: elevation of the maxillary sinus floor using lateral approach with grafting material, and simultaneous implant placement (one-stage) (Fig. 50-49).
5. Residual bone height of 3–4 mm and flat or oblique sinus floor: elevation of the maxillary sinus floor using lateral approach with grafting material, and simultaneous implant placement (one-stage) (Fig. 50-50).
6. Residual bone height of 1–2 mm and flat or oblique sinus floor: elevation of the maxillary sinus floor using lateral approach with grafting material and delayed implant placement 4–8 months later (two-stage) (Fig. 50-51).

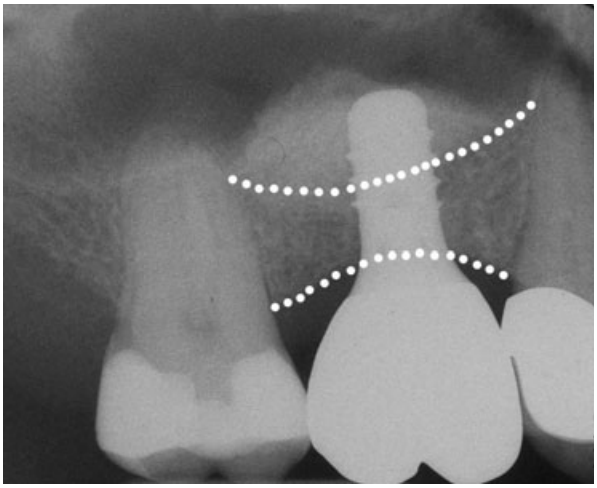

Fig. 50-48 Radiograph of an implant inserted in the posterior maxilla with a flat sinus floor and a residual bone height of 5–6 mm. The osteotome technique with grafting material was used. The radiograph shows a dome-shaped formation covering the entire apex of the implant (the dotted lines represent the outlines of the residual bone).

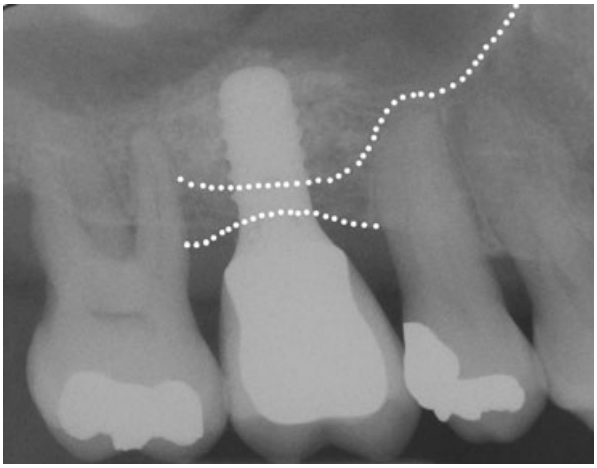

Fig. 50-50 Radiograph of an implant inserted in the posterior maxilla with a flat sinus floor and a residual bone height between 2 and 3 mm. The maxillary sinus floor was elevated using the lateral approach, and one implant was inserted simultaneously (the dotted lines represent the outlines of the residual bone).

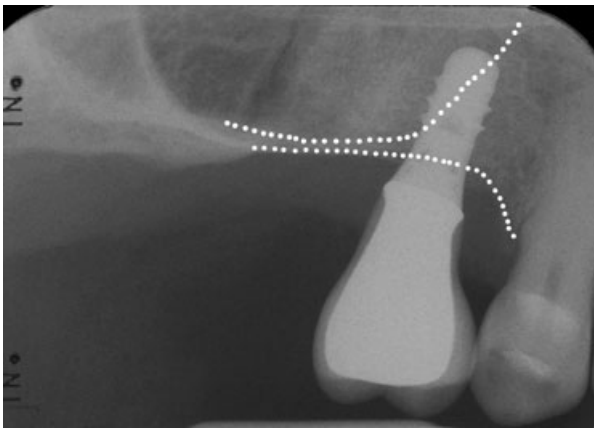

Fig. 50-49 Radiograph of an implant inserted in the posterior maxilla with a oblique sinus floor and a residual bone height between 2 and 8 mm. The maxillary sinus floor was elevated using the lateral approach, and one implant was inserted simultaneously (the dotted lines represent the outlines of the residual bone).

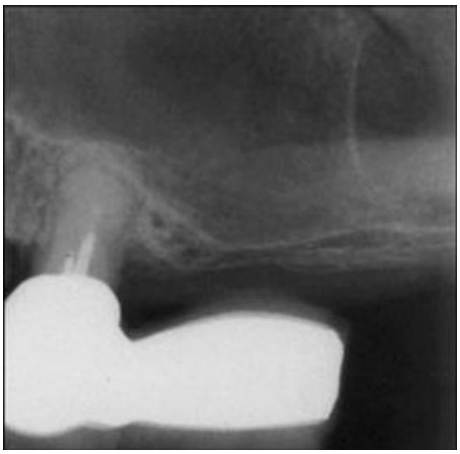

Fig. 50-51 Radiograph showing a large pneumatized maxillary sinus, where a two-stage sinus floor elevation with a delayed implant insertion has to be used.

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Part 16: Occlusal and Prosthetic Therapy

Chapter 51

Tooth-Supported Fixed Partial Dentures

Jan Lindhe and Sture Nyman

Clinical symptoms of trauma from occlusion

Angular bony defects

It has been claimed that *angular bony defects* and *increased tooth mobility* are important symptoms of trauma from occlusion (Glickman 1965, 1967). The validity of this suggestion has, however, been questioned (see Chapter 14). Thus, angular bony defects have been found at teeth affected by *trauma from occlusion* as well as at teeth with normal occlusal function (Waerhaug 1979). *This means that the presence of angular bony defects cannot* per se *be regarded as an exclusive symptom of trauma from occlusion*.

Increased tooth mobility

Increased tooth mobility, determined clinically, is expressed in terms of amplitude of displacement of the crown of the tooth. Increased tooth mobility can, indeed, be observed in conjunction with *trauma from occlusion*. It may, however, also be the result of a reduction of the height of the alveolar bone with or without an accompanying angular bony defect caused by plaque-associated periodontal disease (see Chapter 14). Increased tooth mobility resulting from occlusal interferences may further indicate that the periodontal structures have become adapted to an altered functional demand, i.e. a widened periodontal ligament with a normal tissue composition has become the end result of a previous phase of progressive tooth mobility (see Chapter 14) associated with trauma from occlusion.

Progressive (increasing) tooth mobility

In Chapter 14, it was concluded that the diagnosis trauma from occlusion should be used solely in situations where a progressive mobility could be observed. Progressive tooth mobility can be identified only through a series of repeated tooth mobility measurements carried out over a period of several days or weeks.

Tooth mobility crown excursion/root displacement

Initial and secondary tooth mobility

A tooth which is surrounded by a normal periodontium may be moved (displaced) in horizontal and vertical directions and may also be forced to perform limited rotational movements. Clinically, tooth mobility is usually assessed by exposing the crown of the tooth to a certain force and determining the distance the crown can be displaced in buccal and/or lingual direction. The mobility (= movability) of a tooth in a horizontal direction is closely dependent on the height of the surrounding supporting bone, the width of the periodontal ligament, and the shape and number of roots present (Fig. 51-1).

The mechanism of tooth mobility was studied in detail by Mühlemann (1954, 1960) who described a

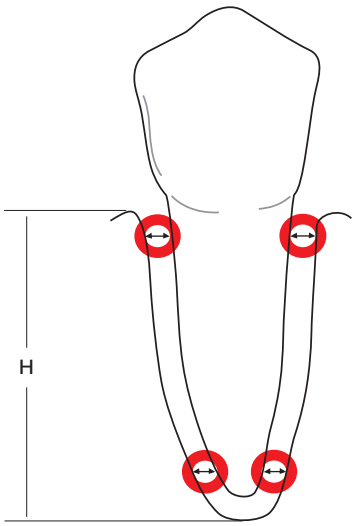


Fig. 51-1 The mobility of a tooth in horizontal direction is dependent on the height of the alveolar bone (H), the width of the periodontal ligament (encircled arrows), and the shape and number of roots.

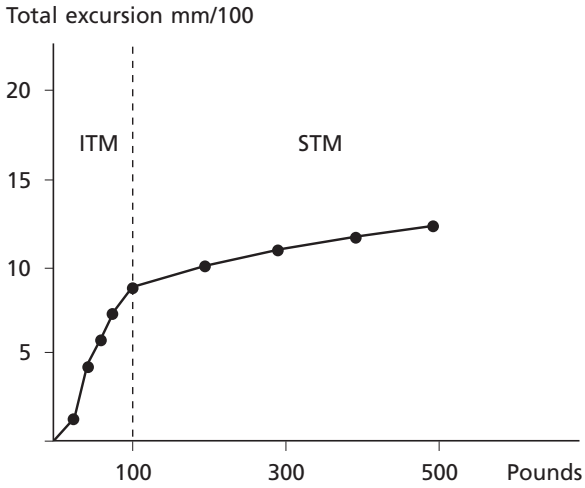


Fig. 51-3 Initial tooth mobility (ITM) means the excursion of the crown of a tooth when a force of 100 pounds is applied to the crown. Secondary tooth mobility (STM) means the excursion of the crown of the tooth when a force of 500 pounds is applied.

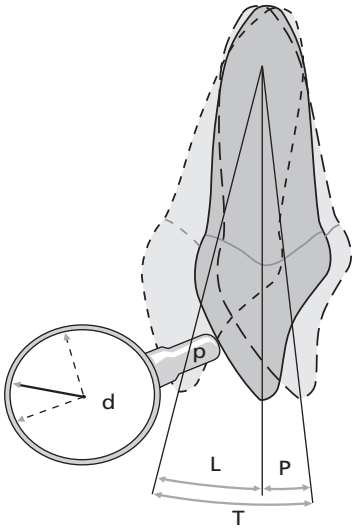


Fig. 51-2 Tooth mobility measurements by means of the Periodontometer. d = dial indicator; p = pointer; L = labial excursion of the crown; P = palatal excursion of the crown; T = L + P = total excursion of the crown.

standardized method for measuring even minor tooth displacements. By means of the "Periodontometer" a small force (~45 kg (100 pounds)) is applied to the crown of a tooth (Fig. 51-2). The crown starts to tip in the direction of the force. The resistance of the tooth-supporting structures against displacement of the root is low in the initial phase of force application and the crown is moved only 5/100–10/100 mm. This movement of the tooth was called "*initial tooth mobility*" (ITM) by Mühlemann (1954) and is the result of an *intra-alveolar* displacement of the root (Fig. 51-3). In the pressure zone (see Chapter 14) there is a 10% reduction in the width of the periodontal ligament and in the tension zone there is a corresponding increase. Mühlemann and Zander (1954) stated that "there are good reasons to assume that the initial displacement of the root (ITM) corresponds to a reorientation of the periodontal membrane fibers into a position of functional readiness towards tensile strength". The magnitude of the ITM varies from individual to individual, from tooth to tooth, and is mainly dependent on the structure and organization of the periodontal ligament. The ITM value of ankylosed teeth is therefore zero.

When a larger force (~225 kg (500 pounds)) is applied to the crown, the fiber bundles on the tension side cannot offer sufficient resistance to further root displacement. The additional displacement of the crown that is observed in "*secondary tooth mobility*" (STM) (Fig. 51-3) is allowed by distortion and compression of the periodontium in the pressure side. According to Mühlemann (1960) the magnitude of STM, i.e. the excursion of the crown of the tooth when a force of 500 pounds is applied, (1) varies between different types of teeth (e.g. incisors 10–12/100 mm, canines 5–9/100 mm, premolars 8–10/100 mm and molars 4–8/100 mm), (2) is larger in children than in adults, and (3) is larger in females than males and increases during, for example, pregnancy. Furthermore, tooth mobility seems to vary during the course of the day; the lowest value is found in the evening and the largest in the morning.

A new method for determining tooth mobility was presented by Schulte and co-workers (Schulte 1987; Schulte *et al*. 1992) when the Periotest® (SiemensAG, Bensheim, Germany) system was introduced. The Periotest device measures the reaction of the periodontium to a defined percussion force which is applied to the tooth and delivered by a tapping instrument. A metal rod is accelerated to a speed of 0.2 m/s with the device and maintained at a constant velocity. Upon impact the tooth is deflected and the

rod decelerated. The contact time between the tapping head and the tooth varies between 0.3 and 2 milliseconds and is shorter for stable than mobile teeth. The Periotest scale (the Periotest values) ranges from –8 to +50 and the following ranges should be considered:

- –8 to +9: clinically firm teeth
- 10–19: first distinguishable sign of movement
- 20–29: crown deviates within 1 mm of its normal position
- 30–50: mobility is readily observed.

The Periotest values correlate well with (1) tooth mobility assessed with a metric system, and (2) degree of periodontal disease and alveolar bone loss. The simple Periotest device is likely to be used in both the clinic and research settings in the future.

Clinical assessment of tooth mobility (physiologic and pathologic tooth mobility)

If, in the traditional clinical measurement of tooth mobility, a comparatively large force is exerted on the crown of a tooth which is surrounded by a normal periodontium, the tooth will tip within its alveolus until a closer contact has been established between the root and the marginal (or apical) bone tissue. The magnitude of this tipping movement, which is normally assessed using the tip of the crown as a reference point, is referred to as the "*physiologic*" tooth mobility. The term "*physiologic*" implies that "*pathologic*" tooth mobility may also occur.

What, then, is "pathologic" tooth mobility?

1. If a similar force is applied to a tooth which is surrounded by a periodontal ligament with an increased width, the excursion of the crown in horizontal direction will become increased; the clinical measurement consequently demonstrates that the tooth has an increased mobility. Should this increased mobility be regarded as *pathologic*?
2. An increased tooth mobility, i.e. an increased displacement of the crown of the tooth after force application, can also be found in situations where the height of the alveolar bone has been reduced but the remaining periodontal ligament has a normal width. At sites where this type of bone loss is extensive, the degree of tooth mobility (i.e. excursion of the crown) may be pronounced. Should this increased tooth mobility be regarded as "pathologic"?

Figure 51-4b illustrates a tooth which is surrounded by alveolar bone of reduced height. The width of the remaining periodontal ligament, however, is within normal limits. A horizontally directed force applied to the crown of the tooth in this case will result in a larger excursion of the crown than if a similar force is applied to a tooth with normal height of the alveolar bone and normal width of the periodontal ligament (Fig. 51-4a). There are reasons to suggest that the *so-called increased mobility* measured in the case of Fig. 51-4b is, indeed, *physiologic*. The validity of this statement can easily be demonstrated if the displacement of the two teeth is assessed not from the crown but from a point on the root at the level of the bone crest. If a horizontal force is directed to the teeth as indicated in Fig. 51-4 the reference points (*) on the root surfaces will be displaced a similar distance in both instances. *Obviously, it is not the length of the excursive movement of the crown that is important from a biologic point of view, but the displacement of the root within its remaining periodontal ligament*.

In plaque-associated periodontal disease, bone loss is a prominent feature. Another so-called classical symptom of periodontitis is "increased tooth mobility". It is important to realize, however, that in many situations with even or "horizontal" bone loss patterns, the increased crown displacement (tooth mobility) assessed in clinical measurements should, according to the above discussion, also be regarded as physiologic; the movement of the root within the space of its remaining "normal" periodontal ligament is normal.

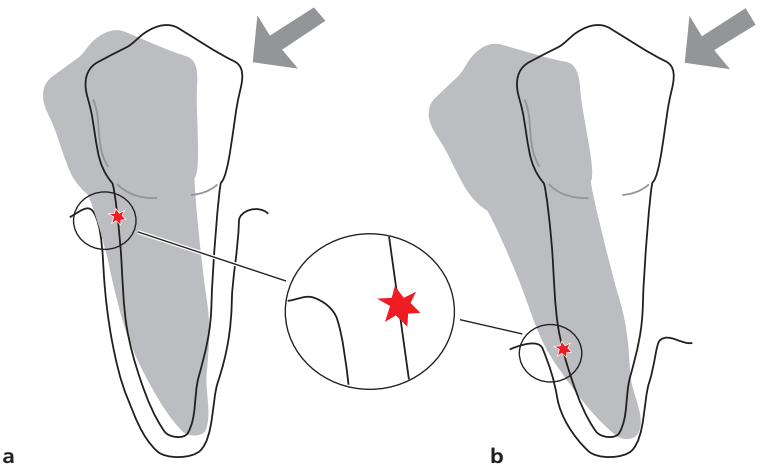


Fig. 51-4 (a) The normal "physiologic" mobility of a tooth with normal height of the alveolar bone and normal width of the periodontal ligament. (b) The mobility of a tooth with reduced height of the alveolar bone. The distance of the horizontal displacement of the reference point (*) on the roots is the same in the two situations (a,b).

3. Increased crown displacement (tooth mobility) may also be detected in a clinical measurement where a "horizontal" force is applied to teeth with angular bony defects and/or increased width of the periodontal ligament. If this mobility does not increase gradually – from one observation interval to the next – the root is surrounded by a periodontal ligament of increased width but normal composition. This mobility should also be considered *physiologic* since the movement is a function of the height of the alveolar bone and the width of the periodontal ligament.
4. Only *progressively increasing tooth mobility*, which may occur in conjunction with trauma from occlusion, is characterized by active bone resorption (see Chapter 14) and which indicates the presence of inflammatory alterations within the periodontal ligament tissue, may be considered *pathologic*.

Treatment of increased tooth mobility

A number of situations will be described below which may call for treatment aimed at reducing an increased tooth mobility.

Situation I

Increased mobility of a tooth with increased width of the periodontal ligament but normal height of the alveolar bone

If a tooth (for instance a maxillary premolar) is fitted with an improper filling or crown restoration, occlusal interferences develop and the surrounding periodontal tissues become the seat of inflammatory reactions, i.e. trauma from occlusion (Fig. 51-5). If the restoration is so designed that the crown of the tooth in occlusion is subjected to undue forces directed in a buccal direction, bone resorption phenomena develop in the buccal–marginal and lingual–apical pressure zones with a resulting increase of the width of the periodontal ligament in these zones. The tooth becomes hypermobile or moves away from the "traumatizing" position. Since such traumatizing forces in teeth with normal periodontium or overt gingivitis cannot result in pocket formation or loss of connective tissue attachment, the resulting increased mobility of the tooth should be regarded as a physiologic adaptation of the periodontal tissues to the altered functional demands. A proper correction of the anatomy of the occlusal surface of such a tooth, i.e. occlusal adjustment, will normalize the relationship between the antagonizing teeth in occlusion, thereby eliminating the excessive forces. As a result, apposition of bone will occur in the zones previously exposed to resorption, the width of the periodontal ligament will become normalized and the tooth stabilized, i.e. it reassumes its normal mobility (Fig. 51-5). In other words, resorption of alveolar bone which is caused by trauma from occlusion is a reversible process which can be treated by the elimination of occlusal interferences.

The capacity for bone regeneration after resorption following trauma from occlusion has been documented in a number of animal experiments (Waerhaug & Randers-Hansen 1966; Polson *et al*. 1976a; Karring *et al*. 1982; Nyman *et al*. 1982). In such experiments, the induced bone resorption not only involved the bone within the alveolus but also the alveolar bone crest. When the traumatizing forces were removed, bone tissue was deposited not only in the walls of the alveolus, thereby normalizing the width of the periodontal ligament, but also on the bone crest area, whereby the height of the alveolar bone was normalized (Fig. 51-6) (Polson *et al*. 1976a). In the presence

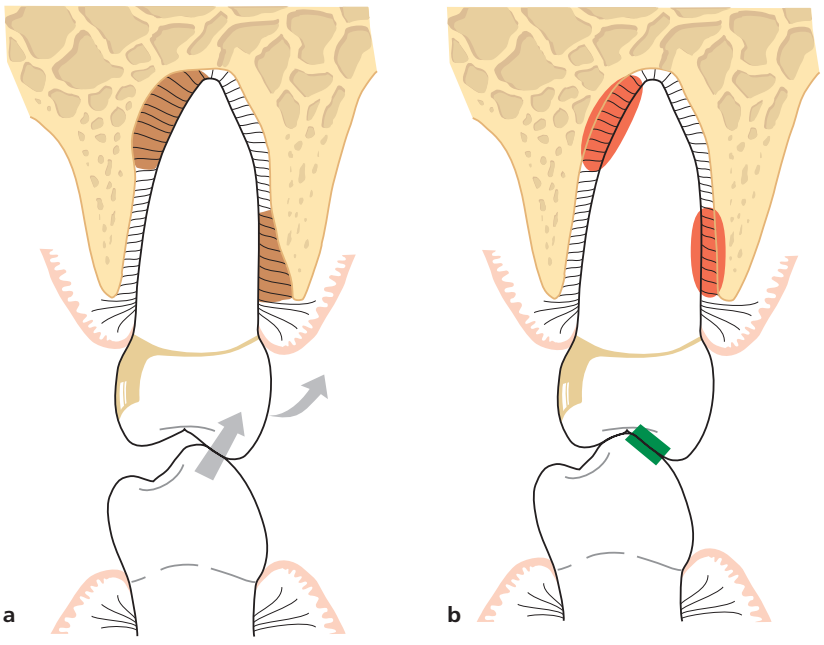


Fig. 51-5 (a) Contact relationship between a mandibular and a maxillary premolar in occlusion. The maxillary premolar is fitted with an artificial restoration with an improperly designed occlusal surface. Occlusion results in horizontally directed forces (arrows) which may produce an undue stress concentration within the "brown" areas of the periodontium of the maxillary tooth. Resorption of the alveolar bone occurs in these areas. A widening of the periodontal ligament can be detected as well as increased mobility of the tooth. (b) Following adjustment of the occlusion, the horizontal forces are reduced. This results in bone apposition ("red areas") and a normalization of the tooth mobility.

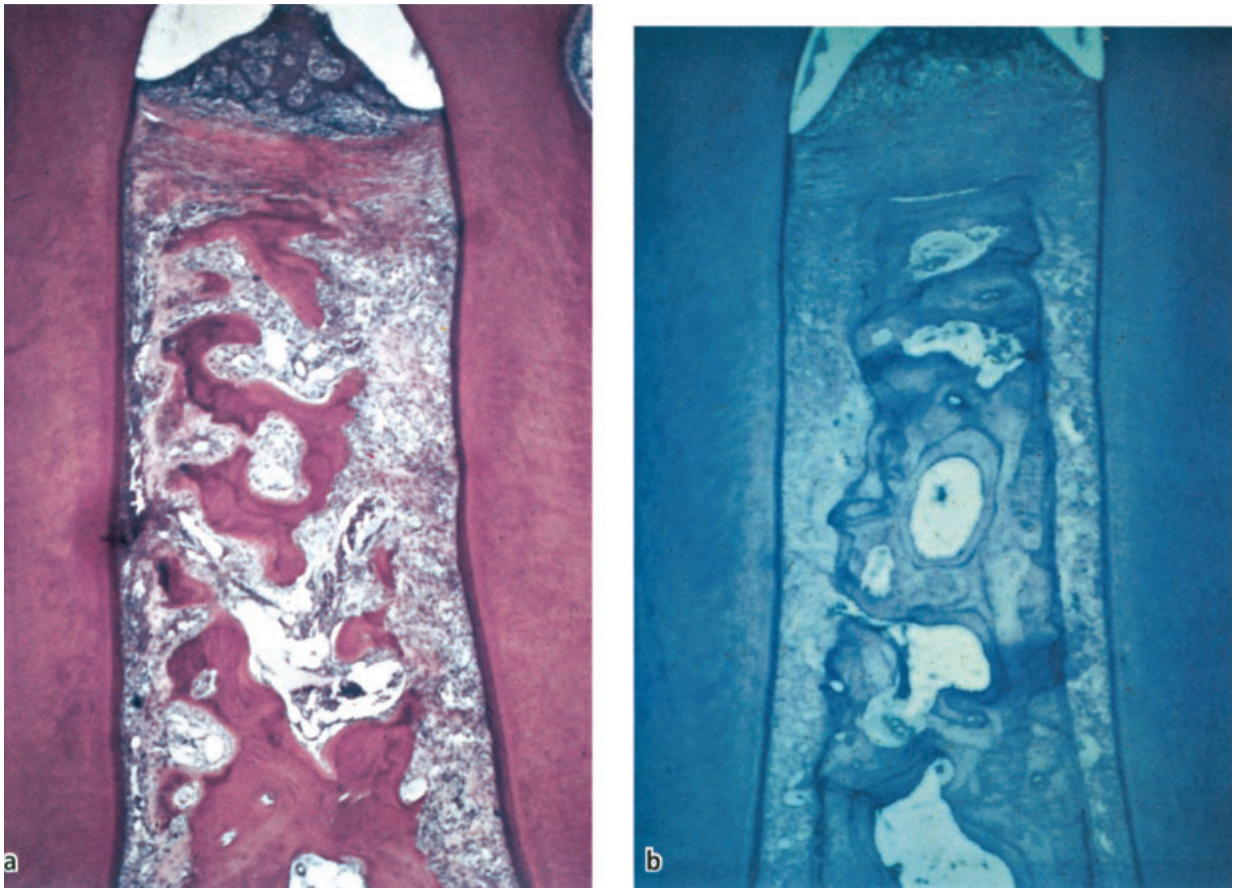


Fig. 51-6 Photomicrographs illustrating the interdental area between two mandibular premolars in the monkey. In (a) the two premolars are exposed to jiggling forces. Note the reduction of alveolar bone in the area and the location of the bone crest. Ten weeks after the elimination of the jiggling forces (b) a considerable regeneration of bone has occurred. Note the increase of the height of the interdental bone and the normalization of the width of the periodontal ligaments. The apical end of the junctional epithelium is located at the cemento-enamel junction. (Courtesy of Dr. A.M. Polson; from Polson *et al*. (1976a).)

of an untreated, plaque-associated lesion in the soft tissue, however, substantial bone regrowth did not always occur (Fig. 51-7) (Polson *et al*. 1976b).

Situation II

Increased mobility of a tooth with increased width of the periodontal ligament and reduced height of the alveolar bone

When a dentition has been properly treated for moderate to advanced periodontal disease, gingival health is established in areas of the dentition where teeth are surrounded by periodontal structures of reduced height. If a tooth with a reduced periodontal tissue support is exposed to excessive horizontal forces (trauma from occlusion), inflammatory reactions develop in the pressure zones of the periodontal ligament with accompanying bone resorption. These alterations are similar to those which occur around a tooth with supporting structures of a normal height; the alveolar bone is resorbed, the width of the periodontal ligament is increased in the pressure/tension zones and the tooth becomes hypermobile (Fig. 51-8a). If the excessive forces are reduced or eliminated by occlusal adjustment, bone apposition to the "pre-trauma" level will occur, the periodontal ligament will regain its normal width and the tooth will become stabilized (Fig. 51-8b).

Conclusion: situations I and II

Occlusal adjustment is an effective therapy against increased tooth mobility when such mobility is caused by an *increased width* of the periodontal ligament.

Situation III

Increased mobility of a tooth with reduced height of the alveolar bone and normal width of the periodontal ligament

The increased tooth mobility which is the result of a reduction in height of the alveolar bone without a concomitant increase in width of the periodontal membrane cannot be reduced or eliminated by occlusal adjustment. In teeth with normal width of the periodontal ligament, no further bone apposition on the walls of the alveoli can occur. If such an increased

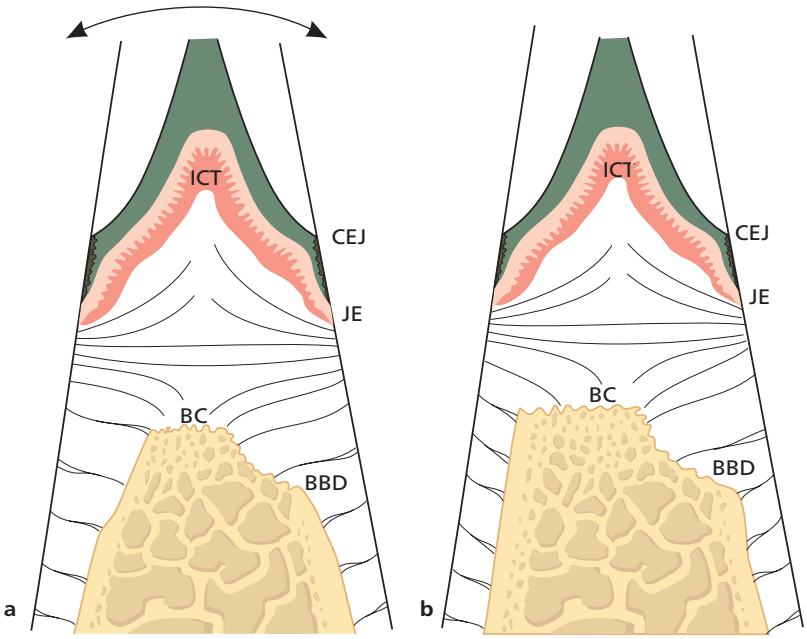


Fig. 51-7 In the presence of an existing marginal inflammation, alveolar bone, lost by jiggling trauma (a), will not always regenerate following elimination of the traumatic forces (b). ICT = infiltrated connective tissue; CEJ = cemento-enamel junction; JE = apical end of junctional epithelium; BC = alveolar bone crest; BBD = bottom of angular bony defect. From Polson *et al.* (1976b).

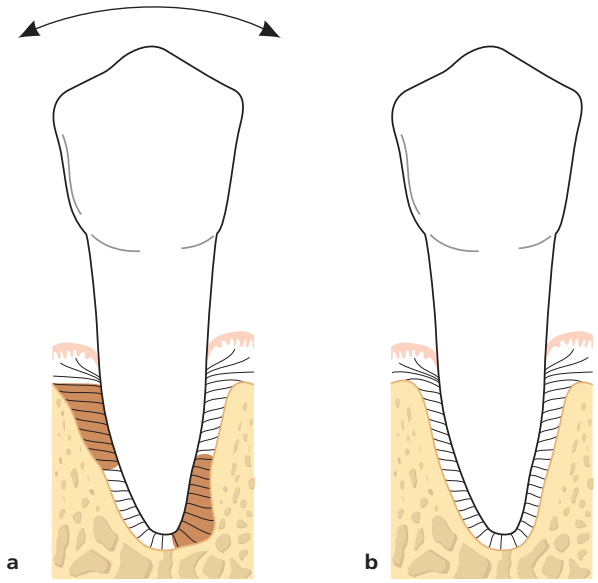


Fig. 51-8 If a tooth with reduced periodontal tissue support (a) has been exposed to excessive horizontal forces, a widened periodontal ligament space ("brown" areas) and increased mobility (arrow) result. (b) Following reduction or elimination of such forces, bone apposition will occur and the tooth will become stabilized.

tooth mobility does not interfere with the patient's chewing function or comfort, no treatment is required. If the patient experiences the tooth mobility as disturbing, however, the mobility can only be reduced in this situation by splinting, i.e. by joining the mobile tooth/teeth together with other teeth in the jaw into a fixed unit – a splint.

A splint, according to the Glossary of Periodontic Terms (1986) is "an appliance designed to stabilize mobile teeth". A splint can be fabricated in the form of joined composite fillings, fixed bridges, removable partial prostheses, etc.

Example: Case A, 64-year-old male

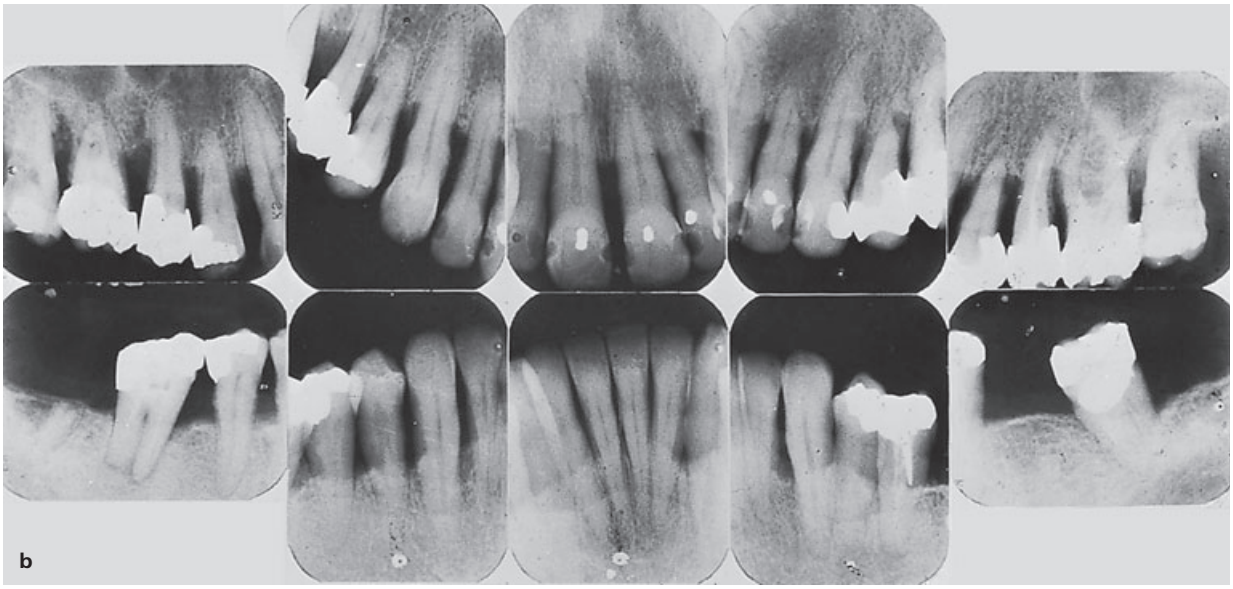
The periodontal condition of this patient is illustrated by the probing depth, furcation involvement and tooth mobility data as well as the radiographs from the initial examination in Fig. 51-9. Periodontal disease has progressed to a level where, around the maxillary teeth, only the apical third or less of the roots is invested in supporting alveolar bone. The following discussion is related to the treatment of the maxillary dentition.

In the treatment planning of this case it was decided that the first premolars (teeth 14 and 24) had to be extracted due to advanced periodontal disease and furcation involvement of degree III. For the same reasons, teeth 17 and 27 were scheduled for extraction. Teeth 16 and 26 were also found to have advanced loss of periodontal tissue support in combination with deep furcation involvements. The most likely *definitive* treatment should include periodontal and adjunctive therapy in the following parts of the dentition: 15 and 25, and 13, 12, 11, 21, 22, 23. For functional and esthetic reasons, 14 and 24 obviously had to be replaced. The question now arose as to whether these two premolars should be replaced by two separate unilateral bridges, using 13, 15 and 23, 25 as abutment teeth, or if the increased mobility of these teeth and also of the anterior teeth (12, 11, 21, 22) (Fig. 51-9) called for a bridge of cross-arch design, with the extension 15–25, to obtain a splinting effect. If 14 and 24 are replaced by two unilateral bridges, each one of these three-unit bridges will exhibit the same degree of mobility in a bucco-lingual direction as the individual abutment teeth (degree 2) (Fig. 51-9), since a unilateral straight bridge will not have a stabilizing effect on the abutment teeth in this force direction.

a

Periodontal chart

Tooth	Pocket depth M	B	D	L	Furcation involvement	Tooth mobility
~~18~~						
17	6	6	8	8	b2, m2, d1	
16	6	6	8	8	m1, d2	2
15	8	8	6	7		2
14	7	7	7	4	3	2
13	8	4	8	4		2
12	8	4	8	4		2
11	6	4	7	4		1
21	6	4	6	4		1
22	6	5	7			2
23	6		6	4		2
24	7		8		3	2
25	6	8	8	4		2
26	8		6		b2, m2, d2	
27	6	6	10	8	b2, d2	1
~~28~~						
~~48~~						
~~47~~						
46	8	6	6	7	b1, l2	
45	6		7	4		1
44	6		6	4		
43	7	7	6	4		
42	4		4	4		1
41	6	4				1
31	6					1
32	4		6	4		1
33	6		6	6		2
34	4		7	4		
35	7		4	6		2
~~36~~						
37	8	5	6	4	b2, l2	3
~~38~~						



b

Fig. 51-9 Case A, 64-year-old male. Periodontal status (a) and radiographs (b) prior to therapy.

From the radiographs it can be seen that the increased mobility observed in the maxillary teeth of this patient is associated mainly with reduced height of the alveolar bone and not with increased width of the periodontal ligaments. This means that the mobility of the individual teeth should be regarded as normal or "physiologic" for teeth with such a reduced height of the supporting tissues. This in turn implies that the increased tooth mobility in the present case does not call for treatment unless it interferes with the chewing comfort or jeopardizes the position of the front teeth. This particular patient had not recognized any functional problems related to the increased mobility of his maxillary teeth. Consequently, there was no reason to install a cross-arch bridge in order to splint the teeth, i.e. to reduce tooth mobility.

Following proper treatment of the plaque-associated periodontal lesions, two separate provisional bridges of unilateral design were produced (15, 14, 13; 23, 24, 25, 26 palatal root). The provisional acrylic bridges were used for 6 months during which the occlusion, the mobility of the two bridges and the position of the front teeth were all carefully monitored. When, after 6 months, no change of position of the lateral and central incisors had occurred and no increase of the mobility of the two provisional bridges had been noted, the definitive restorative therapy was performed.

Figure 51-10 presents radiographs obtained 10 years after initial therapy. The position of the front teeth and the mobility of the incisors and the two bridges have not changed during the course of the maintenance period. There has been no further loss of periodontal tissue support during the 10 years of observation, no further spread of the front teeth and no widening of the periodontal ligaments around the individual teeth, including the abutment teeth for the bridgework.

Conclusion: situation III

Increased tooth mobility (or bridge mobility) as a result of reduced height of the alveolar bone can be accepted and splinting avoided, provided the occlusion is stable (no further migration or further increasing mobility of individual teeth), and provided the degree of existing mobility does not disturb the patient's chewing ability or comfort. Consequently, splinting is indicated when the mobility of a tooth or a group of teeth is so increased that chewing ability and/or comfort are disturbed.

Situation IV

Progressive (increasing) mobility of a tooth (teeth) as a result of gradually increasing width of the reduced periodontal ligament

Often in cases of advanced periodontal disease the tissue destruction may have reached a level where extraction of one or several teeth cannot be avoided. In such a dentition, teeth which are still available for periodontal treatment may, after therapy, exhibit such a high degree of mobility, or even signs of progressively increasing mobility, that there is an obvious risk that the forces elicited during function may mechanically disrupt the remaining periodontal ligament components and cause extraction of the teeth.

It will only be possible to maintain such teeth by means of a splint. In such cases a fixed splint has two objectives: (1) to stabilize hypermobile teeth and (2) to replace missing teeth.

Example: Case B, 26-year-old male

Figure 51-11 presents radiographs taken prior to therapy and Fig. 51-12 those obtained after periodon-

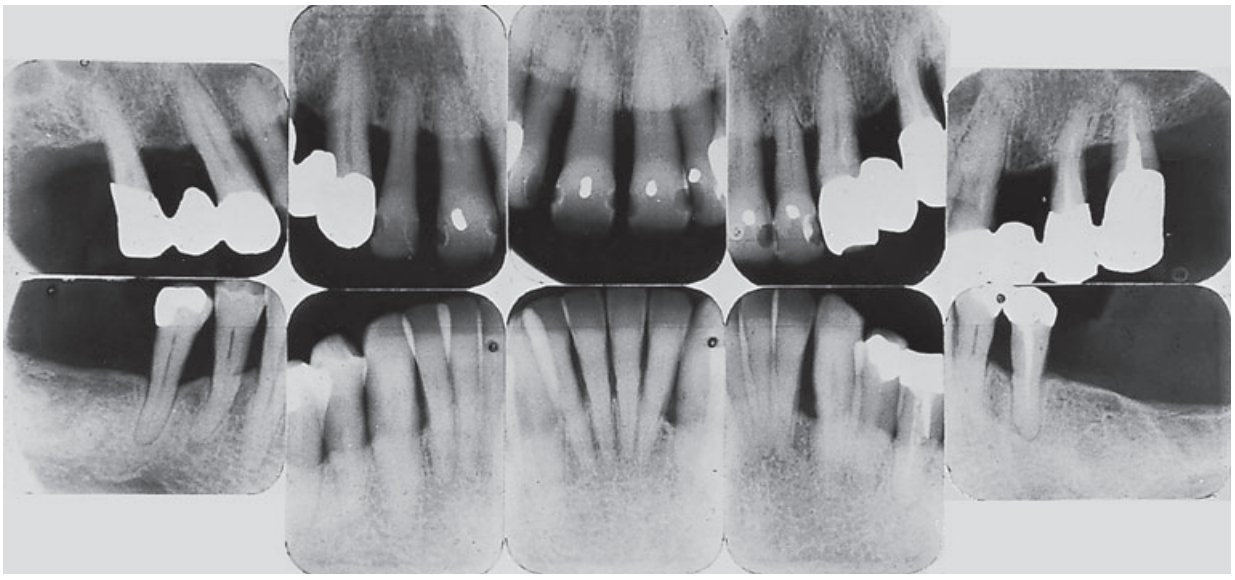


Fig. 51-10 Case A. Radiographs obtained 10 years after periodontal therapy and installation of two unilateral bridges in the maxilla.

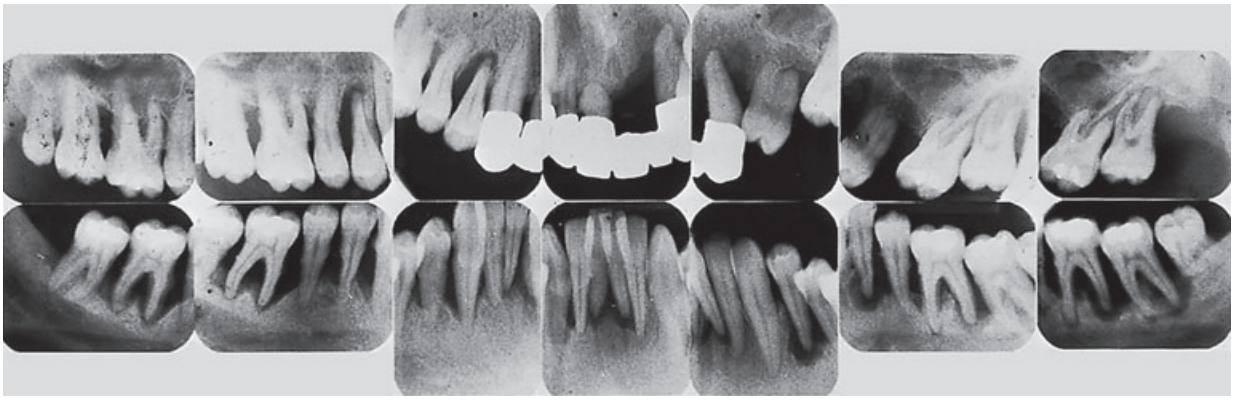


Fig. 51-11 Case B, 26-year-old male. Radiographs illustrating the periodontal conditions prior to therapy.

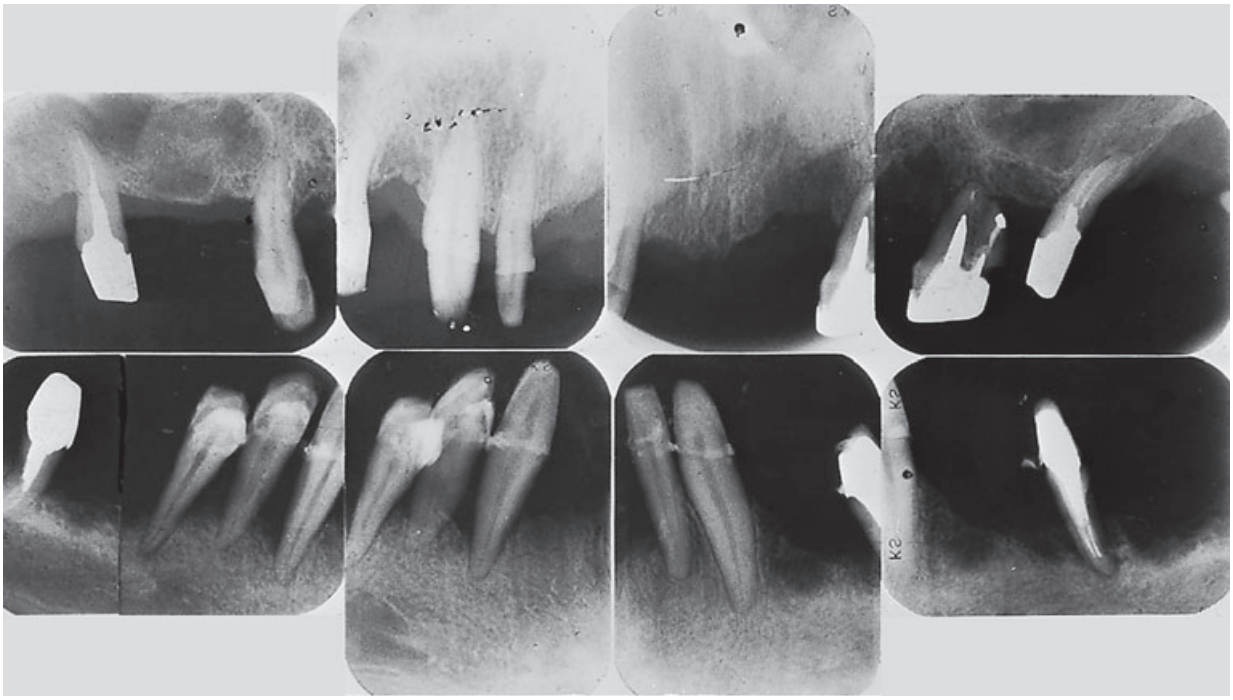


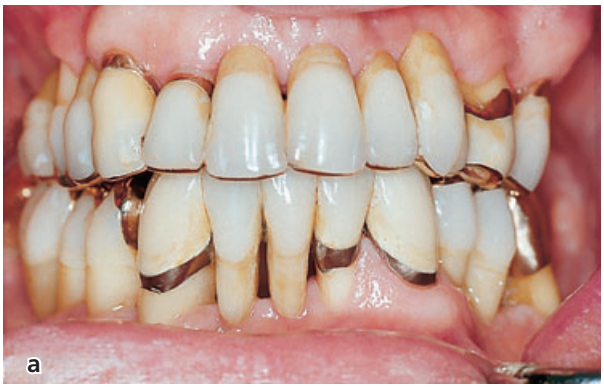
Fig. 51-12 Case B. Radiographs obtained after periodontal treatment and preparation of the abutment teeth for two fixed splints.

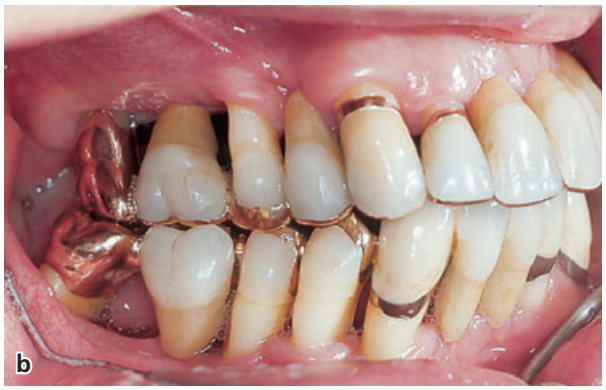
tal treatment and preparation of the remaining teeth as abutments for two fixed splints. All teeth except 13, 12, and 33 have lost around 75% or more of the alveolar bone and widened periodontal ligaments are a frequent finding. The four distal abutments for the two splints are root-separated molars, the maintained roots being the following: the palatal root of 17, the mesio-buccal root of 26, and the mesial roots of 36 and 47. It should be observed that tooth 24 is root-separated and the palatal root maintained with only minute amounts of periodontium left. Immediately prior to insertion of the two splints, all teeth except 13, 12, and 33 displayed a mobility varying between degrees 1 and 3. From the radiographs in Fig. 51-12 it can be noted that there is an obvious risk of extraction of a number of teeth such as 24, 26, 47, 45, 44, 43, and 36 if the patient is allowed to bite with a normal chewing force without the splints in position.

Despite the high degree of mobility of the individual teeth, the splints were entirely stable after insertion, and have maintained their stability during a maintenance period of more than 12 years. Figure 51-13 describes the clinical status and Fig. 51-14 presents the radiographs obtained 10 years after therapy. From these radiographs it can be observed (compare with Fig. 51-12) that during the maintenance period there has been no further loss of alveolar bone or widening of the various periodontal ligament spaces.

Conclusion: situation IV

Splinting is indicated when the periodontal support is so reduced that the mobility of the teeth is progressively increasing, i.e. when a tooth or a group of teeth are exposed to extraction forces during function.





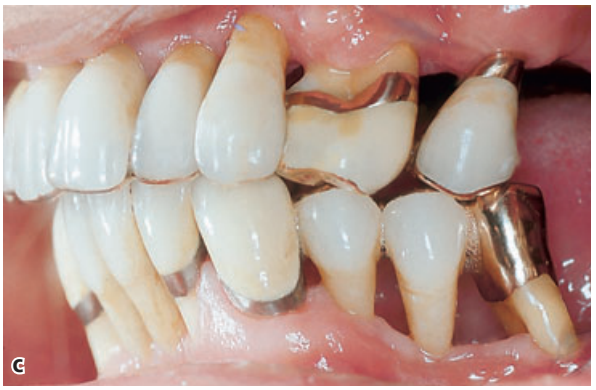


Fig. 51-13 Case B. Clinical status 9 years after therapy.

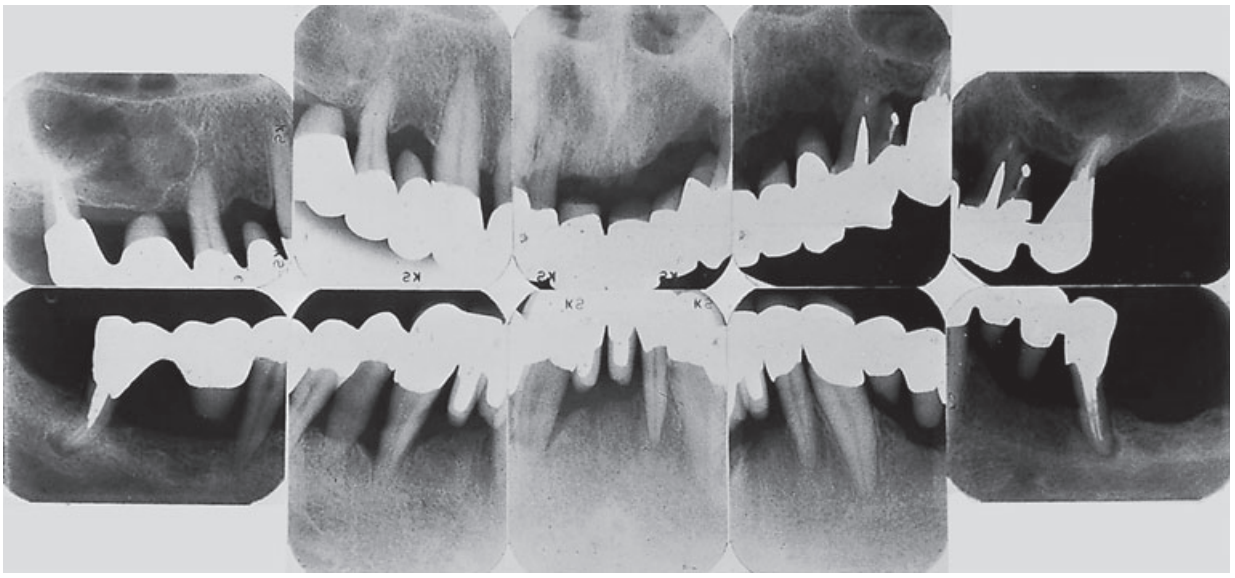


Fig. 51-14 Case B. Radiographs obtained 10 years after therapy.

Situation V

Increased bridge mobility despite splinting

In patients with advanced periodontal disease it can often be observed that the destruction of the periodontium has progressed to varying levels around different teeth and tooth surfaces in the dentition. Proper treatment of the plaque-associated lesions often includes multiple extractions. The remaining teeth may display an extreme reduction of the supporting tissues concomitant with increased or progressive tooth mobility. They may also be distributed in the jaw in such a way as to make it difficult, or impossible, to obtain a proper splinting effect even by means of a cross-arch bridge. The entire bridge/splint may exhibit mobility in frontal and/or lateral directions.

It was stated above (situation III) that a certain mobility of a tooth or a bridge of unilateral design

can be accepted provided this mobility does not interfere with the patient's chewing ability or comfort. This is also valid for a cross-arch bridge/splint. From a biologic point of view there is no difference between increased tooth mobility on the one hand and increased bridge mobility on the other. However, neither progressive tooth mobility nor progressive bridge mobility are acceptable. In cases of extremely advanced periodontal disease, a cross-arch splint with an increased mobility may be regarded as an acceptable result of rehabilitation. The maintenance of status quo of the bridge/splint mobility and the prevention of tipping or orthodontic displacement of the total splint, however, requires particular attention regarding the design of the occlusion. Below, a case is reported which may serve as an interesting illustration of this particular clinical problem.

Example: Case C, 52-year-old female

Figure 51-15 shows radiographs obtained at the initial examination. A 12-unit maxillary bridge was installed 10–15 years prior to the present examination using 18, 15, 14, 13, 12, 11, 21, 22, 23, and 24 as abutments. After a detailed clinical examination it was obvious that 15, 14, 22, and 24 could not be maintained because of severe symptoms of caries and periodontal disease. The remaining teeth were subjected to periodontal therapy and maintained as abutments for a new bridge/splint in the maxilla extending from tooth 18 to the region of 26, i.e. a cross-arch splint was installed which carried three cantilever units, namely 24, 25, and 26. The mobility of the individual abutment teeth immediately prior to insertion of the splint was the following: degree 1 (tooth 18), degree 0 (tooth 13), degree 2 (teeth 12 and 11), degree 3 (tooth 21), and degree 2 (tooth 23).

Radiographs obtained 5 years after therapy are shown in Fig. 51-16. The bridge/splint had a mobility of degree 1 immediately after its insertion and this mobility was unchanged 5 years later. The radiographs demonstrate that no further widening of the periodontal ligament occurred around the individual teeth during the maintenance period.

When a cross-arch bridge/splint exhibits increased mobility, the center (fulcrum) of the movement must be identified. In order to prevent further increase in the mobility and/or to prevent displacement of the bridge, it is essential to design the occlusion in such a way that when the bridge/splint is in contact with the teeth of the opposing jaw, it is subjected to a balanced load, i.e. equal force on each side of the fulcrum. If this can be achieved, the force to which the bridge is exposed in occlusion can be used to retain the fixed prosthesis in proper balance (a further increase of mobility being thereby prevented).

Balanced loading of a mobile bridge/splint has to be established not only in the intercuspal position (IP) and centric occlusion (CP) but also in frontal and lateral excursive movements of the mandible if the bridge shows mobility or a tendency for tipping in the direction of such movements. In other words, a force which tends to displace the bridge in a certain direction has to be counteracted by the introduction of a balancing force on the opposite side of the fulcrum of the movement. If, for instance, a cross-arch splint in the maxilla exhibits mobility in frontal direction in conjunction with protrusive movements of the mandible, the load applied to the bridge in the frontal region has to be counterbalanced by a load in the distal portions of the splint; this means that there must be a simultaneous and equal contact relationship between the occluding teeth in both the frontal and the posterior regions of the splint. If the splint is mobile in a lateral direction, the force acting on the working side of the jaw must be counteracted by a force established by the introduction of balancing contacts in the non-working side of the jaw. The prin-

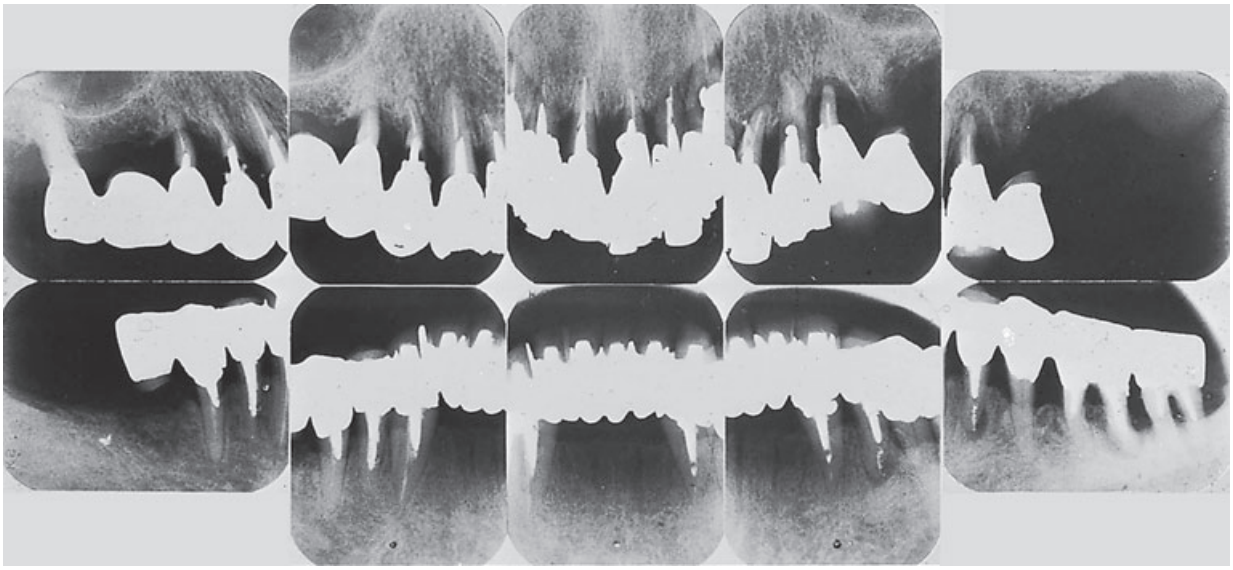


Fig. 51-15 Case C, 52-year-old female. Radiographs obtained at the initial examination.

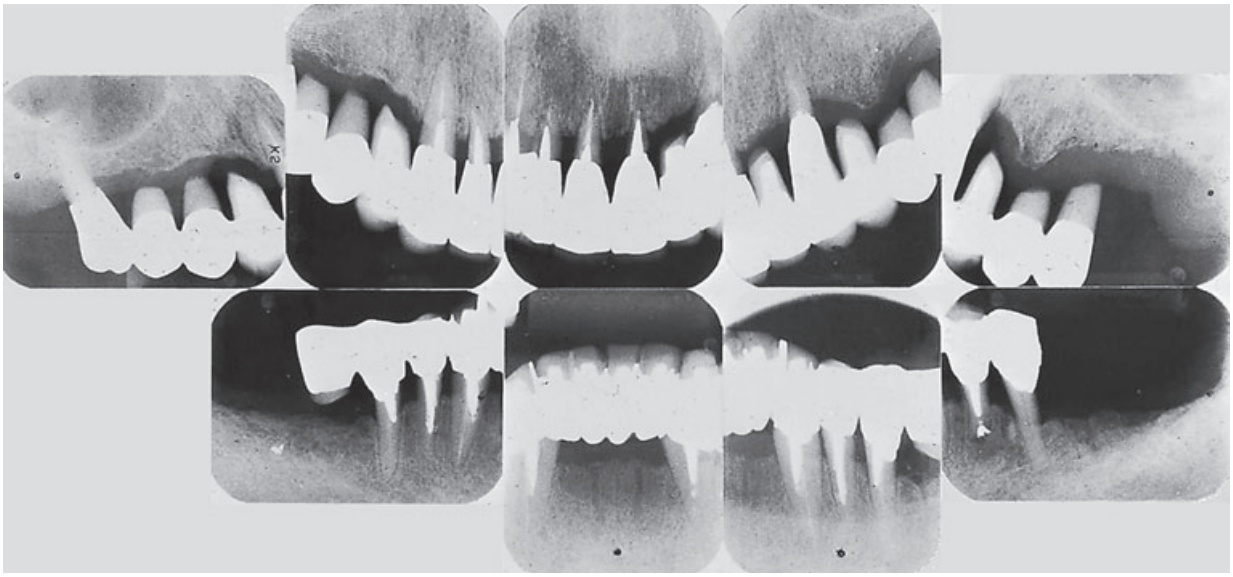


Fig. 51-16 Case C. Radiographs obtained 5 years after therapy.

ciple for establishing stability of a *mobile* cross-arch splint is consequently the same as that used to obtain stability in a complete denture. In situations where distal abutment teeth are missing in a cross-arch bridge/splint with increased mobility, balance and functional stability may be obtained by means of cantilever units. It is important in this context to point out that balancing contacts on the non-working side should not be introduced in a bridge/splint in which no increased mobility can be observed.

The maxillary splint in the patient described in Figs. 51-15 and 51-16 exhibited increased mobility in a frontal direction. Considering the small amount of periodontal support left around the anterior teeth, it is obvious that there would have been a risk of frontal displacement of the total bridge had the bridge terminated at the last abutment tooth (23) on the left side of the jaw. The installation of cantilever units in the 24 and 25 region prevented such a displacement of the bridge/splint by the introduction of a force counteracting frontally directed forces during protrusive movements of the mandible (Fig. 51-17). In addition, the cantilever units provide bilateral contact relationship towards the mandibular teeth in the intercuspal position, i.e. bilateral stability of the bridge.

In cases similar to the one described above, cantilever units can thus be used to prevent increasing mobility or displacement of a bridge/splint. It should, however, be pointed out that the insertion of cantilever units increases the risk of failures of a technical and biophysical character (fracture of the metal frame, fracture of abutment teeth, loss of retention, etc.).

In cases of severely advanced periodontal disease it is often impossible to anticipate in the planning phase whether a bridge/splint will show signs of instability and increasing (progressive) mobility after

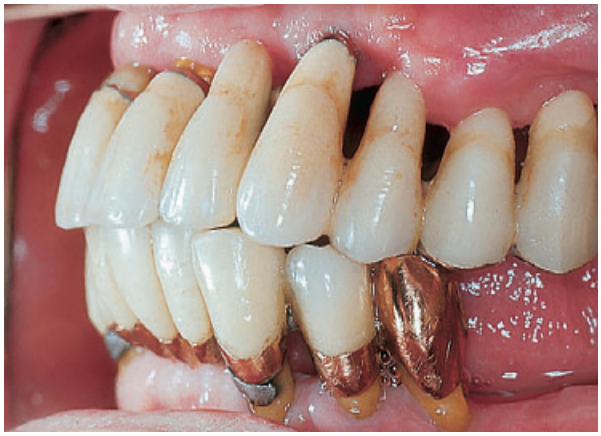


Fig. 51-17 Case C. The cantilever section including teeth 24, 25, and 26.

insertion. In such cases, a provisional splint should always be inserted. Any alterations of the mobility of the bridge/splint can be observed over a prolonged period of time and the occlusion continuously adjusted until, after 4–6 months, it is known whether stability (i.e. no further increase of the mobility) can be achieved. The design of the occlusion of the provisional acrylic bridge is then reproduced in the permanent bridge construction. If, on the other hand, stability cannot be obtained, the rehabilitation of the case cannot be achieved with a fixed splint. The alternative treatment then is a complete denture or an implant-supported restoration.

Conclusion: situation V

An increased mobility of a cross-arch bridge/splint can be accepted provided the mobility does not disturb chewing ability or comfort and the mobility of the splint is not progressively increasing.

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Chapter 52

Implants in Restorative Dentistry

Niklaus P. Lang and Giovanni E. Salvi

Introduction

Ever since oral titanium implants were shown to yield high predicability (97–98%) for incorporation (Berglundh *et al*. 2002; Pjetursson *et al*. 2007) and satisfactory longevity (survival rates of approximately 89% after 10 years of service) (Pjetursson *et al*. 2007), the choice of oral implants as abutments for reconstructing the dentition has revolutionized restorative dentistry. Without adequate evidence, some clinicians trust an implant abutment even more than a natural tooth, and there is an erroneous belief that oral implants now solve most prosthetic problems with a lot more ease and less risk than traditional reconstructive dentistry did.

Even though there is an increasing body of evidence documenting that implant-supported reconstructions have a three-times higher incidence of technical complications than tooth-supported reconstructions (Lang *et al*. 2004; Pjetursson *et al*. 2004a,b; Tan *et al*. 2004) and that the incidence of biologic complications remains approximately the same for the two alternatives, the trend in dentistry, unfortunately, is to prefer the implant over the tooth abutment.

It has to be clearly stated that the decision to maintain and treat or to extract a compromised tooth has to precede the decision regarding the need for and the modalities of tooth replacement. In this sense, "*implants are here to replace missing teeth, they are not supposed to replace teeth*".

If properly evaluated, the indication for oral implants as abutments in restorative dentistry is complementary to traditional approaches and helps to facilitate treatment planning in many instances.

Treatment concepts

When reconstructing a mutilated dentition, it has to be realized that teeth were usually lost due to the two most frequently encountered oral diseases, caries and periodontitis. Only a small proportion of teeth are lost due to trauma or are not present due to agenesis. Hence, the vast majority of patients in need of reconstructions present with an oral biofilm infection of variable severity and extent. It is evident that such patients need to be treated with a cause-related approach, i.e. systematic periodontal therapy has to precede any type of reconstructive therapy. It is of utmost importance that oral biofilm infections be under control prior to the placement of oral implants, since residual periodontal pockets or untreated ecologic niches within the oral cavity may serve as a source of infection and jeopardize the health of the peri-implant region (Mombelli *et al*. 1995). Hence, implant installation and prosthetic reconstruction is generally not a treatment in itself, but belongs to a systematic approach of comprehensively establishing esthetic and functional demands under healthy conditions (see Chapter 31).

It is obvious that chewing function is affected both by tooth loss and the type of prosthetic reconstruction chosen to replace missing teeth. A quantitative comparison by measuring bite force and chewing efficiency with identical methods in subjects with overdentures, complete full dentures, and natural dentitions was performed (Fontijn-Tekamp *et al*. 2000). In the latter group, chewing efficiency was significantly greater than that of patients with full dentures irrespective of the nature of their mandibular ridge. By installing implants, bite force and

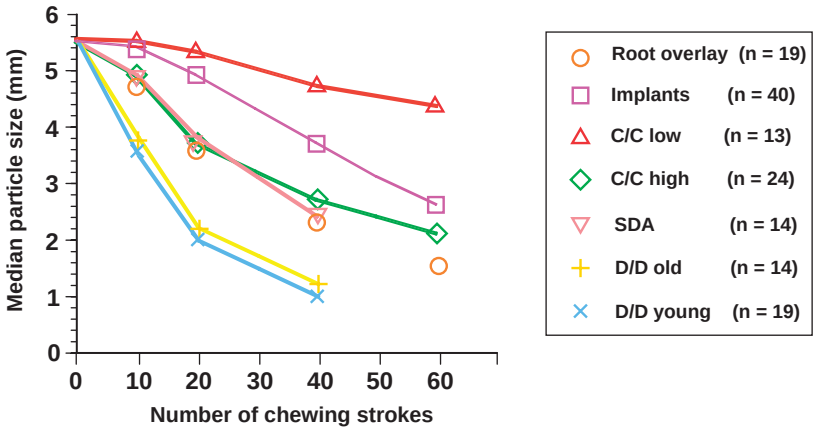

Fig. 52-1 Masticatory chewing efficiency. Number of chewing strokes needed to reach respective particle sizes of the same test food. From Fontijn-Tekamp *et al*. (2000).

chewing efficiency could be significantly improved, although it did not reach that of the dentate patients. Shortened dental arch patients exerted bite forces similar to those of patients with a complete natural dentition, but their chewing efficiency was slightly limited due to the reduced occlusal area. This, in turn, meant that patients with a shortened dental arch would have to perform approximately twice as many chewing strokes to reach the same efficiency as the fully dentate patient (Fig. 52-1).

Limited treatment goals

Generally, efforts are made to completely reconstruct a partially edentulous dentition. The question arises whether or not missing teeth have to be replaced at all and to the full extent. Usually, single teeth are replaced because of predominantly esthetic demands, while multiple missing teeth may also affect functionality and chewing capacity and, hence, are replaced to improve these aspects. However, it is evident from a number of cross-sectional and longitudinal studies (Käyser 1981; Battistuzzi *et al*. 1987; Witter *et al*. 1988, 1990a,b, 1991, 1994) that not all teeth lost are to be replaced. The loss of one or more molars has been thoroughly studied by the Nijmegen group of clinical researchers. No clinically significant differences were found in these studies between subjects with a complete dentition and those with reduced dental arches regarding masticatory capacity, signs and symptoms of temporomandibular disorders, migration of remaining teeth, periodontal support, and oral comfort.

Shortened dental arch concept

Studies on shortened dental arches (SDA) have shown that dentitions comprising anterior and premolar teeth generally fulfil the requirements of a functional dentition, including patient-assessed oral comfort and chewing ability. A review of the literature on SDA concluded that the concept deserves serious consideration in treatment planning for partially edentulous patients. However, with ongoing changes, e.g. in dental health and economy, the concept requires continuing research, evaluation, and discussion (Kanno & Carlsson 2006).

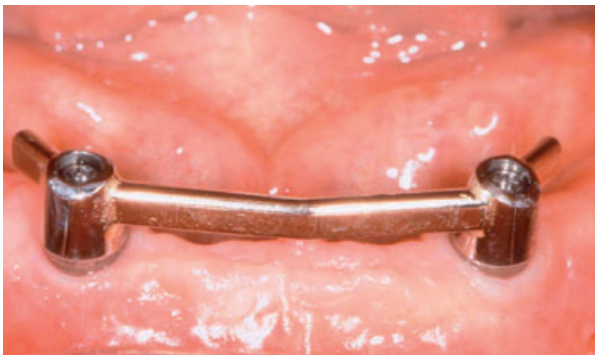

Fig. 52-2 Increasing subjective chewing comfort for completely edentulous patients. Two implants in the canine region united with a bar device (or solely with a retention element without the bar) can dramatically improve masticatory ability and efficacy.

Special attention has to be given to the patient's own needs and desires for increased chewing capacity when considering the SDA as a limited treatment goal. Clinical observation, as well as research findings, indicate that elderly patients can function at an acceptable level with a reduced dentition consisting of ten or even fewer occluding pairs of teeth (Käyser 1990). The WHO goal for the year 2020, namely to maintain a natural dentition of no less than 20 teeth throughout life, is also substantiated by a recent literature review as this proposed dentition will assure oral function (Gotfredsen & Walls 2007).

The choice of implants as abutments to fulfil individual needs may, therefore, become a welcome treatment option within the concept of a shortened dental arch.

Indications for implants

Three major indications can be defined for the use of oral implants:

- To increase subjective chewing comfort
- To preserve natural tooth substance and adequate, existing reconstructions
- To replace strategically important missing teeth.

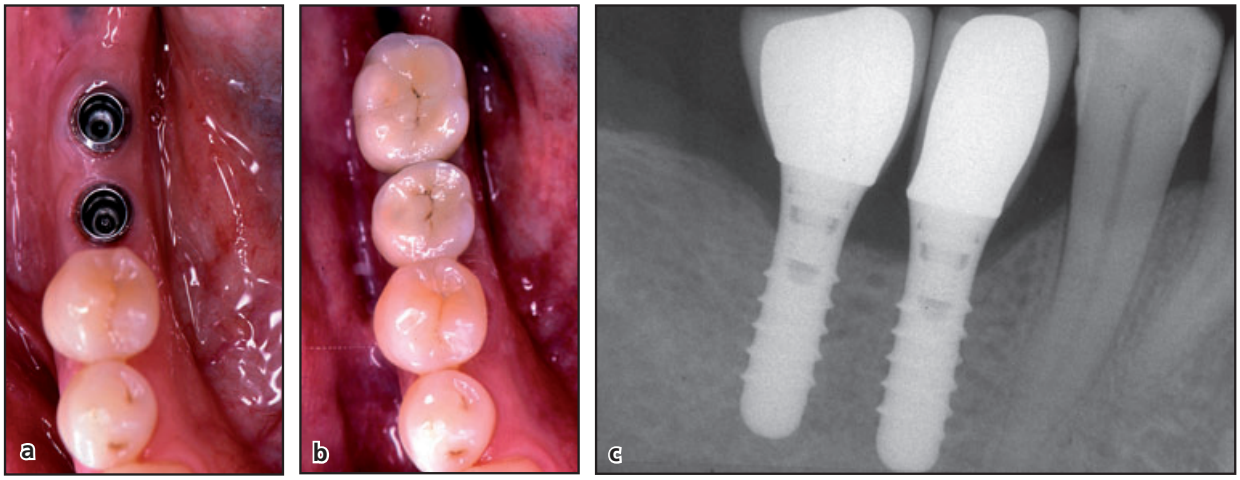

Fig. 52-3 Increasing subjective chewing comfort by replacing missing teeth in a free-end edentulous situation. (a) Installation of two standard size (4.1 mm diameter) Straumann® implants (10 mm), 5 and 11 mm distal to the distal aspect of tooth 45. (b) Chewing units are replaced as a premolar on implant in position 46 and a molar in position 46/47. (c) Radiographic view 5 years after the reconstruction.

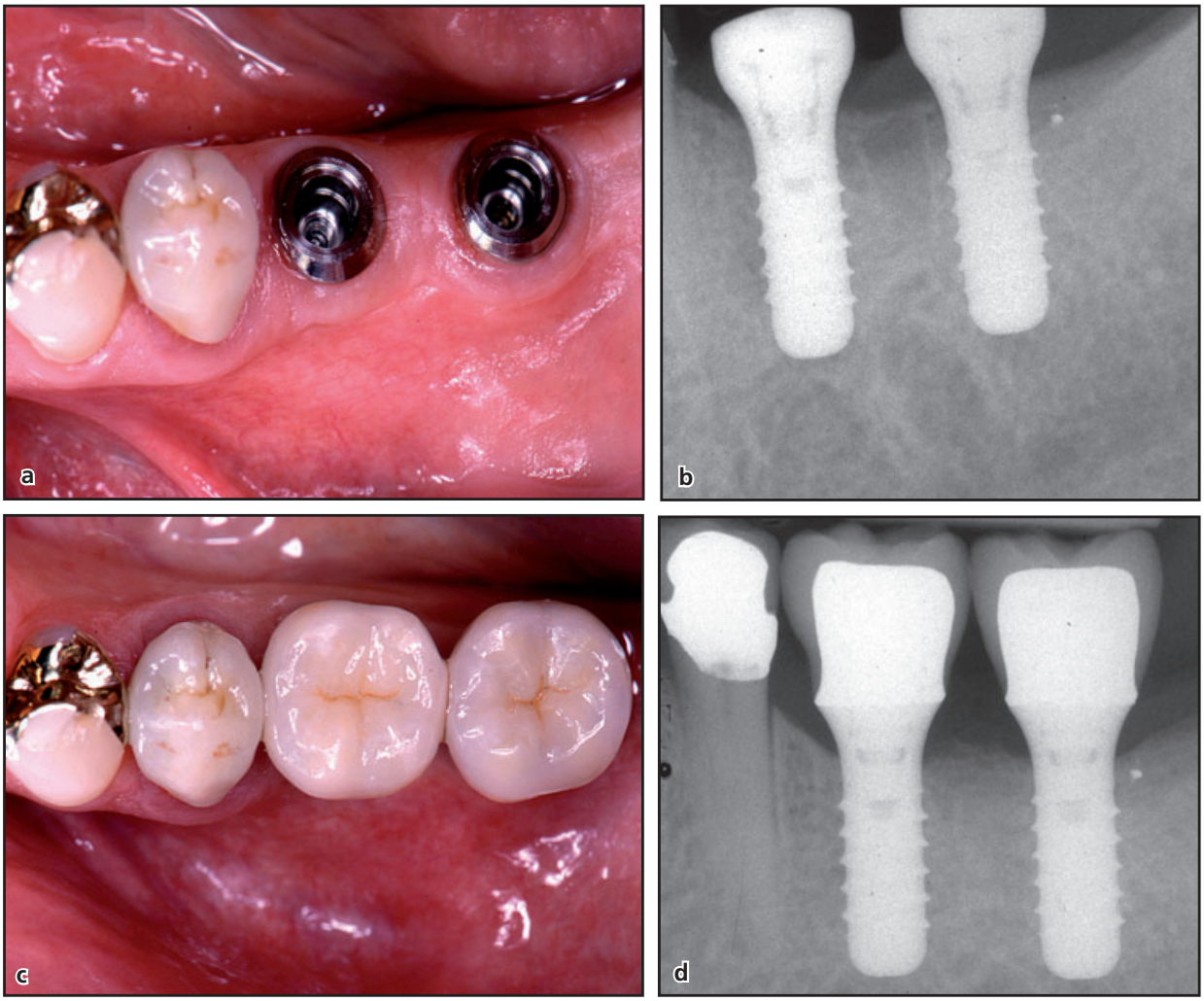

Fig. 52-4 Increasing subjective chewing comfort by replacing missing molars in a mandibular free-end situation. (a) Installation of two standard (4.1 mm diameter) Straumann® implants (8 mm), 6 and 14 mm distal to the distal aspect of tooth 35. (b) Radiographic view at the time of implant installation. (c) Two molar crowns on implants in position 36 and 37, 8 years after installation. (d) Radiographic view, 8 years after loading of the implants.

Increase the subjective chewing comfort

Studies have demonstrated that the installation of a small number of mandibular implants (two to four) may dramatically improve chewing function, especially if the edentulous mandibular ridge showed severe resorption (Fontijn-Tekamp *et al.* 2000, 2004a,b). Hence, it is evident that the completely edentulous patient will benefit from as few as two oral implants installed in the mandibular canine region (Fig. 52-2).

Likewise, subjective chewing comfort may be improved by supplementing single premolar chewing units in the posterior region in order to fulfill individual demands for more chewing capacity under a shortened dental arch concept (Fig. 52-3). It is imperative that the implants be placed in the prosthetically correct location leaving enough space for an interdental (inter-implant) space and observing the dimensions of a premolar width (7 mm).

Instead of adding chewing comfort in premolar units, implant systems with wider necks or platforms may be installed in order to truly mimic the replacement of the missing molars. In these instances, an inter-implant distance of 8 mm has to be observed in order to create enough space for the molars and the inter-implant space (Fig. 52-4).

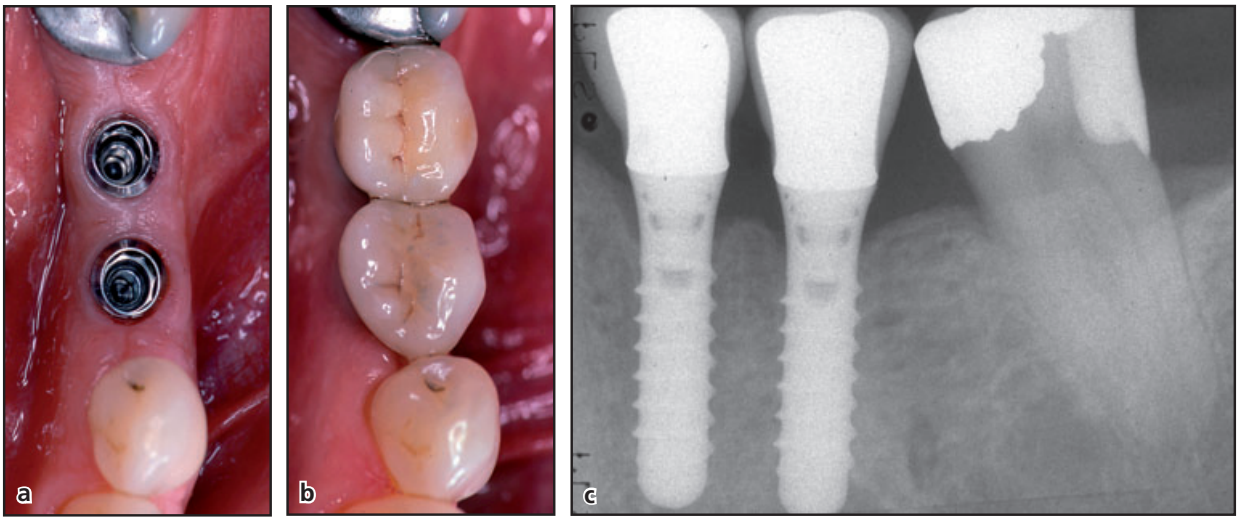

Fig. 52-5 Increasing subjective chewing comfort by closing a mandibular gap. (a) Installation of two standard (4.1 mm diameter) Straumann® implants (10 mm), 5 mm distal to the distal aspect of tooth 34 and 12 mm distal to tooth 34 (= 6 mm mesial to tooth 37). Total extension of the gap: 18 mm. (b) Reconstruction of the implants in premolar units to fit the size of the gap. (c) Radiographic documentation, 6 years after loading. The filling on tooth 37 was satisfactory and did not need replacement.

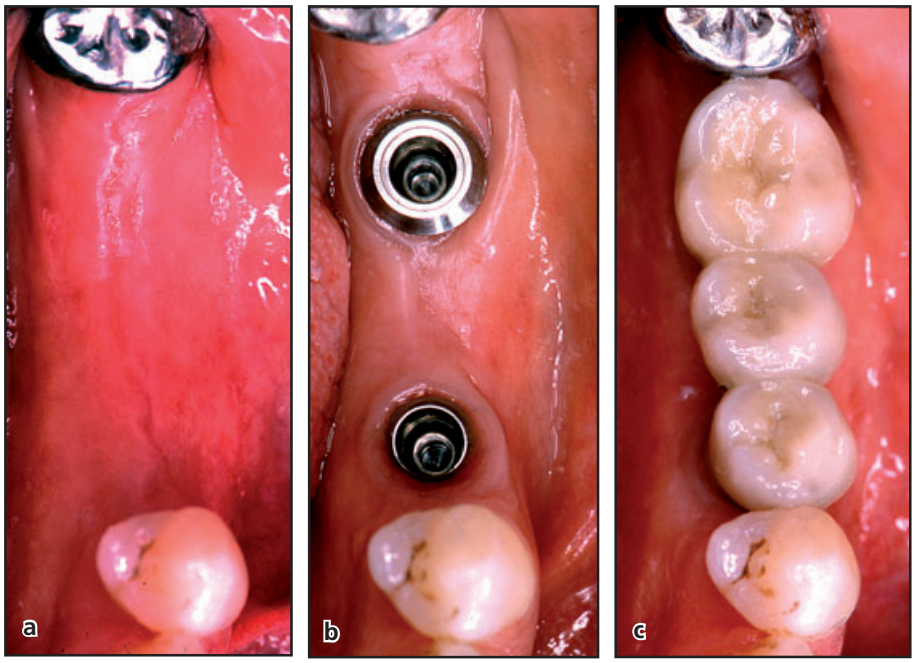

Fig. 52-6 Increasing subjective chewing comfort by filling a large mandibular gap. (a) Edentulous ridge between teeth 34 and 38 is 28 mm. (b) Installation of a standard (4.1 mm diameter) Straumann® implant, 5 mm distal to the distal aspect of tooth 34 and a wide-body (4.8 mm diameter), wide-neck Straumann® implant, 20 mm distal to the distal aspect of tooth 34 and 8 mm mesial to the mesial aspect of tooth 38. (c) Three-unit implant-supported fixed prosthesis filling the gap.

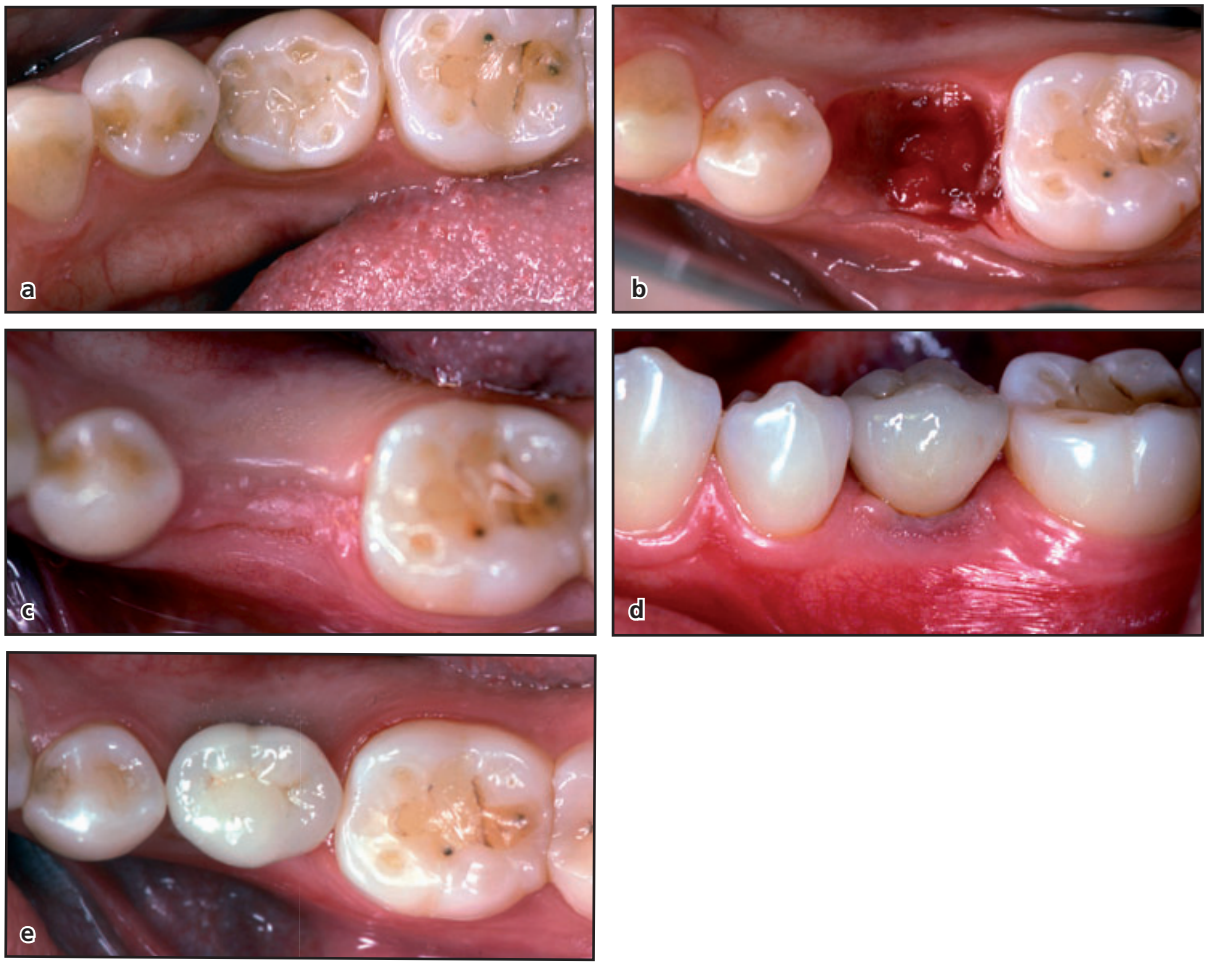

Fig. 52-7 Preservation of natural tooth substance. (a) Deciduous molar 75 has to be replaced owing to the advanced root resorption. (b) Following extraction of tooth 75, the site would be ideal for replacing the missing tooth with a three-unit bridge or a single implant. (c) The single implant is chosen to avoid jeopardizing the integrity and vitality of the two adjacent teeth, 34 and 36. Cutting preparations for full coverage of crowns will result in 10% of the prepared teeth loosing vitality after 10 years. (d) Single tooth replacement of 75, 5 years after reconstruction. (e) Occlusal view of the single implant-supported crown to replace a deciduous molar, 5 years after reconstruction. The adjacent teeth remain unsevered.

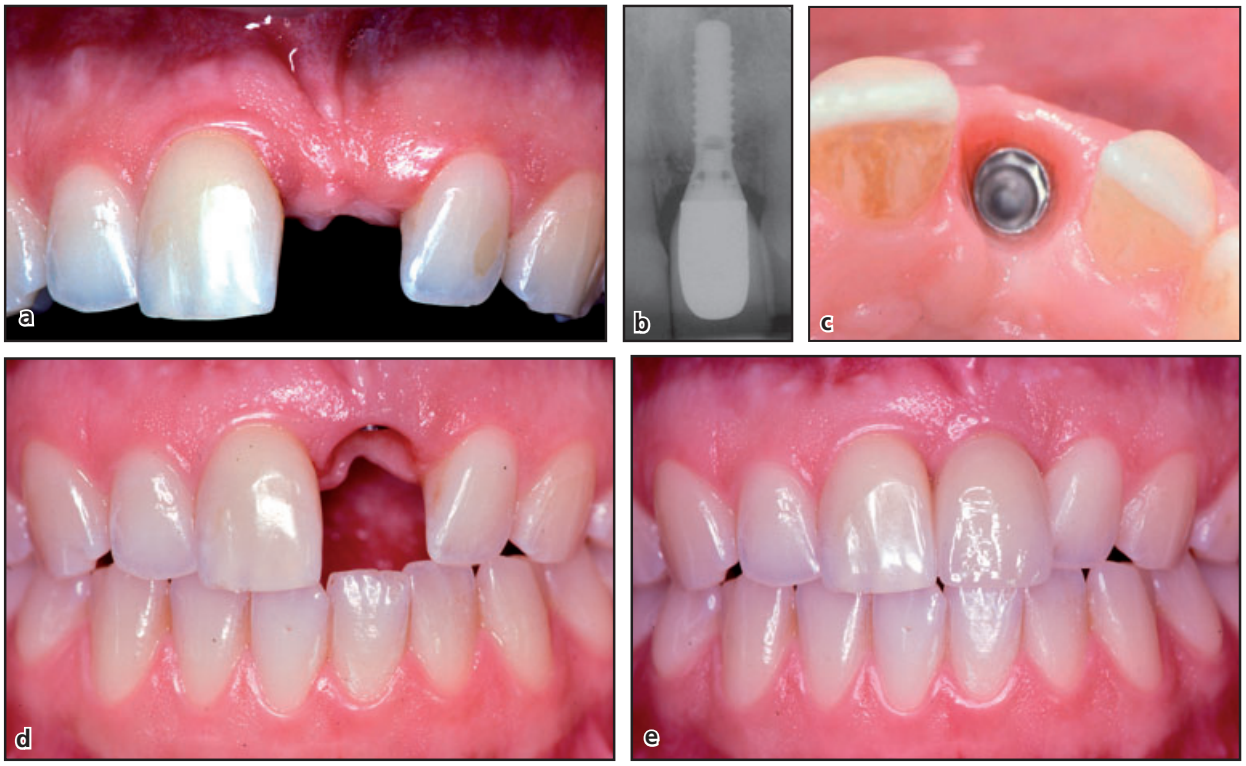

Fig. 52-8 Preservation of intact tooth substance. Single tooth replacement of a missing central incisor 21. (a) The teeth 11 and 22 adjacent to the edentulous space 21 are intact teeth with no fillings and with periodontally healthy conditions. Both mesial and distal papillae are intact and reach coronally to the contact area in this juvenile patient. (b) Following the installation of a Standard Plus (4.1 mm diameter) Straumann® implant with a length of 12 mm, the mucosal tissue is conditioned to achieve a perfect emergence profile. (c) Radiographic documentation 2 years after the prosthetic reconstruction of the implant. (d) Tissue conditioning due to a more apical insertion of the implant for esthetic sites. (e) Implant-supported single tooth replacement 21, 2 years after reconstruction.

Considering the dimensions of premolars (7 mm) and molars (8 mm) and adequate space for the interdental/inter-implant space (4–5 mm), edentulous ridges between existing teeth may be reconstructed and chewing comfort increased without involving adjacent teeth (Fig. 52-5). Obviously, risks can be minimized by reducing the length of bridge spans.

In combinations of molar and premolar reconstructions (Fig. 52-6), the surgical positioning of the implants has to be calculated in detail and restoration-driven stents may have to be used in order to create adequate conditions for prosthetic reconstruction.

Preservation of natural tooth substance and existing functional, satisfactory reconstructions

Oral implants are ideal abutments if natural tooth substance can be preserved. The preparation of a tooth to serve as an abutment for a crown or a bridge anchor opens about 40 000 to 70 000 dentinal tubules per mm^2. This, in turn, means that the integrity of a

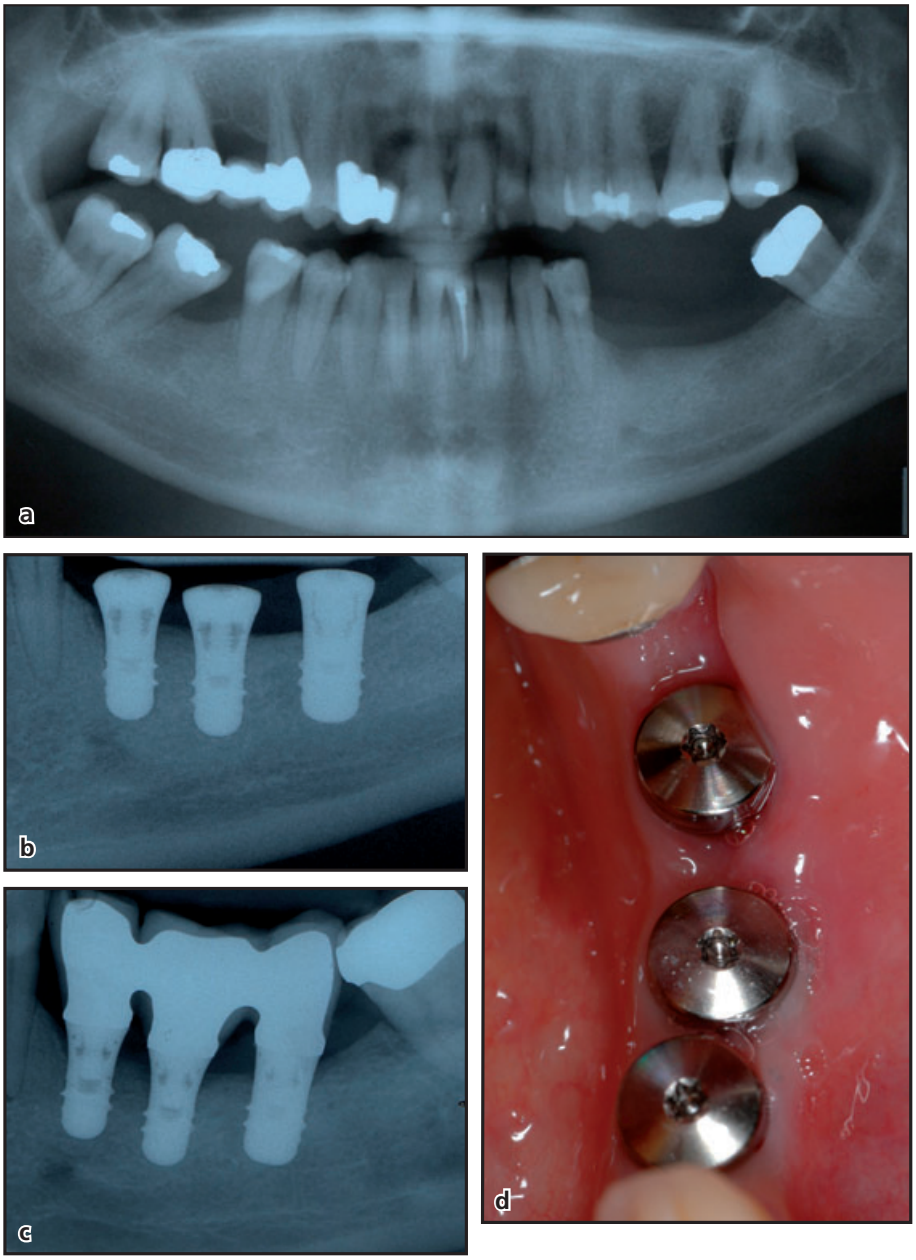

Fig. 52-9 Mandibular edentulous area after the extraction of teeth 35, 36 and 37. (a) Orthopantomogram revealing the neighboring anatomic structures (inferior mandibular nerve) and intact reconstructions on the teeth adjacent to the edentulous ridge. (b) Installation of two standard (4.1 mm diameter) and one wide-body (4.8 mm diameter) Straumann® implants at a distance of 5 mm, 11 mm and 20 mm distal to the distal aspect of tooth 34. (c) Transmucosal implant installation for two premolar and one molar unit. Implants covered with healing caps. The intact crown on tooth 38 is visible. (d) Radiographic documentation after 5 years. Implant crowns are splinted because of the short (6 mm) implants (in the neighborhood of the inferior mandibular nerve).

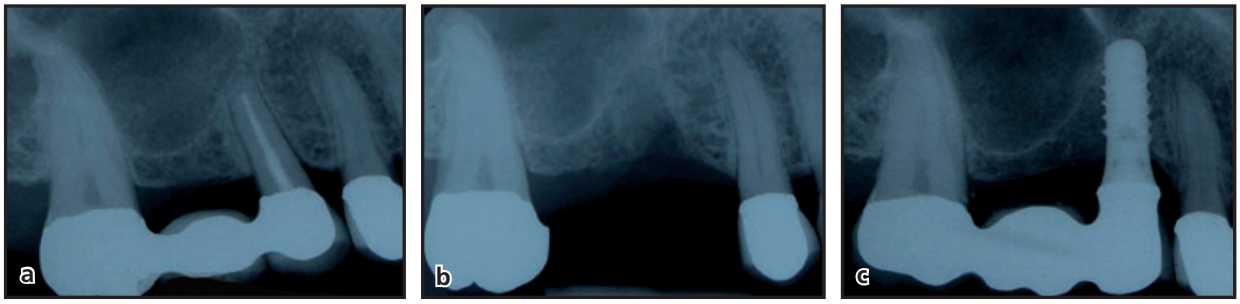

Fig. 52-10 Replacing strategically important teeth. (a) A fixed dental prosthesis is seated on two abutment teeth, 17 and 15. Tooth 15 was root canal treated and suffered from a root fracture jeopardizing the integrity of the entire reconstruction. (b) The bridge is separated between 17 and pontic 16. (c) A new fixed dental prosthesis was seated on the implant 15 and soldered to the existing, still satisfactory crown 17. In this manner, the implant helped to avoid a costly and extensive reconstruction.

vital tooth is severely compromized. Even though a small proportion of abutment teeth will lose their vitality immediately as a sequelae of the preparation procedure, it has been documented that approximately 10% of all vital abutments will have lost vitality after 10 years (Bergenholtz & Nyman 1984; Pjetursson *et al*. 2004b; Tan *et al*. 2004). Hence, it is obvious that an implant installation avoiding tooth preparation represents the most biologically sound way of replacing a missing tooth (Fig. 52-7).

In areas of esthetic priority, the replacement of a missing tooth with a single implant may, beyond any doubt, provide the best and most esthetic treatment option (Fig. 52-8). This is especially true in a periodontally healthy dentition and in situations where the papillae towards the adjacent teeth are still present. By placing the implant in a slightly (1–2 mm) submucosal location, an optimal emergence profile can be achieved.

Instead of preserving natural tooth substance, the clinician may choose to save existing, still satisfactory reconstructions, thereby simplifying the restoration of a mutilated dentition (Fig. 52-9). Occasionally, the reconstruction may have a smaller extent and, hence, have a reduced chance of encountering technical complications during the years of service.

Replacement of strategically important missing teeth

The loss of a strategically important tooth often creates a whole chain reaction of therapeutic measures to be taken. Treatment planning may become highly involved and extensive reconstructions may result from the loss of such a tooth. Especially in dentitions that have received multiple reconstructions, the loss of one strategic abutment may lead to time-consuming and costly therapy (Fig. 52-10). Oral implants provide valuable and indispensable treatment alternatives to redoing existing reconstructions. By the installation of oral implants in strategically correct locations, partial reconstruction of a dentition may be possible. Obviously, such implants have to be installed at locations that are restoration driven, at the proper location for prosthetic reconstruction. In cases with bone dehiscence or lack of adequate bone volume, bone augmentation procedures may have to be performed (Fig. 52-11).

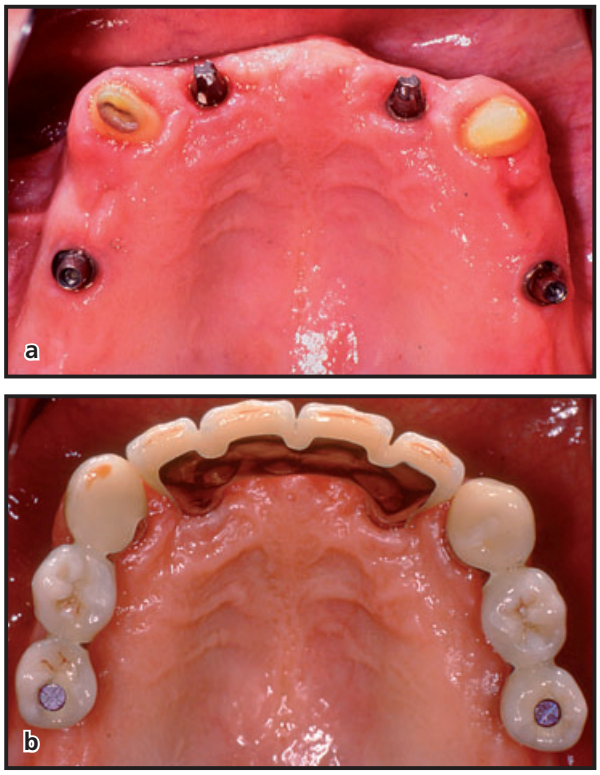

Fig. 52-11 Replacing strategically important abutments. (a) Only the two periodontally healthy maxillary canines 13 and 23 remain. To reconstruct this maxilla with a fixed dental prosthesis requires the installation of oral implants in strategically correct locations. An implant-supported maxillary front reconstruction and two mixed tooth–implant-supported reconstructions in the posterior segments are planned. (b) Eight years following implant installation. The maxillary front reconstruction is cemented on solid abutments that have been installed in the positions of 12 and 22, i.e. 5 mm mesial to the mesial aspects of the canines. The posterior segment reconstructions are cemented on the canines and screw-retained on two implants in the positions of 15 and 25, i.e. the implants are placed 11 mm distal to the distal aspects of the canines allowing the placement of three-unit reconstructions with minimal risks. A shortened dental arch as a limited treatment goal provides satisfactory chewing function.

Conclusions

Oral implants are best used as abutments in restorative dentistry if subjective chewing comfort has to be increased, natural tooth substance or existing satisfactory reconstructions have to be preserved or strategically important missing teeth have to be replaced.

Hence, oral implants have become valuable, indispensable, and welcome treatment alternatives to traditional dental reconstructions. Obviously, oral implants should only be incorporated in oral cavities with healthy conditions, i.e. a thorough periodontal treatment has to precede restorative therapy.

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Chapter 53

Implants in the Esthetic Zone

Urs C. Belser, Jean-Pierre Bernard, and Daniel Buser

Basic concepts

The clinical replacement of lost natural teeth by osseointegrated implants has represented one of the most significant advances in restorative dentistry. Numerous studies on various clinical indications have documented high implant survival and success rates with respect to specific application criteria (Ekfeldt *et al*. 1994; Laney *et al*. 1994; Andersson *et al*. 1995, 1998; Brånemark *et al*. 1995; Lewis 1995; Jemt *et al*. 1996; Lindqvist *et al*. 1996; Buser *et al*. 1997, 2002; Ellegaard *et al*. 1997a;b; Levine *et al*. 1997; Bryant & Zarb 1998; Eckert & Wollan 1998; Ellen 1998; Lindh *et al*. 1998; Mericske-Stern 1998; ten Bruggenkate *et al*. 1998; Wyatt & Zarb 1998; Gunne *et al*. 1999; Lekholm *et al*. 1999; Van Steenberghe *et al*. 1999; Wismeijer *et al*. 1999; Behneke *et al*. 2000; Hosny *et al*. 2000; Hultin *et al*. 2000; Weber *et al*. 2000; Boioli *et al*. 2001; Gomez-Roman *et al*. 2001; Kiener *et al*. 2001; Mengel *et al*. 2001; Oetterli *et al*. 2001; Zitzmann *et al*. 2001; Bernard & Belser 2002; Haas *et al*. 2002; Leonhardt *et al*. 2002; Romeo *et al*. 2002). Several recently published studies have focused on treatment outcome of implant therapy in partially edentulous patients in general, and related to maxillary anterior implant restorations in particular. Belser (1999) reviewed selected publications which appear to have impact when it comes to the discussion of esthetic aspects which will be addressed in this chapter. In a prospective longitudinal study involving a total of 94 implants (50 in the anterior maxilla) restored with fixed partial dentures (FPDs), Zarb and Schmitt (1993) published an average success rate of 91.5% for an observation period up to 8 years. The respective data concerning the maxillary implants demonstrated a success rate of 94% (100% for the prosthesis success). It was concluded that implant therapy in anterior partial edentulism can replicate the data established in the literature for fully edentulous patients. The same authors (Schmitt & Zarb 1993) published an 8-year implant survival rate of 97.9% for single-tooth replacement in partially edentulous patients. These results were confirmed by Avivi-Arber and Zarb in 1996.

Andersson *et al*. (1998) published similarly favorable prospective 5-year data on single-tooth restorations, performed either in a specialist clinic or in general practices, while Eckert and Wollan (1998) presented a retrospective evaluation up to 11 years on a total of 1170 implants inserted in partially edentulous patients, and found no differences in survival rates with respect to the anatomic location of the implants. A meta-analysis concerning implants placed for the treatment of partial edentulism was carried out by Lindh *et al*. (1998). The 6–7-year survival rate for single implant crowns corresponded to 97.5%, while the survival rate of implant-supported FPDs was 93.6%. The influence of implant design and surface texture was investigated by Norton (1998) by means of a radiographic follow-up of 33 implants loaded for up to 4 years. A most favorable maintenance of marginal bone around the conical collar was revealed, with a mean marginal bone loss of 0.32 mm mesially and 0.34 mm distally for the whole group.

Soft tissue stability around implant restorations and adjacent teeth is of paramount importance within the appearance zone (Bengazi *et al*. 1996; Chang *et al*. 1999; Ericsson *et al*. 2000; Grunder 2000; Choquet *et al*. 2001; Cooper *et al*. 2001; Mericske-Stern *et al*. 2001; Bernard & Belser 2002; Engquist *et al*. 2002; Haas *et al*. 2002; Krenmair *et al*. 2002). Scheller *et al*. (1998) specifically addressed this parameter in their 5-year prospective multicenter study on 99 implant-supported single-crown restorations. The authors reported overall cumulative success rates of 95.9% for implants and 91.1% for implant crowns. Soft tissue levels around implant restorations and adjacent teeth remained stable over the entire evaluation period. Wyatt and Zarb (1998) published a longitudinal study on 77 partially edentulous patients, involving a total of 230 implants and 97 fixed partial dentures, with an observation period of up to 12 years (mean 5.41 years) after loading. The average implant success rate was 94%, while the continuous stability of the prostheses (fixed partial dentures) corresponded to 97%. This study comprised 70 anterior and 31 posterior maxillary implants. No significant differences with respect to longevity could be detected either between anterior and posterior locations or between maxillary and mandibular implant restorations.

Along with osseointegration and restoration of function, the patient's subjective satisfaction is a key element of the success of implant therapy. Especially when the implant is located in the anterior part of the oral cavity, an essential part of the therapy aims at creating appropriate conditions, so that the implant prosthesis cannot be distinguished from the adjacent natural teeth at the end of treatment. In this context, a variety of specific procedures have been developed, including novel bone augmentation protocols, connective tissue grafting and reconstruction of lost papillary tissue (Bahat *et al*. 1993; Salama & Salama 1993; Bahat & Daftary 1995; Salama *et al*. 1995; Price & Price 1999; Choquet *et al*. 2001).

Being part of a comprehensive textbook about clinical periodontology, this chapter will focus primarily on fixed implant restorations located in the esthetic zone.

General esthetic principles and related guidelines

The basic parameters related to dental and gingival esthetics in general and to the maxillary anterior segment in particular are well established in the dental literature (Goldstein 1976; Belser 1982; Schärer *et al*. 1982; Seibert & Lindhe 1989; Goodacre 1990; Rüfenacht 1990; Nathanson 1991; Magne *et al*. 1993a,b, 1994, 1996; Chiche & Pinault 1994; Kois 1996; Kokich 1996; Kokich & Spear 1997; Jensen *et al*. 1999) and have been recently summarized in the form of an updated integral check-list by Magne and Belser (2002). When it comes to the characteristics of the natural maxillary anterior dentition, a number of fundamental objective criteria, including gingival health and its normal morphology as well as dimension, form, specific structural composition, color, opalescence, translucency, transparency, and surface texture of incisors and canines, have been identified (Table 53-1, Fig. 53-1). This list is completed by an addition of subjective criteria associated with esthetic integration, such as variations in the arrangement and positioning of front teeth, relative crown length and negative space.

Depending on the type of a given initial clinical situation requiring the replacement of one or several teeth, the patient's expectations may vary from the achievement of an almost perfect illusion, i.e. that the untrained eye cannot easily distinguish the restoration from the surrounding natural dentition, to the

Table 53-1 Fundamental objective esthetic criteria (Magne & Belser 2002, copyright © Quintessence Publishing Co, Inc)

1	Gingival health
2	Interdental closure
3	Tooth axis
4	Zenith of the gingival contour
5	Balance of the gingival levels
6	Level of the interdental contact
7	Relative tooth dimensions
8	Basic features of tooth form
9	Tooth characterization
10	Surface texture
11	Color
12	Incisal edge configuration
13	Lower lip line
14	Smile symmetry
Subjective criteria (esthetic integration)	
	Variations in tooth form
	Tooth arrangement and positioning
	Relative crown length
	Negative space

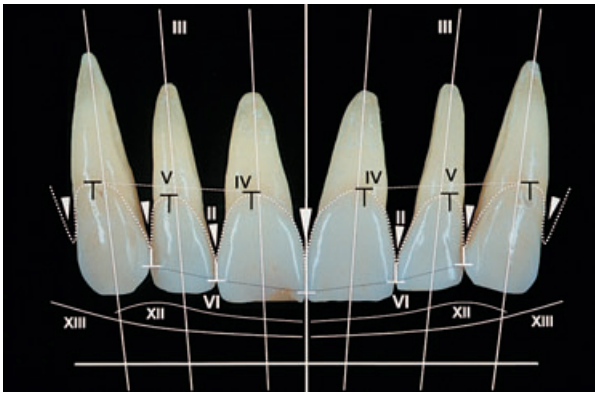

Fig. 53-1 The esthetic checklist, describing a number of respective fundamental objective criteria as they relate to the maxillary anterior segment (detailed description presented in Table 53-1). (Reprinted from Magne & Belser 2002, with permission, copyright © Quintessence Publishing Co, Inc.)

Table 53-2 Patient expectations related to maxillary anterior edentulous segments

- Long-lasting esthetic and functional result with a high degree of predictability
- Minimal invasiveness (preservation of tooth structure)
- Maximum subjective comfort
- Minimum risk for complications associated with surgery and healing phase
- Avoidance of removable prostheses
- Optimum cost effectiveness

Table 53-3 Therapeutic modalities for tooth replacement in the esthetic zone

- Conventional fixed partial dentures (FPDs), comprising cantilever units
- Resin-bonded ("adhesive") bridges
- Conventional removable partial dentures (RPDs)
- Tooth-supported overdentures
- Orthodontic therapy (closure of edentulous spaces)
- Implant-supported prostheses (fixed, retrievable or removable suprastructures)
- Combinations of the above

acceptance of various degrees of compromise from a purely esthetic point of view. The latter case is not infrequent after multiple anterior tooth loss in combination with significant hard and soft tissue deficiencies. In relation to maxillary anterior edentulous segments, patients generally expect a long-lasting functional and esthetic result with a high level of predictability (Table 53-2). To this primary objective are normally added a number of secondary goals which include parameters such as minimal invasiveness, low risk associated with eventual surgery, overall simplicity, and cost effectiveness.

Prior to selecting an implant-based solution, one should comprehensively review all of the possible treatment modalities available (Table 53-3) which have the potential to solve a given clinical problem, and carefully ponder their respective advantages and eventual shortcomings, and only then take the decision together with the adequately informed patient. Currently, the restorative spectrum in the case of missing maxillary anterior teeth comprises conventional FPDs, resin-bonded bridges, removable partial dentures (RPDs), tooth-supported overdentures and implant-supported fixed or removable prostheses. Furthermore, one should not forget that occasionally orthodontic therapy, e.g. closure of limited edentulous spaces, can represent an effective and elegant alternative or adjunct to a prosthetic treatment. However, the availability of scientific evidence – when possible at its highest level – for the planned treatment modality, should be the key parameter for the final choice.

Table 53-4 Criteria favoring implant-borne restorations

- Normal wound healing capacity
- Intact neighboring teeth
- Unfavorable ("compromised") potential abutment teeth
- Extended edentulous segments
- Missing strategic abutment teeth
- Presence of diastemas

In this clinical decision-making process certain criteria, for example the compromised structural, periodontal and/or endodontic status of potential natural abutments, or the extended dimension of the edentulous segment, are among the factors favoring an implant-borne restoration rather than a tooth-supported fixed prosthesis (Table 53-4).

Esthetic considerations related to maxillary anterior implant restorations

In the context of the natural dentition, long clinical crowns, the irregular contour of the gingival margin, i.e. any abrupt change in vertical tissue height between neighboring teeth, and the loss of papillary tissue often have an adverse influence on dental–facial esthetics (Seibert & Lindhe 1989). Furthermore, the same authors have underlined that in the case of a *high scalloped gingival morphotype* (in contrast to a rather *low scalloped gingival morphotype*) there is mostly an unpredictable relationship between the underlying bone and the gingival contour, often leading to so called "black hole cases" and presenting a high risk for losing soft tissue (e.g. gingival or mucosal recession at the labial aspect of teeth or implants), particularly in relation to restorative procedures, as for example insertion of retraction cords and impression taking.

Another esthetically relevant concern lies in the fact that under normal conditions a maxillary front tooth extraction leads on average to approximately 2 mm loss in vertical tissue height. The mean length of the clinical crown of a maxillary central incisor is 10.2 mm, the one of a lateral incisor 8.2 mm and that of a canine 10.4 mm. Consequently, any kind of maxillary anterior restoration should aim at staying within reasonable limits of these average morphologic dimensions, if a harmonious and esthetically pleasing result is to be achieved. Ultimately, an anterior implant restoration should correspond closely to an ovate pontic of a conventional FPD with respect to the relevant soft tissue parameters (Kois 1996).

Numerous publications, mostly in the form of textbooks, book chapters, reviews, case reports and descriptions of clinical and laboratory procedures and techniques, have addressed various aspects specifically related to esthetics and osseointegration (Parel & Sullivan 1989; Gelb & Lazzara 1993; Jaggers *et al*. 1993; Vlassis *et al*. 1993; Bichacho & Landsberg

Table 53-5 Evaluation of anterior tooth-bound edentulous sites prior to implant therapy

- Mesio-distal dimension of the edentulous segment, including its comparison with existing contralateral control teeth
- Three-dimensional analysis of the edentulous segment regarding soft tissue configuration and underlying alveolar bone crest (ref. "bone-mapping")
- Neighboring teeth:
  - volume (relative tooth dimensions), basic features of tooth form and three-dimensional position and orientation of the clinical crowns
  - structural integrity and condition
  - surrounding gingival tissues (course/scalloping of the gingival line)
  - periodontal and endodontic status/conditions
  - crown-to-root ratio
  - length of roots and respective inclinations in the frontal plane
  - eventual presence of diastemata
- Interarch relationships:
  - vertical dimension of occlusion
  - anterior guidance
  - interocclusal space
- Esthetic parameters:
  - height of upper smile line ("high lip" versus "low lip")
  - lower lip line
  - course of the gingival-mucosa line
  - orientation of the occlusal plane
  - dental versus facial symmetry
  - lip support

Table 53-6 Optimal three-dimensional implant positioning ("restoration-driven implant placement") in anterior maxillary sites

- Correct vertical position of implant shoulder (sink depth) using the cemento-enamel junction of adjacent teeth as reference:
  - no visible metal
  - gradually developed, flat axial profile
- Correct orofacial position of point of emergence for future suprastructure from the mucosa:
  - similar to adjacent teeth
  - flat emergence profile
- Implant axis compatible with available prosthetic treatment options (ideally: implant axis identical with "prosthetic axis")

Implant = apical extension of the ideal future restoration.

1994; Ghalili 1994; Landsberg & Bichacho 1994; Neale & Chee 1994; Studer *et al*. 1994; Carrick 1995; Corrente *et al*. 1995; De Lange 1995; Garber 1995; Garber & Belser 1995; Jansen & Weisgold 1995; Khayat *et al*. 1995; Touati 1995; Brugnolo *et al*. 1996; Davidoff 1996; Grunder *et al*. 1996; Hess *et al*. 1996; Marchack 1996; Mecall & Rosenfeld 1996; Bain & Weisgold 1997; Bichacho & Landsberg 1997; Chee *et al*. 1997; Garg *et al*. 1997; Spear *et al*. 1997; Salinas & Sadan 1998; Jemt 1999; Price & Price 1999; Belser *et al*. 2000; Tarnow *et al*. 2000).

In view of maxillary anterior implant restorations, the systematic and comprehensive evaluation of edentulous sites, including the surrounding natural dentition, is of paramount importance (Table 53-5). Key parameters comprise the mesio-distal dimension of the edentulous segment, the three-dimensional analysis of the underlying alveolar bone crest, the status of the neighboring teeth, and interarch relationships as well as specific esthetic parameters.

As one should consider the implant as the apical extension of the ideal future restoration and not the opposite, a respective optimal three-dimensional ("restoration-driven") implant position is mandatory (Table 53-6). Consequently, parameters addressing vertical (sink-depth) and oro-facial implant shoulder location, have been defined, as well as guidelines related to the long axis of the implant, as the latter has a significant impact on the subsequent technical procedures during suprastructure conception and fabrication.

Recently, the ITI Consensus Conference has approved the distinctly submucosal implant shoulder location in the maxillary anterior segment in order to respond to natural esthetic demands (Buser & von Arx 2000). As the current implant design – in contrast to the scalloped cemento-enamel junction – features a straight horizontal, "rotation–symmetrical" restorative interface, interproximal implant crown margins are often located several millimeters submucosally, and are thus difficult to reach by the patient's routine oral hygiene efforts (Belser *et al*. 1998). Mainly for this reason a screw-retained implant suprastructure (Sutter *et al*. 1993; Hebel & Gajjar 1997; Keller *et al*. 1998) is preferred to a cemented one, as it benefits from the surface quality and marginal fidelity of prefabricated, machined components, and avoids potential problems associated with cement excess that may be difficult to reach and thoroughly eliminate.

Anterior single-tooth replacement

Favorable 5-year multicenter results for 71 single-tooth replacements in the anterior maxilla (implant success rate of 96.6%) were reported by Henry *et al*. (1996); however, this group mentioned an associated 10% esthetic failure rate. In a retrospective study on 236 patients treated with single-tooth implant restorations in the anterior maxilla (Walther *et al*. 1996), a Kaplan–Meier survival rate of 89% was found for an observation period of 10 years. The failure rate for lateral incisor replacement was lower than that for central incisors. Furthermore, 5% of the related prosthetic suprastructures had to be replaced during the 10 years of observation. Kemppainen *et al*. (1997) prospectively documented 102 implants (ASTRA/ITI) for single-tooth replacement in the anterior maxilla of 82 patients and found survival rates of 97.8% and 100%, respectively, after 1 year. Still related to single-tooth maxillary anterior implants, a prospec-

tive study on 15 patients revealed a 100% implant survival rate after 2 years of function (Palmer *et al*. 1997). At crown insertion (6 months after implant placement) the mean bone level was located 0.47 mm apically to the top of the implants. No significant additional changes in crestal bone level occurred during the remainder of the study.

Today, it is generally accepted that the final implant shoulder sink depth for esthetic fixed single-tooth restorations can be determined primarily by the location of the cemento-enamel junction (CEJ) of the neighboring teeth and by the level of the free gingival margin at the vestibular aspect of these same teeth. This means that the implant shoulder is positioned 1–2 mm more apically to the labial CEJ of the adjacent teeth (Belser *et al*. 1998, 2000). However, the noticeable esthetic progress made in this kind of implant restoration is the result of recent developments in the absence of extensive long-term documentation. Because the exclusive use of clinical signs for establishing peri-implant health or disease may not be sufficient, the evaluation of additional objective parameters is needed. A number of diagnostic tests have been utilized by clinicians to supplement clinical signs with objective methods. These tests include microbiologic monitoring, proteolytic bacterial enzyme markers, markers of tissue destruction, and finally, markers of tissue repair and regeneration. In this context peri-implant crevicular fluid (PICF) analysis has become the focus of intense investigation. It has been observed that the volume of crevicular fluid did not differ between implant sites and natural teeth and that the features of inflammation seem to be the same around teeth and implants. In addition, the histologic arrangement of peri-implant soft tissues resembles basically that observed around natural teeth, although there are also some aspects of scar tissue (Abrahamson *et al*. 1996, 1997; Berglundh & Lindhe 1996; Lindhe & Berglundh 1998).

Giannopoulou *et al*. (2003) investigated the effect of intracrevicular restoration margins on peri-implant health of 61 maxillary anterior implants – mainly single-tooth replacements – in 45 patients for up to 9 years. Results revealed that the only statistically significant differences between baseline and follow-up examination concerned pocket probing depth (PPD) and the distance between the implant shoulder and the mucosal margin (DIM measurements), which increased slightly over time. The remainder of the clinical measurements and almost all of the microbiologic and biochemical parameters analyzed did not change significantly. Probably the most critical parameter from a purely esthetic point of view is the DIM value, particularly on the labial aspect of the maxillary anterior implants investigated in this study. A mean value of –1.5 ± 1.1 mm was found at baseline examination, and a slight increase (–1.7 ± 1.1 mm) at the follow-up. This indicates that the risk for exposure of the implant-to-crown interface or margin can be considered low. These findings corroborate recently published data addressing similar parameters (Grunder 2000). The consistently negative Periotest scores confirmed the stability and osseointegrated status of the implants examined. Furthermore, no associations were observed between the above results and the number of years that the implants had been in function. Based on these clinical, microbiologic, and biochemical data, and on an observation period of 4–9 years (mean 6.8 years), it was concluded that in patients with appropriate oral hygiene, implant-supported maxillary anterior crowns with distinctly intracrevicular margins did not predispose to unfavorable peri-implant host and microbial responses. In particular, overall healthy and stable peri-implant tissue conditions – a paramount criterion when it comes to esthetic implant crowns – were consistently encountered and maintained longitudinally. One of the patients participating in this study and who recently passed the 10-year clinical and radiographic follow-up control, is presented in Figs. 53-2 to 53-6. An adequate esthetic integration of the two single-tooth restorations, replacing the congenitally missing lateral incisors, could be achieved and maintained over time.

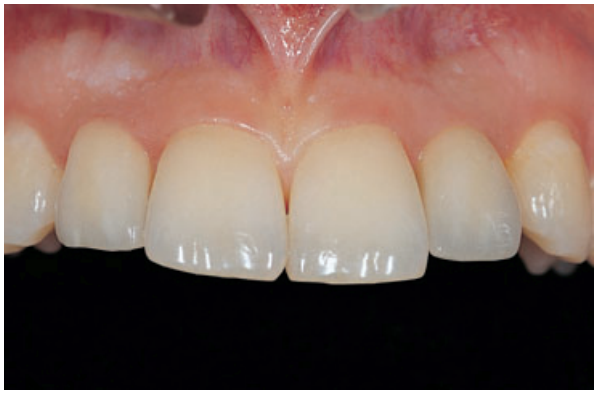

Fig. 53-2 Ten-year follow-up of a 28-year-old female patient. Both congenitally missing lateral incisors were replaced by implants, restored with screw-retained porcelain-fused-to-metal crowns.

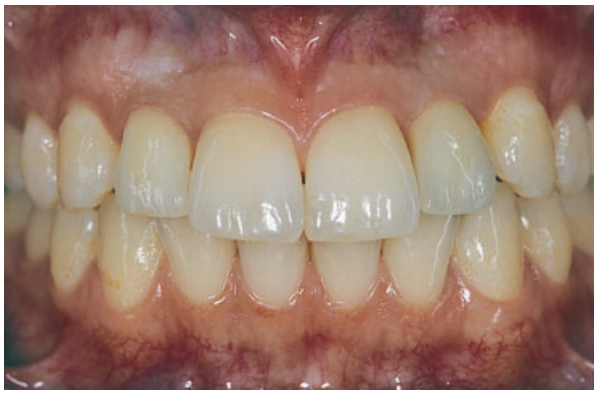

Fig. 53-3 The frontal view in centric occlusal position documents the harmonious integration of the two implant restorations after 10 years of clinical service.

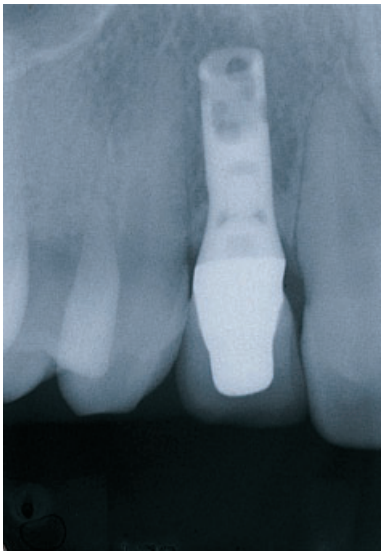

Fig. 53-4 Ten-year post operative radiograph of the maxillary right lateral single-tooth implant restoration.

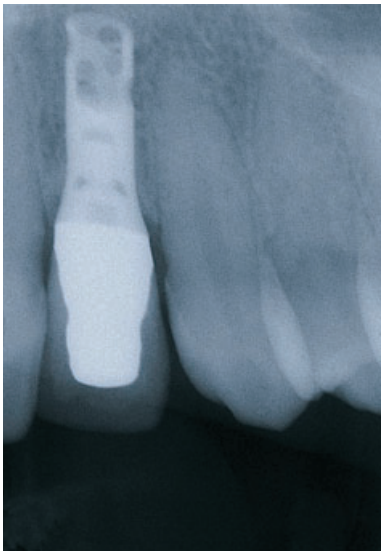

Fig. 53-5 Ten-year post-operative radiograph of the maxillary left lateral single-tooth implant restoration.

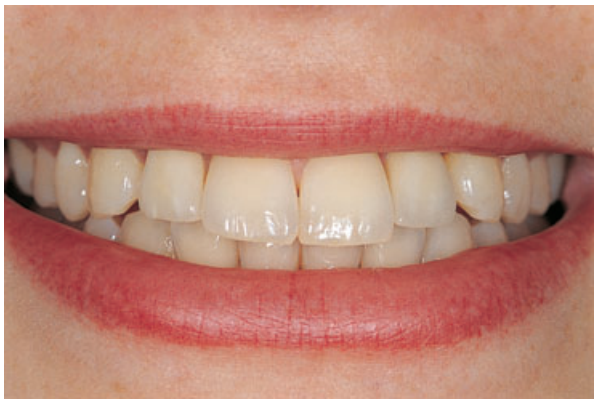

Fig. 53-6 During unforced smiling an adequate balance between implant-crowns and natural dentition can be noticed.

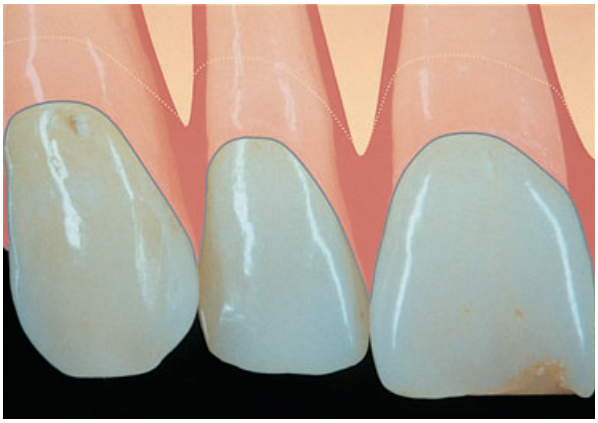

Fig. 53-7 Schematic representation of an intact maxillary right anterior segment. The alveolar bone follows the scalloped course of the cemento-enamel junction for a distance of approximately 2 mm (white dotted line), whereas, accordingly, the gingival tissue occupies the interdental area completely.

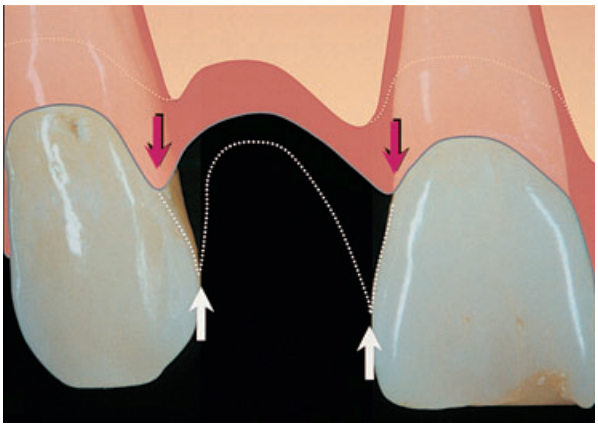

Fig. 53-8 Schematic representation of the same segment after loss of the lateral incisor. While the interproximal bone height has basically been maintained, the corresponding gingival tissue is flattened due to a lack of support originally provided by the now missing tooth.

In a simplistic way, the morphologic and esthetic consequences in the frontal plane of the loss of a single maxillary incisor, when compared to the original intact situation, can be summarized as follows: maintenance of the tooth-sided interproximal bone height at the neighboring teeth, and vertical loss ("flattening") of the corresponding gingival tissue due to a lack of support originally provided by the now missing tooth (Figs. 53-7, 53-8). In case of an anterior single-tooth replacement, the related implant restoration should aim at replicating the clinical crown of the contralateral control tooth from the line of soft tissue emergence to the incisal border. Additionally, a gradually developed, flat emergence profile from the implant shoulder to the peri-implant mucosal margin is mandatory (Figs. 53-9, 53-10).

The basic considerations related to maxillary anterior single-tooth replacement, including the respective general achievements and limitations, and

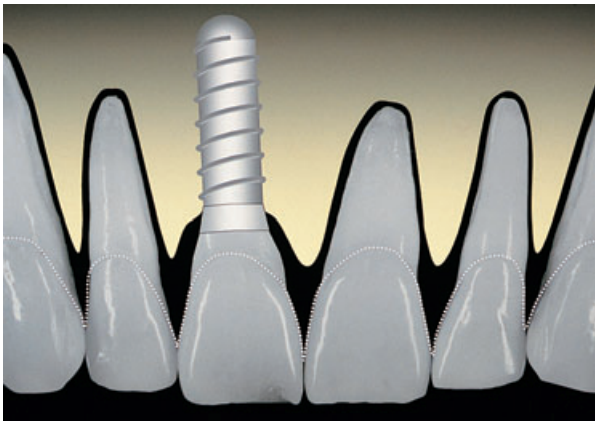

Fig. 53-9 The treatment objective in the case of an anterior single-tooth replacement is an implant restoration with a gradually developed, flat emergence profile from the implant shoulder to the peri-implant mucosal surface. Ideally, the clinical crown of the implant restoration should aim at replicating the clinical crown of the corresponding contralateral tooth.

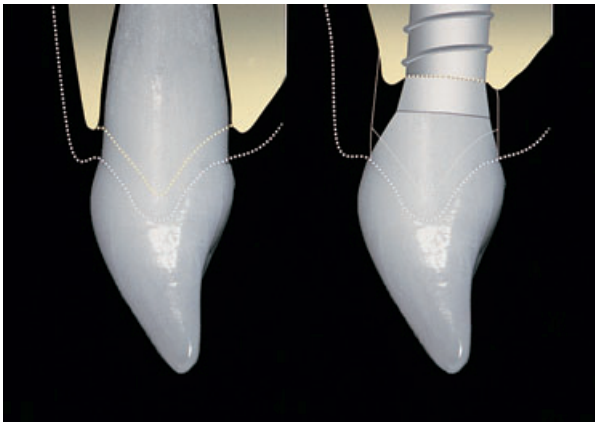

Fig. 53-10 Schematic comparison in the sagittal plane between a natural maxillary incisor and a respective implant borne single-tooth restoration. The decrease of alveolar bone height on the labial and palatal aspect following tooth loss leads to a more palatal implant position when compared to the original root position, which in turn influences the axial profile of the restoration.

addressing edentulous segments with different types of labial bone deficiencies, are presented in Table 53-7.

Sites without significant tissue deficiencies

An increasing body of evidence indicates that the most determinant parameter for achieving an esthetic single-tooth restoration is the interproximal bone height at the level of the teeth confining the edentulous gap. The related bone should be within a physiologic distance, i.e. approximately 2 mm, of the CEJ and thus provide the essential support for the overlaying soft tissue compartments. Consequently, preoperative diagnosis will include interproximal radiographic bone height assessment and periodontal probing of the soft tissue attachment level.

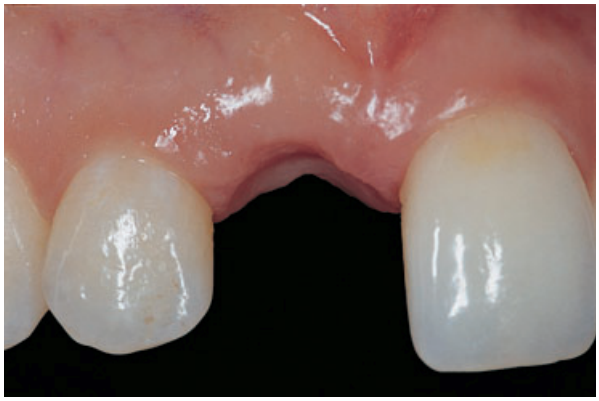

Fig. 53-11 Pre-operative close-up view of the upper right anterior region of a 22-year-old female patient with a missing right central incisor. The scalloped course of the gingiva is maintained, featuring interproximal soft tissue at the level of the cemento-enamel junction.

Table 53-7 Basic considerations related to anterior single-tooth replacement

Achievements	Predictable and reproducible results regarding both esthetic parameters and longevity in sites without significant vertical tissue deficiencies Well defined and well established surgical protocols: • *restoration-driven* implant placement Adequate and versatile restorative protocols and prosthetic components: • occlusal/transverse screw-retention • angulated abutments • high-strength ceramic components
Sites with buccal bone deficienies	Lateral bone augmentation using *autografts* and *barrier membranes*: • technique offers efficacy and predictability • *simultaneous* or *staged approach* depending on defect extension and defect morphology Lateral bone augmentation by means of *alveolar bone crest splitting* and/or various *osteotome techniques*: • limited clinical long-term documentation
Limitations	Combined vertical bone and soft tissue deficiencies: • following removal of ankylosed teeth or failing implants • advanced loss of periodontal tissues, including gingival recession, on neighboring teeth • limited scientific documentation related to *vertical bone augmentation* and *distraction osteogenesis*

If the comprehensive presurgical analysis of a given maxillary anterior single-tooth gap has confirmed a favorable vertical level of both soft tissue and underlying alveolar bone at the interproximal aspect of the two adjacent teeth on the one hand (Figs. 53-11 to 53-13), and no major vestibular bone deficiencies on the other hand, the site can be consid-

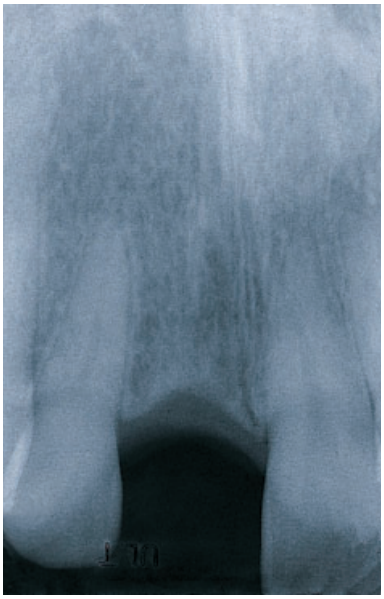

Fig. 53-12 The corresponding radiograph displays favorable bony conditions in view of implant therapy. Note in particular the interproximal bone height, following the cemento-enamel junction for a distance of less than 2 mm.

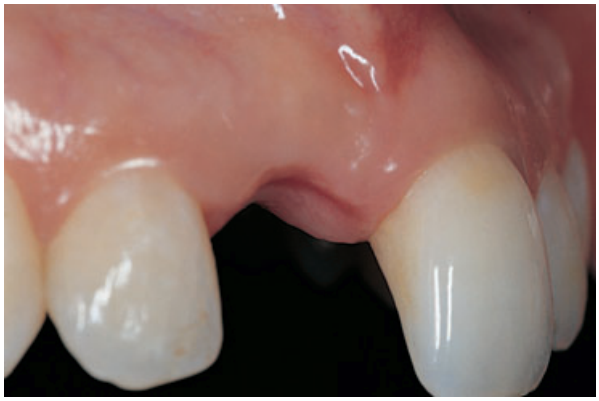

Fig. 53-13 The oblique close-up view confirms optimal conditions for the insertion of an implant, namely interproximal soft tissue height and no significant loss of the buccal bone plate.

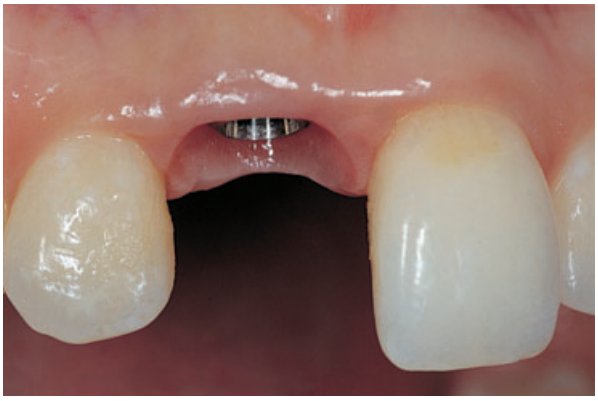

Fig. 53-14 Clinical view of the maxillary anterior implant site 8 weeks after insertion of a solid screw implant according to a one-stage transmucosal surgical protocol. A harmonious peri-implant soft tissue profile has been established by means of a titanium healing cap featuring a respective emergence profile and thus offering adequate interproximal soft tissue support.

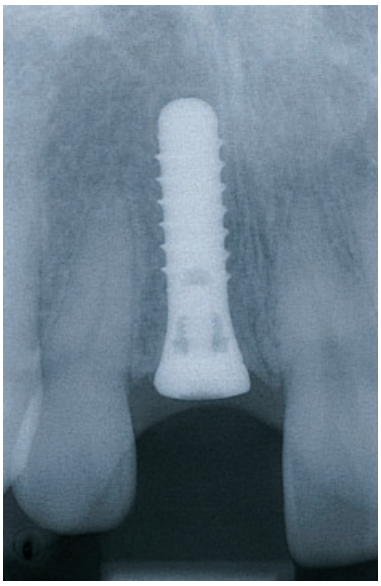

Fig. 53-15 The corresponding radiograph displays a continuous close contact between bone and implant and confirms that the vertical interproximal bone level has been maintained.

ered compatible with a straightforward implant surgical protocol. In order to ensure the best probability of a successful and long-lasting esthetic treatment outcome, the actual implant placement has to be carried out meticulously according to the surgical guidelines defined in Table 53-6. These guidelines include key parameters such as low-trauma surgical principles in general and precise three-dimensional ("restoration-driven") implant positioning in particular. In the case of standard single-tooth sites, most surgeons do not advocate the use of a surgical guide or stent, as the adjacent teeth and associated anatomic structures normally offer sufficient morphologic landmarks to reach the therapeutic objective safely. As far as the detailed surgical protocol is concerned, readers are referred to Chapter 48. Buser and von Arx (2000) have published the surgical step-by-step procedure related to maxillary anterior single-tooth implants, and insisted on a slightly palatal incision technique to preserve a maximum of keratinized mucosa on the labial aspect of the future implant restoration. Another crucial parameter is the maintenance of at least 1 mm of bone plate on the vestibular aspect of the implant in order to minimize the risk for peri-implant soft tissue recessions, a factor parameter when it comes to esthetics. Under such conditions one may consistently achieve post-surgical treatment outcomes featuring unaltered vertical soft tissue and underlying bone levels at the interproximal aspect of the adjacent natural teeth (Figs. 53-14 to 53-16).

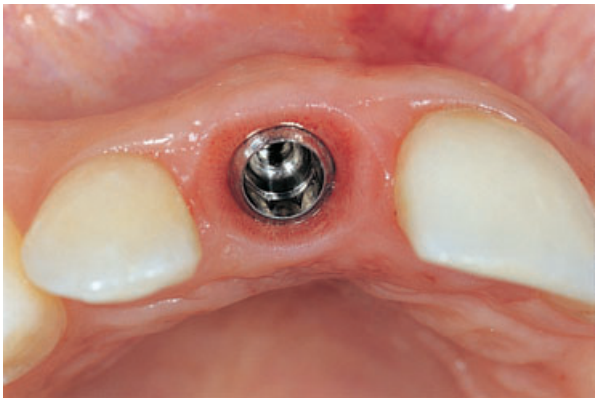

Fig. 53-16 The occlusal view reveals an implant position in the orofacial plane that is in accordance with the adjacent natural roots and thus permits development of a flat emergence profile.

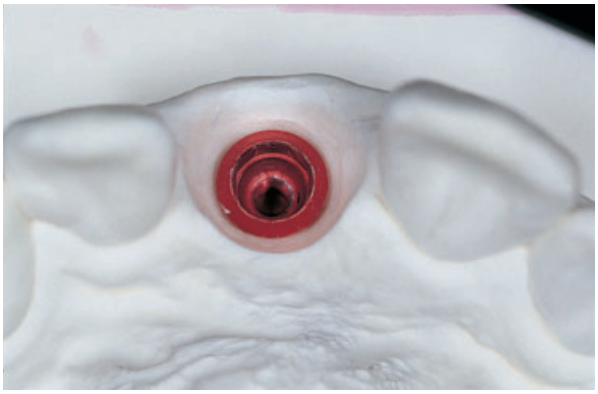

Fig. 53-18 The configuration of the peri-implant soft tissue is subsequently adapted on the stone model according to the diagnostic wax-up. Ultimately, it will be the restoration itself that completes the last phase of soft tissue conditioning by subtle respective physical displacement.

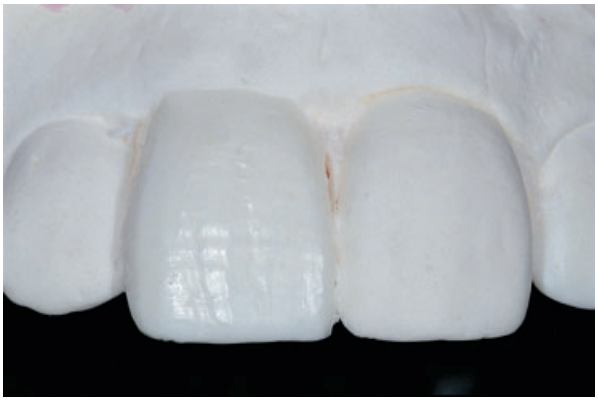

Fig. 53-17 On a stone model derived from the clinical situation, the laboratory technician defines the treatment objective in wax. At this stage priority is given to esthetic principles and maintenance of symmetry rather than to the actual position of the underlying implant.

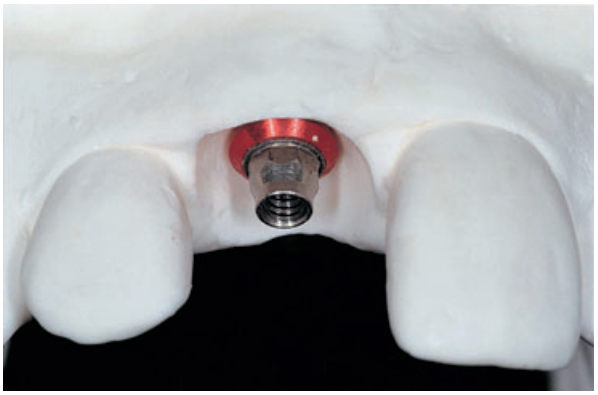

Fig. 53-19 An appropriate secondary titanium component (abutment) is selected as support for the planned screw-retained implant restoration.

Once osseointegration is confirmed radiologically and clinically, the clinical situation is transferred to the master model by means of an impression, normally assisted by auxiliary components in the form of prefabricated impression copings. On the master model, which in turn contains a replica (analogue) of the implant, the laboratory technician defines the final configuration of the single-tooth implant restoration by means of a diagnostic wax-up (Fig. 53-17). Under normal circumstances, i.e. when the natural contralateral control tooth corresponds mostly to the esthetic and functional requirements of an appropriate "target model", the technician basically copies the clinical crown of this control tooth in wax, regardless of the actual underlying implant position. At this stage a close-to-ideal restoration is planned, while its connection to the underlying implant will be addressed later. This approach comprises the minute shaping of the peri-implant soft tissue configuration (on the master model in the form of stone), in view of an identical emergence from the labial and interproximal soft tissue margin, to the one observed on the natural tooth site (Fig. 53-18). Only after having completed this preparatory step, will the ceramist select the most adequate secondary component (i.e. abutment), depending on the three following cardinal criteria (Fig. 53-19):

1. Implant shoulder depth in relation to the labial mucosal margin
2. Oro-facial implant shoulder position with respect to the future line of emergence of the suprastructure
3. Long axis of the implant.

In most instances, preference will be given to a screw-retained implant suprastructure, unless a combination of mesiostructure and cemented restoration is chosen. Screw-retention is primarily preferred due to a marked submucosally located implant shoulder, in particular at the interproximal aspect, which may render the removal of excess cement difficult, and which is mostly not within reach of the patient's routine oral hygiene measures. In addition, screw-retained suprastructures benefit from the close-to-perfect surface quality characteristics and the

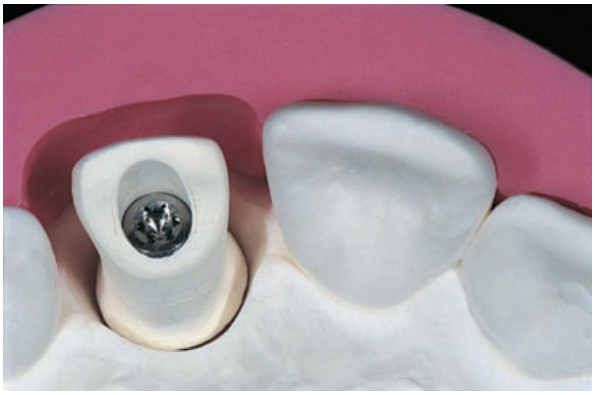

Fig. 53-20 Using a silicon template as guide, a prefabricated ceramic blank is inserted and subsequently reduced to provide adequate space for the external layers of cosmetic porcelain.

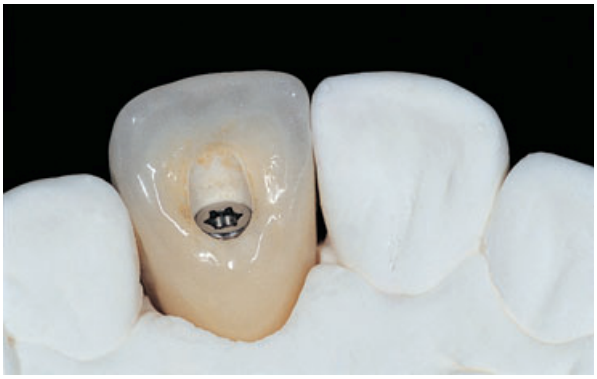

Fig. 53-22 In particular, the completed screw-retained all-ceramic restoration displays a high degree of translucency on its incisal third.

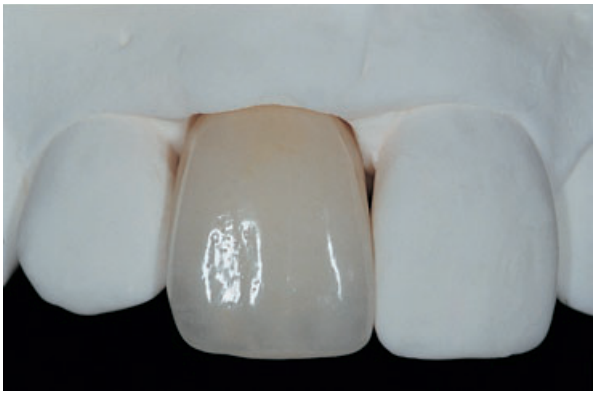

Fig. 53-21 Labial view of the completed ceramo-ceramic restoration on the master cast.

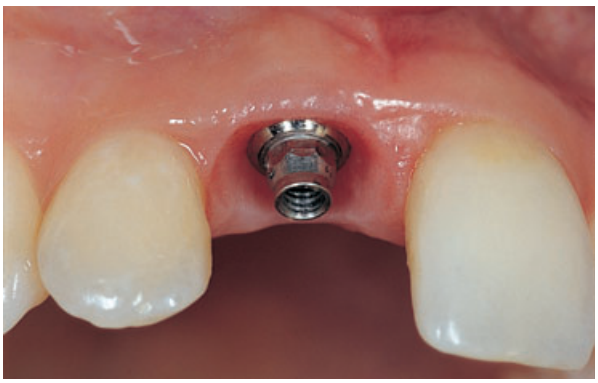

Fig. 53-23 A titanium abutment will serve as infrastructure for the transocclusally screw-retained high-strength all-ceramic restoration.

marginal precision of machined, prefabricated components. Nowadays several of the leading implant systems also offer high-strength ceramic tertiary components which may positively contribute to the esthetic treatment outcome, particularly in the case of a rather thin labial peri-implant mucosa (Fig. 53-20). Another parameter which is of primary importance when it comes to esthetic considerations relates to maxillary anterior implant restorations and is associated with the suprastructure design itself at the interproximal aspect. In order to provide optimal conditions for the related soft tissue, a long interdental contact line is established, located slightly more towards the palatal aspect of the restoration (Figs. 53-21, 53-22). This design offers optimal support for the interproximal soft tissue and thereby reduces the potential hazard of a so-called "black triangle" (Figs. 53-23 to 53-25). In this context some studies have indicated that there exists a predictable relationship between the location of the interdental contact point and the associated alveolar bone crest when it comes to presence or absence of interdental papillae fully occupying the interdental space of maxillary anterior teeth (Tarnow *et al*. 1992; Tarnow & Eskow 1995).

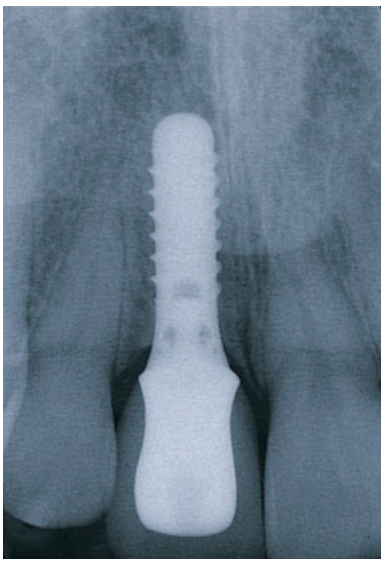

Fig. 53-24 The 1-year post-operative radiograph confirms favorable conditions at the bone-to-implant interface. Note a high degree of radio-opacity of the all-ceramic substrate, permitting the evaluation of the fidelity of the marginal adaptation.

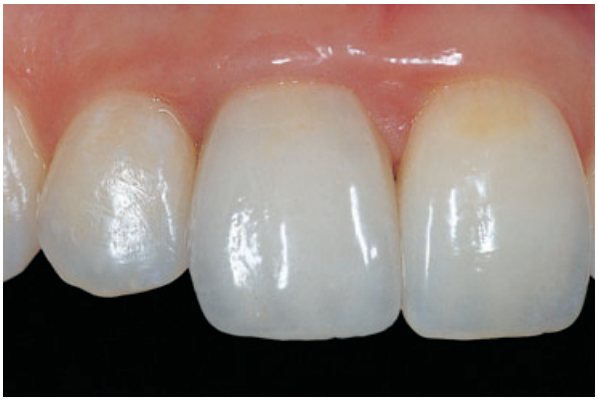

Fig. 53-25 An acceptable overall integration of the metal-free implant-borne restoration on site 11 can be noted.

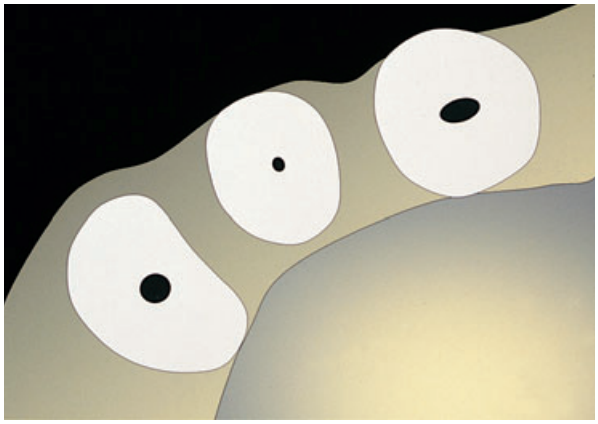

Fig. 53-26 Schematic representation of a horizontal section at the cemento-enamel junction level of the maxillary right anterior segment.

Sites with localized horizontal deficiencies

In a case of a localized (minor) horizontal deficiency, i.e. a confined vestibular alveolar bone crest defect at the vestibular aspect of a maxillary anterior single-tooth gap, one prefers to place the implant and simultaneously undertake a lateral bone augmentation procedure, on condition that several well defined prerequisites are fulfilled. These include an implant placement in accordance with the guidelines presented in Table 53-6 ("restoration-driven" implant placement), the achievement of an adequate primary stability and a resulting cervical dehiscence-type bony defect which is compatible with a predictable bone augmentation procedure. More specifically, the dehiscence should have the form of a two-wall bony defect, and the labial aspect of the inserted implant should not exceed the surrounding bone contours. Under such conditions, the treatment of choice consists of the application of autogenous bone chips, harvested at the site of the implant surgical intervention. The bone chips, which can be combined with one of the numerous available bone substitutes (e.g. BioOss®) if necessary, will provide adequate support for a subsequently adapted barrier membrane. The described grafting material is finally complemented with "bone slurry", constantly collected during the entire procedure. Subsequently, a bioabsorbable membrane is applied prior to repositioning and tension-free suturing of the mucoperiosteal flap. This implicates a rather extended flap design, comprising vertical releasing incisions.

In conclusion, a simultaneous lateral augmentation procedure is recommended if the three following conditions are present:

1. Ideal three-dimensional ("restoration-driven") implant position
2. Adequate primary implant stability
3. Localized two-wall bony defect, exceeding the labial contour of the implant and hereby assuring an appropriate bone regeneration potential and providing the necessary stability to the applied bone graft.

Under these specific conditions, the implant can be functionally loaded after 2–4 months, depending on size and configuration of the respective bone defect.

It is not infrequent in the anterior maxilla, due to its specific alveolar bone crest morphology, that "restoration-driven" rather than "bone-driven" implant positioning leads to a fenestration-type defect in the apical area of the implant. If adequate primary implant stability can be obtained, a similar simultaneous lateral bone augmentation procedure, as described for localized dehiscence-type defects, appears feasible. Under such circumstances the healing time prior to functional implant loading remains the same as advocated for standard implant protocols (i.e. 2 months for SLA-coated screw-type titanium implants).

Sites with extended horizontal deficiencies

In the case of more extended horizontal alveolar bone crest deficiencies, a simultaneous implant placement and lateral bone augmentation procedure becomes technically more difficult and less predictable, as the ultimate goal remains an optimal "restoration-driven" implant positioning (Figs. 53-26, 53-27). The described extended horizontal bone deficiency, on the one hand, may often not permit acceptable primary implant stability to be achieved, and, on the other hand, may lead to a vestibular bone dehiscence that does not have a distinct two-wall morphology. Furthermore, the labial implant contour would be more prominent than the respective surrounding bone (Fig. 53-28). Under these specific circumstances the principal prerequisites for a simultaneous approach are clearly not present, thus leading to the recommendation to proceed according to a staged surgical protocol, which will address the lateral bone augmentation first and the actual implant placement in a second stage.

This may represent a major problem for some patients, as two surgical interventions, normally

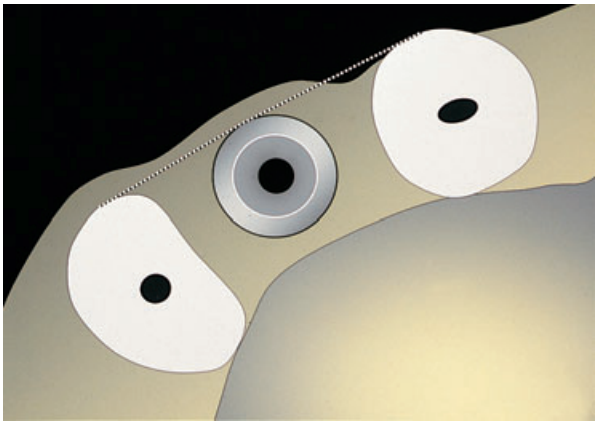

Fig. 53-27 "Restoration-driven" implant placement in the horizontal plane at the site of the maxillary right lateral incisor. In order to maintain at least 1 mm of alveolar bone also on the labial aspect, the implant has to be inserted approximately 1–2 mm more towards the palate when compared to the adjacent roots.

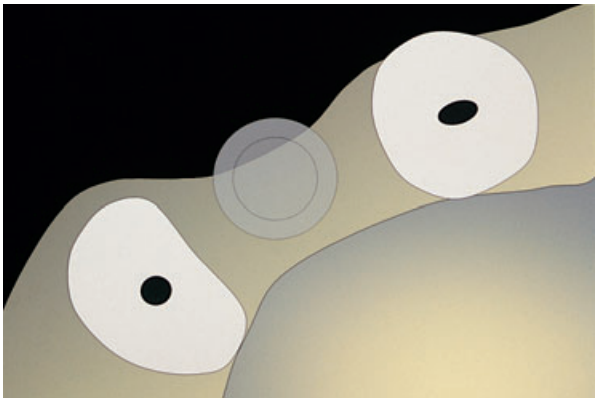

Fig. 53-28 In the case of an extended lateral bone deficiency, where an adequately placed implant would largely exceed the vestibular border of the alveolar bone crest, a lateral bone augmentation procedure (staged approach) is indicated.

separated by approximately 6 months, are necessary, leading to a total treatment time of 8 months or more. It is therefore indispensable to inform the patient thoroughly about both the reasons for the staged approach associated to implant therapy, and the possible conventional prosthodontic alternatives (e.g. a traditional tooth-borne FPD, eventually in combination with a connective tissue grafting procedure to optimize the deficient edentulous ridge in view of an optimal and esthetic pontic). The patient will then be in a position to give his or her informed consent to either of the two therapeutic modalities, according to individual preference.

In the case of implant therapy, the first step consists of the elevation of a rather extended mucoperiosteal flap featuring vertical releasing incisions, as the added site volume (due to the block graft and barrier membrane) will require subsequent splitting of the periosteum prior to flap repositioning and suturing (Fig. 53-29). Numerous studies reporting results of various bone augmentation techniques

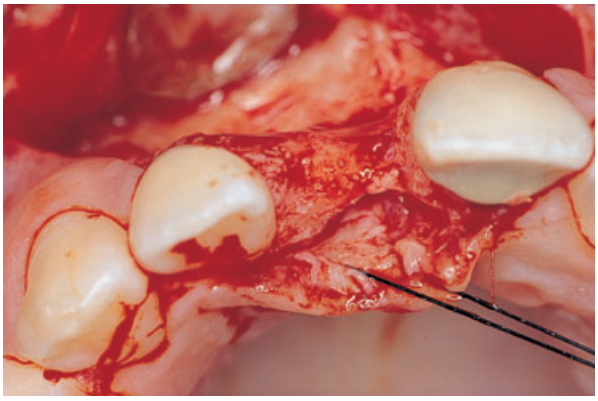

Fig. 53-29 After elevation of a mucoperiosteal flap a severe extended resorption on the vestibular aspect of the edentulous alveolar ridge becomes apparent. Such a morphology is hardly compatible with "restoration-driven" implant placement.

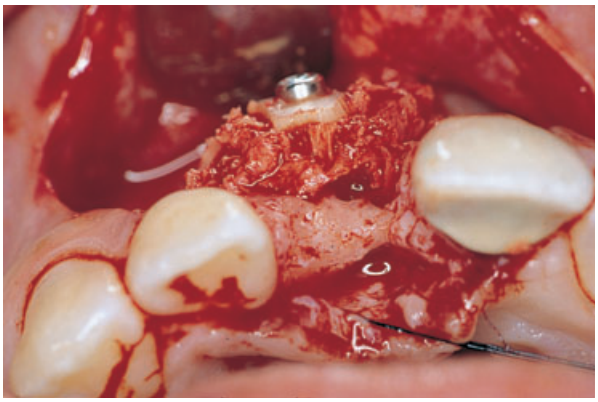

Fig. 53-30 An autogenous bone graft, harvested from the patient's chin region, has been secured with a fixation screw and its periphery filled in with additional bone chips prior to membrane placement.

and related materials have been published (Hürzeler *et al*. 1994; Buser *et al*. 1996; Ellegaard *et al*. 1997b; Chiapasco *et al*. 1999, 2001; von Arx *et al*. 2001a; Zitzmann *et al*. 2001). To date, autogenous bone block grafts, mostly harvested from the chin or the retromolar area, in combination with e-PTFE barrier membranes, still have the best clinical long-term documentation (Buser *et al*. 2002). These authors presented prospectively documented 5-year data of 40 consecutively treated patients, according to a staged protocol. Implants could subsequently be inserted on all laterally augmented sites. It was concluded that the clinical results of implants placed in regenerated bone were comparable to those reported for implants in non-regenerated bone. A clinical example of the described approach is presented in Figs. 53-29 to 53-37.

Sites with major vertical tissue loss

When it comes to maxillary anterior single-tooth gaps with significant vertical tissue loss, the predictable achievement of an esthetically pleasing

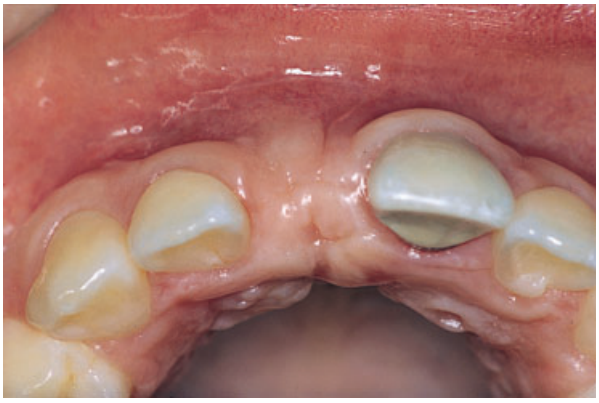

Fig. 53-31 Six months after the lateral ridge augmentation procedure the clinical occlusal view documents that uneventful healing has occurred and that the orofacial ridge profile has been improved.

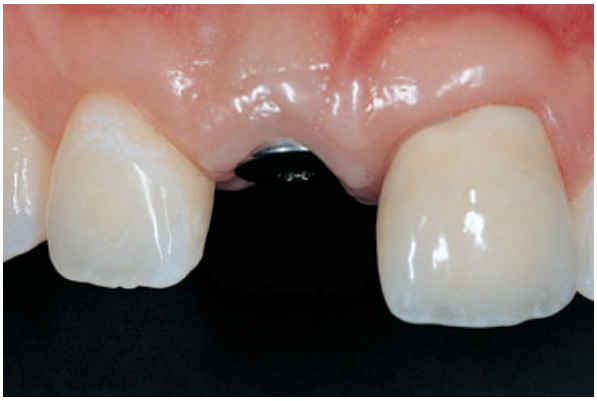

Fig. 53-34 Two weeks after mucosaplasty and exchange of healing caps the initiation of a harmoniously scalloped labial soft tissue course is apparent. Furthermore, the access from the surface to the underlying implant shoulder has been established.

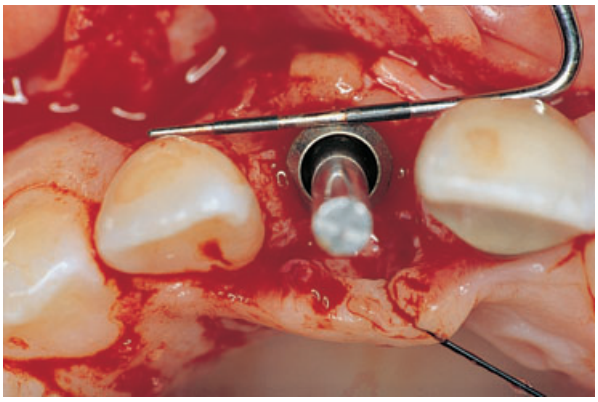

Fig. 53-32 During implant surgery. All key parameters characterizing an optimal implant position (shoulder sink depth, orofacial point of emergence, implant axis) could be satisfied.

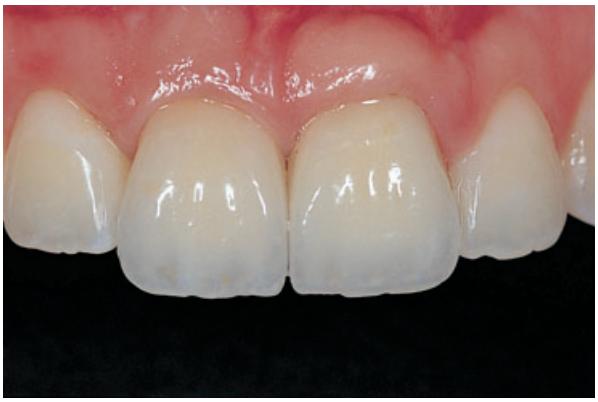

Fig. 53-35 The two ceramo-metal crown restorations – one tooth-borne (site 21) and one implant-borne (site 11) – display little difference in appearance since symmetry has been respected from the line of mucosal emergence to the incisal edge.

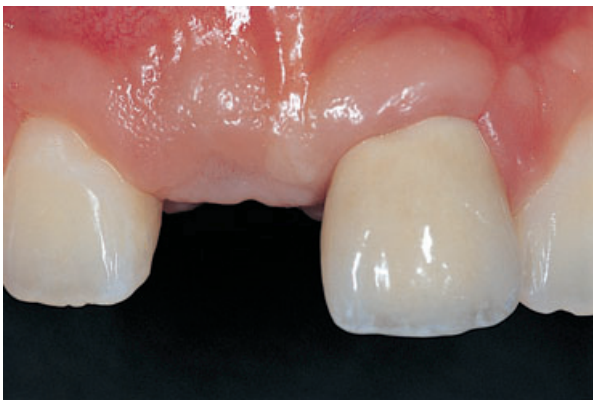

Fig. 53-33 After 3 months of healing the labial view documents a slight excess of keratinized peri-implant mucosa in a coronal direction, which is a prerequisite for the development of the final esthetic soft tissue contours. The first step of the subsequent procedure will consist of the insertion of a longer titanium healing cap, following a minor mucosaplasty.

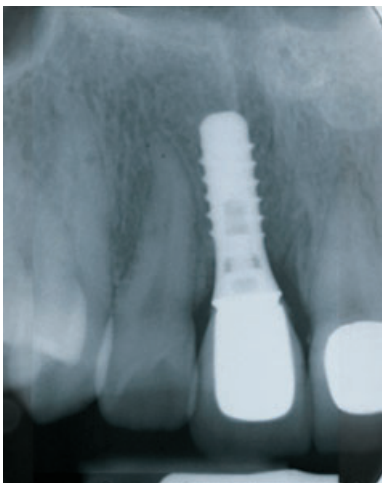

Fig. 53-36 The 1-year follow-up radiograph confirms the stability of the osseointegrated 10 mm titanium screw implant.

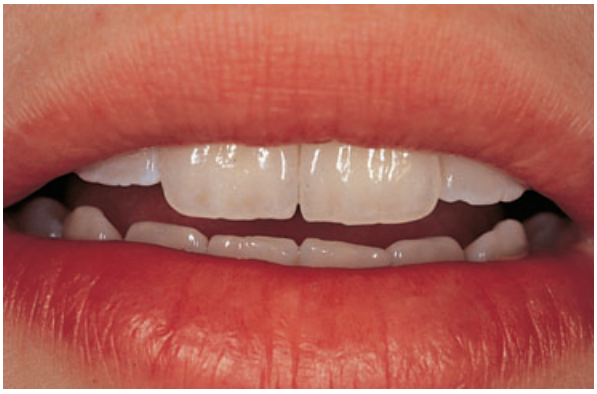

Fig. 53-37 An esthetically pleasing overall integration of the two maxillary anterior restorations is underlined by a close-up view of the patient's unforced smile.

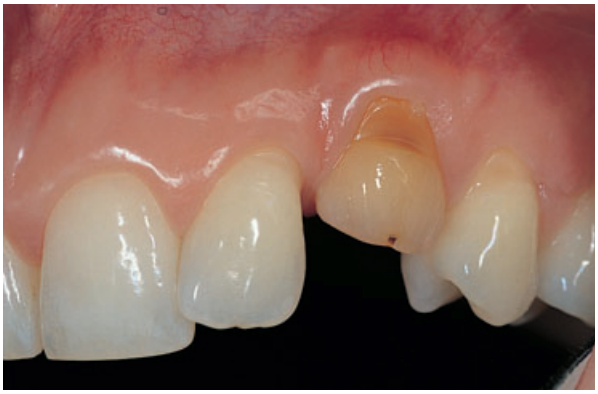

Fig. 53-38 Pre-operative view of a 35-year-old female patient consulting with a persistant primary tooth in the position of the maxillary left canine. Note the irregular course of the adjacent gingiva in general and the loss in vertical tissue height in particular.

treatment outcome, ideally providing a so-called perfect illusion with respect to its integration in the surrounding natural dentition, gets difficult. As pointed out earlier in this chapter, a close relationship exists between the interproximal bone height and the associated soft tissue level (Figs. 53-7, 53-8). If the coronal border of the alveolar bone is no longer within the physiologic distance of approximately 2 mm from the interproximal CEJ of the teeth confining the edentulous space, there is an increased risk of an altered respective soft tissue course (due to a lack of underlying bony support) and its adverse impact on the appearance. Such situations can be encountered following the removal of ankylosed teeth or failing implants, or in case of advanced periodontal tissue loss – including gingival recession – on neighboring teeth. Under these specific circumstances, the final decision whether or not to use implants will ultimately depend on (1) the careful and comprehensive evaluation of all of the therapeutic modalities available for anterior tooth replacement (Table 53-3), and (2) the patient's individual smile line and expectations. This process includes an objective analysis of the advantages and eventual shortcomings associated with each modality.

To illustrate these clinically relevant aspects, the initial situation and the subsequent implant treatment of a 35-year-old female patient consulting with an ankylosed maxillary deciduous left canine, are presented in Figs. 53-38 to 53-46. The preoperative analysis had led to the conclusion that the fabrication of a conventional tooth-borne three-unit FPD, using the intact lateral incisor and first premolar as abutments and featuring a canine pontic, was not opportune from several points of view. Among these should be particularly mentioned aspects related to the questionable mechanical resistance of the resulting conventional prosthesis, specific occlusal considerations (e.g. canine guidance in a pontic area), lack of esthetic superiority when compared to a virtual implant-borne fixed restoration, and, last but not least, the conflict with the general principle of

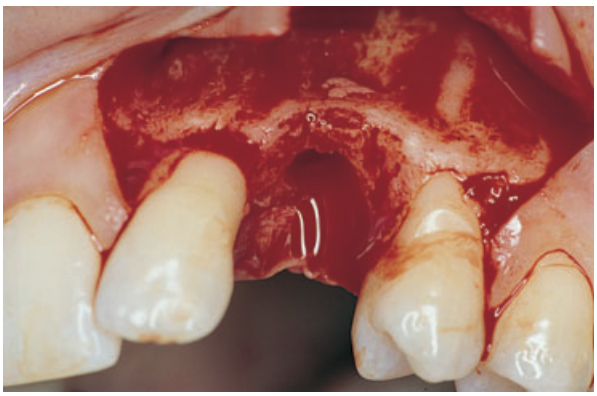

Fig. 53-39 One month after removal of the deciduous canine, the root of which was severely resorbed, a mucoperiosteal flap with vertical releasing incisions is elevated and the preparation of a calibrated implant bed performed. One can note an increased distance between the cemento-enamel junction and the coronal border of the alveolar bone and the left lateral incisor.

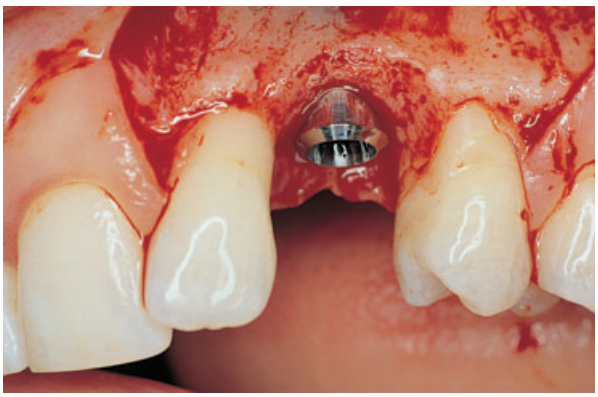

Fig. 53-40 Buccal view after insertion of the implant.

minimal invasiveness (maximum preservation of intact tooth structure).

Once the decision was made, both the implant surgical and the restorative strategies focused on improving or at least optimally exploiting the

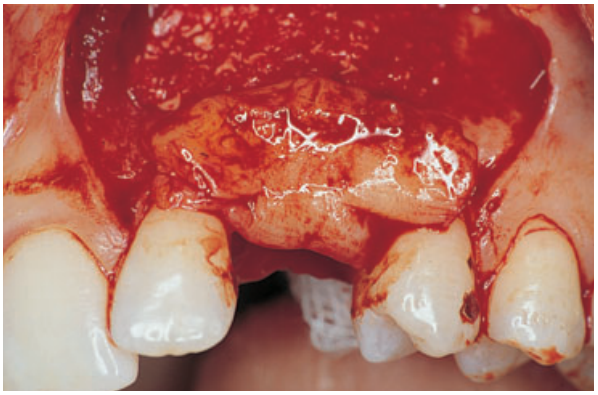

Fig. 53-41 In a case of rather thin mucosa, the utilization of a connective tissue graft, harvested from the palate, may be indicated to create a sufficient thickness of soft tissue at the implant site.

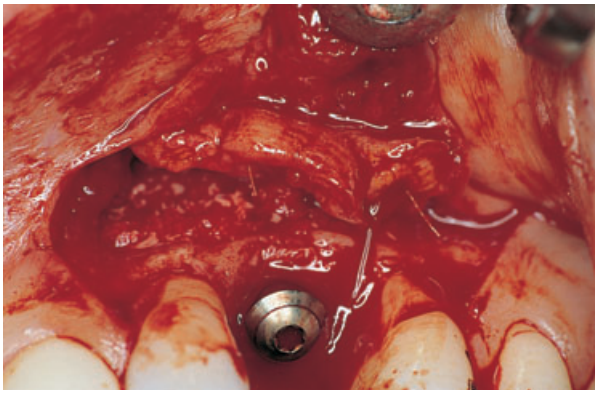

Fig. 53-42 Prior to flap closure, the connective tissue graft is secured to the flap with bioabsorbable sutures.

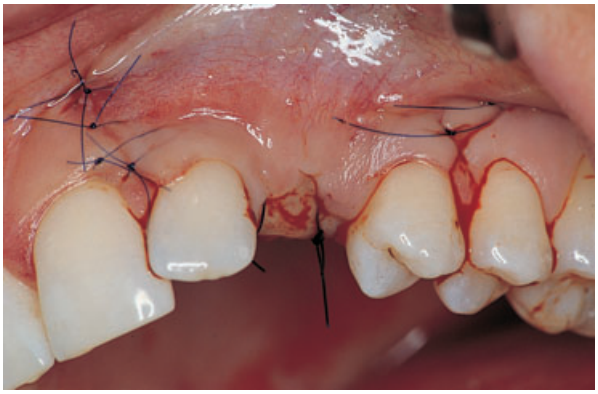

Fig. 53-43 Coverage of most of the healing cap during suturing is recommended, leading to a submerged or at least to a "semi-submerged" healing mode.

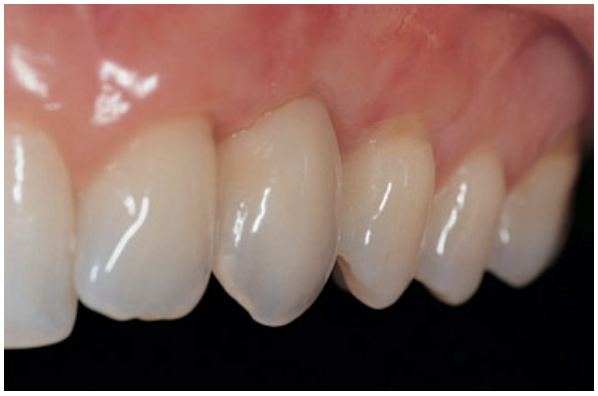

Fig. 53-44 The clinical aspect after insertion of the ceramo-metal implant crown reveals stable and esthetic peri-implant soft tissue contours.

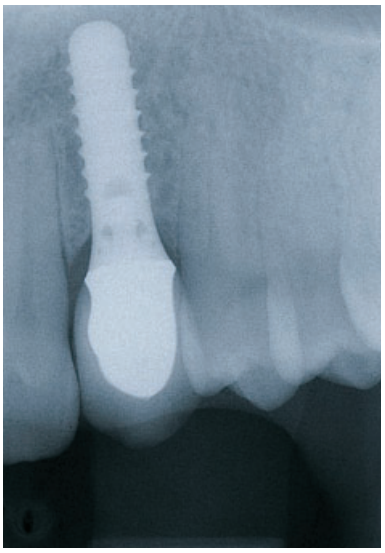

Fig. 53-45 The 2-year follow-up radiograph confirms the stability of the osseointegrated 10 mm solid screw titanium implant.

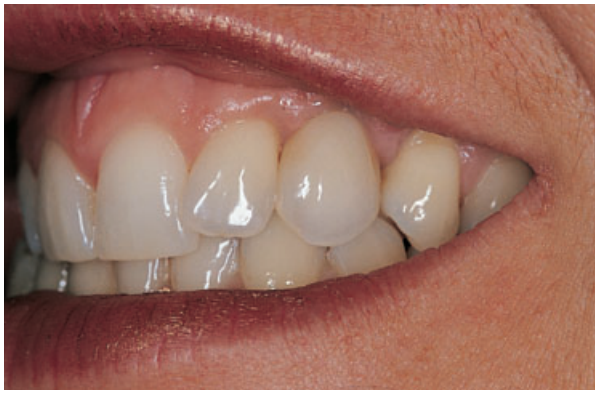

Fig. 53-46 On a left lateral view, during the patient's forced smiling, one can note that the lack of vertical soft tissue in the interproximal area has been compensated for with an apically extended interdental contact line.

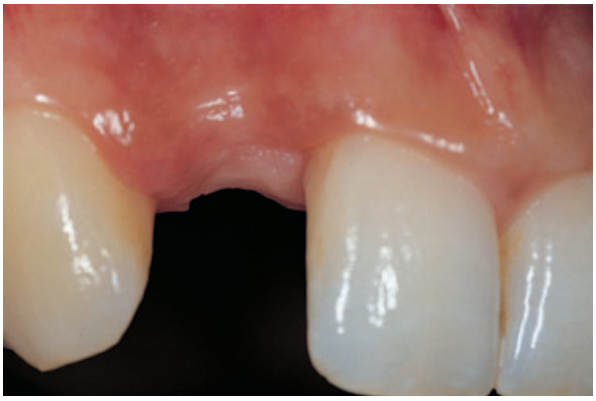

Fig. 53-47 Labial close-up view of the maxillary right anterior region of a 19-year-old female patient. The interdental soft tissue height distal to the central incisor and the corresponding underlying alveolar bone height are markedly reduced, leading to exposure of the cemento-enamel junction.

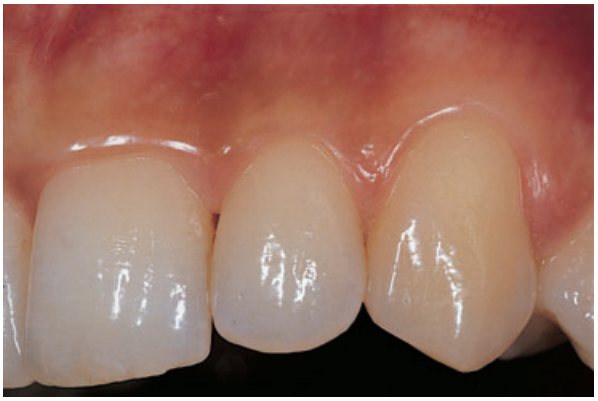

Fig. 53-48 The contralateral side of the dental arch shows perfectly intact and harmonious conditions with respect to the course of the gingiva.

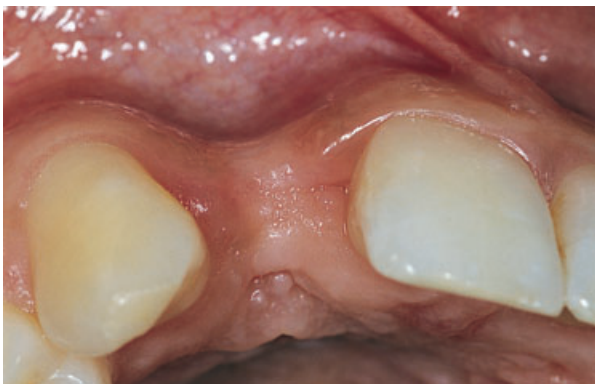

Fig. 53-49 On the occlusal view of the edentulous site a significant lateral crest deficiency becomes apparent, which calls for both a bone and soft tissue augmentation procedure, particularly if an implant solution is planned.

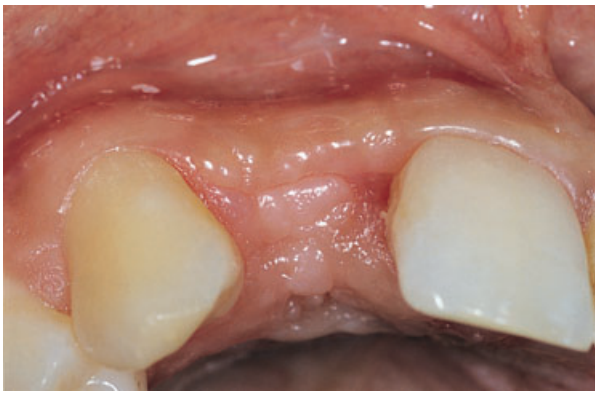

Fig. 53-50 Six months after combined lateral bone and soft tissue augmentation, the site appears to be compatible with "restoration-driven" implant placement.

pre-existing limited esthetic potential of the site. From the surgical side, this comprised a deeper than normal implant shoulder sink depth (Fig. 53-40), the use of a connective tissue graft on the vestibular aspect (Fig. 53-41), a localized lateral bone augmentation (simultaneous approach) procedure (Fig. 53-42) and a coronally repositioned flap (Fig. 53-43). The metal–ceramic implant restoration featured a transverse screw-retention to provide maximum space for esthetic porcelain stratification and a long contact line on the mesial aspect to compensate for the missing interdental soft tissue height (Figs. 53-44 to 53-46).

A more severe preoperative situation of vertical tissue deficiency, combined with a marked horizontal bone defect, is presented in Figs. 53-47 to 53-49. This 19-year-old female patient lost her maxillary right lateral incisor due to a localized periodontal problem. Again, the comprehensive site analysis concluded that a single-tooth implant restoration was the best compromise in view of major disadvantages associated with all of the conventional prosthodontic options. From a purely esthetic point of view, none of the therapeutic modalities had the potential to predictably lead to a perfect re-establishment of a symmetrical, harmoniously scalloped soft tissue course at its original physiologic level. However, a rather low lip-line during the patient's normal communication and unforced smiling permitted the least invasive approach to be chosen. Following a lateral connective tissue and bone augmentation procedure (Fig. 53-50), an implant could be inserted in an acceptable position and subsequently restored with a screw-retained crown. The final frontal view, allowing a direct comparison between the intact (Fig. 53-51) and the restored side, clearly demonstrates the current esthetic limitations associated with implant therapy in sites with a marked vertical tissue deficiency (Fig. 53-52).

Multiple-unit anterior fixed implant restorations

The normal consequence following loss of two or more adjacent upper anterior teeth comprises a flattening of the edentulous segment. In particular one can observe the disappearance, in an apical direction, of the crestal bone originally located between the

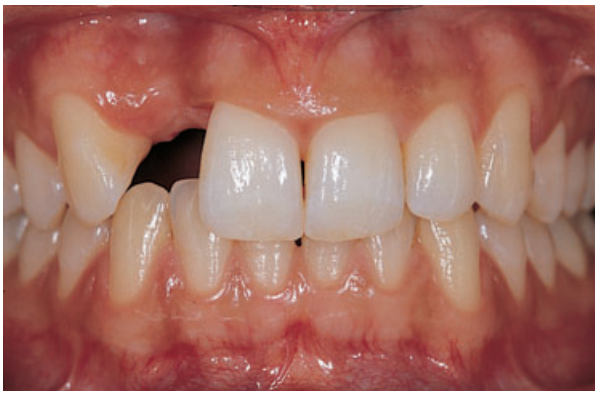

Fig. 53-51 The buccal view in centric occlusion position before therapy summarizes the problems associated with localized vertical tissue deficiencies: lack of a harmoniously scalloped soft tissue course in general and missing interdental papillae in particular.

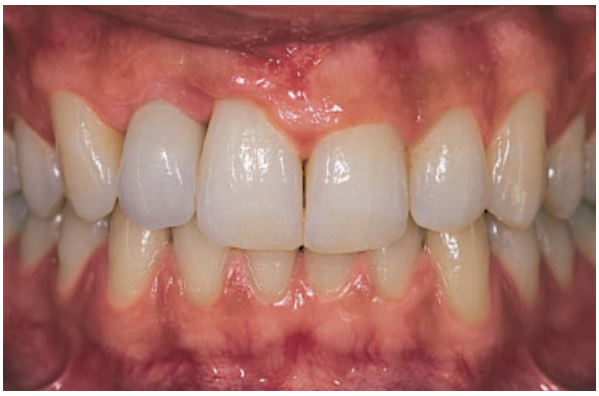

Fig. 53-52 The corresponding view after lateral bone and soft tissue augmentation and insertion of an implant-borne single-tooth restoration on the site of the right lateral incisor, underlines the resulting shortcomings with respect to esthetic parameters. Vertical tissue deficiencies – which at present cannot be predictably compensated for – clearly compromise the overall integration of an otherwise successful treatment.

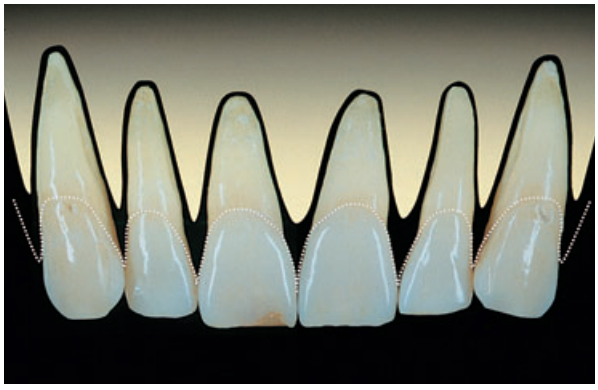

Fig. 53-53 Schematic representation of the six maxillary anterior teeth, including their bony support and the course of the marginal soft tissue, corresponding ideally approximately to the cemento-enamel junction (dotted line).

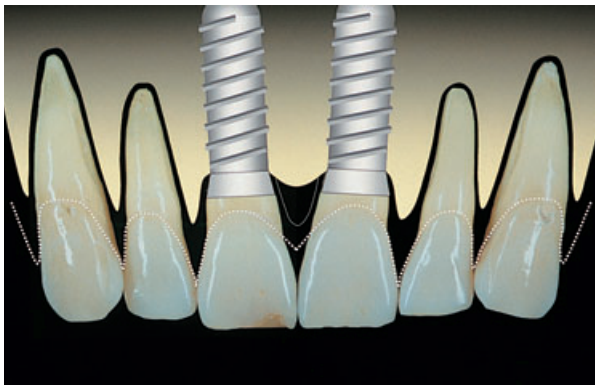

Fig. 53-54 Loss of the two central incisors and their subsequent replacement by implant restorations normally leads to well defined bone loss ("micro-gap", establishment of a "biologic width") around the implant sites. The main consequence from an esthetic point of view consists of vertical soft tissue deficiencies, namely between adjacent implants (dotted lines).

incisor teeth. This phenomenon is not, or only minimally, present at the interproximal aspect of the remaining anterior teeth and thus explains the fundamental difference between a maxillary anterior single-tooth gap and a multi-unit edentulous segment.

If two standard screw-type titanium implants are inserted to replace two missing maxillary central incisors (Figs. 53-53, 53-54), an additional peri-implant bone remodeling process will take place. In the frontal plane, two different characteristic processes, one between the natural tooth and the implant and the other between the two implants, can be distinguished. At the site between tooth and implant, the tooth-sided interproximal bone height should theoretically remain at its original location, i.e. within 2 mm from the CEJ, from where the implant-sided interproximal bone height drops in an oblique manner towards the first implant-to-bone contact, normally located approximately 2 mm apically of the junction ("microgap") between the implant shoulder and the abutment or suprastructure. This phenomenon has been referred to in the literature as "saucerization" or establishment of a "biologic width" (Hermann *et al*. 1997, 2000, 2001a,b). In contrast, the inter-implant bone height normally decreases further in an apical direction, once the respective abutments or suprastructures are connected to the implant shoulder. This process is mostly accompanied by a loss of interimplant soft tissue height and hence may lead to unsightly, so-called "black interdental triangles". The schematic close-up views comparing the original dentate situation with the status after integration of two adjacent implant restorations, clearly demonstrate the negative consequences on the course of the marginal soft tissue line in a case of multiple adjacent maxillary anterior implants (Figs. 53-55, 53-56).

The basic considerations related to the current state of achievements and limitations of maxillary anterior fixed multiple-unit implant restorations in sites with and without horizontal and/or vertical soft

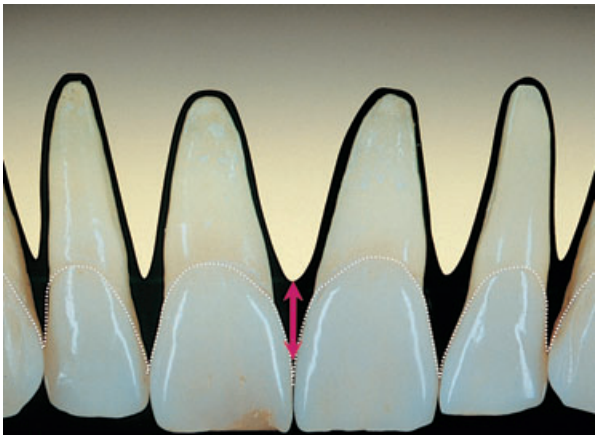

Fig. 53-55 Schematic close-up view of the relationship between cemento-enamel junction, alveolar bone, and course of the gingiva in the maxillary incisor area.

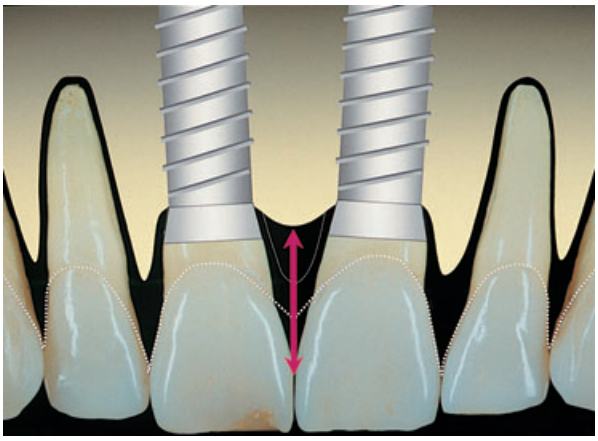

Fig. 53-56 Same area after implant therapy. The red arrow represents the distance between the inter-implant bone crest and the interdental contact point. The lack of bony support for the interdental soft tissue often causes the appearance of black triangles, compromising the esthetic treatment outcome.

and hard tissue deficiencies are summarized in Table 53-8.

Sites without significant tissue deficiencies

Due to the previously described shortcomings inherent in multiple adjacent implant restorations, the clinical decision-making process will thus address both the height of the patient's smile line (low, medium, high) and the individual gingival phenotype (thick and low scalloped or thin and high scalloped). In the presence of a favorable gingival morphotype, some restorative "tricks", including peri-implant soft tissue conditioning and particular interproximal crown design, need to be implemented to predictably achieve an acceptable esthetic compromise (Figs. 53-57 to 53-62). Peri-implant soft tissue conditioning is primarily achieved by using either healing caps featuring an appropriately shaped, continuously increasing (in a coronal direction) axial emergence profile, or by means of plastic components permitting the customization of the best suited axial contour in the region from the implant shoulder or abutment to the mucosal margin (Fig. 53-58). The particular suprastructure design concerns the inter-implant aspect, where, instead of an interdental contact point, a long and slightly palatal contact line is developed in the form of two adjacent "wings",

Table 53-8 Basic considerations related to anterior fixed multiple-unit implant restorations in sites with horizontal and/or vertical soft and hard tissue deficiencies

Achievements	Predictable and reproducible results regarding lateral bone augmentation using barrier membranes supported by autografts: • allows implant placement in patients with a low lip line
Limitations	Vertical bone augmentation is difficult to achieve and related surgical techniques lack prospective clinical long-term documentation Inter-implant papillae cannot predictably be re-established as of yet

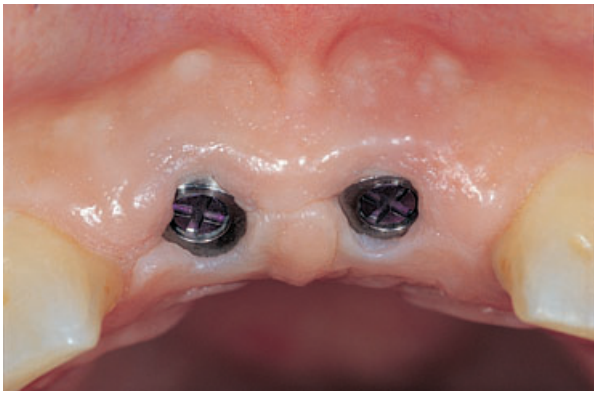

Fig. 53-57 Clinical close-up view of the maxillary anterior segment of a 32-year-old female patient following placement of two 12-mm solid screw implants according to a one-stage transmucosal surgical protocol.

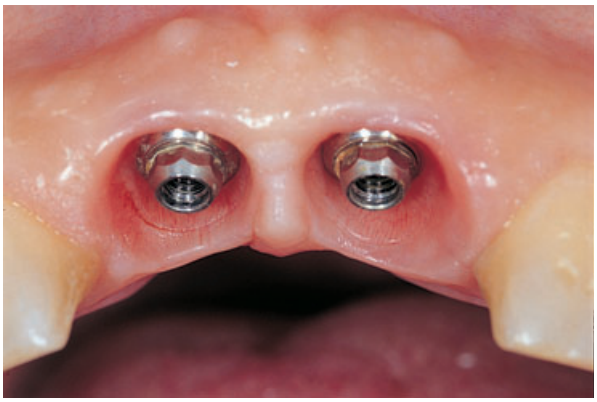

Fig. 53-58 Conditioning of the peri-implant mucosa, in view of the future restorations, has been performed by means of auxiliary plastic components with the possibility of individualizing the emergence profile.

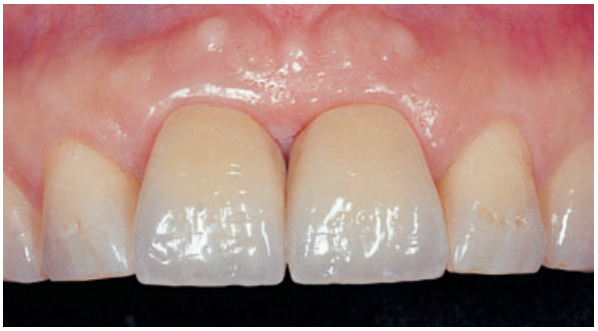

Fig. 53-59 The corresponding clinical close-up view, taken shortly after insertion of the two screw-retained ceramo-metal restorations, documents the effect of a long interdental contact line, the presence of pronounced mesial ridges, and a slight increase of color saturation in the cervico-interdental area. Such technical measures contribute to the compensation of a flat and more apically located labial mucosa line.

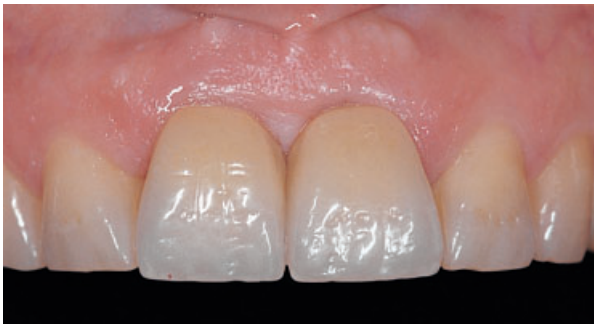

Fig. 53-60 Clinically, a slight fill-in of inter-implant mucosa and an overall stable soft tissue situation can be noted after 6 years of clinical service.

which are more color-saturated in order to create a discrete shade transition ("blending-in") at the mucosal margin. If the mesial oblique triangular ridges of the two adjacent implant restorations are located at their normal location, the ceramic crowns will not – despite their increased vestibular diameter – optically appear larger (Fig. 53-61). This design reduced the inter-implant cervical triangle to a minimum at the moment of the crown insertion (Fig. 53-59), and favored a coronal soft tissue increase, clearly visible at the 6-year clinical follow-up (Fig. 53-60).

Sites with extended horizontal deficiencies

If the absence of multiple adjacent teeth in the anterior maxilla is accompanied by a marked, but primarily horizontal, resorption of the edentulous alveolar bone crest towards the palate, one can adopt two different strategies. One consists of a so-called "bone-driven" implant placement which will lead to a distinct palatal implant position. In most instances this strategy calls for an implant assisted overdenture-type prosthesis which can more easily compensate for the discrepancy between the required position of the teeth to be replaced and the actual implant location, when compared to a fixed implant prosthesis. Furthermore, the denture flange can quite efficiently solve shortcomings related to esthetics, phonetics, and/or insufficient labial and facial tissue support. Normally, denture stability and subjective comfort are excellent and – owing to its removable nature – access for oral hygiene is easy (Mericske-Stern 1998; Kiener *et al*. 2001). One should be aware, however, that this approach also has its inherent limits and has to take into account crucial parameters such as phonetics and minimal room required for the tongue. As this chapter focuses primarily on fixed maxillary anterior implant restorations, we refer to the relevant respective literature.

Another approach consists of one of the various lateral bone augmentation procedures reported in

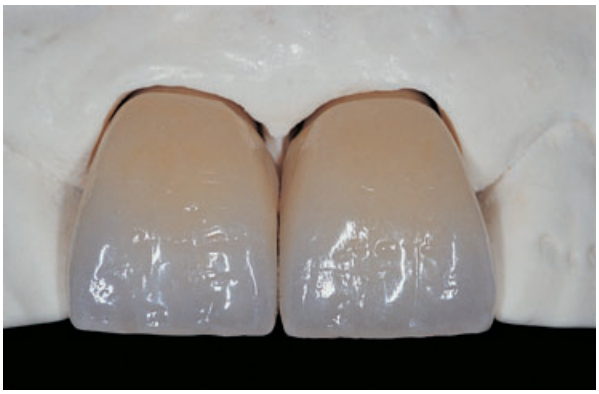

Fig. 53-61 In order to compensate for the reduced height of the inter-implant soft tissue, the ceramist has used an apically prolonged interdental contact line in the form of so-called "mini-wings". These interdental ceramic extensions are made of a more saturated root-like porcelain and are slightly displaced to the palatal aspects of the crowns. This approach results in restorations that integrate successfully, although they are physically larger than the original anatomic crowns.

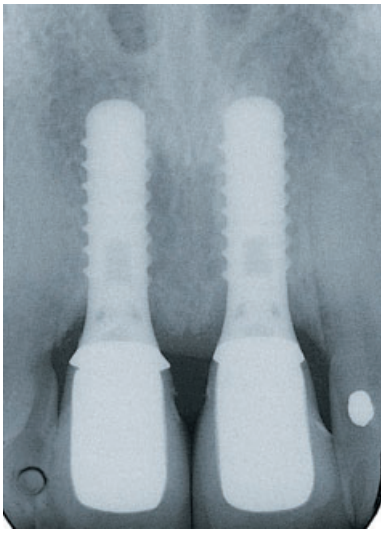

Fig. 53-62 Six years after placement of the 12 mm solid screw titanium implants, the respective radiographs reveal stable conditions at the osseointegrated interface and adequate marginal adaptation.

the literature (Buser *et al*. 1996, 1999, 2002; Chiapasco *et al*. 1999; von Arx *et al*. 2001a,b; Zitzmann *et al*. 2001), which ultimately should lead to a more "restoration-driven" implant placement, ideally compatible with a straightforward fixed implant prosthesis featuring a continuous, flat axial emergence profile. To date a scalloped course of the peri-implant mucosa cannot be predictably achieved around multiple adjacent maxillary anterior fixed implant restorations, and as an increased clinical crown length is normally inherent in this approach as well, the pre-operative assessment of the patient's lip line or smile line (Jensen *et al*. 1999) is of primary importance during the related decision-making process.

Sites with major vertical tissue loss

The replacement of multiple missing adjacent maxillary anterior teeth with a fixed implant prosthesis still represents a major therapeutic challenge in the presence of combined major horizontal and vertical alveolar ridge deficiencies. Vertical bone augmentation techniques, for example the distraction osteogenesis procedure (Chiapasco *et al*. 2001), hold promise for the future but lack clinical long-term documentation at present.

As a consequence, the treatment of choice consists in most instances of an implant-assisted (e.g. spherical attachments, bar devices) removable overdenture.

Conclusions and perspectives

When implants are to be inserted within the esthetic zone in view of a fixed restoration, deep placement – close to or at the alveolar bone crest level – of the shoulder of implants, often specifically designed for this indication, permits the suprastructure margin to be hidden below the mucosa, and the development of a gradual harmonious emergence profile from the implant shoulder to the surface. The resulting clinical crown replicates the profile of the natural control tooth despite a slightly more palatal implant position. This in turn leads to a secondary peri-implant bone loss or bone remodeling – particularly in a case of multiple adjacent implants – due to the reorganization of a biologic width (Hermann *et al*. 1997, 2000, 2001a,b). Under these particular circumstances, screw-retained restorations, based on prefabricated, machined components, will assure a maximum marginal adaptation, favoring the maintenance of the long-term stability of the esthetic result (Belser 1999; Belser *et al*. 1998, 2000). The currently flat, "rotation–symmetrical" design of standard screw-type titanium implants, leading to a marked submucosal implant shoulder position at the interproximal aspect, may not, however, represent the optimal design, in particular in the context of multiple adjacent implants.

Scalloped implant design

As pointed out earlier in this chapter, the traditional implant design may lead to esthetic shortcomings in a case of multiple adjacent maxillary anterior fixed implant restorations. One could hypothesize in this context whether a modified design at the coronal end of the implant, in the sense of a scalloped, more "CEJ-like" configuration, might lead to an improved preservation of peri-implant bone at the interproximal aspect in general, and between adjacent implants in particular. One of the possible design solutions and its anticipated theoretical impact on bone and esthetic parameters are presented in Figs. 53-63, 53-64, and 53-68. More specifically, this approach ultimately aims at creating an inter-implant bone height and resulting soft tissue level situation compatible with generally accepted esthetic criteria. Among these one should primarily mention the establishment and/or maintenance of a harmoniously scalloped course of the marginal peri-implant mucosa. At present, the combination of the following three elements appears important:

Fig. 53-63 Instead of the traditional implant design, featuring a flat rotation–symmetrical coronal aspect, a scalloped connection, inspired by the natural cemento-enamel junction, may lead to a more superficial implant insertion and by this to the preservation of more bone in the interproximal area.

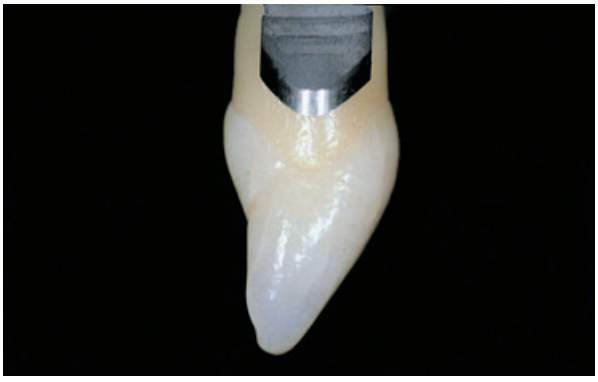

Fig. 53-64 Comparison in the sagittal plane of a natural maxillary central incisor and a titanium implant featuring a scalloped design at its coronal end. The radius corresponds to the amount of bone which might theoretically be preserved.

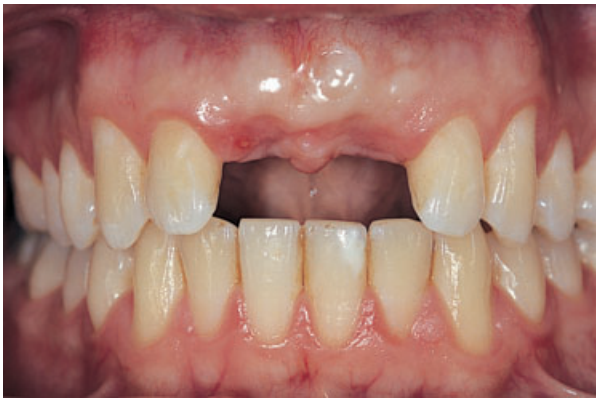

Fig. 53-65 Vestibular view in centric occlusion position of a 24-year-old male patient. The two maxillary central incisors have been lost due to a traumatic injury.

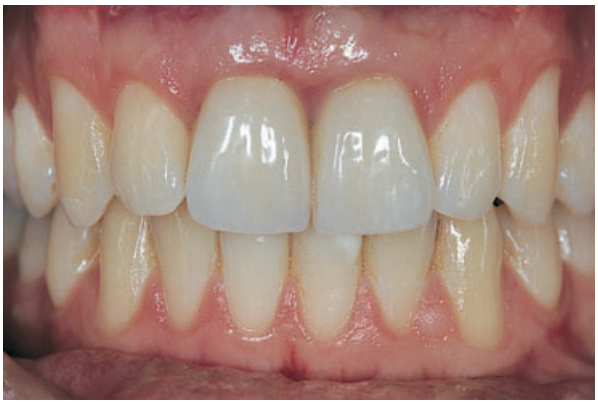

Fig. 53-66 After 1 year of clinical service, there is a harmoniously scalloped marginal soft tissue course, including the most critical inter-implant area.

1. Screw-type titanium implant body, featuring optimal surface characteristics
2. Tooth-colored transmucosal portion with adequate axial emergence profile and scalloped coronal end
3. Mechanically sound suprastructure connection, permitting both screw retention and cementation.

The clinical potential of such a novel, scalloped implant design is documented in Figs. 53-65 to 53-67, presenting a 24-year-old male patient who had lost his two maxillary central incisors in the course of an accident. The 1-year clinical and radiographic follow-up appears to support – at least short-term – the hypothesis that such an approach may preserve inter-implant crestal bone and overlying soft tissue to a certain extent.

Segmented fixed implant restorations in the edentulous maxilla

Another particular challenge from both a surgical and a prosthodontic point of view represents the

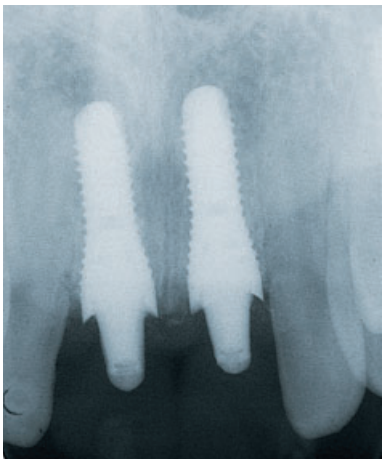

Fig. 53-67 The 1-year follow-up radiograph shows prototype of titanium implants featuring a scalloped design at their coronal end. This design permits a more superficial implant insertion, aiming at a better preservation of inter-implant alveolar bone.

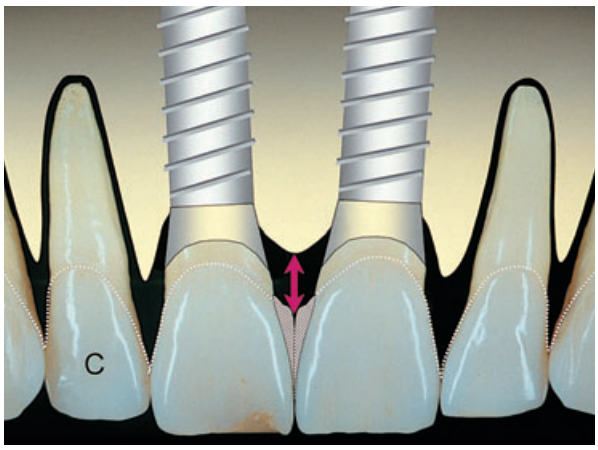

Fig. 53-68 Schematic representation of the theoretical advantages of a scalloped implant design: more superficial implant placement, increased bone and soft tissue preservation particularly in the inter-implant area, and improved esthetics (in combination with interdental "mini-wings").

implant-supported fixed prosthetic rehabilitation of the edentulous maxilla. Undoubtedly esthetic considerations and certain aspects associated with the patient's subjective comfort – both during the actual treatment phase and once the prosthesis is completed – also play a major role in this context. We will limit our reflections to (1) specific aspects of pre-implant diagnosis, (2) the importance of implant number, alignment and spatial distribution, and (3) conception of the suprastructure.

These elements are addressed in the form of a respective clinical case presentation, involving a 67-year-old female patient, edentulous in the maxilla (Figs. 53-69 to 53-89). Besides the traditional clinical and radiologic investigation, an in-mouth try-in of the envisioned treatment objective in the form of a

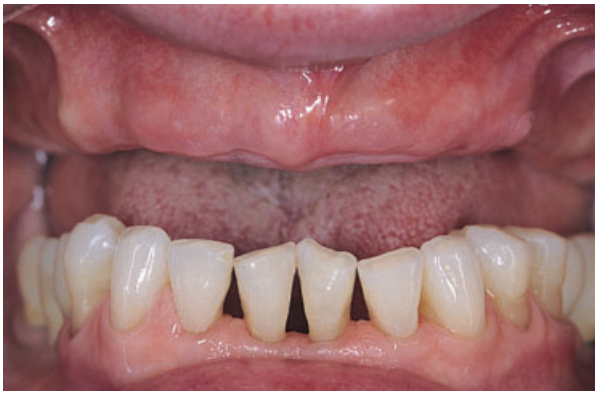

Fig. 53-69 Vestibular view of a 67-year-old female patient, edentulous in the maxilla for 18 months. The pre-existing fixed prosthetic rehabilitation had to be removed due to periodontal disease and was replaced by an immediate complete upper denture to which she never adapted. In the mandible a natural dentition is present to the premolar area.

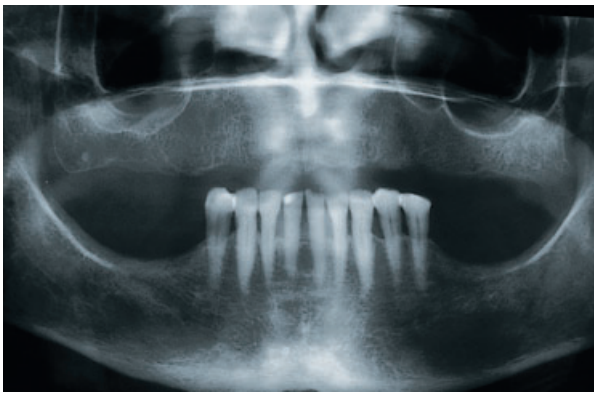

Fig. 53-70 The corresponding panoramic radiograph reveals – at least as far as the vertical bone volume is concerned – favorable conditions in view of implant therapy in both the upper and the lower posterior jaw.

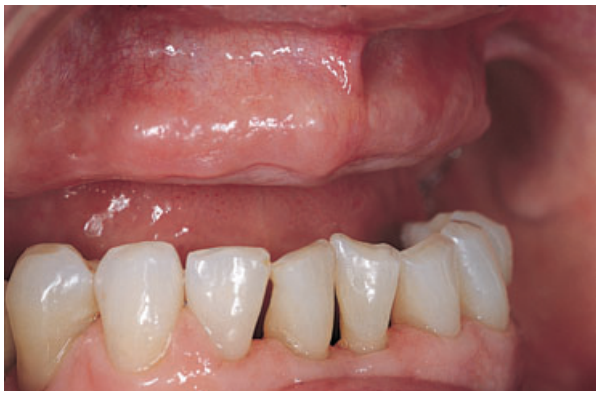

Fig. 53-71 The oblique view confirms the presence of an appropriate intermaxillary relationship which is essential for a fixed implant-supported prosthesis.

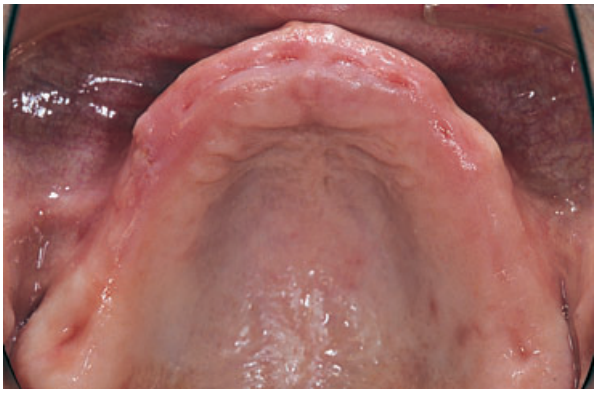

Fig. 53-72 On the occlusal view of the edentulous maxilla, one can note overall favorable conditions for implant therapy and the clinical signs of the recently performed tooth extractions.

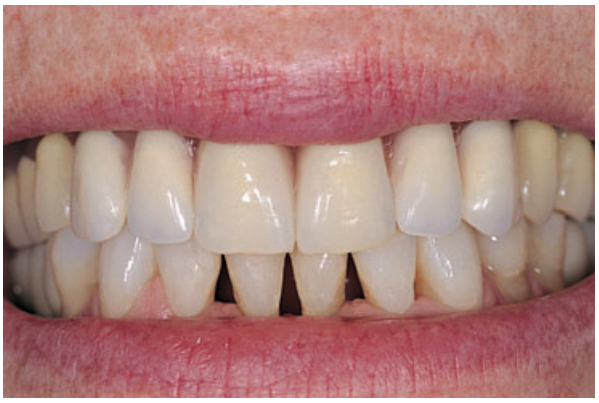

Fig. 53-73 During an unforced smile, the height of the smile line and the eventual need for additional lip support, are evaluated. Both parameters are decisive for the selection between a fixed implant prosthesis or an implant overdenture.

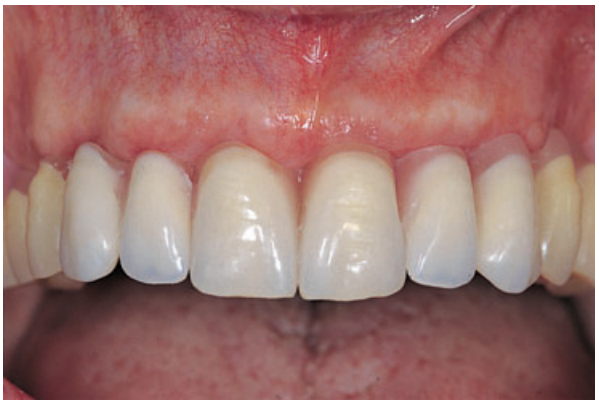

Fig. 53-74 In order to evaluate the feasibility of a fixed implant prosthesis, the clinical try-in of a diagnostic tooth set-up is of paramount importance. One should perform this tooth set-up without vestibular denture flange, so that the patient can realize how long the clinical crowns will be.

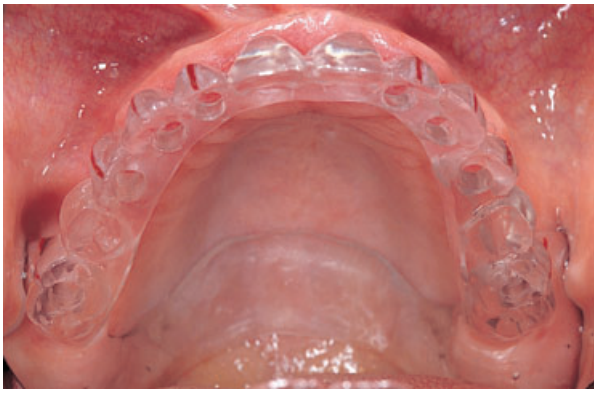

Fig. 53-75 A duplicate of the diagnostic tooth set-up in transparent acrylic will serve as a surgical guide. For optimal stability during surgery, the guide is extended to the posterior palate, an area which will not be concerned by the flap elevation.

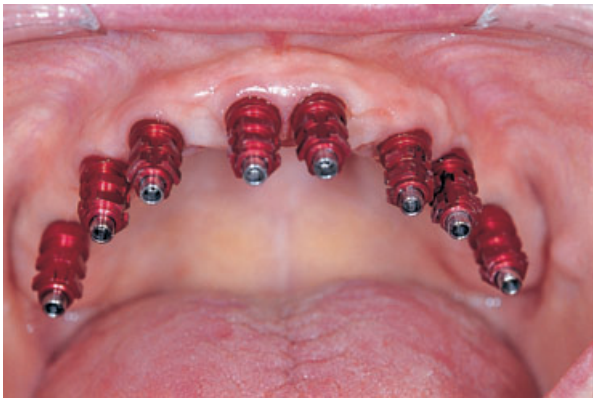

Fig. 53-78 Eight weeks after implant surgery, osseointegration is confirmed radiologically and clinically. Screw-retained impression copings are inserted to perform an implant-level impression.

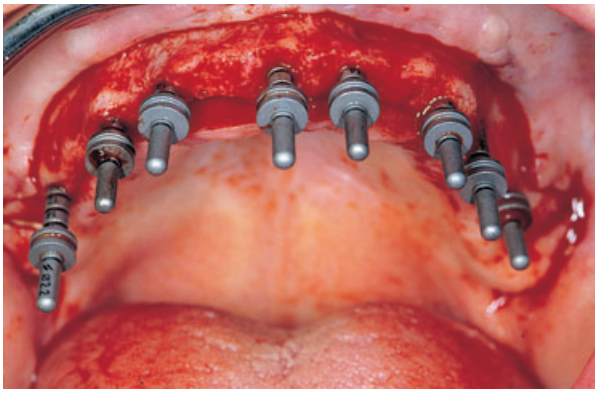

Fig. 53-76 Intrasurgical view of the edentulous maxilla, prepared for the insertion of eight implants to support a fixed prosthesis. Particular attention has been paid to achieving optimal parallelism of the implants by means of a respective surgical guide.

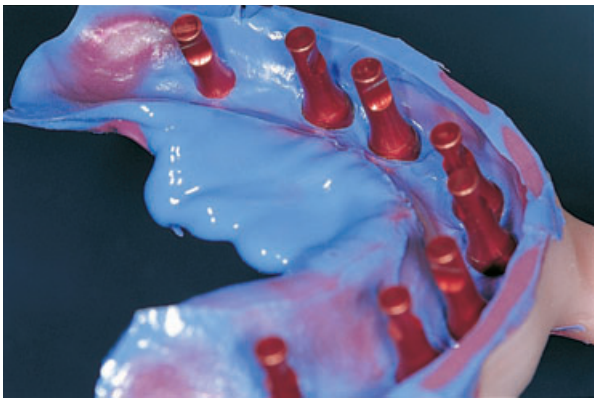

Fig. 53-79 Prior to the master cast fabrication, color-coded implant replicas (analogues) are secured to the respective impression copings.

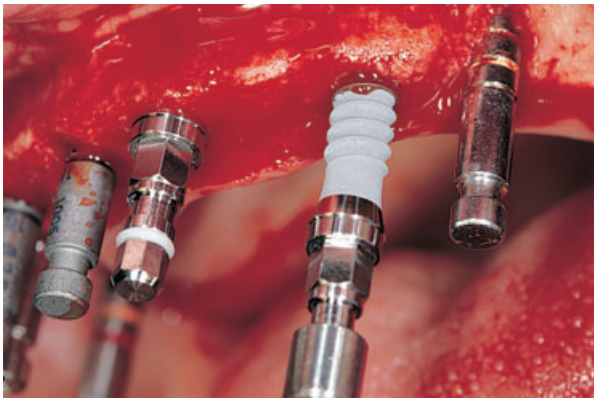

Fig. 53-77 Insertion of a titanium solid screw implant, featuring an SLA surface, in the area of the maxillary left canine.

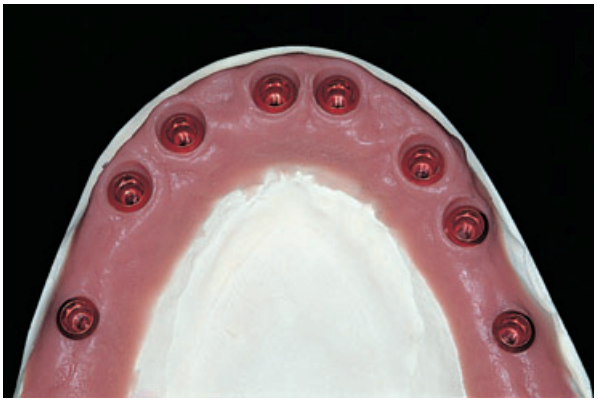

Fig. 53-80 The maxillary master cast features a removable silicon representation of the peri-implant soft tissues.

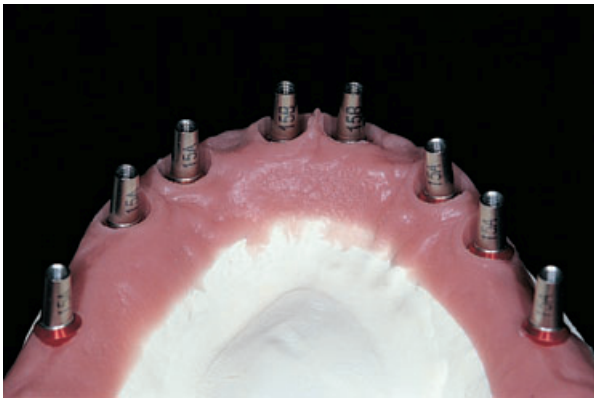

Fig. 53-81 After mounting the master cast in a second-generation, semi-adjustable articulator, the most suitable secondary components (abutments) in view of a cementable fixed implant prosthesis are selected.

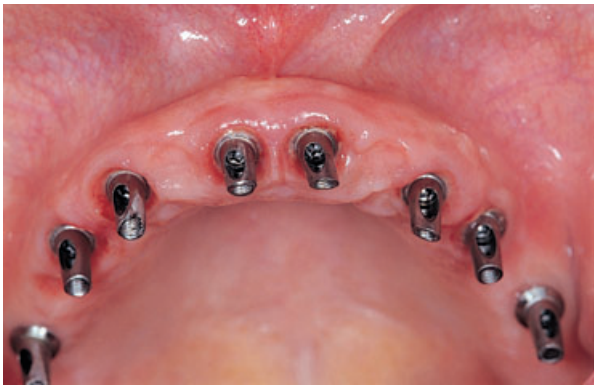

Fig. 53-84 Prior to cementation of the described ceramo-metal suprastructure, the secondary implant components (abutments) are tightened to 35 Ncm with a calibrated torque wrench.

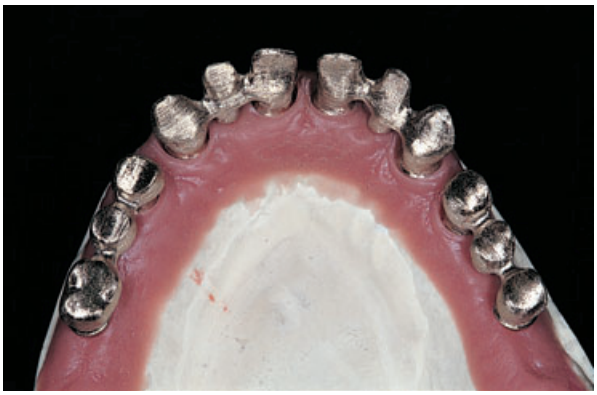

Fig. 53-82 Using a silicon key, derived from the diagnostic wax-up, as a guide, the laboratory technician has fabricated the cast metal framework in the form of four independent three-unit segments. Each segment will be supported by two implants.

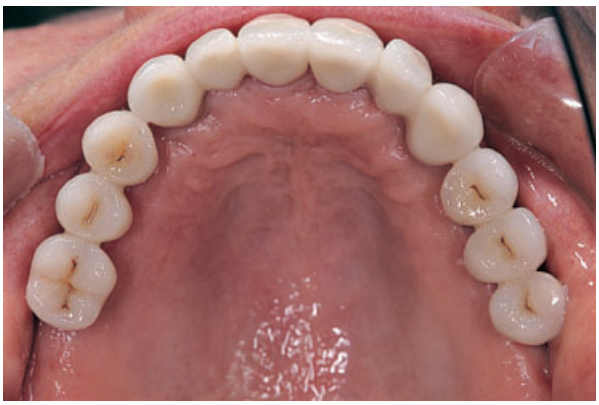

Fig. 53-85 The corresponding clinical view documents that a design similar to that applied in the natural dentition has been used.

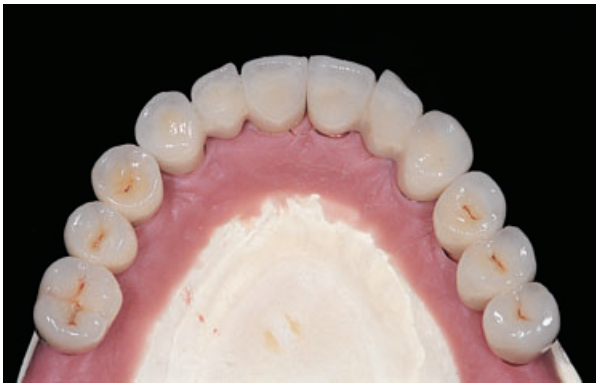

Fig. 53-83 The completed ceramo-metal implant prosthesis on the master cast, ready to be inserted in the patient's mouth.

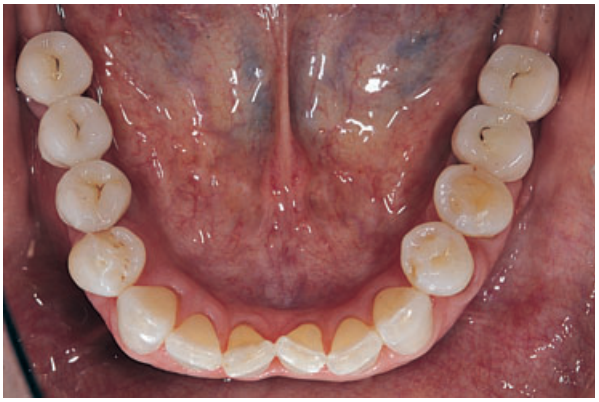

Fig. 53-86 In the mandible the bilaterally shortened arch has been prolonged to the first molar area by means of two fixed cemented ceramo-metal implant prostheses.

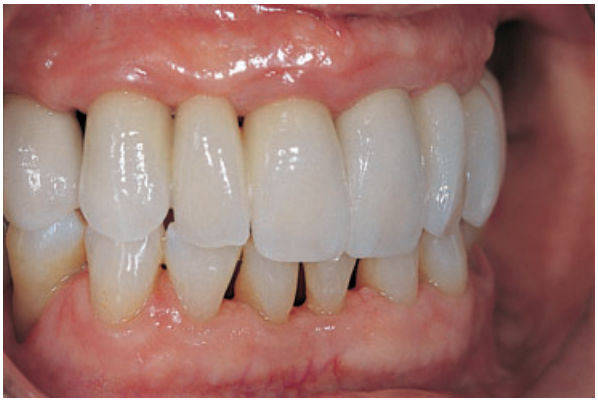

Fig. 53-87 The oblique clinical close-up view of the final implant restoration reveals an acceptable integration both from a functional and an esthetic point of view.

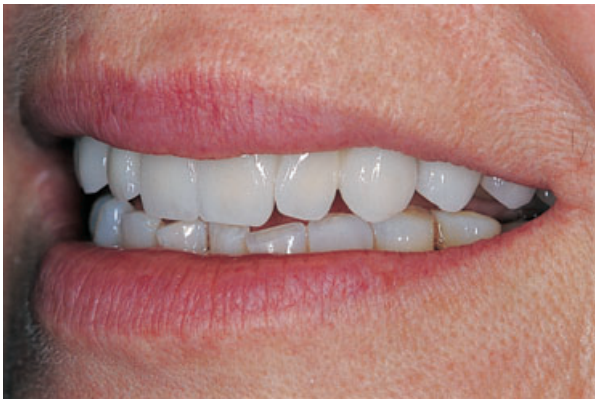

Fig. 53-88 Finally, an esthetically pleasing result could be achieved by means of a fixed implant-supported prosthesis.

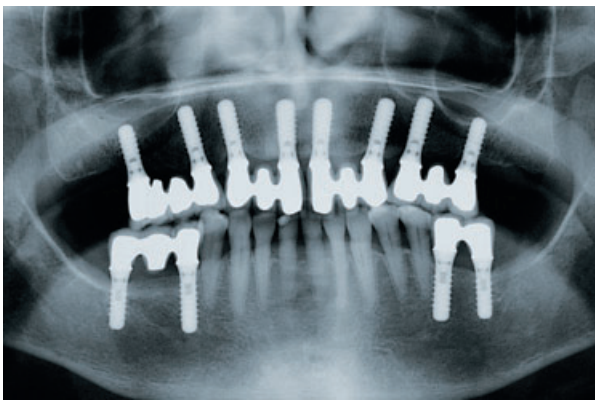

Fig. 53-89 The 1-year post-operative panoramic radiograph confirms osseointegration and documents that the maxillary prosthesis has been completed in four independent segments.

set-up of teeth without vestibular denture-type flange is of primary importance (Fig. 53-73). Among other aspects, this approach will allow the visualization of the length of the clinical crowns of the future fixed implant prosthesis, and the evaluation of whether a fixed prosthesis will provide sufficient lip and facial support (Fig. 53-74). A surgical guide, derived from the described tooth set-up, will guarantee that the future implant positions are in accordance with the determined tooth positions. Whenever possible, parallelism of implants is recommended, as it permits an eventual early or immediate loading approach (Szmukler-Moncler *et al*. 2000; Cooper *et al*. 2001; Andersen *et al*. 2002; Cochran *et al*. 2002), and facilitates the subsequent clinical and laboratory procedures. Although little scientific evidence exists to indicate how many implants of which dimension and in what position are required for a predictable and long-lasting fixed implant rehabilitation of an edentulous maxilla, some clinical trends – mostly derived from traditional prosthodontic experience – do exist. If one plans to extend the prosthesis to the first molar area, and if the anatomic conditions allow the use of standard-size (length and diameter) implants, between six and eight implants seem reasonable. However, in order to increase the overall prosthetic versatility and to be able to apply the principle of segmenting, which includes the ease of eventual re-interventions in a case of localized complications (Priest 1996; Goodacre *et al*. 1999; Lang *et al*. 2000; Johnson & Persson 2001), eight implants may be considered adequate. The recommended respective positions are on both sides of the jaw: the sites of the central incisors, the canines, the first premolars, and the first molars (Fig. 53-76). This approach will ultimately allow the fabrication of four independent three-unit FPDs, with all the related technical and clinical advantages (Figs. 53-78 to 53-89). Some of the scientific data available to date and supporting the concept of smaller segments rather than full-arch splinting will be presented and discussed in Chapter 54.

In conclusion, the concepts and therapeutic modalities do exist nowadays to solve – by means of implants – elegantly as well as predictably a majority of clinical situations requiring the replacement of missing teeth in the esthetic zone, and the most promising novel approaches and perspectives can already be identified on a not too distant horizon.

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Chapter 54

Implants in the Posterior Dentition

Urs C. Belser, Daniel Buser, and Jean-Pierre Bernard

Basic concepts

General considerations

The overall favorable long-term survival and success rates reported in the recent literature for osseointegrated implants in the treatment of various types of edentulism (Brånemark *et al*. 1995; Jemt *et al*. 1996; Lindqvist *et al*. 1996; Buser *et al*. 1997, 1998b, 2002; Andersson *et al*. 1998; Eckert & Wollan 1998; Lindh *et al*. 1998; Mericske-Stern 1998; ten Bruggenkate *et al*. 1998; Wyatt & Zarb 1998; Gunne *et al*. 1999; Lekholm *et al*. 1999; Van Steenberghe *et al*. 1999; Wismeijer *et al*. 1999; Behneke *et al*. 2000; Hosny *et al*. 2000; Hultin *et al*. 2000; Weber *et al*. 2000; Boioli *et al*. 2001; Gomez-Roman *et al*. 2001; Kiener *et al*. 2001; Mengel *et al*. 2001; Oetterli *et al*. 2001; Zitzmann *et al*. 2001; Bernard & Belser 2002; Haas *et al*. 2002; Leonhardt *et al*. 2002; Romeo *et al*. 2002) permit consideration of dental implants as one of the reliable therapeutic modalities during the establishment of any prosthetic treatment plan. In numerous clinical situations implants can clearly contribute to a notable simplification of therapy, frequently enabling removable prostheses to be avoided, keeping it less invasive with respect to remaining tooth structure or rendering the treatment both more elegant and versatile as well as more predictable (Belser *et al*. 2000).

As part of a textbook focusing essentially on clinical periodontics, this chapter will address primarily implant therapy performed in the posterior segments of partially edentulous patients. In this context, the use of implants may often significantly reduce the inherent risk of a "borderline" conventional tooth-borne fixed prosthesis (e.g. compromised or missing "strategic" abutment teeth, long-span fixed partial dentures, cantilevers) by implementing the principle of segmentation. It is currently widely accepted that – in comparison with extended splinted prosthetic segments – small ones are preferable as they are easier to fabricate, generally provide improved "passive fit" and marginal fidelity, offer better access for the patient's oral hygiene, and ultimately are less complicated to handle where there is need for re-intervention. When it comes to treatment planning in general, and to the choice *implant versus tooth-borne fixed partial denture (FPD) versus tooth* in particular, the related decision-making criteria should be essentially derived from scientific evidence and objective prosthetically oriented risk assessment in the broad

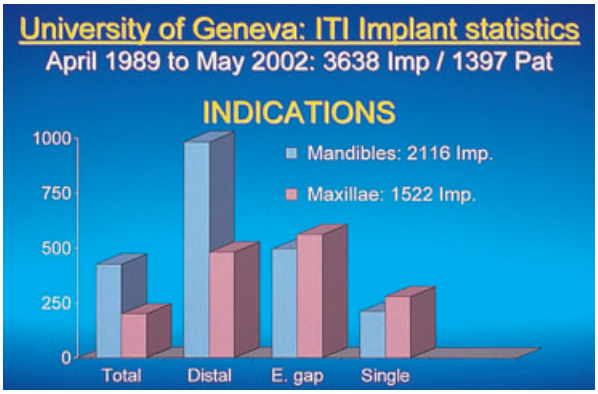


Fig. 54-1 University of Geneva implant statistics, 1989–2002. Indications.

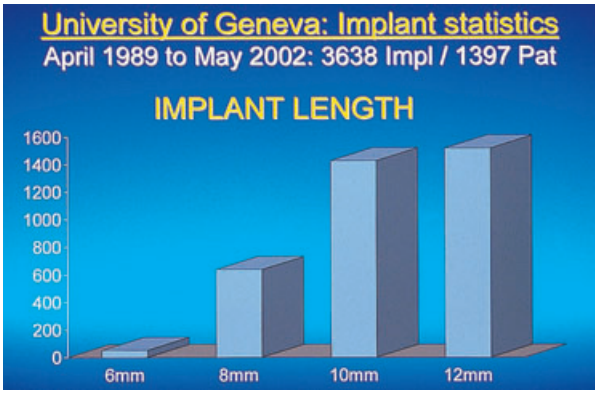


Fig. 54-2 University of Geneva implant statistics, 1989–2002. Implant length distribution.

sense, including additional parameters such as simplicity, cost effectiveness, and quality of life. Beyond any doubt, the advent of osseointegration has had a fundamental impact on the therapeutic approach and strategies implemented today in the field of prosthetic rehabilitation of the compromised posterior dentition. The implant statistics of the University of Geneva School of Dental Medicine, for example, reveal that from April 1989 until May 2002 more than 3600 implants of 6–12 mm length were inserted in about 1400 patients presenting with different types of edentulism (Figs. 54-1, 54-2). This treatment method is increasingly applied worldwide and has had a tremendous influence on traditional prosthodontic attitudes (Beumer *et al*. 1993; Zarb & Schmitt 1995; Tarnow *et al*. 1997; Zitzmann & Marinello 1999; Belser *et al*. 2000; Schwarz-Arad & Dolev 2000; Brägger *et al*. 2001; Deporter *et al*. 2001; Zitzmann & Marinello 2002). Since most of the established dental implant systems today comprise a wide range of mostly screw-type implants with different diameters and dimensions to replace missing premolars and molars (Fig. 54-3), the versatility of implant therapy in the load-carrying part of the dentition of partially edentulous patients has been significantly enhanced.

Numerous other indications have been added to the so-called classical indications for the use of

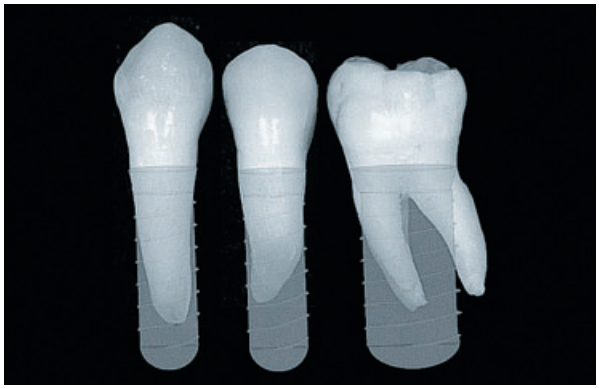


Fig. 54-3 Different implant diameters are available for the replacement of posterior teeth.

implants, i.e. severely atrophied edentulous jaws, missing teeth in otherwise intact dentitions (congenitally missing teeth; tooth loss due to trauma or due to a localized endodontic/restorative/periodontal complication or failure), and the distally shortened dental arch (particularly when premolars are missing). Among these other indications one should mention all the strategies aiming at either reducing the prosthodontic risk in general or rendering the treatment simpler and more cost effective. Virtually no limits for the placement of implants seem to exist any more owing, for example, to advanced bone augmentation techniques, comprising anterior sinus floor elevation and distraction osteogenesis (Buser *et al*. 1993, 1995, 1996, 1998a, 2002; Chiapasco *et al*. 1999, 2001a; Buser & von Arx 2000; Simion *et al*. 2001; von Arx *et al*. 2001a,b).

When it comes to the technique of placing implants in the posterior segments of the jaws, a one-step non-submerged surgical protocol can be associated with notable advantages. On the one hand, healing of the peri-implant soft tissues occurs simultaneously with osseointegration, and on the other hand the location of the junction between the implant shoulder and the secondary components is normally positioned close to the mucosal surface. It is ultimately the position of this junction which determines the apical migration of the peri-implant epithelium and the crestal bone level, once the so-called biologic width has been established (Abrahamson *et al*. 1997; Hermann *et al*. 1997, 2000, 2001a,b; Lindhe & Berglundh 1998; Engquist *et al*. 2002; Wyatt & Zarb 2002). Positioning of the transition between implant shoulder and secondary components at the level of the mucosa rather than at the crestal bone also represents a biomechanical advantage, as it contributes to the reduction of the lever effect and resulting bending moments acting on the junction between implant and suprastructure. This is clinically relevant, as one should be aware of the existence of an increasing body of evidence reporting technical complications, such as loosening/fracture of screws or fracture of components/veneers, related to implant-supported prosthetic suprastructures (Lundgren & Laurell 1994; Wie 1995;

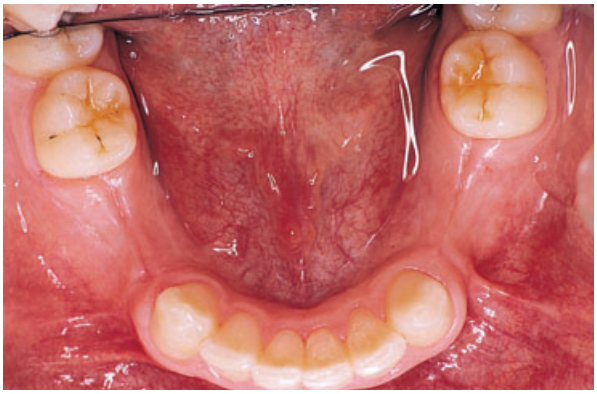


Fig. 54-4 Occlusal view of the mandible of a 22-year-old male patient. All premolars are congenitally missing, the remainder of the dentition is intact.

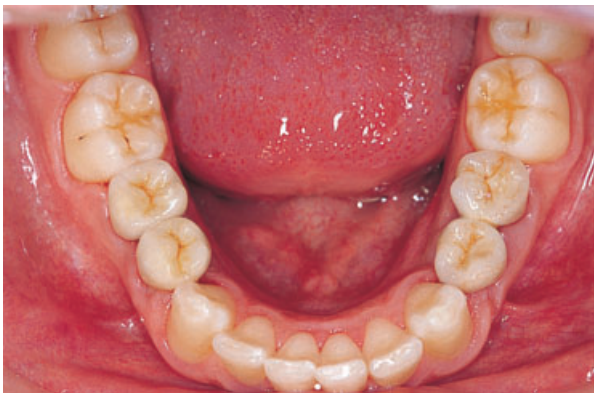


Fig. 54-5 Final view after insertion of four implants, restored with cemented metal–ceramic suprastructures.

Hebel & Gajjar 1997; Rangert *et al*. 1997; Bosse & Taylor 1998; Glantz & Nilner 1998; Taylor 1998; Brägger 1999; Goodacre *et al*. 1999; Isidor 1999; Keith 1999; Schwarz 2000; Johnson & Persson 2001). Besides mechanical types of complications, a number of other conditions that are rather biologic in nature, for example peri-implantitis, are reported in the recent literature (Ellegaard *et al*. 1997a,b; Ellen 1998; Lang *et al*. 2000; Brägger *et al*. 2001; Quirynen *et al*. 2001, 2002). As these are addressed in detail in another chapter, we will only focus on aspects related to fixed posterior implant restoration design and maintenance.

It is the aim of this chapter to present clinically oriented guidelines and procedures for implant therapy of various types of edentulism located in the load-carrying part of the dentition, addressing primarily the partially dentate patient and mainly focusing on fixed implant-supported prostheses.

Indications for implant restorations in the load carrying part of the dentition

When it comes to partial edentulism in the posterior segments of the jaws, implants are increasingly used either to preserve sound mineralized tooth structure or to avoid removable partial dentures (RPDs) and high-risk conventional fixed partial dentures (FPDs). This includes situations with missing teeth in otherwise intact dentitions (Figs. 54-4, 54-5), the distally shortened dental arch (Figs. 54-6 to 54-8), extended edentulous segments, missing "strategic" tooth abutments, and structurally, endodontically or periodontally compromised potential abutment teeth (Table 54-1).

The rapid advance in terms of the broad utilization of dental implants is not exclusively based on the associated favorable long-term reports for this treatment modality. Other parameters such as purely "mechanical" advantages and the availability of prefabricated components and auxiliary parts, which in turn contribute notably to the simplification of the treatment, had a significant impact on current con-

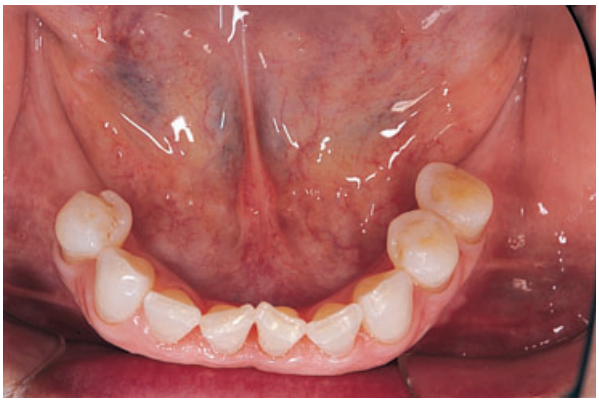


Fig. 54-6 Bilaterally distally shortened dental arch in the mandible of a 66-year-old female patient.

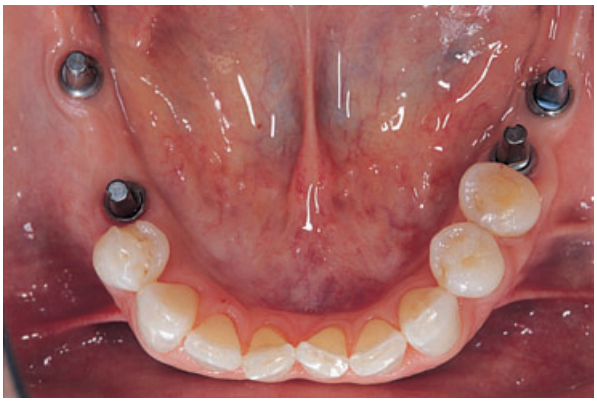


Fig. 54-7 Four implants have been inserted to lengthen the arch bilaterally to the region of the first molars.

cepts and strategies as well (Table 54-2). Furthermore, clinical decision making based on prosthetically oriented risk assessment (Table 54-3), frequently leads to the need for an increased number of abutments. The objective is to reduce the overall risk associated with a given prosthetic solution on the one hand, and to implement the principle of segmenting on the other.

A representative clinical example is given in Figs. 54-9 and 54-10. Instead of a conventional five-unit

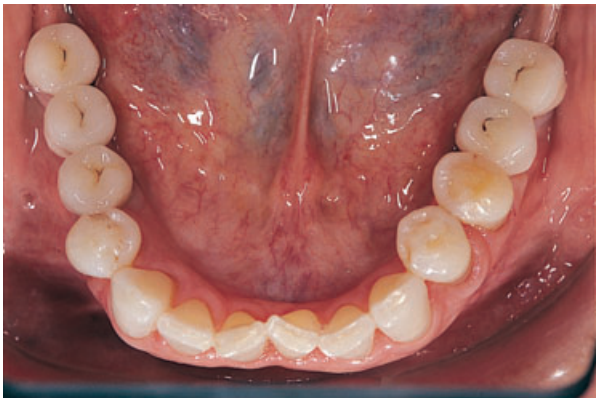


Fig. 54-8 Five premolar-sized metal–ceramic elements were used to restore the four implants.

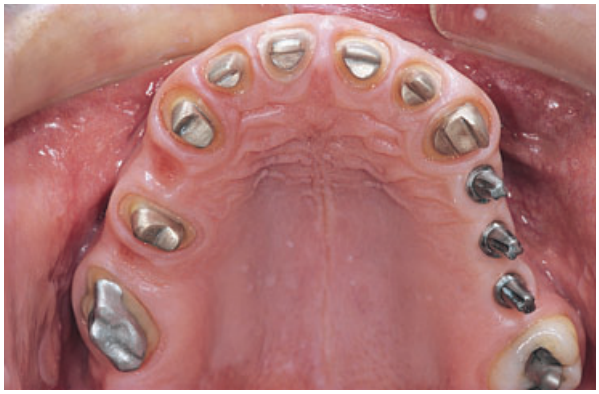


Fig. 54-9 Maxillary occlusal view displaying natural and implant abutments prior to the insertion of an extended porcelain-fused-to-metal restoration. In order to avoid a high-risk long-span FPD, three implants have been added in the left posterior segment.

Table 54-1 Indications for posterior implants

- Replacement of missing teeth in intact dentitions (e.g. congenitally missing premolars), i.e. preservation of tooth structure
- Avoidance of removable partial dentures (RPDs)
- Increase of the number of abutments:
  - Reduction of the prosthetic risk
  - Application of the principle of segmenting
  - Ease of eventual reinterventions
- Maintenance of pre-existing crowns and FPDs
- Following prosthetic complications and failures

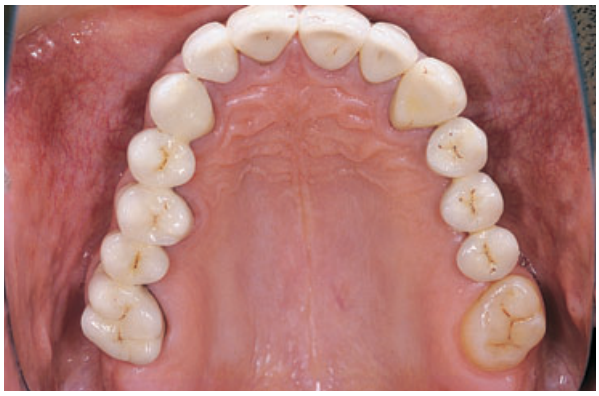


Fig. 54-10 A similar restorative design has been chosen for both natural and implant-supported metal–ceramic suprastructures.

Table 54-2 Impact of dental implants related to the treatment of posterior partial edentulism

- Favorable overall long-term results
- Preservation of mineralized tooth structure
- "Mechanical" advantages:
  - Commercially pure (c.p.) titanium (biocompatibility, mechanical properties, no risk for caries)
  - Reproducible, prefabricated ("machined") primary, secondary and tertiary components and auxiliary parts
- Simplified clinical and laboratory protocols

Table 54-3 "High risk" conventional fixed partial dentures (FPDs)

- Long-span fixed partial bridges
- Cantilever units (mainly distal extensions)
- Missing "strategic" tooth abutments
- Structurally/periodontally/endodontically compromised tooth abutments
- Reduced interarch distance
- Presence of occlusal parafunctions/bruxism

FPD, replacing the missing maxillary left first and second premolars as well as the absent first molar, three implants have been inserted. This approach allowed the avoidance of a long-span bridge, a full coverage preparation of the second molar, and an associated surgical crown-lengthening procedure. The additional cost related to the three implants was justified by an overall reduced prosthodontic risk. The question about adequate number, size, and distribution of implants will be addressed later in this chapter. Prosthetically oriented risk assessment comprises the comprehensive evaluation of potential natural abutment teeth, including their structural, restorative, periodontal, and endodontic status. Several well documented treatment modalities are often possible to replace missing posterior teeth, so this objective evaluation is of primary importance and represents an ever increasing challenge to the clinician. This is illustrated by a maxillary posterior segment where both the first premolar and the first molar were missing (Figs. 54-11 to 54-14). The insertion of a five-unit tooth-borne FPD was discarded because of its too invasive nature related to the intact canine, and owing to a slightly questionable status of

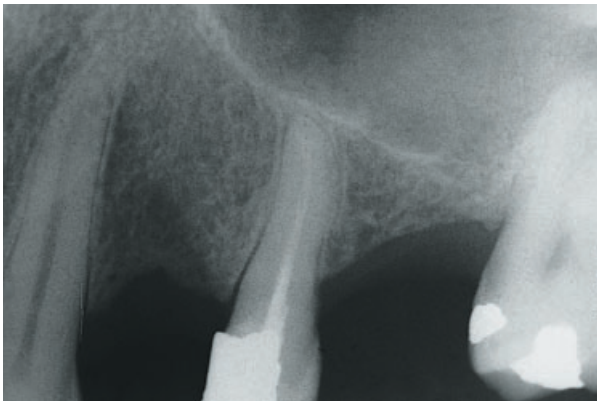


Fig. 54-11 Pre-operative radiograph of the left maxilla, revealing two missing dental elements. One should note in particular an intact canine, a structurally reduced second premolar, and an extended recessus of the sinus in the area of the missing first molar.

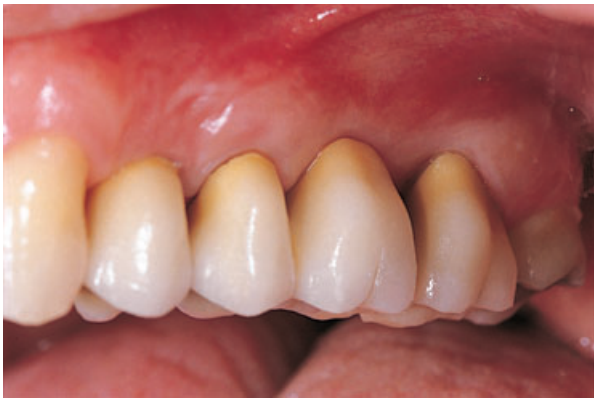


Fig. 54-12 Vestibular view of the prosthetic rehabilitation of the maxillary left quadrant: an implant-supported single-tooth restoration on the site of the first premolar, and a three-unit tooth-borne FPD to replace the missing first molar.

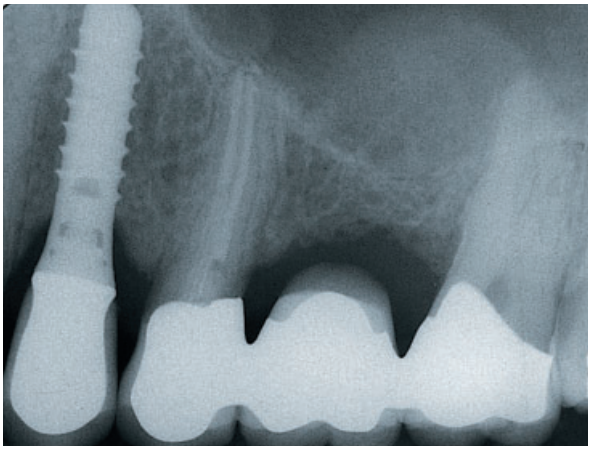


Fig. 54-13 The post-operative radiograph documents that an endodontic revision has been performed on the second premolar prior to its restoration with an adhesive carbon-fibre-post based build-up and a metal–ceramic crown (bridge retainer).

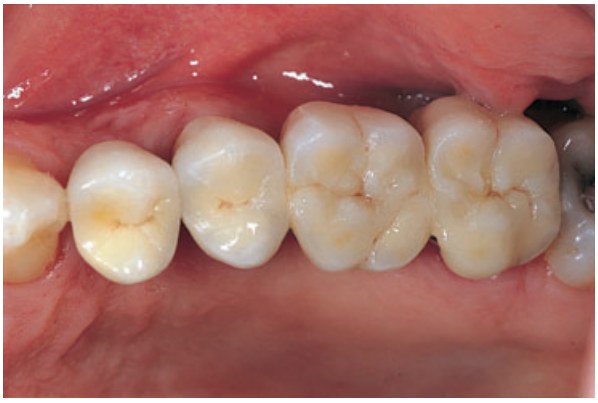


Fig. 54-14 An identical prosthetic design has been applied for both the implant-supported and the tooth-supported restoration.

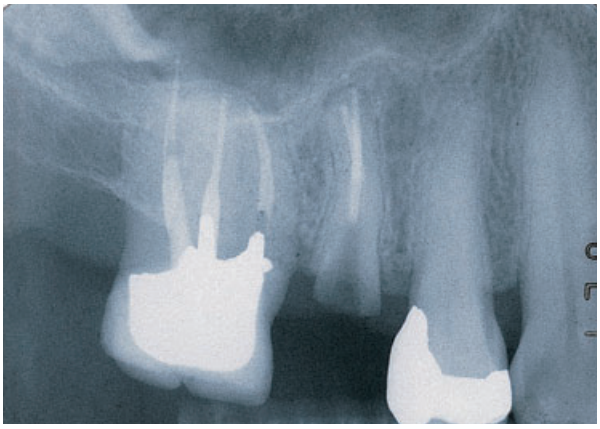


Fig. 54-15 Ad hoc radiograph of the upper right posterior sextant. One notes the presence of a structurally compromised second premolar. The treatment of that particular root would require build-up and crown lengthening (margin exposure, creation of an adequate ferrule) which in turn would negatively affect the adjacent teeth.

the endodontically treated second premolar in view of its eventual use as so-called "peer-abutment". Finally, an implant has been placed at the site of the missing first premolar and subsequently restored with a single-unit restoration. As the proximity of the maxillary sinus at the location of the missing first molar would have required a grafting procedure to make an implant installation possible, a three-unit tooth-supported FPD was ultimately chosen, after having duly discussed the respective advantages and shortcomings with the patient. Having attributed a "strategic value" to the moderately compromised second premolar by using it as abutment of a short-span bridge, there was still a difficulty in consistently establishing clinical treatment plans that were fully based on scientific evidence.

Still under the influence of the high level of predictability and longevity reported for implant therapy, the clinician is currently not only pondering implant-borne restorations versus conventional FPDs, but increasingly implant versus maintaining a compromised tooth (Figs. 54-15, 54-16). In this

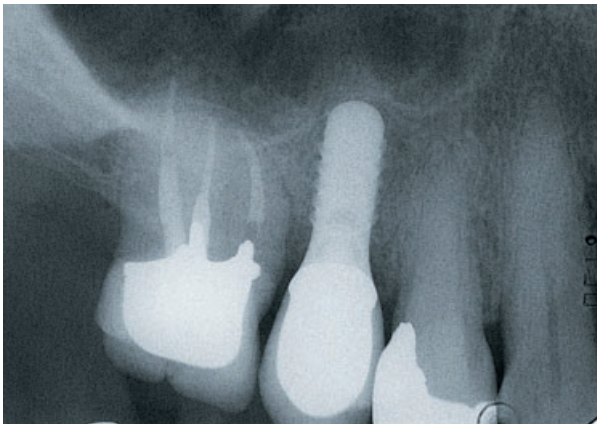


Fig. 54-16 The post-operative radiograph documents that the root of the second premolar has been replaced by a single-tooth implant restoration. In particular, the pre-existing metal–ceramic crown on the first molar could be maintained by this approach.

particular clinical case, the evaluation focused on whether or not it was objectively opportune to restore the structurally compromised root of a maxillary second premolar. This would have required – after elimination of the decayed dentin – a surgical crown-lengthening procedure to create access to the margin, which in turn would have included the risk for an adverse effect (furcation proximity of the adjacent first molar) on the neighboring teeth. Furthermore, a three-unit FPD was out of the question for obvious reasons. Based on this rationale and in the context of a more comprehensive analysis of the situation, it was finally decided to extract a *per se* treatable root and to replace it by an implant. One should never forget, however, that this trend to consider, under certain circumstances, an implant as a better solution than "acrobatically" treating a severely compromised tooth, calls for well defined evidence-based respective criteria and represents a non-negligible ethical responsibility for the clinician.

Controversial issues

Despite the ever-growing body of scientific evidence indicating that implant therapy in the partially edentulous patient is an overall highly predictable treatment modality, several conceptional issues remain controversial to date (Table 54-4). These controversial issues include open questions addressing adequate number, size, and distribution of implants for optimal therapy of a given type and configuration of partial edentulism, as well as parameters related to occlusion and occlusal materials, to implant axis, to the minimal acceptable ratio between suprastructure height and implant length, and – last but not least – related to questions focusing more specifically on the mechanical aspects and requirements of posterior implant prosthodontics. Among these, the kinds of connection between implant and abutment have to be mentioned in particular. Most of these questions will be discussed in the remainder of this chapter, at length where possible and appropriate, or more superficially when solid information is missing or when the topic is more adequately covered by other authors in this book.

Table 54-4 Controversial issues related to posterior implant restorations

- Adequate number, size (length/diameter), configuration and distribution of implants
- Cemented versus screw-retained (transocclusal/transverse screw retention)
- Single units versus splinted adjacent implant restorations
- Longest possible versus shorter implants
- Impact of implant axis
- Optimal implant shoulder sink depth
- Minimal ratio between implant length and suprastructure height
- Combination of natural teeth and implants in the same restoration
- Design of the optimal abutment-to-implant connection
- Implant-specific occlusal concepts, including occluding restorative materials, non-axial loading, type of guidance during mandibular excursions
- Healing times prior to functional loading (immediate/early/delayed)
- Significance of offset/staggered implant positioning

Restoration of the distally shortened arch with fixed implant-supported prostheses

As pointed out earlier in this chapter, from 1989–2002 the distally shortened arch represented the most frequent indication for the use of implants at the University of Geneva School of Dental Medicine. In fact, out of a total of 3638 implants, almost 1500 were placed in distally shortened arches, with close to 1000 implants inserted in the mandible and about 500 in the posterior maxilla (Fig. 54-1). Implants were primarily used when premolars were also missing. Whenever possible, the adopted treatment strategy consisted of restoring the shortened dental arch to the region of the first molars. Occasionally, implant therapy was restricted to the premolar area, according to the principles of the well established premolar occlusion concept, or extended to the second molar area if an antagonistic contact had to be established for an opposing natural second molar.

Number, size, and distribution of implants

It is still unclear to date how many implants of which dimension at which location are required to optimally rehabilitate a given edentulous segment in the load-carrying part of the dentition. Several different respective recommendations and related strategies are currently in use, mostly derived from traditional prosthodontic experience and attitudes, and based on so-called clinical experience and common sense

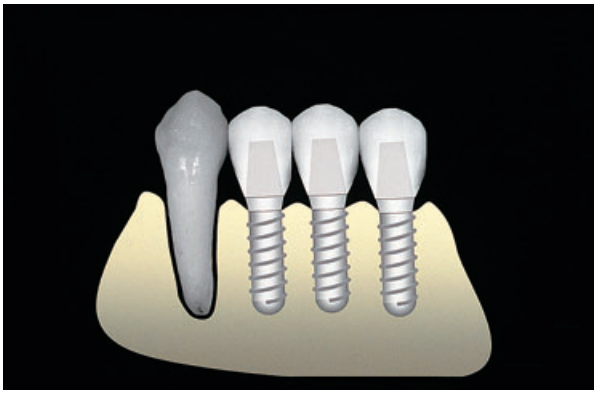


Fig. 54-17 Schematic representation of the distally shortened dental arch. One therapeutic option consists of replacing each missing occlusal unit up to the first molar area with an implant.

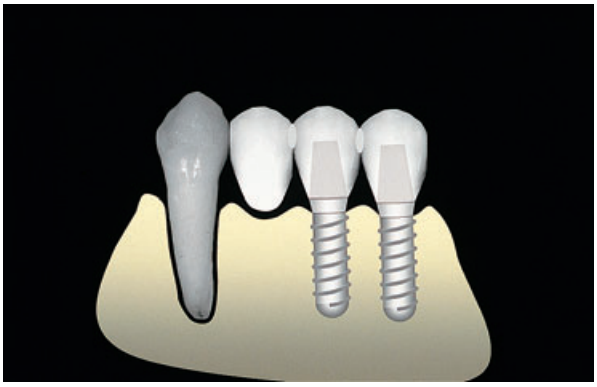


Fig. 54-19 In a case of an inadequate bone volume in the area of the missing first premolar, the placement of two distal implants may be considered, leading to a three-unit suprastructure with a mesial cantilever.

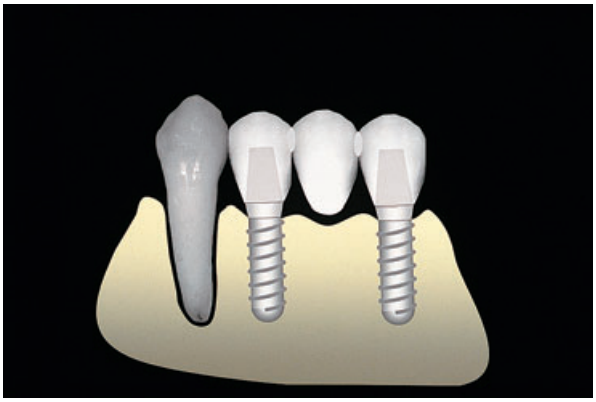


Fig. 54-18 An alternative option would be the replacement of the three missing occlusal units by two implants to support a three-unit suprastructure with a central pontic.

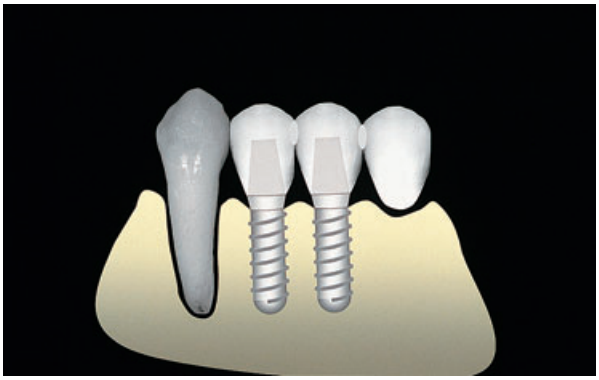


Fig. 54-20 In a case of an inadequate bone volume in the area of the missing first molar, the placement of two mesial implants may be considered, leading to a three-unit suprastructure with a distal cantilever.

rather than on solid scientific evidence. In defense of the situation one should be aware, however, that it is often difficult to design and carry out randomized clinical trials evaluating exclusively and without interference one specific parameter of conceptual relevance.

In a situation where the canine is the most distal remaining tooth of a dental arch, at least five different options can be taken into consideration if one plans to replace the missing teeth up to the first molar area (Figs. 54-17 to 54-21). These include the replacement of each missing occlusal unit by one implant (Fig. 54-17), a mesial and a distal implant to support a three-unit FPD with a central pontic (Fig. 54-18), two distal implants to permit the insertion of a three-unit FPD with a mesial cantilever (Fig. 54-19), two mesial implants to sustain a three-unit FPD with a distal cantilever (Fig. 54-20) and, finally, only one distally inserted implant in view of a four-unit FPD combining implant and natural tooth support (Fig. 54-21).

As far as the recommendation to use premolar-sized units for implant-borne posterior FPDs is concerned, it has proven its practical validity in more than 10 years of clinical experience (Buser *et al*. 1997;

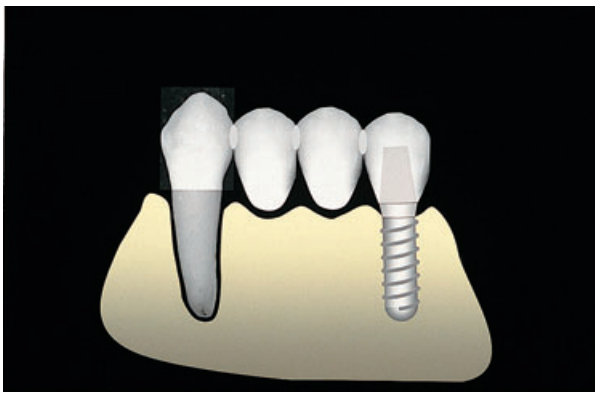
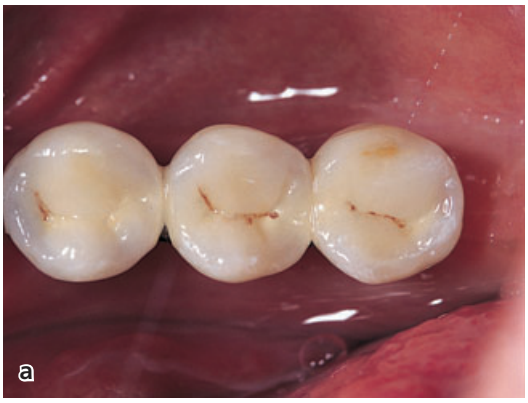


Fig. 54-21 In a case of inadequate bone volume in the area of the two missing premolars, the placement of a distal implant may be considered, leading to a four-unit suprastructure with a mixed (tooth and implant) support.

Bernard & Belser 2002). In fact, a crown featuring a mesio-distal diameter of 7–8 mm at its occlusal surface allows the optimal generation of a harmonious axial profile, gradually emerging from the standard implant shoulder (diameter 4–5 mm on average) to the maximum circumference. In addition, the



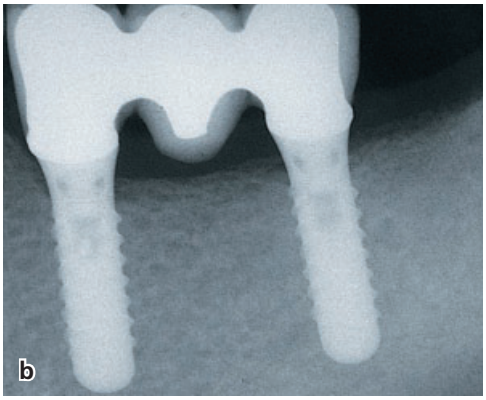


Fig. 54-22 (a) Occlusal view of a cemented three-unit metal–ceramic FPD, supported by a mesial and a distal implant. (b) The corresponding 3-year follow-up radiograph confirms stable conditions at the implant to bone interface of the two 12 mm solid screw implants.

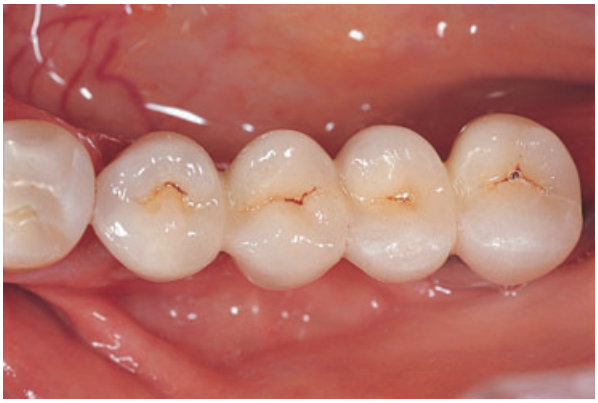


Fig. 54-23 Occlusal view of a cemented four-unit metal–ceramic FPD supported by a mesial and a distal implant.

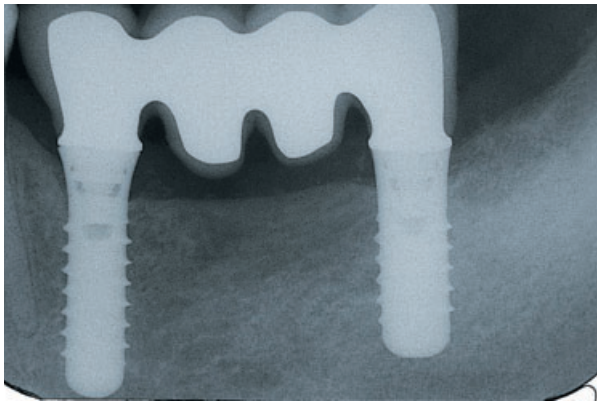


Fig. 54-24 The related 2-year follow-up radiograph documents that at the distal site a 10 mm solid screw implant with an increased diameter ("wide-body implant") has been used.

width of the occlusal table is confined, thereby limiting the risk for unfavorable bending moments to the implant–abutment–suprastructure complex (Belser *et al*. 2000).

Based on an increasing body of scientific evidence, most clinicians' first choice represents the mesial and distal implant and the respective FPD with the central pontic (Fig. 54-22). Prospective long-term multicenter data (Buser *et al*. 1997; Bernard & Belser 2002) have confirmed the efficacy and predictability of this specific modality. In fact, it permits the defined treatment objective with a minimal number of implants and associated costs. Although presently still lacking formal evidence at the level of prospectively documented, randomized clinical trials, it appears from clinical experience that the use of two implants to support a four-unit FPD with two central pontics (Figs. 54-23, 54-24) may be adequate in certain clinical situations. Clinicians tend to use this approach in the presence of favorable bone conditions, permitting standard-size or wide-diameter implants with appropriate length (i.e. 8 mm or more).

If the alveolar bone crest dimension is also sufficient in an oro-facial direction, the utilization of wide-diameter/wide-platform implants is preferred. Due to their increased dimensions a more adapted suprastructure volume and improved axial emergence profile of the implant restoration – when compared to a so-called premolar unit – can be achieved in the molar area (Figs. 54-25 to 54-28). By this token the intercuspation with an opposing natural molar is also facilitated.

Implant restorations with cantilever units

There is strong evidence in the relevant dental literature that cantilever units – in particular distal extensions – of conventional tooth-borne FPDs are associated with a significantly higher complication rate when compared to FPDs featuring a mesial and a distal abutment and a central pontic. Respective failure rates could be attributed to decisive factors such as non-vital abutment teeth as well as specific occlusal conditions such as a reduced interarch distance and/or occlusal parafunctions (Glantz & Nilner 1998). These authors concluded in their review of the current relevant literature that risks were lower for mechanical failures with cantilevered implant-borne reconstructions than with comparable conventional fixed situations. Risks, however, do exist. As loss of

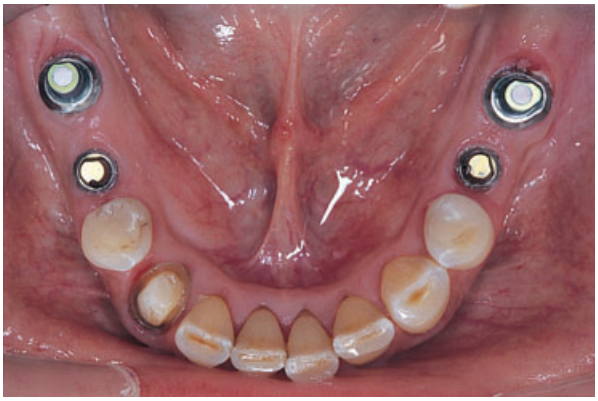


Fig. 54-25 Occlusal view of a bilaterally distally shortened mandibular arch. Two implants have been placed on either side to restore the arch to the area of the first molars. The two distal implants feature an increased diameter, better suited for the replacement of a missing molar.

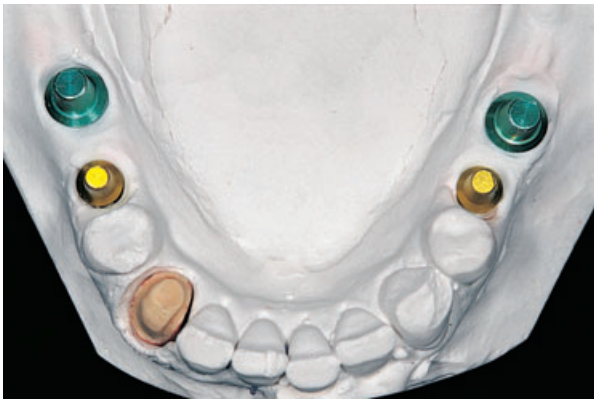


Fig. 54-26 The master model comprises color-coded aluminum laboratory analogues at the implant sites, facilitating the technician's work in view of the suprastructure fabrication. This is in contrast to the site of the prepared natural abutment.

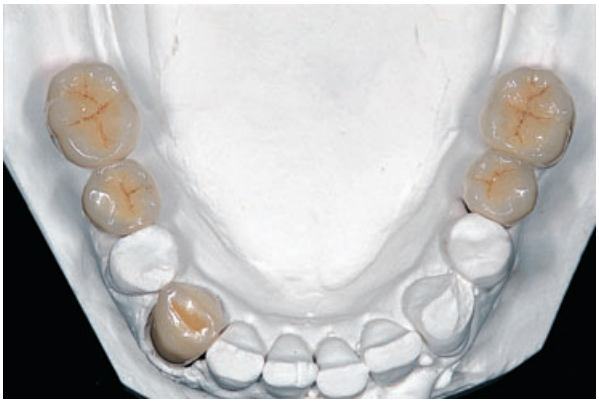


Fig. 54-27 Once the metal–ceramic restorations are completed, no noticeable design difference between implant-supported and tooth-supported suprastructures is apparent.

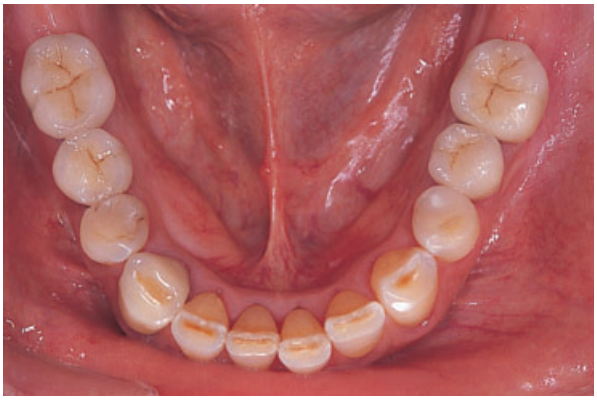


Fig. 54-28 The respective clinical view confirms an acceptable integration of the four implant restorations in the existing natural dentition.

retention, which was one of the frequent complications encountered on conventional cantilevered prostheses, can easily be prevented when it comes to implant-supported restorations of this type, the latter seem to be a viable alternative in cases where the local alveolar bone crest conditions do not allow the insertion of an implant at the most favorable location. In such situations the clinician has to ponder whether a bone augmentation procedure can be objectively justified or if the risk for complications of a more simple, straightforward approach can be considered low.

The 6-year clinical and radiographic follow-up of a three-unit FPD featuring a mesial cantilever is presented in Figs. 54-29 and 54-30.

Combination of implant and natural tooth support

There is general agreement that, from a purely scientific point of view, the combination of implants and natural teeth to support a common FPD is feasible. Clinical studies reporting prospectively documented long-term data did not show adverse effects of splinting teeth to implants (Olsson *et al*. 1995; Gunne *et al*. 1997, 1999; Hosny *et al*. 2000; Lindh *et al*. 2001; Naert *et al*. 2001a,b; Tangerud *et al*. 2002). The issue of connecting implants and teeth by means of rigid or non-rigid connectors, however, remains controversial to date, but intrusion of natural roots has been reported in the literature as a potential hazard of non-rigid connection (Sheets & Earthman 1993). Most of the recently published respective literature reviews conclude with the general clinical recommendation that one should avoid, whenever possible, the direct combination of implants and teeth as it may frequently lead to a more complicated type of prosthesis. If there is no viable alternative available, a rigid type of connection is preferred to prevent an eventual intrusion of the involved abutment teeth (Lundgren & Laurell 1994; Gross & Laufer 1997).

Furthermore, it has been demonstrated that despite the fundamental difference between an osseointe-

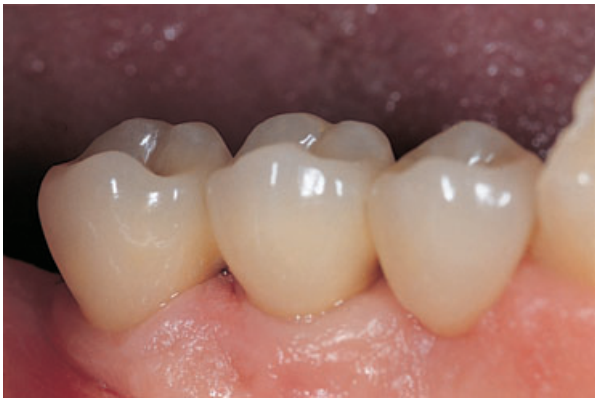


Fig. 54-29 Six-year clinical follow-up view of a mandibular three-unit FPD supported by two distal implants.

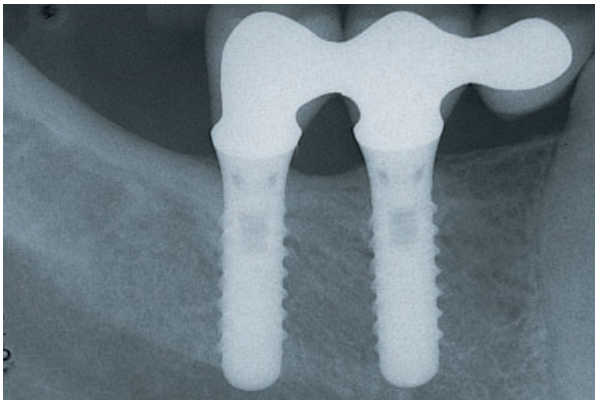


Fig. 54-30 The 6-year radiograph displays stable bony conditions around the two implants supporting a cemented suprastructure with a premolar-sized mesial cantilever unit.

grated implant and a tooth surrounded by a periodontal ligament, the assumption that when these two structures are combined, the entire occlusal load will ultimately go to the implant and hence create an unfavorable "cantilever-type" situation, is not valid from a scientific point of view (Richter, Isidor, Brägger). In fact, under normal function, such as during mastication, the tooth abutment is similarly load-bearing. This may change, however, during severe occlusal parafunctions, like nocturnal bruxism.

Sites with extended horizontal bone volume deficiencies and/or anterior sinus floor proximity

It is not infrequent that distally shortened dental arches do not feature an adequate local bone volume at the prospective implant sites. This may refer to bone height, bone width, alveolar bone crest axis or to the vicinity of noble structures such as the mandibular alveolar nerve canal or the anterior part of the maxillary sinus. Often a combination of several of the mentioned limitations is encountered. As implant insertion is clearly a three-dimensional

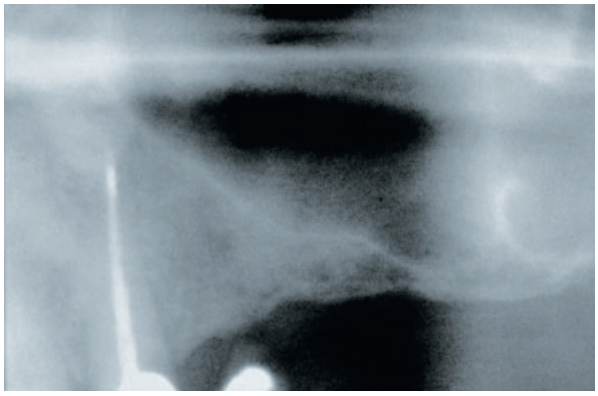


Fig. 54-31 Initial radiograph of the maxillary left posterior segment of a 67-year-old male patient. The canine represents the most distal remaining tooth element. Note the marked extension of the anterior recessus of the sinus.

surgical and restorative procedure on the one hand, and as "restoration-driven" rather than "bone-driven" implant placement is widely recommended on the other hand, a meticulous presurgical site analysis – based on the envisioned treatment objective – is of primary importance. In order to keep the treatment as easy and finally also as cost-effective as possible, one should comprehensively evaluate whether a minor deviation from the ideal implant position could be considered acceptable, i.e. not leading to a compromise which might adversely affect predictability, longevity, and/or subjective comfort. This approach may still permit a professionally defendable result in some cases, but without a complexity of treatment that would be difficult to bear by some patients.

Advanced invasive procedures like lateral bone augmentation, anterior sinus floor elevation, alveolar ridge splitting or distraction osteogenesis, require a high level of skills and respective experience and hence should only be deployed if the relation between benefit and risk/cost is soundly balanced (Buser *et al*. 1993, 1995, 1996, 1999, 2002; Chiapasco *et al*. 1999, 2001a; Simion *et al*. 2001; von Arx *et al*. 2001a,b; Zitzmann *et al*. 2001).

In this specific context, a complex implant treatment of a 67-year-old male patient whose most distal remaining tooth in the left maxilla was an endodontically treated canine, is shown in Figs. 54-31 to 54-44. Pre-operative diagnosis revealed the necessity to perform – according to a staged approach – first a combined lateral bone augmentation procedure and anterior sinus floor elevation and, after a 6 month healing period, the insertion of implants. For the sinus floor elevation the so-called "trap-door" technique was used and the created space grafted with autogenous bone chips and BioOss®. The lateral bone augmentation comprised the fixation of a large block graft in the area of the first premolar. After application of an e-PTFE barrier membrane, primary wound closure was achieved by sectioning of the periosteum of the respective mucoperiosteal flap. This often leads

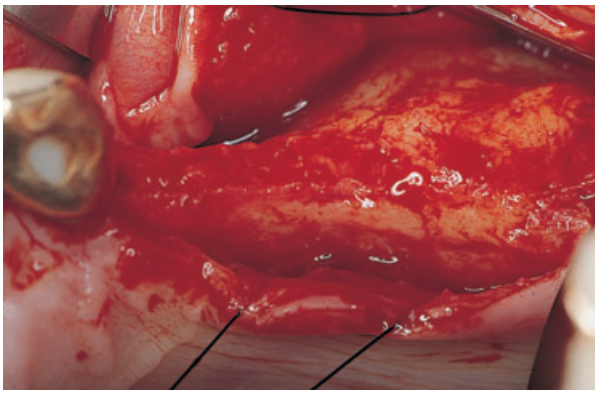


Fig. 54-32 After elevation of a mucoperiosteal flap, an insufficient horizontal bone volume in the region of the premolars becomes apparent.

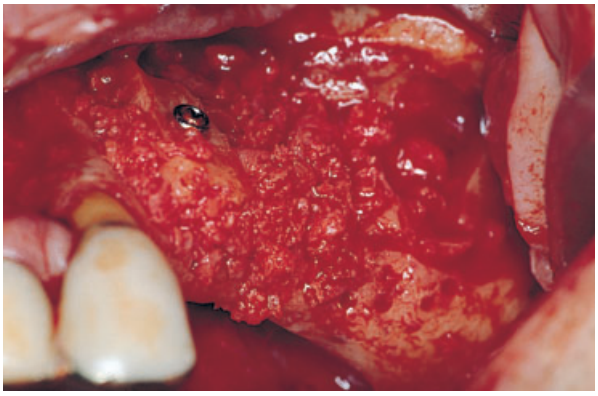


Fig. 54-35 The lateral bone augmentation procedure is completed by adding a combination of autogenous bone chips, bone slurry, and BioOss®.

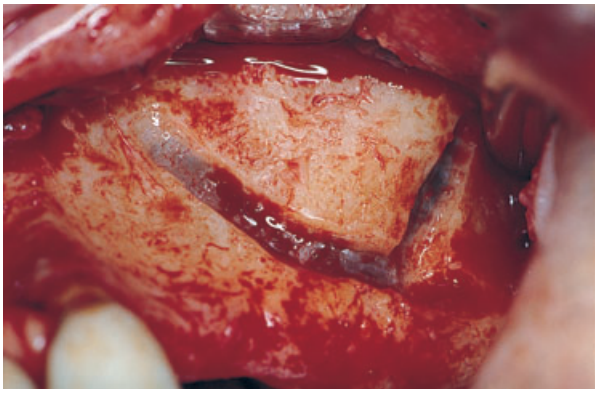


Fig. 54-33 In view of an anterior sinus floor elevation procedure, the first step for a respective osteotomy is performed. Attention is given not to perforate the Schneiderian membrane.

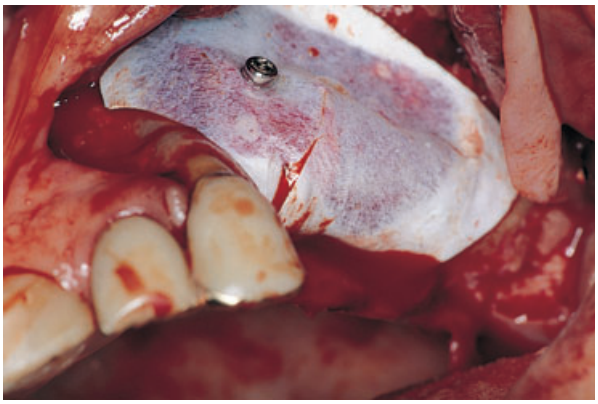


Fig. 54-36 Prior to flap repositioning and suturing, a barrier membrane is applied.

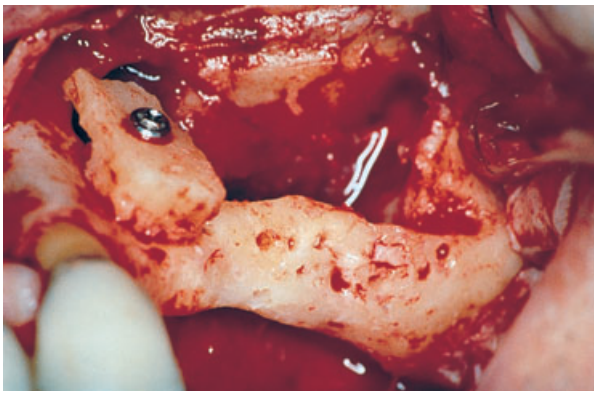


Fig. 54-34 After the so-called "trap-door" procedure in the region of the maxillary sinus, an autogenous bone block graft, harvested from the patient's retromolar area, is positioned and then immobilized by a fixation screw at the location of the missing first premolar.

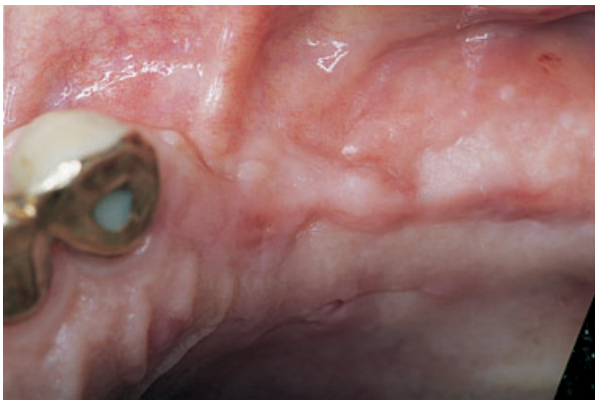


Fig. 54-37 One month after primary wound closure and uneventful healing, the involved soft tissues have recovered their normal appearance.

to a lack of attached keratinized mucosa on the vestibular aspect of the surgical site, which has to be subsequently corrected, most conveniently at the moment of implant placement. When it comes to sites that have been previously grafted, the majority of surgeons advocate inserting one implant per missing occlusal unit. This attitude appears to be based more on the reflection that the overall heaviness of the approach would largely justify this additional security and/or on the hypothesis that augmented bone may not have exactly the same "load-bearing" capacity as the pre-existing bone, than on irrefutable scientific evidence. Accordingly, three adjacent screw-type

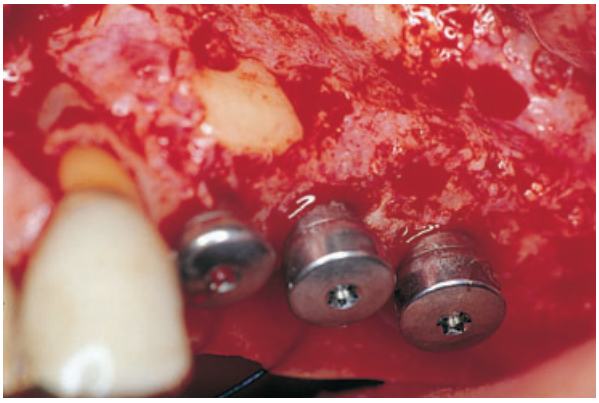


Fig. 54-38 Eight months following the combined anterior sinus floor elevation and lateral bone augmentation procedure, the site is reopened and three implants are inserted.

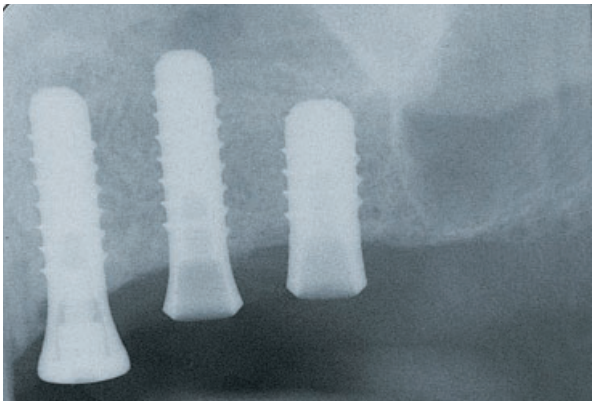


Fig. 54-41 The corresponding radiograph confirms successful osseointegration of the three implants that are mostly located in augmented bone.

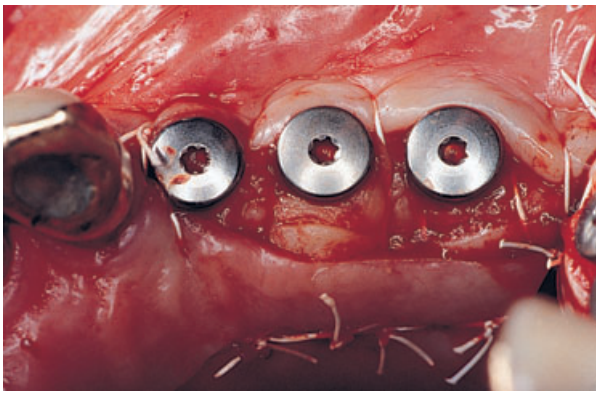


Fig. 54-39 In order to increase the amount of keratinized mucosa on the vestibular aspect of the implants, the flap is repositioned accordingly. The resulting deficiency on the palatal aspect is compensated for by means of a connective tissue being part of the partial-thickness flap.

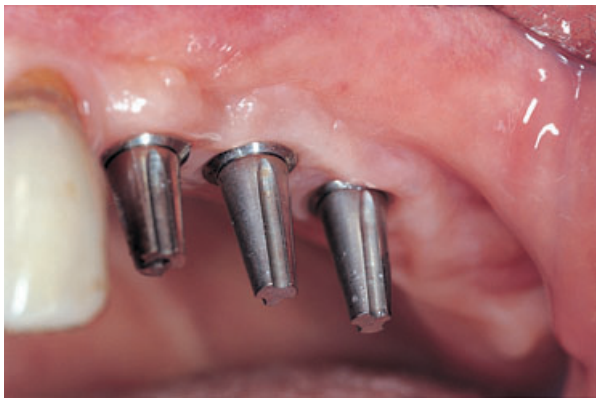


Fig. 54-42 In a case of implant shoulder location compatible with cementation, respective solid abutments are selected and tightened to 35 Ncm with a calibrated torque wrench.

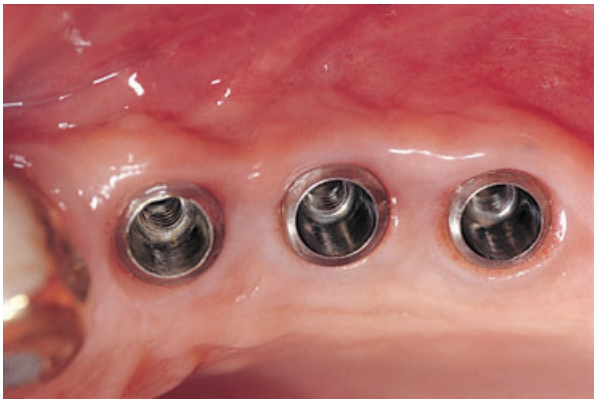


Fig. 54-40 Three months after implant placement, favorable peri-implant soft tissue conditions have been re-established.

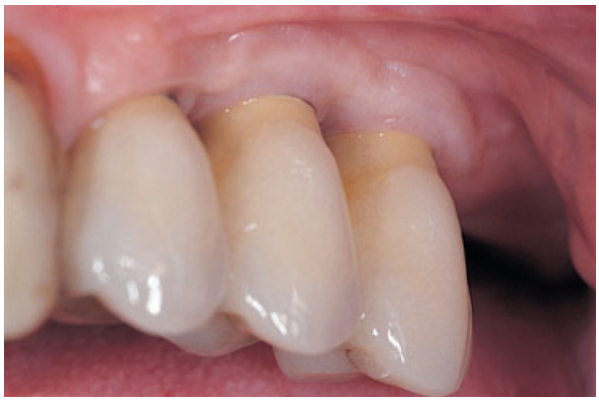


Fig. 54-43 Clinical view of the final three-unit metal–ceramic implant suprastructure, featuring a flat and continuous emergence profile and adequate access for inter-implant oral hygiene.

implants – the most distal one an increased-diameter titanium screw – had been placed and subsequently restored by a three-unit splinted metal-ceramic FPD (Figs. 54-38 to 54-44).

Results from a recently published longitudinal clinical study (Buser *et al*. 2002) on 40 consecutively enrolled patients, who were first treated with a lateral bone augmentation procedure and subsequently, in a second stage, received implants inserted in the previously augmented area. Implants could finally be placed as planned in all the treated sites, and a 97% success rate was revealed at the 5-year clinical and

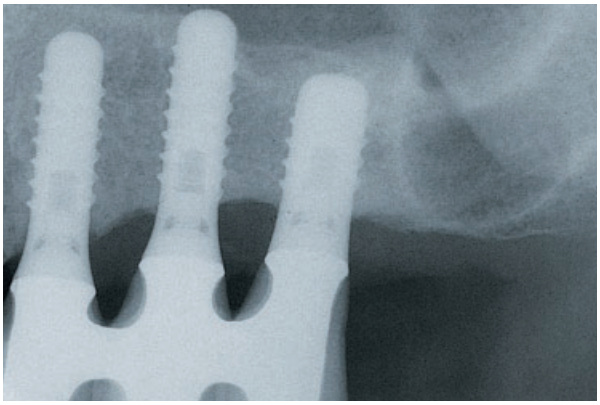


Fig. 54-44 The 4-year follow-up radiograph confirms stable conditions at the osseointegrated interface.

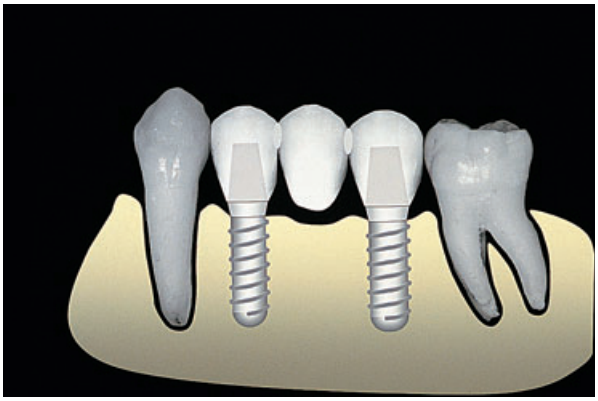


Fig. 54-45 Schematic representation of a tooth-bound posterior edentulous segment, restored by two implants and a three-unit FPD with a central pontic.

radiographic follow-up examination. It was thus concluded that lateral bone augmentation is indeed a predictable procedure and that implants subsequently inserted in augmented sites do have similar success rates to implants placed in comparable non-augmented sites.

Multiple-unit tooth-bound posterior implant restorations

Number, size, and distribution of implants

When it comes to implant therapy in extended posterior edentulous segments confined mesially and distally by remaining teeth, the question about optimal number, size, and distribution of implants has to be raised again. Among the key parameters to be addressed during the decision-making process are the mesio-distal dimension of the edentulous segment, the precise alveolar bone crest volume (including bone height and crest width in an oro-facial direction), the opposing dentition (premolars or molars), interarch distance and specific occlusal parameters, as well as the periodontal, endodontic, and structural conditions of the neighboring teeth.

One feasible approach consists of segmenting the edentulous space in premolar-size units of approximately 7 mm of mesio-distal diameter at the level of the occlusal plane, and of approximately 5 mm at the prospective implant shoulder. On posterior locations, clinicians increasingly prefer a rather superficial implant shoulder location or in many instances even a supramucosal one, so the respective measurements can be carried out at the crest level of study casts. It is important during this process to anticipate a minimal distance between implant shoulders of approximately 2 mm, and between a natural tooth and an implant of about 1.5 mm (to be measured at the interproximal soft tissue level). Again, the treatment objective, i.e. a long-lasting implant-supported FPD, should be predictably reached (1) with optimal efficacy and (2) with a minimum of invasiveness and

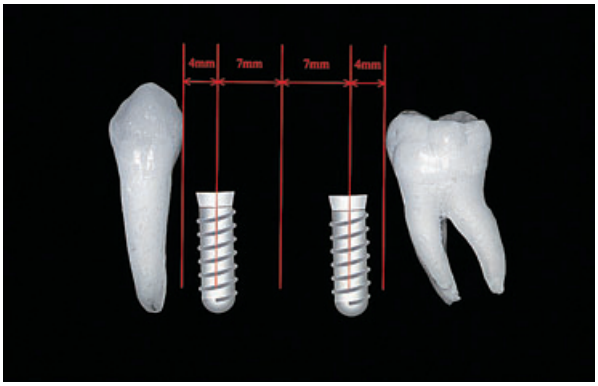


Fig. 54-46 In the case of three missing occlusal units, an implant-supported FPD with a central pontic (approximately 7 mm in width) may be considered as a viable solution.

cost. The still existing controversy of whether each missing occlusal unit should be replaced by one implant or whether a minimal number of implants should be used, has already been addressed earlier in this chapter.

In the case of three missing occlusal units and in the absence of other particular restrictive conditions such as limited local bone volume, the authors recommend the insertion of a mesial and a distal implant to support a three-unit FPD with a central pontic (Fig. 54-45). This approach permits the fabrication of three metal–ceramic elements featuring a mesio-distal diameter of about 7 mm each. Based on an average implant shoulder dimension of approximately 5 mm, one can anticipate a gradually increasing, harmonious emergence profile from the implant shoulder to the occlusal surface. In order to satisfy the remaining important dimensional conditions, i.e. respecting the minimal distance between adjacent implants and in between teeth and implants, one needs to dispose of a minimal total mesio-distal gap distance of 21–22 mm (Fig. 54-46).

In the case of two missing occlusal units, one should try as a general rule to select the largest possible implant diameters with respect to the total mesio-distal distance of the given tooth-bound

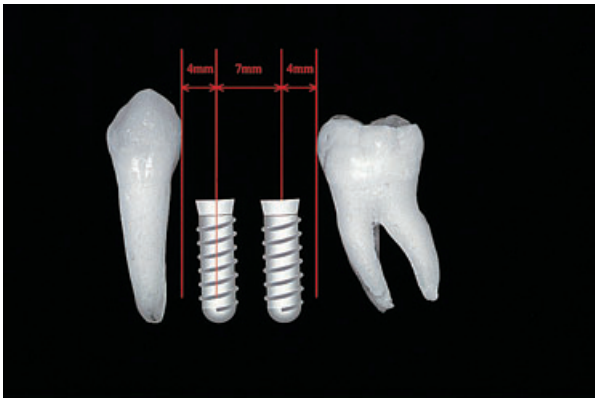


Fig. 54-47 If a given tooth-bound edentulous space only permits the insertion of two adjacent implants, a minimal interimplant distance of 2 mm and a minimal implant-to-tooth distance of 1.5 mm (at the interproximal soft tissue level) should be respected.

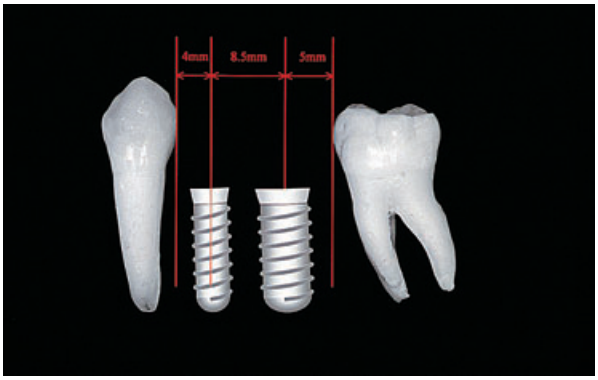


Fig. 54-48 In the presence of a mesio-distal gap width of approximately 17 mm, one may consider the combination of a standard and an increased-diameter ("wide-neck") implant. The same minimal inter-implant and implant-to-tooth distances have to be respected.

edentulous segment. Decisive parameters are again interimplant distance and space between implants and adjacent teeth, as well as oro-facial crest width at the two prospective implant sites. For a total gap diameter of about 14–15 mm, two standard-size implants are most suitable (Fig. 54-47), while for one of 17 to 18 mm the combination of one standard and one wide-diameter/wide-platform implant is considered adequate (Fig. 54-48). It goes without saying that the latter choice also requires the respective oro-facial bone volume.

These are just frequently encountered clinical examples, but in the function of other morphology and dimensions of edentulous tooth-bound segments, additional approaches and implant combinations may be envisioned. Two such clinical situations are presented in Figs. 54-49 to 54-52 and Figs. 54-53 to 54-55. In the first case, the gap diameter required the two adjacent implants to be spaced wider than the normally advocated interproximal 2 mm. The laboratory technician compensated for this excess of space with a root-imitation pontic which in turn

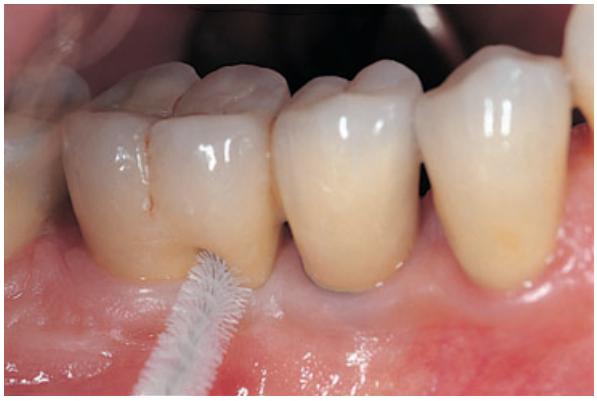


Fig. 54-49 Vestibular aspect of a metal–ceramic restoration supported by two screw-type implants. Due to an excess of mesio-distal space, the implants have been separated by approximately 4 mm. Instead of a traditional pontic, a root imitation has been performed close to the distal implant, providing an adequate guide for an interdental brush in view of an efficient plaque control at the marginal area of the implant restoration.

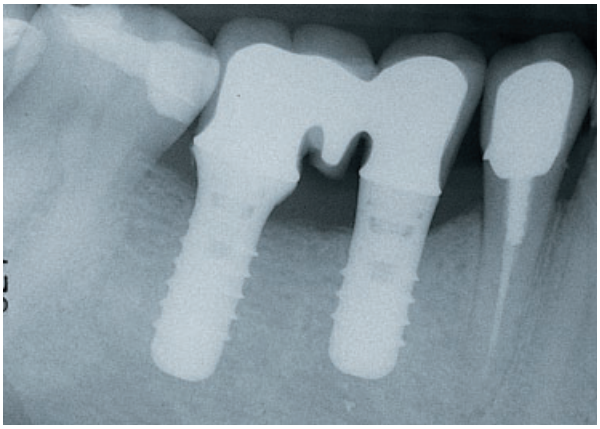


Fig. 54-50 With respect to cleanability, the respective prosthesis design is clearly visible on the post-operative radiograph.

Fig. 54-51 The corresponding master model visualizes the different dimensions and distances involved in this individual case.

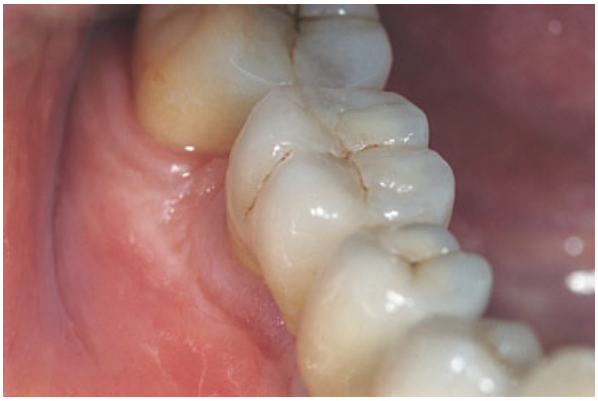


Fig. 54-52 On an oblique view the vestibular axial profile of the implant restoration becomes visible. Soft tissue (cheek and tongue) support and harmony with adjacent teeth are of paramount importance.

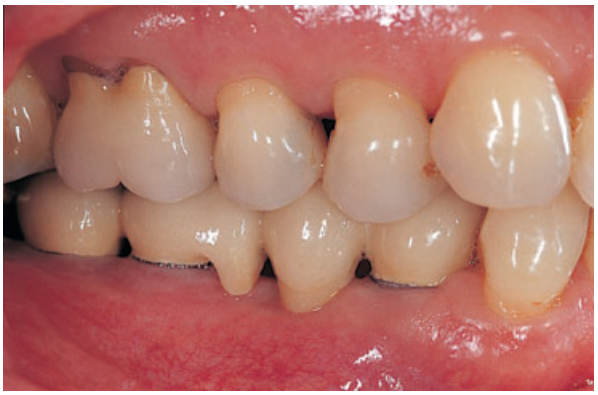


Fig. 54-53 Buccal view of an extended edentulous right mandibular tooth-bound gap treated with an implant restoration. In the pontic area a design favoring the efficacy of an interdental brush close to the implant margins has been applied.

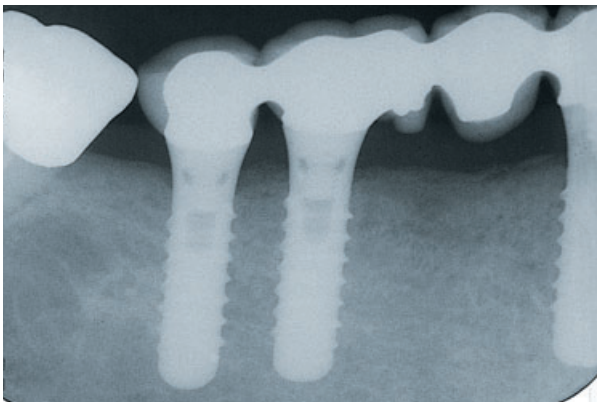


Fig. 54-54 The related radiograph illustrates the chosen design in the pontic area in terms of access to and efficacy of interproximal plaque control.

provided an excellent guide facilitating the use of an interdental brush (Fig. 54-49). In the second case, only the placement of three standard-size implants was possible due to a restricted bone volume in oro-facial direction. Again, the technician could optimally distribute the different restoration volumes but still

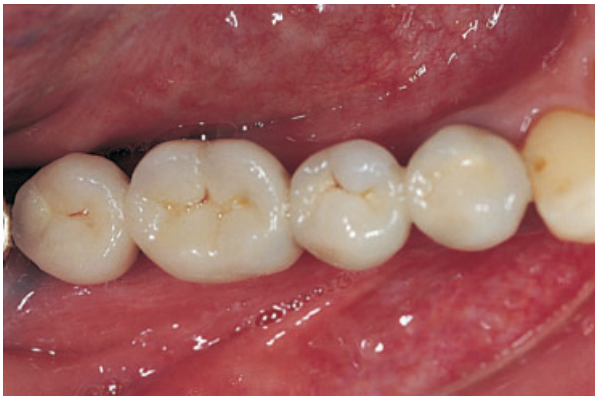


Fig. 54-55 Occlusal view of the completed 4-unit implant-borne fixed porcelain-fused-to-metal prosthesis.

Table 54-5 Splinting of multiple adjacent posterior implants

Parameters to consider:
• Access for oral hygiene
• Marginal adaptation/"passive fit"
• Technical simplicity/ease of eventual reinterventions
• "Overload" of the osseointegrated interface
• "Rotational forces" on implant components
• Screw-loosening/fatigue fractures

comply with basic prerequisites such as a flat axial emergence profile and optimal access for the patient's oral hygiene (Figs. 54-53, 54-54).

Splinted versus single-unit restorations of multiple adjacent posterior implants

Another persisting controversial issue relates to the question whether multiple adjacent implants in the load-carrying part of the dentition should support splinted or segmented single-unit restorations (Table 54-5). There still appears to be a confrontation between rather "biological" considerations versus more "mechanical" thinking.

Generally speaking, the biologically oriented considerations, insisting on easy access for oral hygiene and optimal marginal adaptation, represent probably the more scientifically-based point of view. Clinicians advocating splinting of multiple adjacent implants do so primarily for mechanical reasons. They hypothesize that this approach decreases forces and force moments at the level of the suprastructures and the various underlying implant components, and that relatively frequent mechanical complications such as screw-loosening and fractures may be significantly reduced or prevented by this measure. The related literature does not at present provide a clear answer, as randomized long-term clinical trials addressing this particular parameter are still scarce. Some more general reports do exist, however, addressing mainly type and frequency of mechanical complications (Goodacre *et al*. 1999).

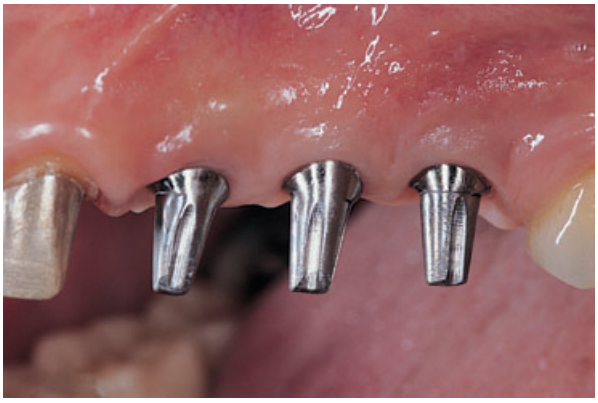


Fig. 54-56 The implant shoulder-abutment complex of the three left maxillary posterior implants has been prepared with fine-grain diamond burrs under abundant water cooling in order to facilitate the configuration of the related suprastructure. Particular emphasis was given to margins following closely the scalloped course of the soft tissue.

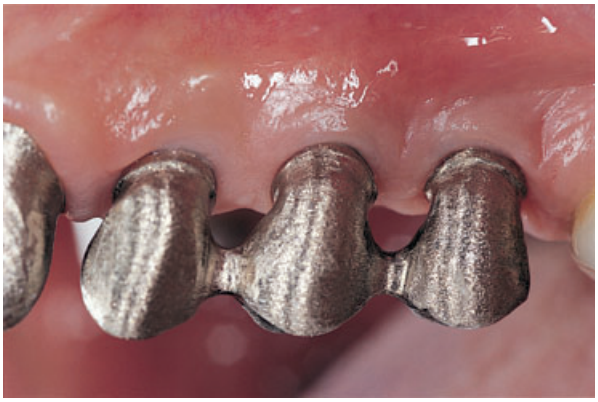


Fig. 54-57 In a case of reduced-diameter implants, splinting of adjacent units may reduce the risk for technical complications. A metal framework try-in prior to the application of the ceramic veneering may help to detect and eliminate an eventual non-passive fit at an early stage.

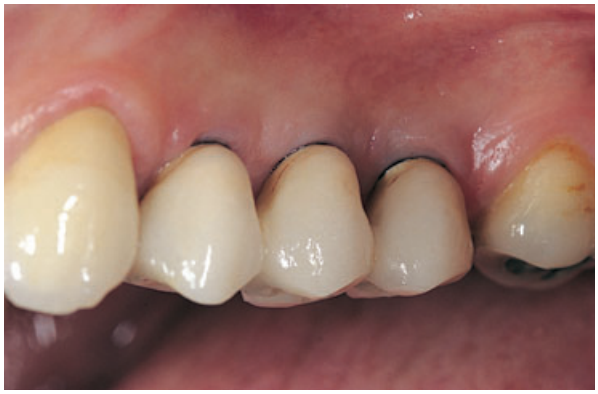


Fig. 54-58 The vestibular view of the final metal–ceramic restoration illustrates the impact on esthetics of a metal margin. This aspect should be discussed with the patient before treatment. In case of a high smile line, one may consider an increased sink depth during implant surgery.

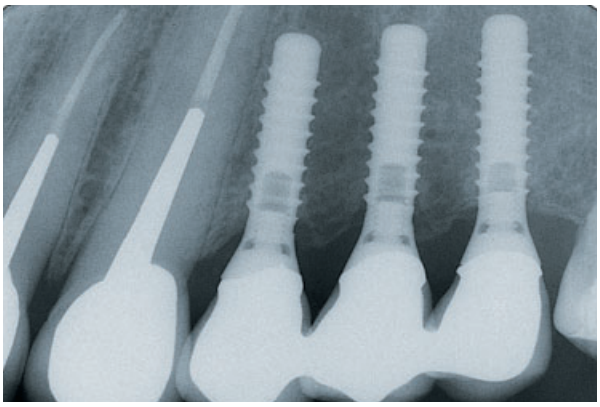


Fig. 54-59 On the 1-year follow-up radiograph an acceptable marginal fidelity can be assessed.

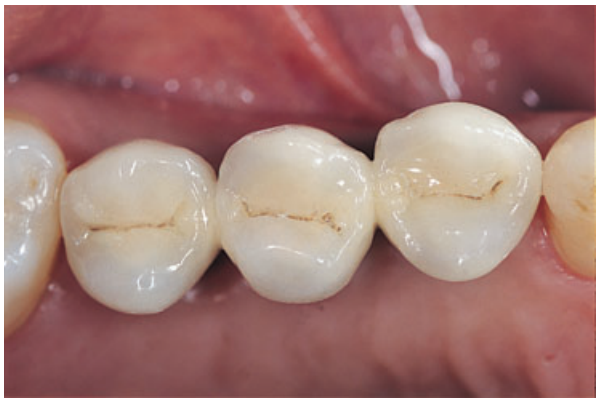


Fig. 54-60 Occlusal view of a right maxillary posterior three-unit implant restoration featuring premolar-sized segments.

Among the frequently forwarded arguments to plead the case of splinting are reduced-diameter (Figs. 54-56 to 54-59) or short (i.e. less than 8 mm) implants, implants inserted in low-density bone, implants placed in augmented or grafted (e.g. after anterior sinus floor elevation) bone, or implant restorations in the posterior segments of patients with verified notable occlusal parafunctions or bruxism. One should be aware, however, that the majority of these arguments are primarily based on clinical opinions and eventually common sense, and that to date they lack formal scientific evidence. In fact, there is increased indication, derived from prospective multicenter studies (although not addressing this parameter in particular), that splinting does not appear to be a prerequisite for preventing excessive crestal bone resorption or even loss of osseointegration. Nowadays, the authors would seriously reconsider their respective choice related to the suprastructure design presented in Figs. 54-60 and 54-61. In the presence of standard-size (i.e. addressing both diameter and length) implants, which are placed in normal density, original (non-augmented or grafted) bone, single-unit restorations are definitely recommended as they comply better with the various parameters that are important from a more biologic point of view, as demonstrated by the clinical example presented in Figs. 54-62 and 54-63.

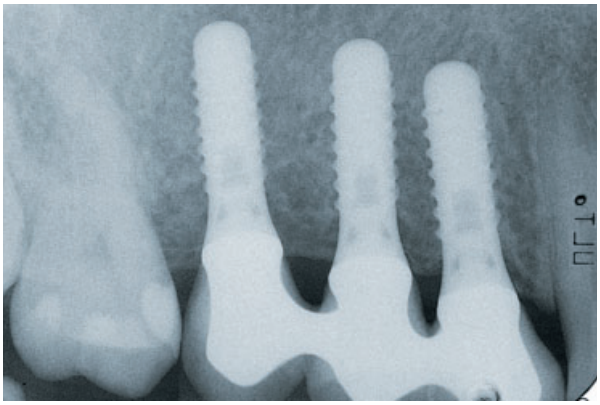


Fig. 54-61 The corresponding follow-up radiograph confirms acceptable peri-implant conditions.

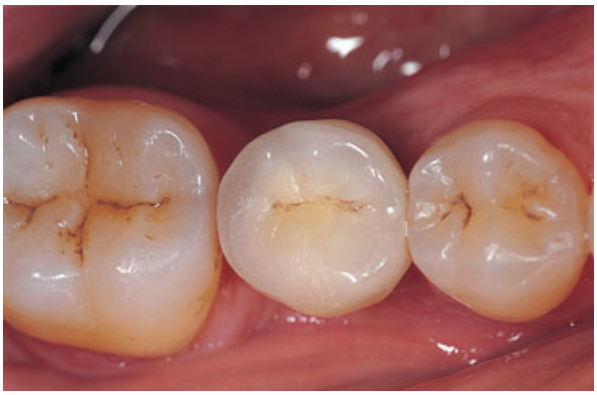


Fig. 54-64 Occlusal view of a single-tooth implant restoration replacing a missing mandibular right second premolar.

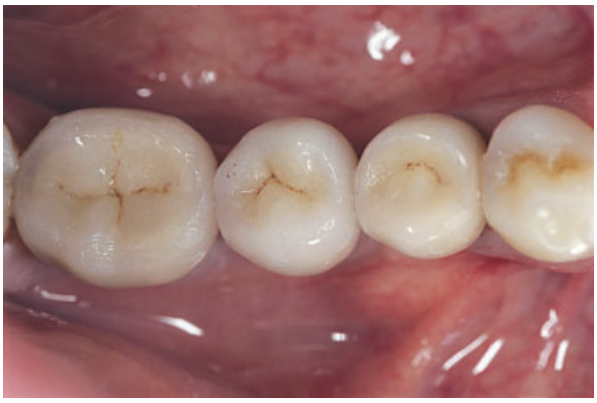


Fig. 54-62 Occlusal view of three independent, implant-supported fixed metal–ceramic restorations in the right posterior mandible.

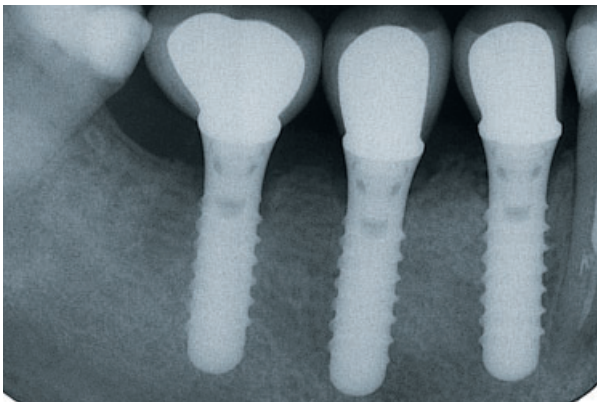


Fig. 54-63 As confirmed by the follow-up radiograph, an increased (more molar-like) dimension has been given to the most distal restoration, despite the fact that a standard-sized implant had to be used for restricted bone volume reasons.

Posterior single-tooth replacement

At the time when most implant systems had basically only one "standard" dimension at disposition, this corresponded to approximately 4–5 mm at the implant shoulder and thus was optimally suited for premolar-size restorations, featuring a continuously increasing (towards coronally) flat axial emergence profile and a mesio-distal diameter of about 7–8 mm at the occlusal surface. Clinicians were not infrequently faced with posterior single-tooth sites, however, that did not comply with these dimensions, for example in the case of missing first molars or after the loss of persisting deciduous (primary) second molars. As a consequence, the resulting implant restorations featured either unfavorable excessive interproximal overcontour or wide open embrasures. The first situation was difficult to clean, while the second led to undesired food retention (impaction). Nowadays most of the leading implant manufacturers offer wide-body/wide-platform implants designed for the replacement of multi-rooted teeth (Fig. 54-3).

Premolar-size single-tooth restorations

When it comes to posterior single-tooth gaps that correspond dimensionally to an average premolar, standard-size screw-form implants are well suited. The respective implant dimensions which include both the intrabony part and the implant shoulder, offer the additional advantage of being mostly compatible with a limited bone volume in an oro-facial direction. Whenever feasible, a straightforward low-maintenance restorative design is advocated, which normally consists of a cementable porcelain-fused-to-metal crown with vestibular and oral axial contours that are in harmony with the adjacent teeth and thus provide adequate guidance for cheek and tongue (Figs. 54-64 to 54-66).

Molar-size single-tooth restorations

If a given posterior single-tooth gap corresponds rather to the mesio-distal dimension of a molar, it is recommended, for the reasons quoted in the previous paragraph, that the insertion of a wide-neck implant is planned (Bahat & Handelsman 1996). This approach, however, also requires the respective bone volume in an oro-facial direction. If this is not the case, presurgical site analysis, eventually in the form

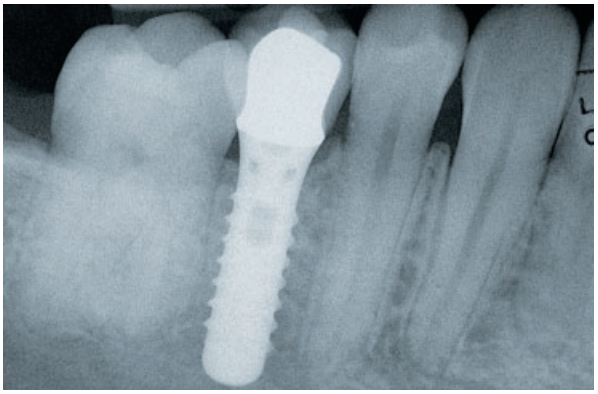


Fig. 54-65 The 5-year radiographic follow-up displays favorable bony conditions around this 12 mm solid screw implant.

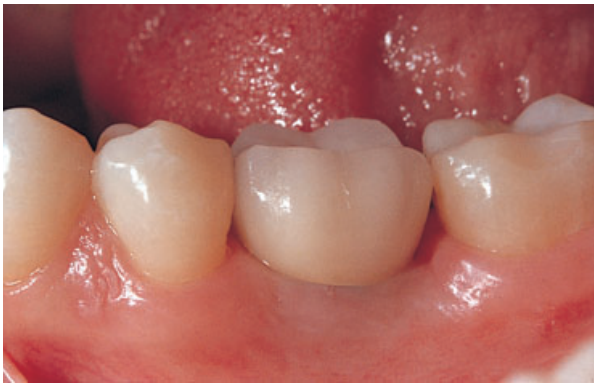


Fig. 54-67 In a case of the replacement of a single missing molar, ideally the use of an implant with corresponding dimensions is recommended to permit a restoration featuring optimal subjective comfort and cleansibility.

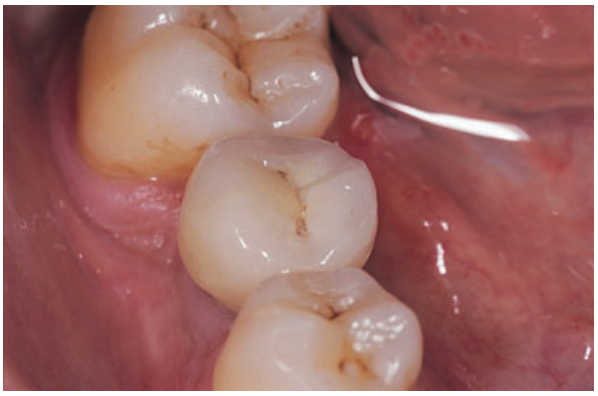


Fig. 54-66 On the oblique view one can notice that an axial contour similar to that present on the adjacent natural teeth has been applied to facilitate oral hygiene and to assure adequate soft tissue (cheek and tongue) guidance and support.

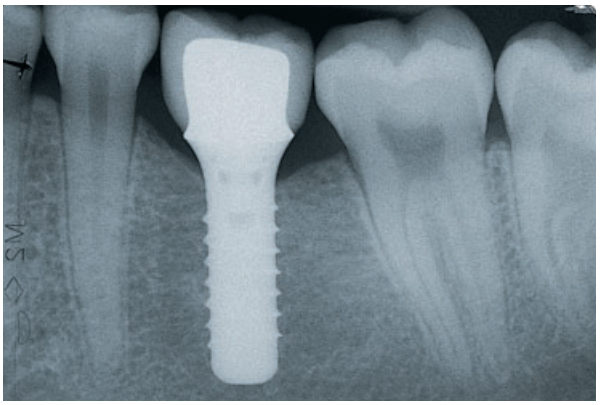


Fig. 54-68 On the 1-year radiographic follow-up a diameter-increased ("wide-neck") implant can be noted which is essential for a suprastructure design without extremely open interdental embrasures, which would be prone to food retention and oral parafunctions.

of a bone-mapping, should identify whether it is possible to have an implant placement in combination with a lateral bone augmentation procedure using a simultaneous approach. If the local bone anatomy requires a bone augmentation according to a staged protocol, one has to carefully ponder and discuss with the patient if this additional effort, risk, and ultimately also cost can be justified by an anticipated implant restoration featuring close-to-ideal axial contours and embrasures.

A clinical example demonstrating the potential of increased-diameter implants for the optimal replacement of a single missing mandibular molar is given in Figs. 54-67 and 54-68.

Sites with limited vertical bone volume

The clinician is quite frequently confronted with posterior single-tooth gaps that present all of the major prerequisites for successful implant therapy listed earlier in this chapter, with the exception of sufficient vertical bone height for the insertion of an implant featuring what is broadly accepted as an adequate length of the implant itself and in relation to the prospective length of the suprastructure. The question that arises is whether there is a minimal implant length required in the context of posterior single-tooth restorations and whether the ratio between implant length and suprastructure length has an influence on crestal bone resorption and ultimately on the longevity of the entire implant–suprastructure complex. The analysis of the respective implant data collected at the University of Geneva School of Dental Medicine in the frame of a prospective multicenter study from 1989 to 2002, permitted the conclusion that shorter implants (6–8 mm) did not show more average crestal bone resorption than longer implants (10–12 mm), and that a so-called unfavorable ratio between implant length and suprastructure height did not lead to more pronounced crestal bone resorption (Bernard *et al*. 1995a; Bernard & Belser 2002). This data is corroborated by other recently published reports (ten Bruggenkate *et al*. 1998; Bischof *et al*. 2001; Deporter *et al*. 2001).

Two examples of respective clinical anecdotal-type evidence, one premolar-size and one molar-size single-tooth restoration, are presented in Figs. 54-69 and 54-70, and Figs. 54-71 and 54-72, respectively.

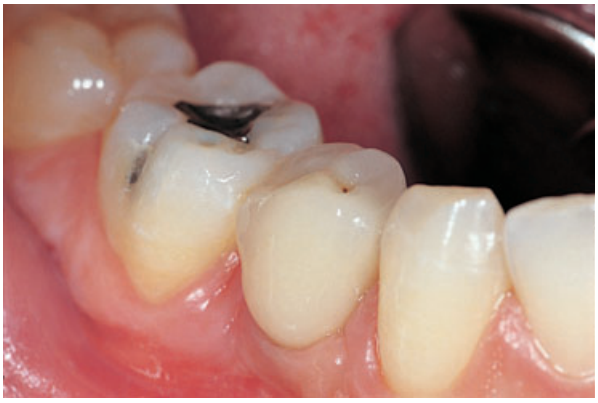


Fig. 54-69 Clinical aspect of a single-tooth implant restoration in the mandibular right premolar area.

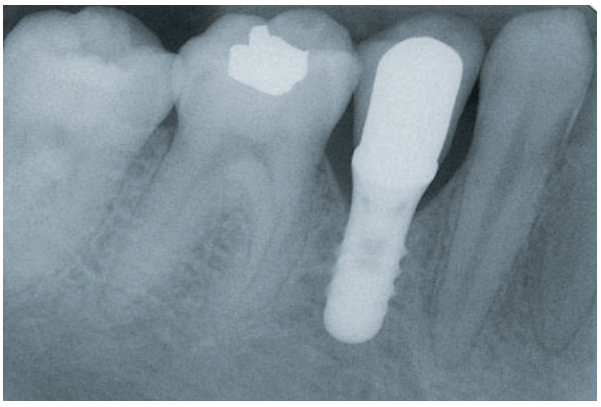


Fig. 54-70 The related 2-year follow-up radiograph shows a so-called unfavorable relationship between the height of the suprastructure and the length of the supporting implant. The placement of a longer implant was not possible due to the limited local bone conditions.

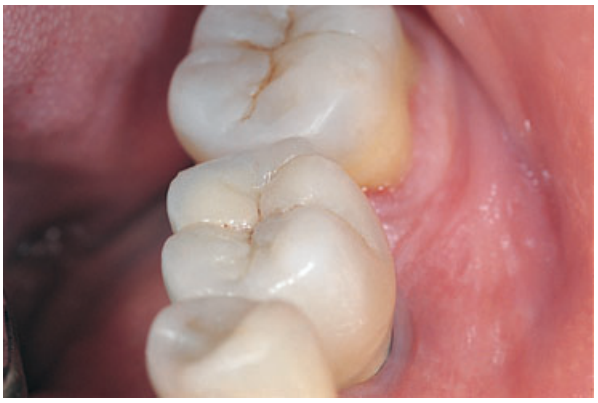


Fig. 54-71 Oblique view of a molar single-tooth implant restoration in the left mandible.

Clinical applications

Screw-retained implant restorations

For many years there was a strong tendency to design most of the fixed implant restorations as screw-retained suprastructures. Retrievability, and by this maintaining the possibility for modification, extension or eventually repair of the prosthesis, was the main rationale for this strategy. One should be aware, however, that this approach also encompasses notable specific inconveniences: colonization of the inner compartments of the implant–abutment–suprastructure complex with mostly anaerobic microorganisms, risk for loosening or fracture of screws, increased technical complexity and related costs, possible interference with structural parameters (weakening of the metal-ceramic design) and esthetics, as well as a "higher maintenance profile" (Sutter *et al*. 1993; Wie 1995; Hebel & Gajjar 1997; Keller *et al*. 1998). As far as the microbial colonization is concerned, it remains unknown to date whether and under which conditions this may have an adverse effect on the longevity of osseointegrated implants.

For these reasons there is currently a distinct trend towards cementable fixed implant restorations in the load-carrying part of the dentition.

The main indications for screw-retention are listed in Table 54-6.

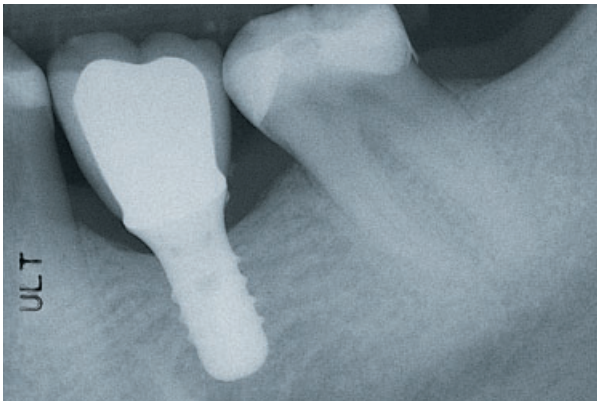


Fig. 54-72 A short diameter-increased screw implant supporting a long molar-sized suprastructure is displayed on the 1-year follow-up radiograph. Note that a normal level of the first bone-to-implant contact has been maintained.

Table 54-6 Indications for screw-retained posterior fixed implant restorations

Parameters to consider:
• Implant shoulder location incompatible with a cemented suprastructure, i.e. inaccessible for meticulous excess cement removal (>2 mm submucosally)
• Reduced intermaxillary distance (<5 mm)
• Foreseeable need for reintervention at the respective implant site
• Extended implant-supported rehabilitations, involving numerous implants
• High overall level of complexity (e.g. non-parallel implants)

Transocclusal screw retention

If for one of the aforementioned reasons a transocclusally screw-retained suprastructure is adopted,

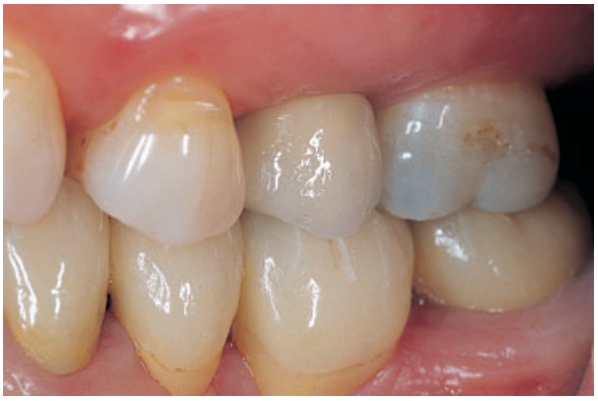


Fig. 54-73 Left lateral view showing the intermaxillary relationship of a young patient in centric occlusion. The missing maxillary second premolar has been replaced by a single-tooth, screw-retained implant restoration. Screw retention was chosen for two reasons: limited interocclusal distance and implant shoulder location incompatible with cementation.

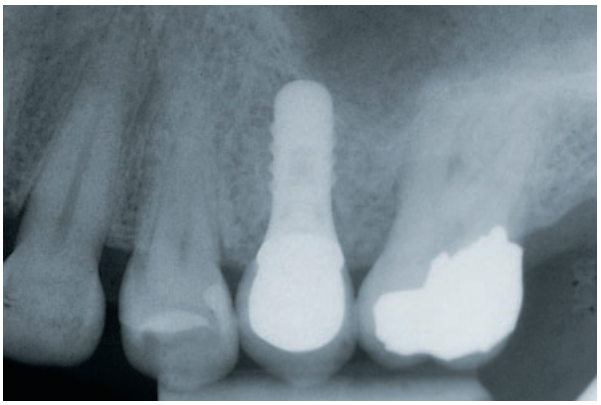


Fig. 54-74 One-year follow-up radiograph of the described 8 mm solid screw implant.

several parameters should be taken into consideration. First, the screw-access channel should be centered on the occlusal surface in order not to interfere too much with the area to be occupied by the cuspids.

A typical clinical example documenting an indication for a screw-retained posterior single-tooth restoration is given in Figs. 54-73 to 54-75. A reduced interarch distance has led to a deeper than usual implant shoulder location which in turn is neither accessible for well controlled excess cement removal nor in reach for the patient's routine oral hygiene. In order to benefit from their superior surface quality characteristics and marginal precision, prefabricated machined cast-on components have been used for the respective suprastructure fabrication. Ideally, the screw-access channel occupies a restricted area in the centre of the occlusal table, and the distance from the head of the screw to the occlusal surface should be sufficient for a subsequent composite cover-restoration (Fig. 54-75).

Furthermore, the principles of the metal–ceramic technology require a well defined space for developing an adequate metal support for a uniform thickness of the overlaying stratification of porcelain. Even in a case of a well centered occlusal perforation, the latter occupies close to half of the mesio-distal and oro-facial diameter of the occlusal table, and thereby significantly weakens the overall mechanical resistance of the structure. If the screw-access channel is not centered, however, additional problems are created in the sense of both weakening the restoration and interfering with esthetic criteria. Under such circumstances one should consider, for example, the use of angled abutments as currently offered by most of the leading implant systems.

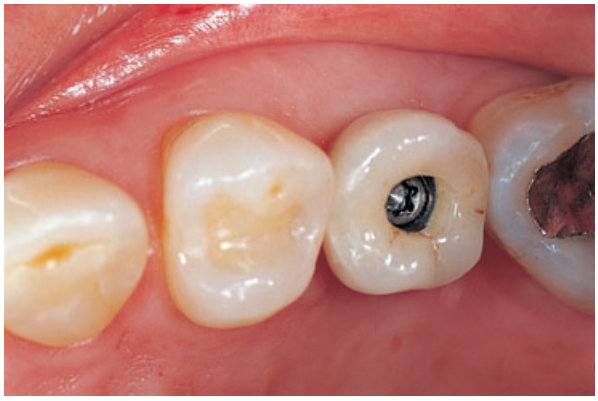


Fig. 54-75 Ideally, the screw-access channel should be located in the center of the occlusal surface. This reduces both the risk for interference with an appropriate metal–ceramic design in general, and the risk for porcelain fractures in particular.

Another key parameter represents the interarch distance, or more specifically, the distance between the implant shoulder and the plane of occlusion. According to our experience this distance should be at least equal to 5 mm. This is minimal and does not permit – for esthetic reasons – the occlusal screw to be subsequently covered with a composite resin restoration. In this context 6–7 mm are clearly more adequate.

A combination of several well known problems, which are frequently encountered after implant placement in the posterior mandible, are shown in Figs. 54-76 to 54-78. Two implants have been inserted to restore a distally shortened arch with a three-unit FPD. Owing to the local bone anatomy, the implants were placed in a more lingual position than the original teeth (Fig. 54-76). The implant shoulder location was too superficial for these particular circumstances and did not provide sufficient distance to gradually correct the discrepancy between the actual implant shoulder position and the ideal occlusal location. Furthermore, the necessity of keeping the screw access in the center of the occlusal table, and the insufficient room for composite screw-head coverage, ultimately led to a considerable compromise (Fig. 54-77). The final radiograph (Fig. 54-78) clearly shows that the presurgical bone volume would have permitted a vertical reduction of the edentulous bone

Fig. 54-76 Occlusal view of a mandibular master model comprising two posterior implant analogues and a prepared natural second premolar abutment. Note the proximity of the mesial implant and the second premolar on the one hand, and the distinct lingual position of the two implants on the other.

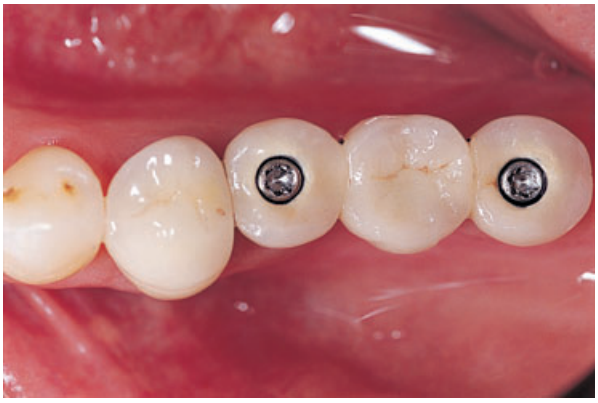


Fig. 54-77 The clinical view of the completed transocclusally screw-retained three-unit implant-supported FPD demonstrates that the lingual implant position did not allow for a suprastructure that is in line with the adjacent teeth. Furthermore, the screws are reaching the occlusal surface, leaving no space for an esthetic coverage with composite resin.

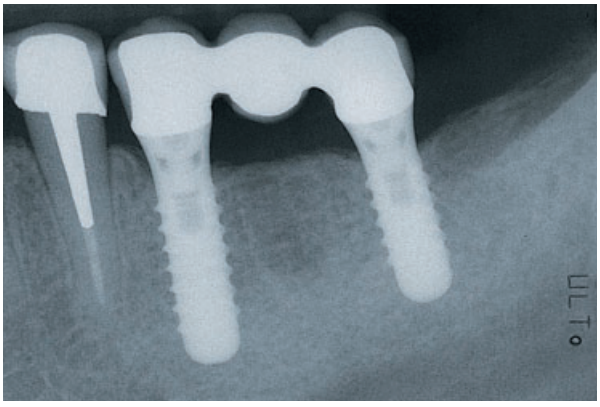


Fig. 54-78 The related 3-year follow-up radiograph documents an only minimal distance between implant shoulder and occlusal surface. Under such conditions, a slight reduction of the alveolar ridge prior to implant placement would have provided more vertical leeway for compensating the lingual implant position and ultimately for covering the occlusal screw.

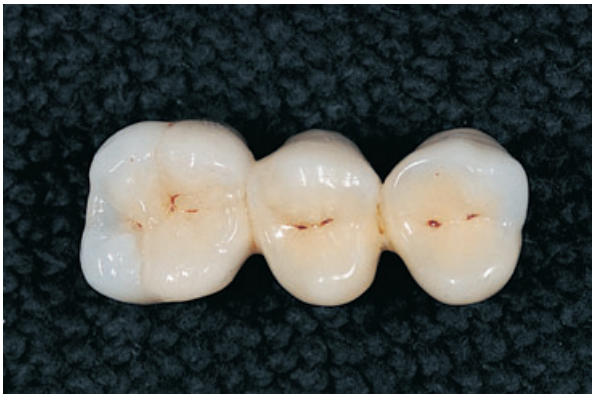


Fig. 54-79 Occlusal configuration of a three-unit metal–ceramic implant restoration designed for transverse screw retention. Note the absence of any interference due to screws on the occlusal aspect of the restoration.

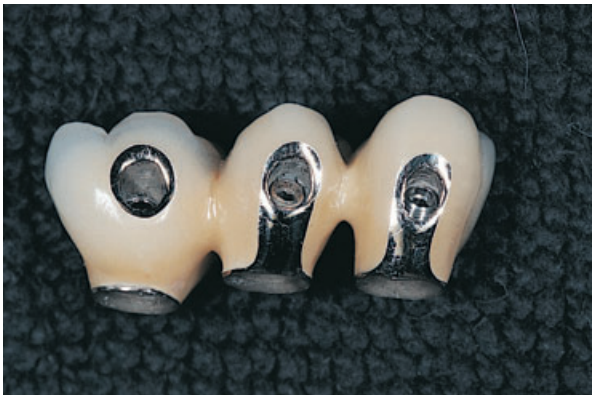


Fig. 54-80 The oral aspect of that same prosthesis features the decisive elements related to the transverse screw retention: improved esthetics, no weakening of the ceramo-metal design. The screw-access channels are completely protected by the metal framework.

crest to be performed prior to implant insertion. By this token the suboptimal implant position could have been partially corrected by the implant restoration, and the occlusal screw covered by composite resin, or a screw-retained restoration eventually avoided as there would be adequate conditions for a cemented suprastructure.

Transverse screw retention

When it comes to screw-retained posterior implant restorations one should not forget the option of transverse screw retention (Figs. 54-79 to 54-84). This specific technical approach leaves the occlusal surface of the restoration free from any screw and permits the design of a screw-access channel on the oral aspect, featuring a metal protection on the entire circumference of the perforation (Fig. 54-80). These two factors significantly improve both the overall mechanical resistance and the esthetic appearance. Furthermore, the metal protects the surrounding porcelain during removal and tightening of the transverse screw and

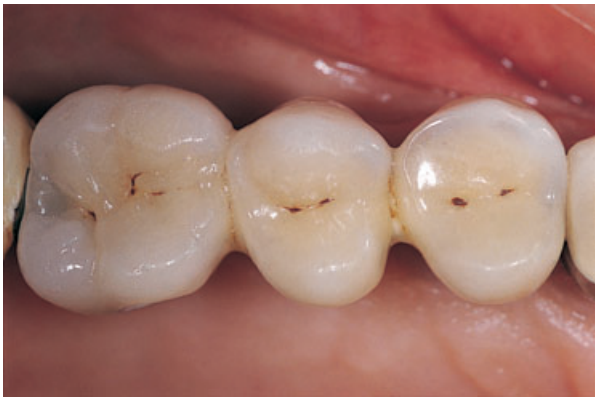


Fig. 54-81 Clinical 5-year follow-up of this three-unit implant restoration. No significant changes can be noticed on the occlusal surface.

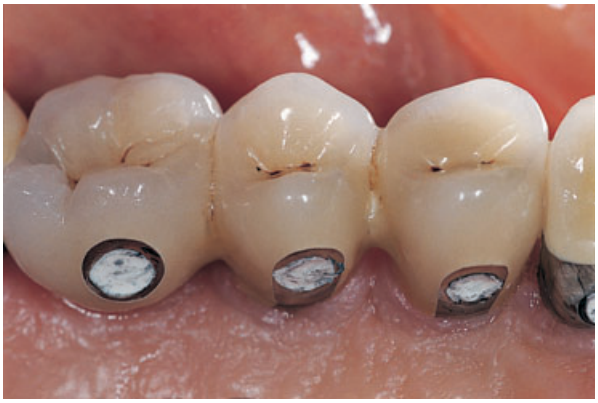


Fig. 54-82 Palatal view of the transverse screw-retained implant prosthesis after 5 years of clinical service. The screw-access channels are blocked by a temporary material.

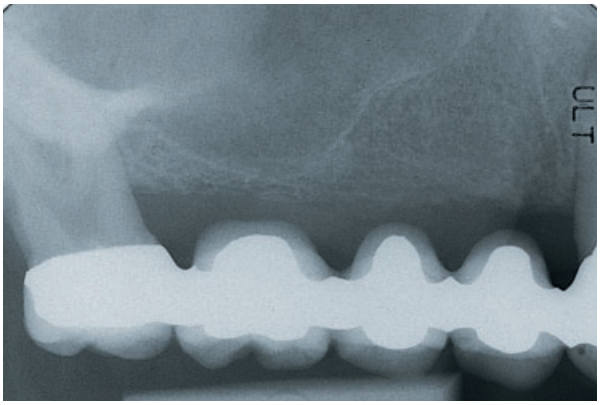


Fig. 54-83 Pre-operative radiograph of the patient's maxillary right posterior segment, revealing a tooth-borne long-span FPD which had failed after 4 years of function due to loss of retention and subsequent damage on the mesial abutment.

thereby prevents the induction of fissures prone to subsequent propagation and ultimately leading to ceramic fractures. One has to be aware, however, that from a purely technical and economic point of view, transverse screw-retained restorations require additional, more complex components and advanced technical skills, and are more expensive. In the long-term, on the other hand, the distinct advantages should clearly outweigh these inconveniences in numerous clinical situations.

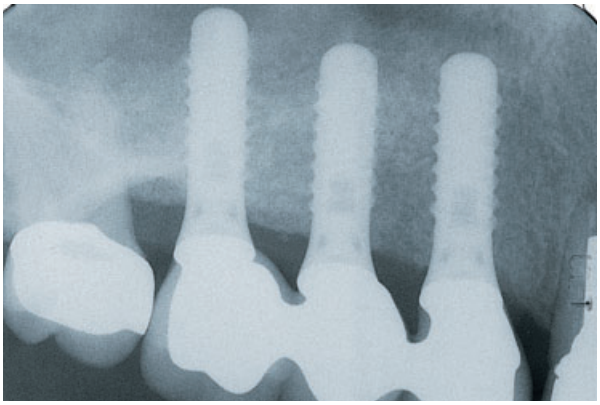


Fig. 54-84 Five-year follow-up radiograph of the same quadrant, now restored with a three-unit transverse screw-retained metal–ceramic implant suprastructure. Note that the distal retainer of the original tooth-borne FPD could be maintained.

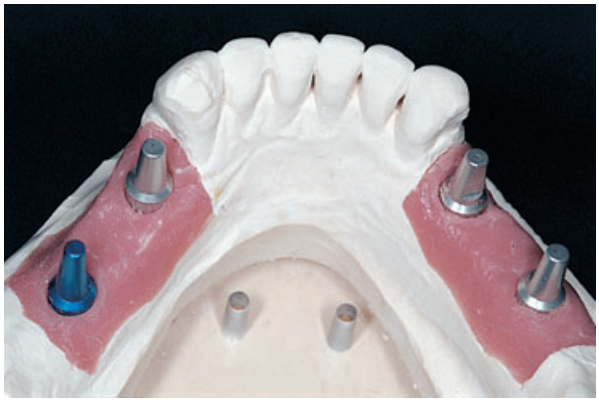


Fig. 54-85 Example of a typical mandibular master model, derived from an impression at the abutment level, comprising four colour-coded implant–abutment analogues.

Abutment-level impression versus implant shoulder-level impression

Most of the leading implant systems currently offer the possibility of taking impressions either at the level of a previously inserted abutment or at the level of the implant shoulder itself (Figs. 54-85 and 54-86). The former approach is mostly indicated if the patient does not wear a removable temporary prosthesis and in the case of optimally placed, "restoration-driven" implants, comprising accessibility of the implant shoulder, point of emergence from the soft tissue, implant axis, interarch distance, and overall easy access for use of simple "pop-on" plastic transfer copings. As shown later, a clear preference is given to cemented suprastructures under such simple, straightforward conditions. In fact, the clinician is only required to keep a limited stock of components, i.e. cementable titanium abutments of various heights

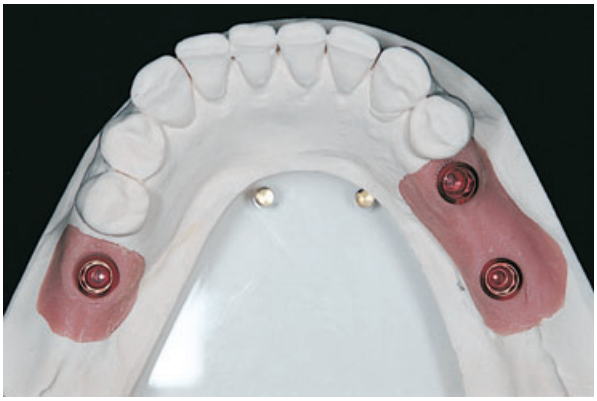


Fig. 54-86 Example of a typical mandibular master model, derived from an impression at the implant shoulder level, comprizing three colour-coded implant analogues.

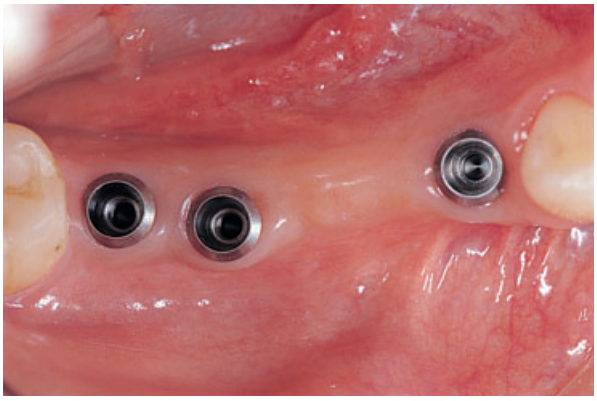


Fig. 54-87 Occlusal view of the mandibular right posterior quadrant with three implants that had been placed according to a single-step transmucosal surgical protocol.

and injection-molded impression copings, in his office. Whenever the clinical situation deviates notably from the previously described conditions, one may consider taking an impression directly at the level of the implant shoulder. For that approach, only transfer copings have to be available in the dental practice. In fact, the patient is leaving the office after the impression session exactly as he came in, i.e. with the same cover screw and with the same unaltered temporary prosthesis. After master model fabrication and articulator mounting, the technician will then select the most appropriate secondary components in the laboratory and ultimately deliver the finished restoration together with the respective supporting abutments.

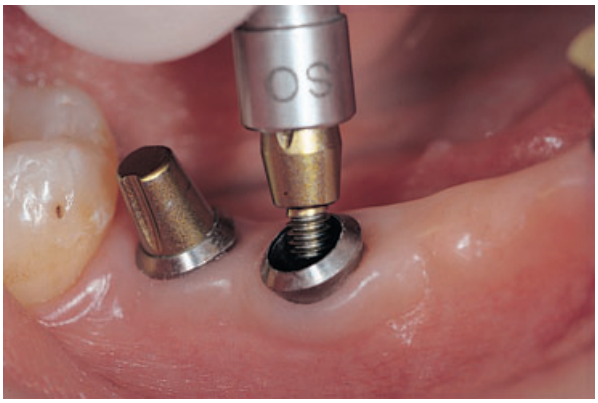


Fig. 54-88 In accordance with the available interocclusal space, adequately dimensioned solid abutments are selected, inserted and subsequently tightened to 35 Ncm in view of a cemented suprastructure.

Cemented multiple-unit posterior implant prostheses

In recent years, an increasing trend towards cemented posterior implant restorations, using either temporary or permanent luting agents, could be observed. The associated original paradigm, indicating that maintaining "retrievability" was one of the fundamental advantages of implant-borne suprastructures, permitting re-intervention, modification, and/or extension at any time, has been lately challenged by parameters such as increased clinical and technical simplicity, low-maintenance design of the restorations, and superior cost effectiveness. As more implants are utilized in clinical situations where conventional FPDs would also be easily possible, but where the latter have become second choice, the sites are more favorable for this type of therapy and these implants come closer to the characteristics currently termed as "restoration-driven". Parallel to this improved mastering of three-dimensional implant positioning, secondary components such as abutments that are optimally designed for subsequent cemented restorations have been developed, in combination with auxiliary parts such as simplified impression copings, laboratory analogues, and burnout patterns. A typical clinical example of the treatment of an extended tooth-bound posterior segment by means of implants and a subsequently cemented suprastructure is presented in Figs. 54-87 to 54-94. Three screw-type implants have been inserted according to a single-step transmucosal (non-submerged) surgical protocol, leading 8 weeks after implant installation to a clinical situation which is well suited for a restorative procedure similar to the one traditionally used in the context of natural tooth abutments. More particularly, all of the involved implant shoulders are easily accessible (Figs. 54-87 to 54-90) for restorative procedures and later for maintenance, and the surrounding peri-implant mucosa healing and tissue maturation has occurred simultaneously with implant osseointegration, both being key factors in facilitating prosthetic procedures. Furthermore, the superficially located interface between implant shoulder and suprastructure or abutment will reduce the length of suprastructure leverage and by this the resulting bending moments. Under the assumption that presurgical site analysis and, derived from that, prosthetic treatment planning has predictably led to optimal implant positioning, the resulting implant

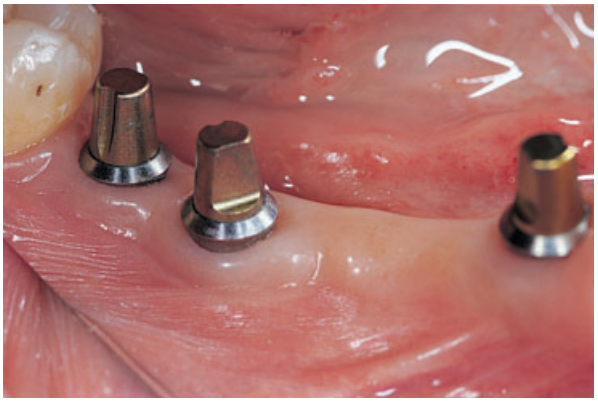


Fig. 54-89 With the solid abutments in place, the inter-implant parallelism is confirmed. Note the easily accessible implant shoulders which will facilitate the following impression and restorative procedures.

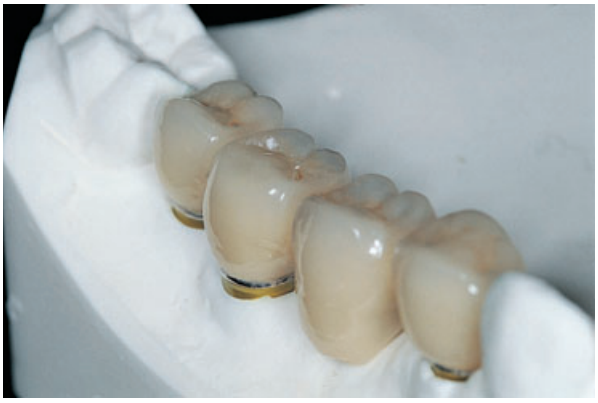


Fig. 54-92 Based on prefabricated burn-out patterns, the final metal–ceramic restoration has been completed. Note the continuous flat axial emergence profile of the individual elements.

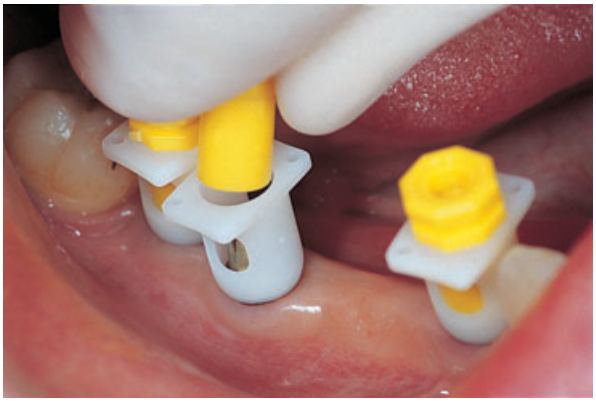


Fig. 54-90 Prefabricated injection-molded, self-centering impression copings and related color-coded positioning cylinders are inserted prior to impression taking with a stock tray.

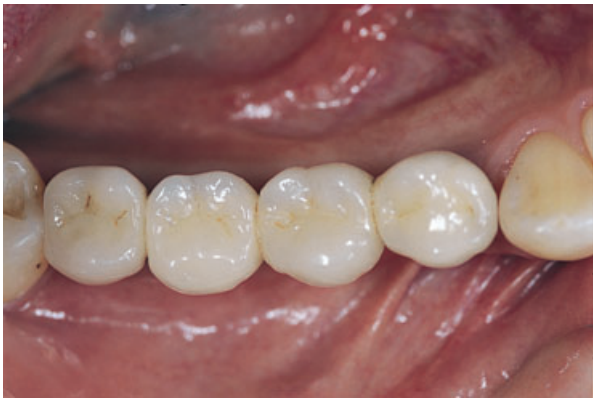


Fig. 54-93 The clinical occlusal view of the cemented four-unit implant prosthesis composed of premolar-sized segments.

Fig. 54-91 The completed master model comprises color-coded aluminum implant analogues.

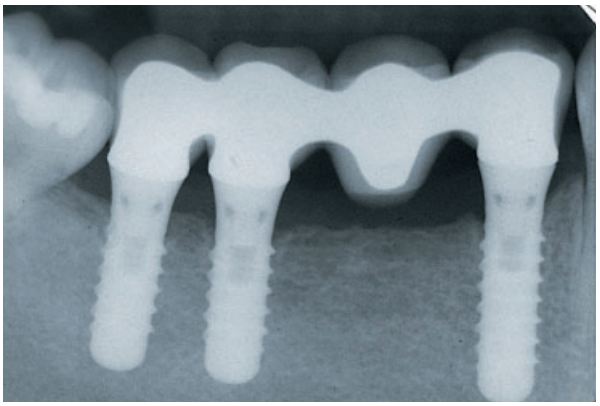


Fig. 54-94 The radiographic control confirms both successful osseointegration of the involved implants and accurate marginal adaptation of the suprastructure.

prosthesis should almost by definition feature a gradually increasing, flat axial emergence profile, adequate embrasures and overall design, and occlusal characteristics similar to those advocated for tooth-borne FPDs (Figs. 54-92 to 54-94).

Angulated abutments

It is not infrequent that all of the parameters defining an optimal three-dimensional implant position cannot be readily reached. Under such conditions the clini-

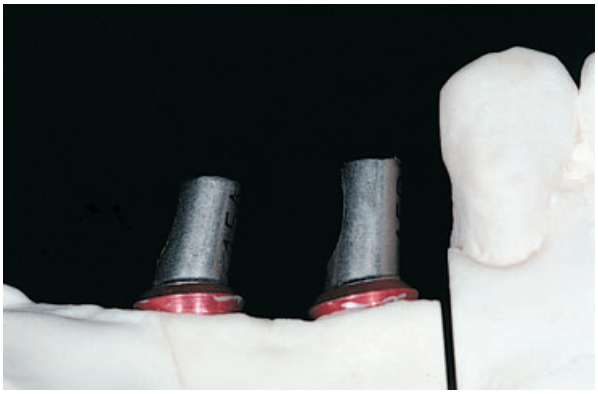


Fig. 54-95 Lateral view of a master model comprising implant level analogues in the right mandibular posterior sextant. Angulated abutments have been selected to correct a too distal implant axis.

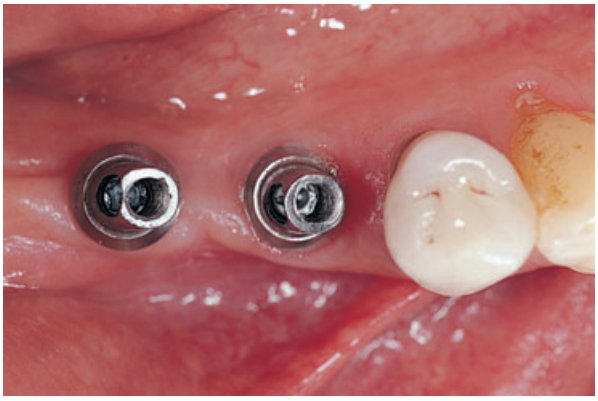


Fig. 54-97 Using an appropriate index, the two angulated abutments are transferred intraorally and subsequently tightened to 35 Ncm with a torque wrench.

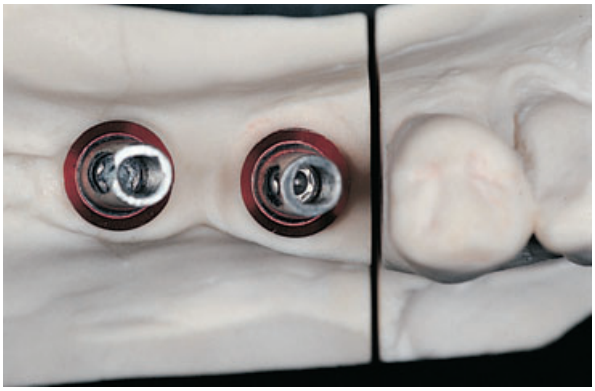


Fig. 54-96 The corresponding occlusal aspect visualizes the amount of axis correction achieved.

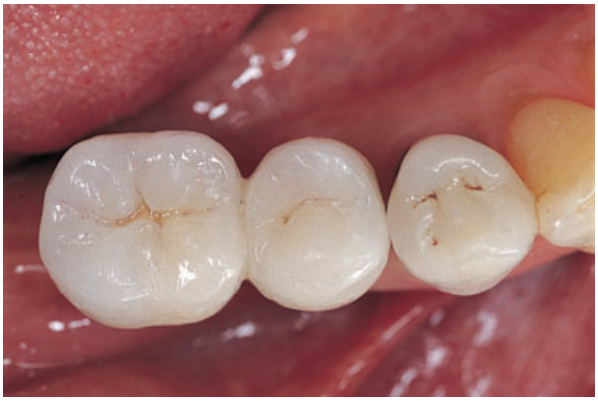


Fig. 54-98 Clinical occlusal view of the cemented two-unit metal–ceramic implant restoration.

cian basically has three options. Either a bone augmentation procedure is undertaken, or a conventional tooth-borne prosthesis is chosen, or one evaluates carefully whether a minor positional compromise can be considered acceptable. The related parameters have to be objectively pondered prior to taking the respective decision together with the duly informed patient. The heaviness of a so-called "site-development" procedure (e.g. lateral or vertical bone augmentation or anterior sinus floor elevation) should definitely be put in direct relation with the expected benefit. In some instances this approach allows significantly invasive procedures to be avoided. Particularly in situations where only the implant axis interferes with an otherwise optimal implant positioning, the subsequent use of angled abutments may still lead to a largely acceptable treatment outcome (Figs. 54-95 to 54-98). In other word, there appears to exist limited room for sometimes considering a slightly "bone-driven" instead of a purely "restoration-driven" implant placement in order to render implant therapy bearable for a given individual patient.

Angled abutments, encompassing various inclinations and dimensions, are currently part of the armamentarium of most of the leading implant systems. They are frequently used and compatible with both a cementable or a screw-retained suprastructure design.

High-strength all-ceramic implant restorations

Additional options, such as milled titanium frameworks as infrastructures for metal–ceramic prostheses or high-strength all-ceramic restorations, have also become recently available in the context of posterior implant restorations. Some of these approaches are based on computer-assisted design and computer-assisted machining (CAD/CAM) technology. As implants and their secondary components are mostly industrially produced or machined, and as their related dimensions and tolerances are well defined, they appear particularly well suited to this kind of technology. In this context, and in order to explain the particular interest associated with this type of technology, it has to be underlined that using either the same metal (i.e. c.p. titanium) or no metal at all for the suprastructure fabrication, would be highly preferable. Porcelain-fused-to-metal alloys with high gold content are primarily utilized due to their superior casting ability.

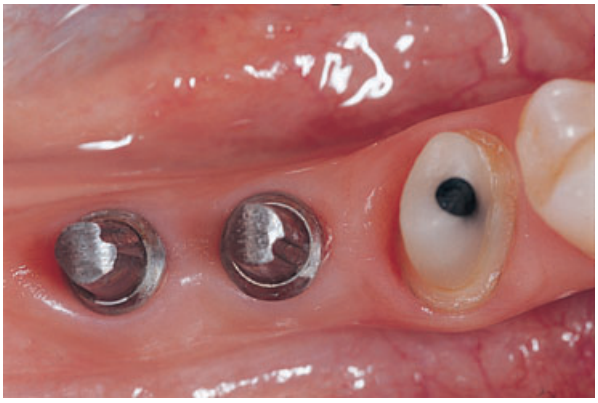


Fig. 54-99 Mandibular right posterior segment, featuring a full-coverage preparation on the non-vital second premolar and two implants equipped with solid abutments in the area of the missing first molar.

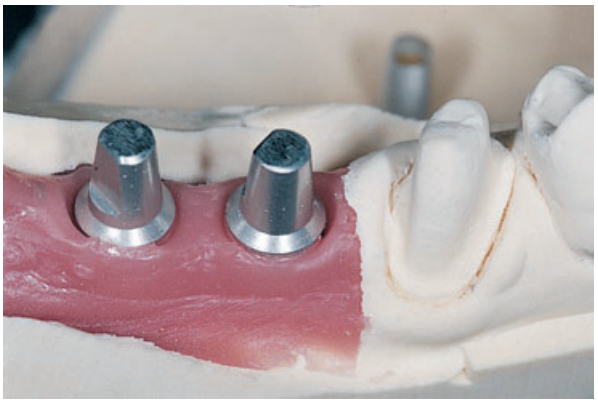


Fig. 54-100 Master model including the stone die of the prepared premolar and the two implant analogues.

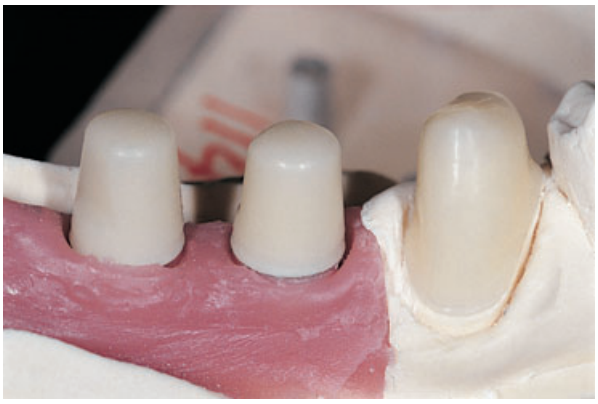


Fig. 54-101 Three respective aluminous oxide copings have been fabricated according to the PROCERA® technique.

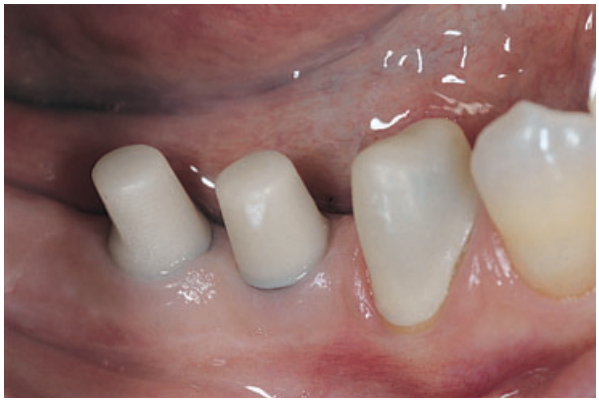


Fig. 54-102 Clinical try-in of the high-strength porcelain infrastructures.

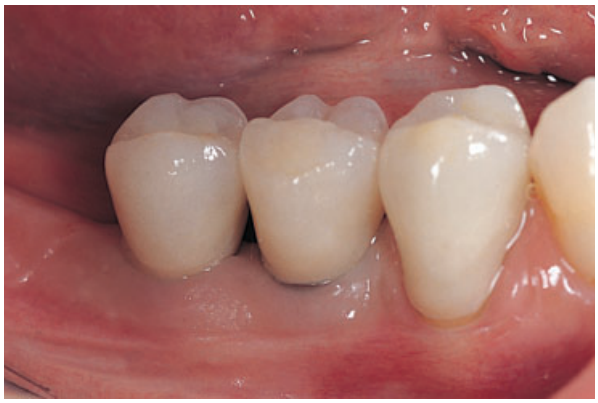


Fig. 54-103 Vestibular view of the cemented final all-ceramic restorations.

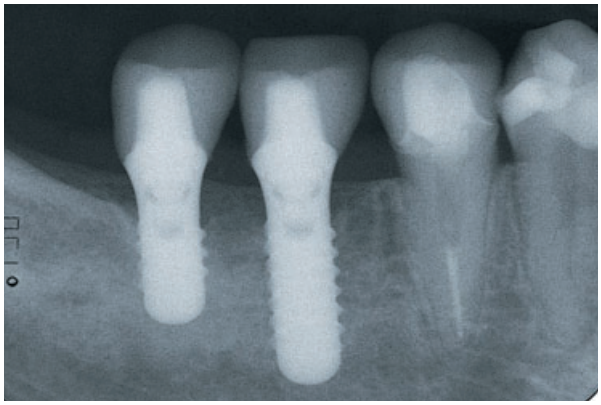


Fig. 54-104 The 1-year radiographic follow-up displays sufficient radio-opacity of the all-ceramic substrate to evaluate the marginal adaptation of the three single-unit restorations.

It would go beyond the scope of this textbook to describe in detail the current evolution in the field of CAD/CAM systems in general and to their impact on implant dentistry in particular. A representative clinical example, however, is given in Figs. 54-99 to 54-105.

All-ceramic implant suprastructures are still preferred as single-unit restorations, primarily for purely technical reasons.

Orthodontic and occlusal considerations related to posterior implant therapy

As one increasingly strives for the best possible biologic, functional and esthetic integration of a given implant restoration in the pre-existing dentition, three-dimensional pre-operative site analysis is of paramount importance. It is not infrequent that this subsequently calls for a pluridisciplinary approach

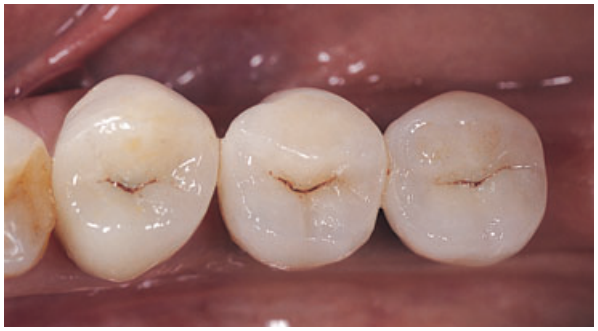


Fig. 54-105 Occlusal view of the two posterior implant-borne premolar-sized suprastructures and the tooth-supported ceramic restoration on the second premolar.

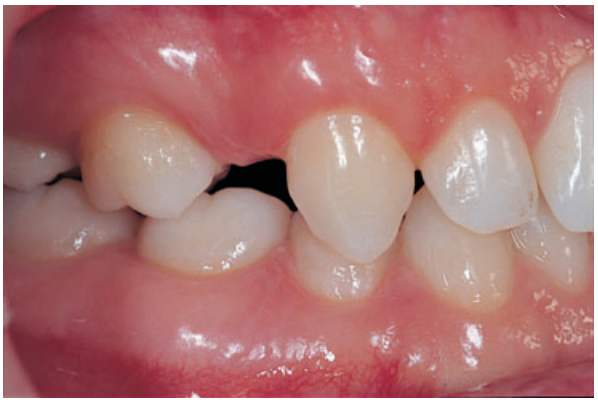


Fig. 54-106 Right lateral view of a 19-year-old female patient, congenitally missing all four permanent maxillary premolars. One can note both an inadequate mesio-distal gap width and a reduced interarch distance.

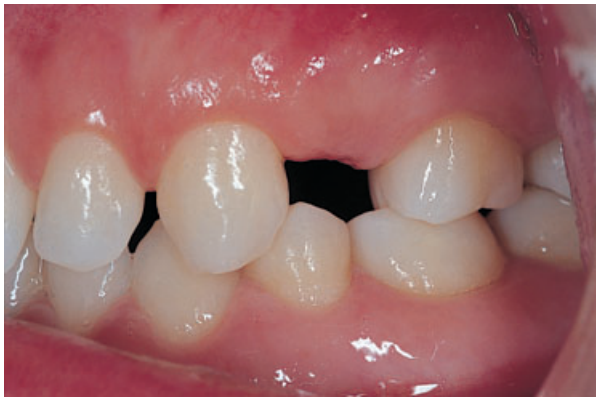


Fig. 54-107 A similar situation regarding interarch distance is present on the patient's left side.

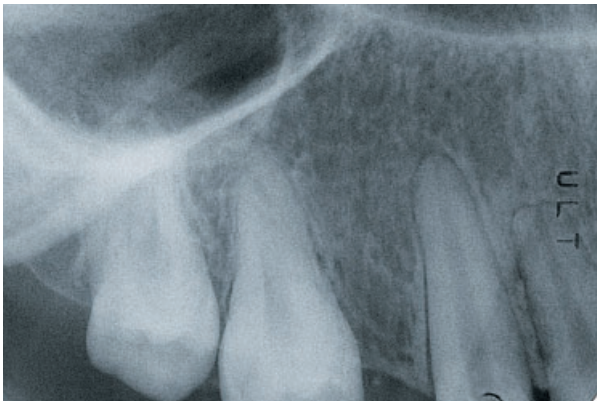


Fig. 54-108 The corresponding radiograph underlines the need for additional orthodontic therapy prior to the insertion of an implant in order to optimize the gap width and the inter-radicular distance.

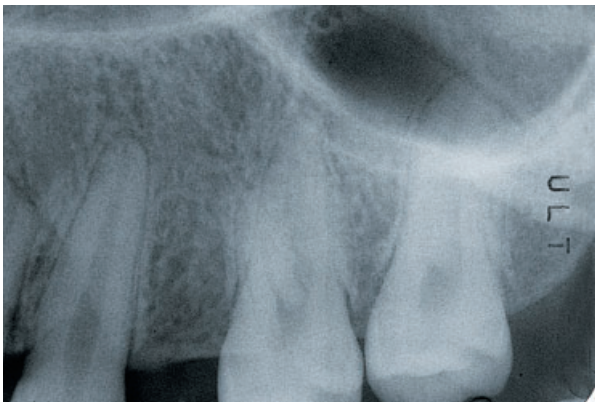


Fig. 54-109 Although to a lesser degree, presurgical orthodontic therapy is also indicated on the maxillary left posterior segment.

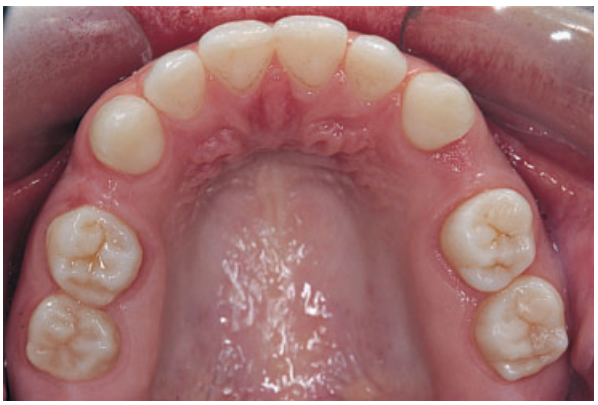


Fig. 54-110 The clinical occlusal view displays the bilateral edentulous spaces in the premolar area. Despite previously performed orthodontic therapy, aiming at reducing the edentulous spaces to the size of one premolar, the mesio-distal gap width on the right side is insufficient for the insertion of an implant.

termed "site development", which may also include presurgical orthodontic therapy (Figs. 54-106 to 54-119). The objective is clearly to create local conditions that are best suited for the type of therapy chosen. If implants are to be involved, the local bone and soft tissue anatomy, as well as the mesio-distal and oro-facial distances of a given edentulous segment, have to comply optimally with the respective most appropriate implant dimensions. Quite often mesio-distal gap dimensions have to be optimized orthodontically and neighboring roots aligned, so that they will not interfere with "restoration-driven" implant positioning. Site development in the broad sense of the term

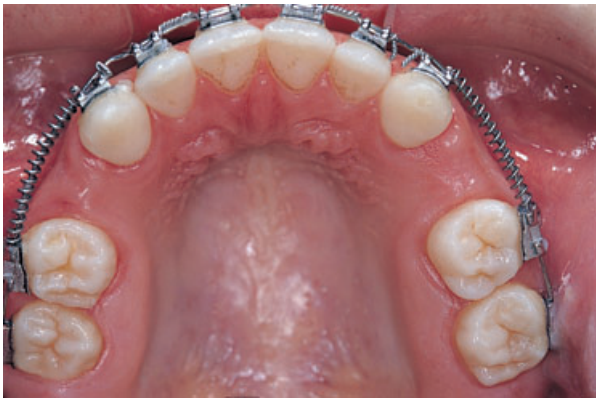


Fig. 54-111 After six months of additional orthodontic treatment using an upper fixed full-arch appliance, the dimensions of the two prospective implant sites appear compatible with this kind of therapy.

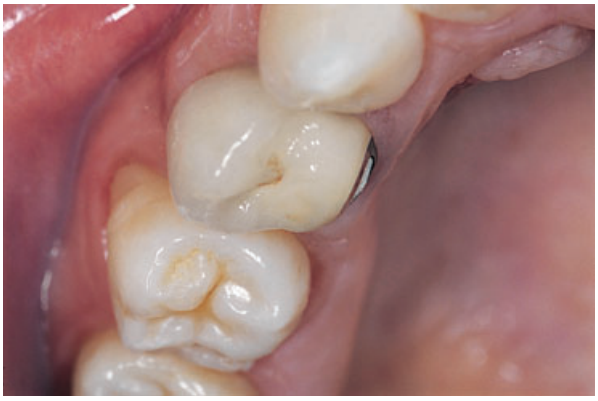


Fig. 54-114 The right oblique occlusal view of the implant restoration clearly demonstrates the advantage of the transverse screw-retention design: no occlusal screw access channel interfering with the functional occclusal morphology and esthetics or with structural requirements inherent to the metal–ceramic technology.

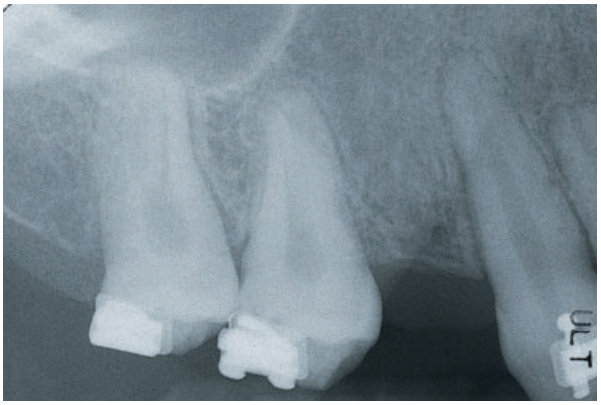


Fig. 54-112 The respective radiograph confirms adequate space in the upper right premolar region for the placement of a standard single-tooth implant.

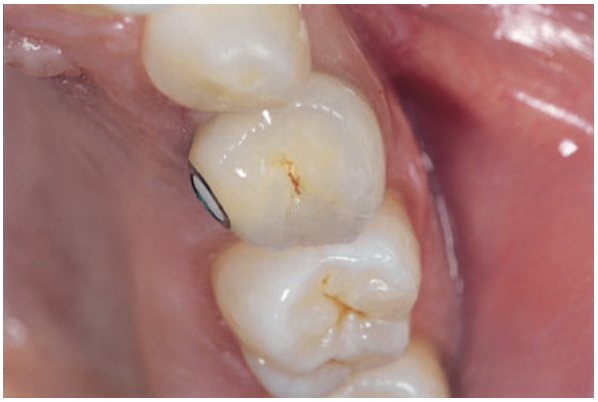


Fig. 54-115 As described for the patient's right side, the left maxillary fixed single-tooth implant restoration integrates appropriately the existing natural dentition.

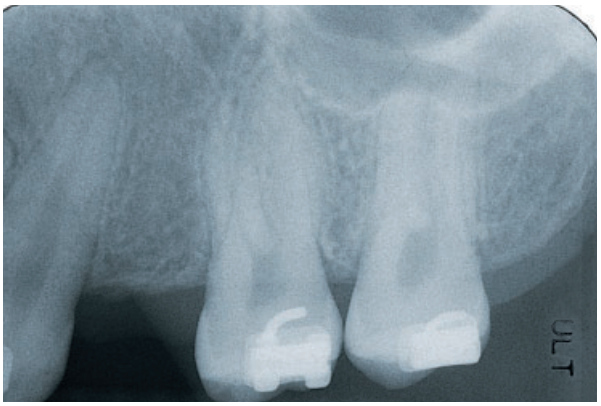


Fig. 54-113 A similar presurgical situation is radiographically confirmed for the upper left premolar site.

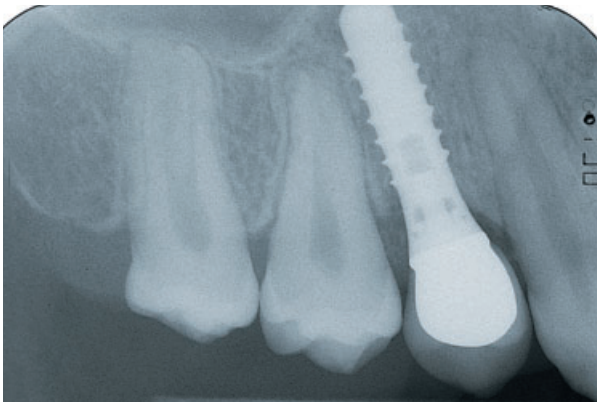


Fig. 54-116 The follow-up radiograph taken 1 year after the insertion of the 12 mm solid screw implant, shows adequate marginal fidelity and stable conditions at the bone-to-implant interface.

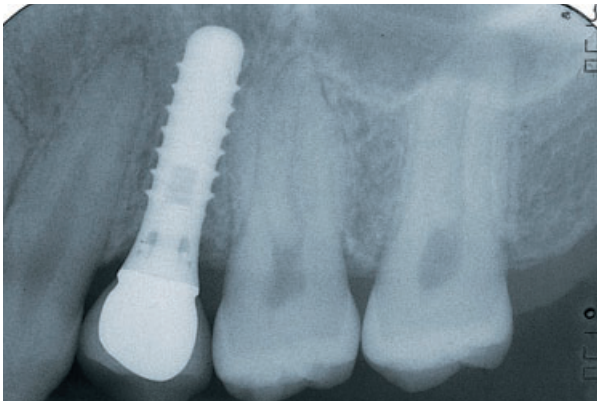


Fig. 54-117 Similar findings are present in the corresponding left-sided follow-up radiograph.

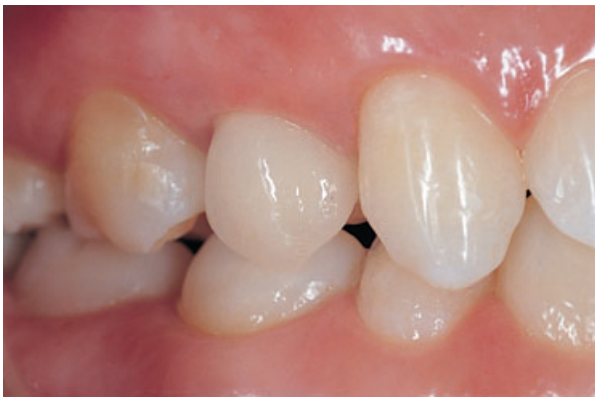


Fig. 54-118 The final right lateral view in centric occlusion features acceptable general interarch conditions and related intercuspation.

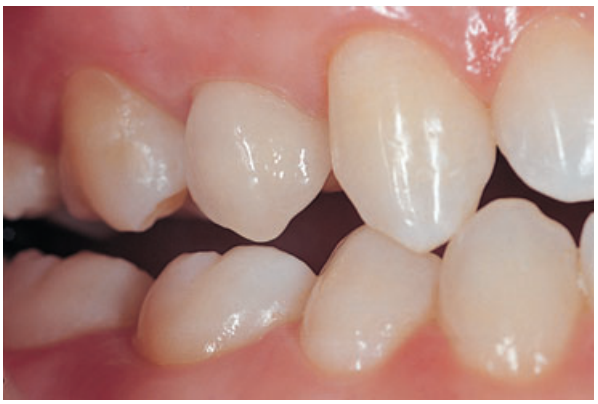


Fig. 54-119 During the right lateral excursion of the mandible (working-side movement), a canine guidance could be established.

also comprises parameters associated with intermaxillary relationships such as occlusal plane, interarch space, and occlusal guidance during mandibular excursions. As osseointegrated implants do provide excellent anchorage for orthodontic appliances (Melsen & Lang 2001), and thus can significantly contribute to the efficacy and simplicity of such a treatment, one may also consider implant insertion prior to orthodontic therapy. This, however, requires meticulous pre-operative analysis and precise three-dimensional implant positioning, anticipating perfectly the ideal location with respect to the final treatment objective.

Table 54-7 Hypothetical implant-specific occlusal concept

- "Light infraocclusion" in centric occlusion position (CO) on posterior implant restorations
- "Narrow" occlusal table
- Only "axial" loading on implant restorations
- No or only "minimal contacts" on implant restorations during "mandibular excursions"
  - No canine guidance on implants
  - Eventually "minimal" group function on the working side

When it comes to occlusal considerations related to posterior implant restorations, one should note that most of the relevant literature available to date addresses eventual effects of occlusal loading on the various components of the implant–abutment–suprastructure complex (Brägger 1999, 2001; Bassit *et al*. 2002; Wiskott *et al*. 2002). In fact, various recommendations are derived from such studies, including various occlusal restorative materials, type and mechanical characteristics of different abutment to implant connections, as well as general guidelines for optimal suprastructure design.

Little information is presently available regarding an eventual direct relationship between occlusal loading and maintenance of osseointegration in general and occurrence of peri-implant crestal bone resorption in particular (Wiskott & Belser 1999; Duyck *et al*. 2001; Engel *et al*. 2001; Gotfredsen *et al*. 2001a,b,c; O'Mahony *et al*. 2001; Engquist *et al*. 2002; Wright *et al*. 2002). Attempts have been made to take into account the fundamental differences between a tooth surrounded by a periodontal ligament and an "ankylosed" osseointegrated implant, the latter disposing neither of local mechanoreceptors nor of a so-called "damping" capacity. This led to a hypothetical implant-specific occlusal concept (Table 54-7), featuring parameters such as lighter contacts in centric occlusion when compared with the surrounding natural dentition, and no or only minimal contacts on implant restorations during mandibular excursions. One should clearly note, however, that these guidelines are primarily derived from clinical experience, subjective opinions and eventually common sense, and that there is little or no solid scientific evidence available to date which would support such a concept (Taylor *et al*. 2000).

Concluding remarks and perspectives

Early and immediate fixed implant restorations

Currently, one can observe a strong tendency towards shortened healing delays and ultimately towards

immediate loading or at least "immediate restoration" protocols in association with dental implants (Tarnow *et al*. 1997; Ericsson *et al*. 2000; Gatti *et al*. 2000; Szmuk-ler-Moncler *et al*. 2000; Bernard *et al*. 2001; Chiapasco *et al*. 2001b; Ganeles *et al*. 2001; Gomez-Roman *et al*. 2001; Roccuzzo *et al*. 2001; Romanos *et al*. 2002). Improved implant surface characteristics have contributed to this evolution (Buser *et al*. 1998a; Deporter *et al*. 2001; Gotfredsen *et al*. 2001b; Roccuzzo *et al*. 2001; Cochran *et al*. 2002). Numerous studies have reported that such an approach can be considered predictable under certain well defined conditions. These conditions include four to six implants inserted in the interforaminal part of the edentulous mandible and which are subsequently splinted with a bar device (Gatti *et al*. 2000), as well as multiple implants evenly distributed around an edentulous arch and then immediately restored – according to the principle of "cross-arch stabilization" – with a splinted full-arch FPD (Tarnow *et al*. 1997). Achieving adequate primary stability at the moment of implant installation, and confining, during the crucial first healing period, an eventual mobility below the threshold of approximately 50 microns, appear to be among the decisive parameters for predictably achieving osseointegration (Szmukler *et al*. 2000). With regard to the routine application of immediate loading protocols for posterior single-tooth restorations, it appears advisable to wait for scientific confirmation of its respective potential in the form of randomized controlled clinical trials.

In conclusion, the possibility of performing highly predictable treatments which are more simple, require less time and which can be conducted in a standard dental practice set-up, as well as the associated quality of treatment outcomes, have nowadays made implant therapy in the load-carrying part of the dentition an integral part of the restorative spectrum for any kind of edentulism. This evolution is most dynamic and holds promise for further significant developments.

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Chapter 55

Implant–Implant and Tooth–Implant Supported Fixed Partial Dentures

Clark M. Stanford and Lyndon F. Cooper

Introduction

The restoration of the fully and partially edentulous situation involves a combination of systematic diagnosis, treatment planning, and careful assessment of the therapy choices and the outcomes. The replacement of a continuous span of teeth creates challenges involving assessment of anatomic, physiologic, cost, time, impact on quality of life (QOL), and patient desires. The clinician is faced with balancing each of these aspects when developing a treatment plan for the patient. Modern dental care assures that tooth replacement therapy is provided in an economical and expedient manner. To this end, dental implants offer advantages for many clinical situations. In certain situations, the restoration of missing teeth using individual free-standing implant-supported crowns is a logical and satisfactory treatment option. At other times use of an implant-supported fixed partial denture (FPD) is a satisfactory approach (Fig. 55-1). Because of functional and esthetic priorities, anterior and posterior multi-tooth implant restorations can present different clinical challenges. This chapter will consider implant-to-implant supported FPD (bridges) separately from tooth-to-implant supported prosthesis since there are unique issues with each type of prosthesis. The use of a fixed complete denture to replace all of the teeth in an arch will be considered as a form of a fixed partial denture.

Initial patient assessment

The predictable esthetic and functional outcomes of implant treatment require comprehensive diagnostic and treatment planning (Stanford 2005a). As a member of the implant team, the prosthodontist needs to collaborate with the surgical specialist, laboratory technician, and allied team members such as radiologists, and dental and surgical assistants. The initial assessment of the patient's medical and dental history assists in the determination of the implant system and devices that will meet the patient's therapeutic needs. The initial patient interview should establish the patient's individual esthetic requirements. This assessment should determine a patient's history of bruxism, periodontal disease, tobacco use, uncontrolled diabetes mellitus, and metabolic bone diseases (Moy *et al.* 2005). Recent literature suggests implant therapy in patients with advanced chronic periodontitis may have an altered prognosis, although stabilized with maintenance therapy (Nevins & Langer 1995; Ellegaard *et al.* 1997; Brocard *et al.* 2000; Pjetursson *et al.* 2004; Wennstrom *et al.* 2004a). Maintenance therapy is vital since longitudinal implant bone loss occurs and can be observed after many years of asymptomatic clinical service (Hardt *et al.* 2002; Fransson *et al.* 2005). In addition, the assessment should educate patients about the etiology of tooth loss, reveal their attitudes about treatment as well as the ability to tolerate it,

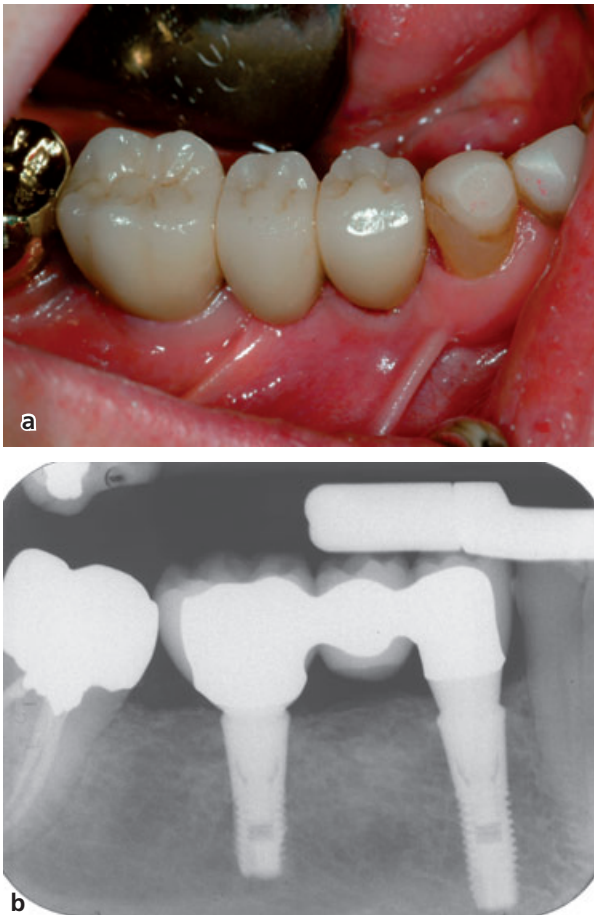

Fig. 55-1 Implant-supported fixed partial denture (FPD). (a) Patient restored with two implants (44 and 46) and three-unit FPD. (b) Five-year recall radiograph demonstrates stability of osseous tissues around the implants.

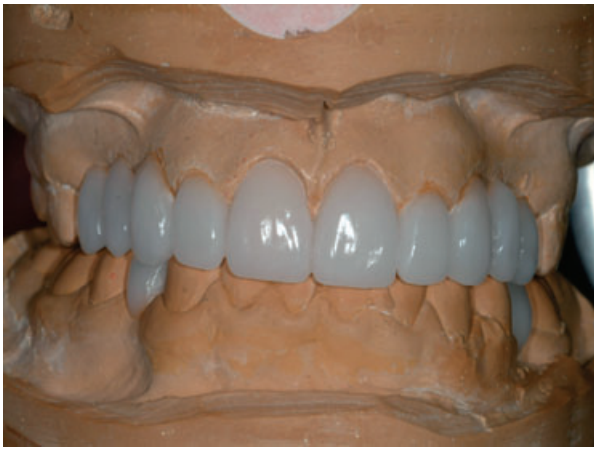

Fig. 55-2 Diagnostic wax-up for implant therapy demonstrating desired contours for the planned definitive restorations.

and inform them of estimated treatment costs (Pjetursson *et al.* 2005; Stanford 2005a). Throughout the surgical and prosthetic phases of the implant reconstruction, the dental practitioner should obtain comprehensive written and verbal informed consent for patient treatment. The consent form should document the risks, benefits, and alternatives discussed with the patient. The option for and consequences of no treatment should be included. This initial assessment phase should provide the clinical team with sufficient information to characterize the patient-related risk factors that will influence treatment.

To assure the implant location, number, and implant dimension are congruent with the anticipated prosthesis, it is essential the dentist design and compose the proposed prosthesis during the diagnostic phase. Pre-operative planning gives insights into both technical aspects (number, implant dimension, position, and angulation) as well as potential surgical site development needed prior to or at the time of implant placement. The complete treatment plan then assimilates clinical, radiographic, and psychologic information gathered using the patient interview, clinical examination, and radiographic survey. During the clinical examination, the dentist carefully evaluates the residual ridge for shape and contour, and evaluates alternative intraoral sites for mucosal recession. A careful evaluation of patient's risk factors for soft and hard tissue changes, whatever final restoration is planned, should be made to comply with the informed consent process and encourage realistic patient expectations. However, to move beyond assessing the feasibility of implant treatment, it is essential to utilize articulated diagnostic study casts to fully assess the tissue architecture and relationship of teeth and mucosa with existing edentulous areas.

Thus, the initial clinical examination should conclude only when sufficient materials are available to accurately mount diagnostic casts and interpret the study casts and screening radiographs using recorded clinical information. Based on this diagnostic information, a surgical guide or denture is fabricated using a process of diagnostic waxing of the planned prostheses, evaluation of the desired implant position, angulation, probable abutment dimension and angulation, and, finally, the need for hard or soft tissue augmentation as supportive therapy to implant placement (Fig. 55-2). The diagnostic waxing process is a key step in the assessment of local risk factors affecting fixed partial dentures supported by dental implants and is critical to the process of strategically planning implant placement to limit these risks.

Implant treatment planning for the edentulous arch

The edentulous mandibular arch can be restored using a fixed complete denture, fixed partial dentures or an overdenture. The fixed complete denture can be a gold casting or CAD/CAM milled titanium framework, either with prosthetic acrylic resin teeth or teeth veneered with porcelain (Adell *et al.* 1990) The edentulous arch can also be restored with a series of FPDs that allows the clinic to manage multiple implants without seeking the precision fit of a full-arch prosthesis (Fig. 55-3). This approach also pro-

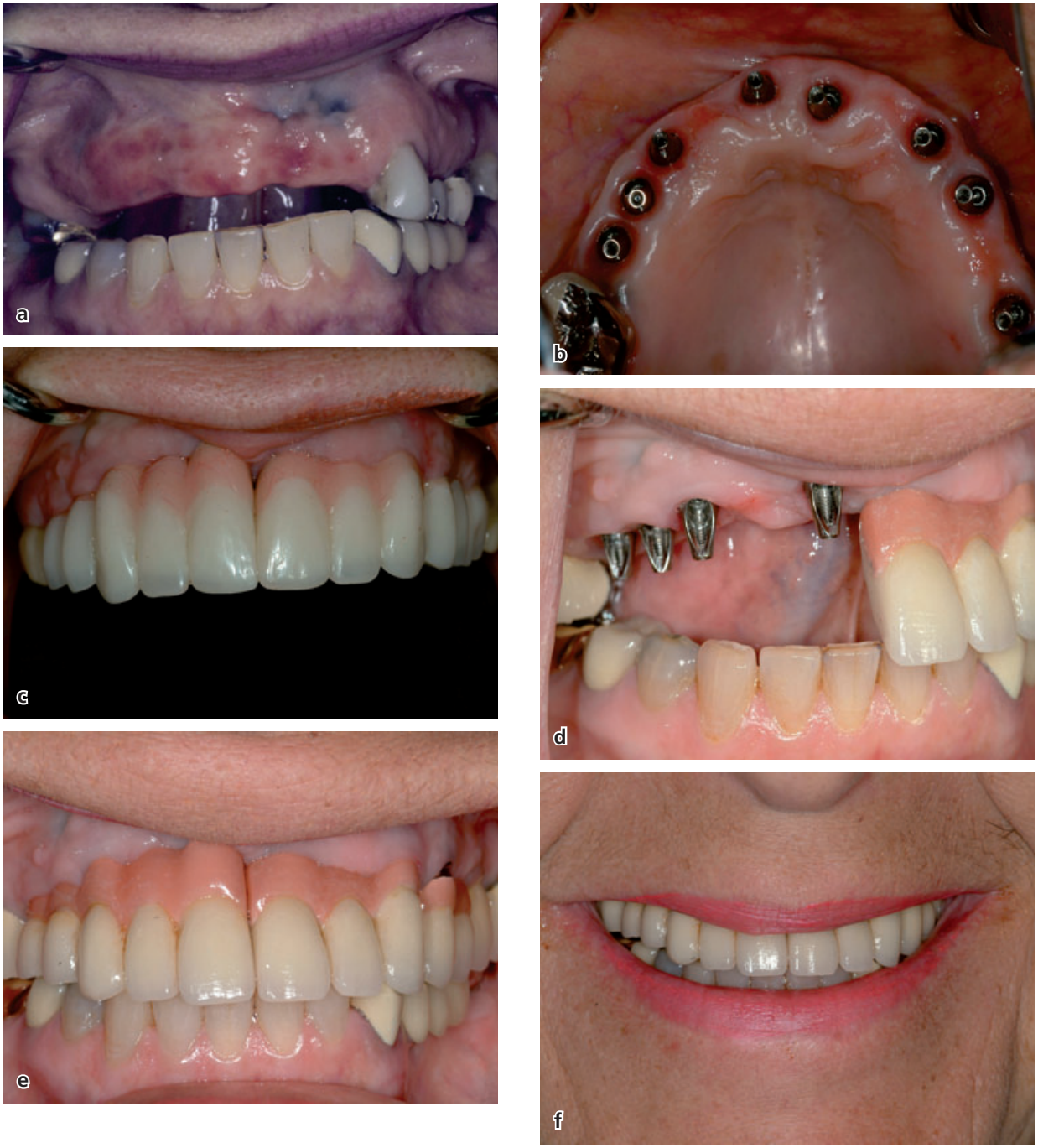

Fig. 55-3 Use of fixed partial dentures to restore missing hard and soft tissue. (a) Patient presented with a 40-year history of an edentulous space in the maxilla. Following placement of eight implants (b), a long-term acrylic resin provisional was fabricated simulating desired tooth and soft tissue dimensions (c). (d) Based on the long-term provisional, a ceramometal fixed prosthesis was fabricated using mucosa-colored ceramic materials on a metal framework. (e,f) Five-year recall demonstrating fixed prosthetic outcomes and anterior esthetics.

vides for greater flexibility in case of complications related to porcelain fracture, recession, wear, etc., and has demonstrated successful long-term outcomes (Bragger *et al.* 2001). An overdenture with attachment to the implant can be fully implant supported and retained or a combination mucosa/implant-borne prosthesis. Clinical studies indicate high patient acceptance of this form of therapy (Feine *et al.* 1994, 2002; Duyck *et al.* 2004; Naert *et al.* 2004a,b; Zitzmann *et al.* 2005).

Prosthesis design and full-arch tooth replacement therapy

If minimal bone resorption exists, restoring the edentulous maxillae with a porcelain-fused-to-metal restoration has a reasonable outcome (Stanford 2005a). The restorative dentist must perform a diagnostic work-up including impressions, jaw relationship records, and an esthetic try-in using prosthetic denture teeth on a trial denture base. The degree of

lip support and smile line (i.e. anterior and posterior occlusal planes) of the diagnostic denture set-up should be evaluated intraorally. It is also useful to evaluate the patient's lip support with and without the anterior facial denture flange (Lewis *et al.* 1992; Stanford 2002). The amount of tooth exposure of the anterior smile line (relaxed and exaggerated), provides clues about the expected crown length, gingival display, and potential need to use gingival tone porcelain for appropriate tooth length and esthetics in a full-arch reconstruction. Communication and discussion with the dental laboratory technician is very helpful at this point prior to finalizing the treatment plan. A fixed maxillary prosthesis has greater incidence of esthetic, phonetic, and oral hygiene problems compared with an overdenture prosthesis, in part associated with excessively long anterior teeth, excessive facial cantilever pontics, and mesial–distal complications with embrasure forms (Lewis *et al.* 1992). Given the clinical and laboratory complexity of these prostheses, a maxillary overdenture on four to six implants may be an alternative (Phillips & Wong 2001; Anon. 2003; Naert *et al.* 2004b).

Complete-arch fixed complete dentures

A complete-arch fixed complete denture (FCD) provides excellent function and patient acceptance (Lewis *et al.* 1992; Feine *et al.* 1994). During the diagnostic phases, the advantages and disadvantages of the FCD compared with those of an overdenture should be discussed with the patient. If using a ceramometal full-arch fixed reconstruction, consider replacing every three teeth with a three-unit fixed partial denture on two implants (e.g. #13–11) using the pontic contours to adjust for implant alignment and esthetic demands (Fig. 55-3) (Stanford 2002). A fixed maxillary reconstruction entails between six and eight implants (first molar, first premolar, canine, and central incisor) with four independent fixed partial dentures (molar to premolar, canine to central incisor, bilaterally) (Stanford 2005a). With care made to limit loading, six implants may be used with distal cantilevers on two fixed partial dentures (cantilever pontics limited to one premolar sized tooth). An overdenture should use a sufficient number of implants for long-term stability, typically four in the maxilla (canine and second premolar region) and two in the lower canine or first premolar region (Mericske-Stern *et al.* 2000). Using the denture set-up, a radiographic guide is fabricated with radio-opaque markers (e.g. gutta-percha or bur shanks) within the denture at the sites of interest. An alternative approach involves duplicating the denture set-up with teeth made using 5% medical grade barium sulfate mixed with clear autopolymerizing resin. This approach allows easy visualization of tooth size, angle, and position on conventional and/or CT-aided treatment planning. In the mandible, the trial set-up evaluates the height and position of the prosthetic teeth relative to the symphyseal cross-sectional anatomy. A conventional fixed complete denture with acrylic teeth requires a minimum of 15 mm from the alveolar crest to the planned incisal edge (Stanford 2005a). If the vertical dimension of occlusion and jaw anatomy is insufficient, one alternative is to perform an aggressive alveoectomy or to rehabilitate with ceramometal restorations (along with treatment planning for the additional cost).

Radiographic information and diagnostic set-up will help determine the type of definitive prosthesis design. Skeletal class I and II relationships with minimal resorption may allow normal contours and lip support with a fixed complete denture. Prognathic class III relationship can increase prosthetic problems, especially if implants cannot be placed distal to the mental foramens. In such cases, an overdenture approach yields a more predictable result (Naert *et al.* 1997).

Prosthesis design and partially edentulous tooth replacement therapy

Clinician or patient preferences for the use of implants for restoration of partial edentulism using FPDs must be carefully weighed against the potential limitations associated with this therapy. Technical complications related to implant components and the suprastructure are more frequently reported than complications related to peri-implant tissues (Berglundh *et al.*, 2002). Also, these complications for implant-supported fixed partial dentures are together more frequent than implant loss or implant fracture. For example, Bragger *et al.* (2001) reported for a 10-year follow-up period that the percentage of reconstructions without any biologic nor technical failure/complication was 66.5% for single-crown implant restorations, 54.4% for implant-supported FPD, and 50% for tooth–implant-supported FPD. Importantly, the authors concluded that prostheses with history of complications were at greater risk of implant failure. It may be possible to infer that complications reflect the functional features of the prosthesis or the patient and, furthermore, that some of these complications are due to limitations in implant and prosthesis planning, placement, construction or the innate limitations of implant components. Complications most frequently observed for FPDs include veneer fracture, opposing restoration fracture, bridge screw loosening or fracture, abutment screw loosening or fracture, and metal framework fractures (Goodacre *et al.* 2003a). The considerations for treatment planning of implant-supported FPDs must include features that affect not only implant success, but also abutment and bridge screw performance, and prosthesis esthetics and longevity.

Primary among clinical considerations for any implant prosthesis is some estimation of the potential forces that will be exerted during function. It is well

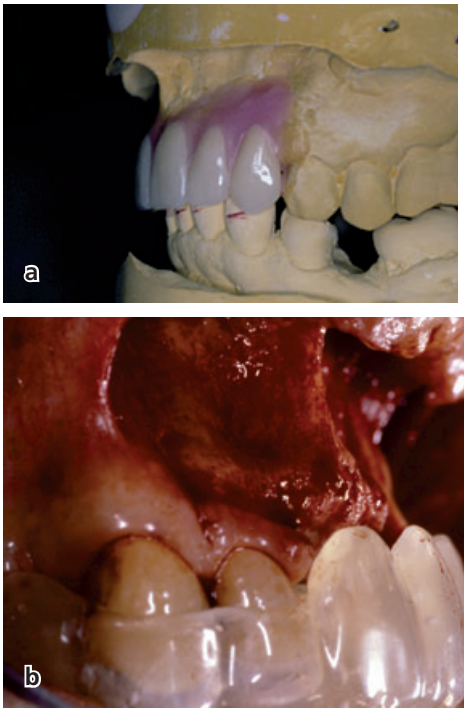

Fig. 55-4 (a) Diagnostic wax-up demonstrating desired tooth position and wax used to demonstrate the amount of planned augmentation needed. (b) At the time of site development, the surgical guide demonstrates the difference between the desired tooth position and the residual ridge.

recognized that masticatory forces increase as the point of interaction moves posterior in the arch. Additionally, damaging bending moments are increased with the acting lever arm length. Greater concern is warranted when implants are planned to support prostheses with large occluso-gingival dimension (extensive resorption) or for prostheses with extensive mesial, buccal or lingual cantilevers or any substantial distal cantilever. Additional immediate considerations typically address the esthetic potential of the prosthesis. This is clearly most relevant for anterior FPDs. Tooth-like restorations are dependent on proper dimensions and, again, greater concern is raised with increasing residual ridge resorption. However, basic features of implant placement such as avoiding encroachment of embrasures are critically important for anterior FPDs. These matters are revealed through the process of evaluating the diagnostic waxing (Fig. 55-4).

The current absence of discrete rules governing the number and dimension of implants (or a particular implant) needed to support a given masticatory function is acknowledged. Krekmanov *et al*. (2002) proposed that support factors can be attributed to implants and that relative risk can be assigned to various clinical scenarios. This approach of recognizing relative risk factors and modifying the clinical approach to therapy – even in a subjective way – merits consideration. At the very least, each clinical scenario should be considered in terms of prosthetic and implant risk both biologically and biomechanically and treatment should be adapted to recognize these risks if possible. Obvious examples would include the use of additional or larger implants to support molar function as opposed to premolar function and the avoidance of distal cantilevers in bruxing patients.

A simple strategy for reducing the biomechanical risks to implants and prostheses of implant-supported FPDs is to plan for implants located beneath the cervical aspect of the terminal mesial and distal FPD retainers whenever possible. This approach reduces the length of bending moments, irrespective of the imposed load, and also assures that the implant and abutment do not encroach on the embrasures to limit oral hygiene or esthetic potential of the restoration (Fig. 55-1).

When multiple implants are placed in an edentulous span, careful treatment planning will indicate mesial and distal width of desired restorative teeth. This plan will in turn indicate proposed sites where implants (e.g. every other tooth) may be placed for stability of the prosthesis. Choice of implant location may depend on available osseous tissues, soft tissue thickness, esthetics, phonetics, and need for ridge development.

Implant per tooth versus an implant-to-implant FPD?

In having a dialog with patients about the desired tooth replacement therapy, clinicians often recommend an implant per tooth approach when replacing multiple contiguous teeth. When this approach is done with individual free-standing crowns, the approach provides potential for a natural tooth-by-tooth replacement. On the other hand, it can create significant issues for the prosthetic restoration if the implants are not placed in exactly the desired location. The use of short-span FPDs therefore has certain general advantages. First, the use of two implants to replace three teeth allows the technician to judiciously use the pontic contours to alter the shape and contour of the prosthesis, compensating for implants that are not optimally positioned. For instance, implants that emerge at the interproximal area can be compensated by the use of angled abutments or custom abutments facilitating the use of the connector dimensions to create an illusion of natural teeth. Another advantage cited by some is the establishment of interproximal contacts between the prosthesis and adjacent teeth.

In order to assess the predictability of these types of restorations, clinical research studies need to be assessed. Randomized, controlled clinical trials of partially edentulous patients with a previous history of periodontal bone loss were evaluated in a 5-year trial by Wennström *et al.* (2004a). This study reported on 149 self-tapping implants (Astra Tech AB, Mölndal, Sweden) placed in the maxilla (n = 83) and mandible (n = 66) in the premolar and molar area. Each patient

received two implants (machined surface versus grit blasted with Ti dioxide) that were allowed to heal for 6 months prior to loading. Screw-retained FPDs were completed and maintenance therapy provided following the CIST program (Lang *et al.* 2004). Implant loss was 5.9% at the subject level. FPDs demonstrated a total 5-year bone loss from implant placement of 0.41 ± 0.78 mm (subject level) (Wennstrom *et al.* 2004a). There was a statistical difference in the frequency of bone loss between those placed in the upper versus those in the lower jaw: 38% of the maxillary implants demonstrated >1 mm bone loss while 9% of the FPD in the lower arch had >1 mm bone loss at 5 years.

Previous studies evaluating bone loss with the implant system used in this study have reported mean marginal bone loss from implant placement to be an average of –0.46 ± 0.38 mm (Olsson *et al.* 1995; Yusuf & Ratra 1996; Karlsson *et al.* 1997, 1998; Makkonen *et al.* 1997; Norton 1997, 2001; Arvidson *et al.* 1998; Astrand *et al.* 1999; Cooper *et al.* 1999, 2001; Palmer *et al.* 2000, 2005; Puchades-Roman *et al.* 2000; van Steenberghe *et al.* 2000; Gotfredsen & Karlsson 2001; Steveling *et al.* 2001; Weibrich *et al.* 2001; Engquist *et al.* 2002; Wennstrom *et al.* 2004a,b, 2005; Rasmusson *et al.* 2005). When implants were placed in the posterior maxilla with the indirect sinus lift technique and restored with FPDs at 6 weeks using a fluoride-modified implant, outcomes demonstrated bone loss –0.19 to –0.4 mm (sd = 0.73) from implant placement with a 98.3% cumulative implant survival rate (CISR) (Stanford 2006). These data support the concept that partially edentulous patients can be restored with FPDs (Gotfredsen & Karlsson 2001). However, post-insertion maintenance is critical. Hardt *et al.* (2002) observed in a population with a history of bone loss associated with periodontitis, that poor oral hygiene and compliance with maintenance therapy resulted in an elevated failure rate of 8% at 5 years; 62% of the implants in patients susceptible to periodontitis vs. 44% in non-perio groups demonstrated more than 2 mm bone loss (Hardt *et al.* 2002). This emphasizes the need for ongoing supportive care for patients undergoing tooth replacement therapy (Lang *et al.* 2004a; Schou *et al.* 2004).

Cantilever pontics

In managing tooth replacement therapy there are times when a mesial or distal extension is needed to the FPD. The use of cantilever extensions increases the mechanical angular moment on the prosthesis and increases the potential for early fatigue and prosthetic complications (Brunski 2003). The use of cantilever extensions were first advocated as a routine prosthetic approach in the Toronto mandibular fixed complete denture designed for the edentulous arch (Zarb 1988; Zarb and Schmitt 1990a,b, 1991). Clinical studies on the use of cantilever extensions suggest greater complications with longer extensions beyond 15 mm, although there are many opinion-based recommendations that range from 10–20 mm (Shackleton *et al.* 1994). Cantilever extensions increase the angular moment on the most distal implant and abutment connection and the complications such as loosening screws, fractured components, etc. are related to a combination of factors including cantilever design, composition, occlusion, jaw relationships, and implant/abutment design (Brunski *et al.* 1986). In a survival analysis though 80 months of fixed complete dentures with an acrylic resin tooth replacement and the external hex Branemark system, Shackleton *et al.* (1994) observed a 100% survival rate for cantilever extension <15 mm but a decline to <30% survival for extension >15 mm.

In the anterior quadrant where esthetics are desired, there are often missing lateral incisors that leave only minimal mesial–distal space for implant placement. One option may be to use narrow diameter implants in such sites but control of occlusion is important (Stanford 2005b). An alternative, especially when there are missing adjacent teeth, is to use cantilever pontics of minimal dimension to replace the missing teeth (Fig. 55-5). This has the potential for more predictable esthetics without excessive site development, expense, and time. The use of cantilever pontics in the posterior quadrants is more controversial. Cantilever pontics in ceramometal FPDs create larger moment arms on the prosthesis and have the potential for increase mechanical complications with the implant–abutment stack (Stanford 1999; Brunski 2000, 2003; Brunski *et al.* 2000; Gratton *et al.* 2001). There are times where posterior cantilever pontics are useful but the clinician should consider these for areas of controlled occlusal forces and primarily for esthetics. Further, in use with ceramometal FPD, their use should be limited with no more than a premolar size pontic (~7 mm mesial-distal dimension) with only light centric occlusal contacts on the pontic (Stanford 2005b).

There are ongoing issues regarding cemented relative to screw-retained FPDs. While the choice of prosthesis is dependent on multiple factors (clinician preference, flexibility, passivity of fit, cost, etc.) there are times when one approach is preferable. For instance, in situations where the patient has multiple clinical signs of recession (thin tissue biotype, recession, lack of keratinized mucosa, etc.) a screw-retained fixed prosthesis may be preferable (Stanford 2005a). This approach will allow the clinician to remove the prosthesis at a later point in time and make repairs which may salvage the prosthesis. Patients with a history of implant loss in the area, difficult implant placement or elevated medical risk are other indications to consider a screw-retained fixed prosthesis. Further, if the prosthesis needs to be routinely removed (e.g. in a research protocol) for accurate measurements of pocket probing depths (PPD) and bleeding on probing (BOP), the clinician may want to chose a screw-retained prosthesis. At times there

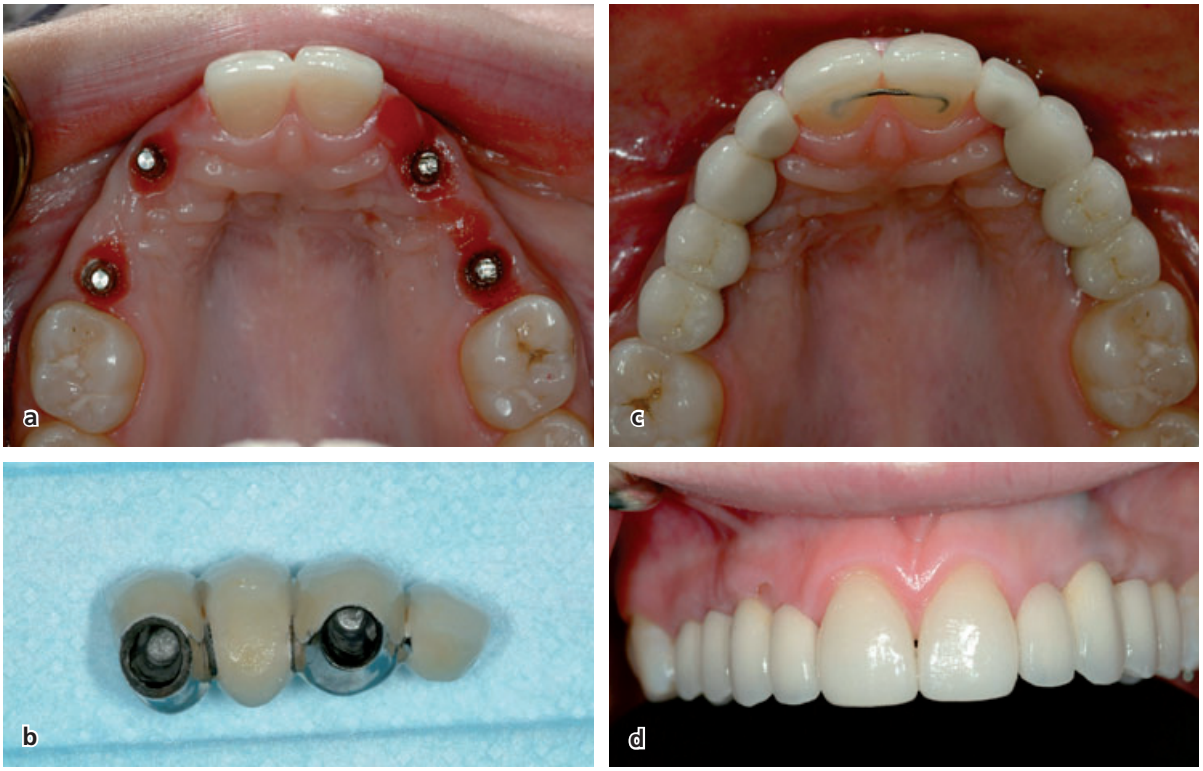

Fig. 55-5 Use of cantilever pontics to replace missing lateral incisors as a part of fixed partial denture (FPD) therapy. (a) Four implants were placed in the maxilla in the second premolar and canine region. (b) A four-unit FPD with cantilever pontics (12 and 22) was fabricated. (c) Restoration of eight missing teeth with four implants allowing establishment of an acceptable esthetic result (d).

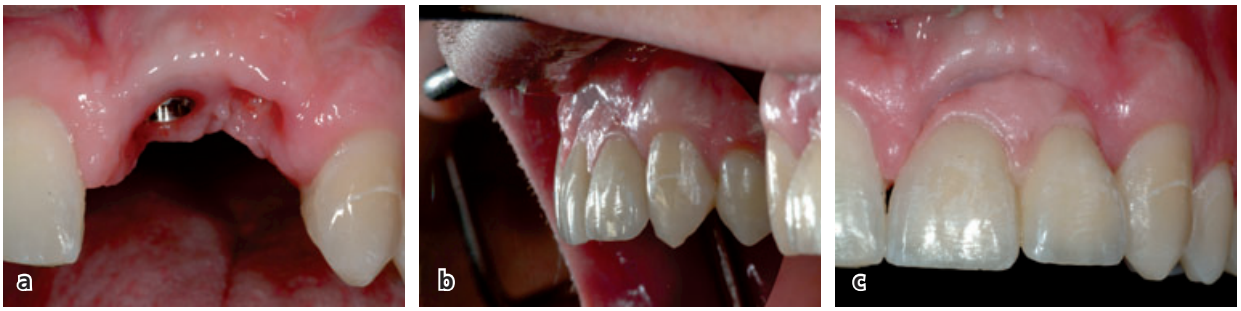

Fig. 55-6 Soft and hard tissue prosthetic replacement. (a) Patient presented with soft tissue loss in the area of 21 and 22. (b) Missing mucosal and hard tissue contours were replaced with a combination of gingival and tooth-colored ceramic materials. (c) A prosthetic solution to a difficult esthetic situation. Ceramic reconstruction by Henry Husemann CDT (University of Iowa).

are indications for fabricating a fixed prosthesis that replaces both hard and soft tissues (Garcia & Verrett 2004). In sites where there has been considerable loss of supporting structures, common following trauma or long-term chronic bone loss such as periodontal disease, it may be necessary to replace both dental and osseous supporting structures (Fig. 55-3). If this cannot be accomplished with biological site development, the clinicians may need to reconstruct this area with a combination of porcelain teeth developed with the appropriate mesial-distal and inciso-gingival dimensions to match the adjacent teeth and blend into the esthetic contours of the dentition and face. In doing so, it may become obvious that the gingival tissues need to be replicated in "mucosal" colored porcelain or acrylic. The development of tissue-matched mucosal shades takes significant laboratory skill and dexterity and often means the patient needs to be seen directly by the technician along with the restorative dentist (Malament 2000; Malament & Neeser 2004). Custom mucosal shades often need to be developed and matched chairside. While these approaches can be quite time consuming the end results can be quite satisfactory and surpass what can be accomplished by repeated soft tissue procedures (Fig. 55-6). The restorative dentist needs carefully to assess the patient early in the diagnostic process for implant therapy and determine if they are at elevated risk for unpredictable loss of soft tissue. Key factors to assess are thin tissue biotype, previous history of

recession, mucosal inflammation, tooth loss due to trauma or chronic progressive osseous disease (e.g. periodontitis). All of these conditions influence the stability and position of the mucosal tissues following implant tooth replacement therapy.

Immediate provisionalization

The application of implant-supported FPDs has a unique role especially in early and immediate loading procedures. While the splinting of implants for long-term osseointegration is not considered routinely necessary, the early splinting of multiple implants during the osseous healing process is considered important (Cooper *et al.* 2002, 2005, 2006; Slaets *et al.* 2005; De Kok *et al.* 2006; Duyck *et al.* 2006). Immediate provisionalization procedures have the potential to provide rapid function, esthetics, and patient satisfaction, and the use of implant-supported FPD prosthetic designs plays an intimate role in controlling micromotion and allowing successful outcomes similar to conventional loading procedures (De Kok *et al.* 2006; Duyck *et al.* 2006; Hall *et al.* 2006; Peleg *et al.* 2006).

The immediate provisionalization of implant-supported fixed dentures has a unique role in the retreatment of failing fixed prostheses. When large fixed prostheses are present with only one or two failing abutments, further tooth-supported restoration often requires extensive restoration. This is particularly true if strategic abutments such as a canine or terminal abutment tooth are not salvageable due to caries, fracture or localized periodontitis. In such cases, segmental resection of the failed tooth and supported pontic teeth can be replaced by dental implants. The advantages are obvious in terms of preventing the retreatment of a much larger FPD and providing an esthetic and functional treatment option for an anterior restoration.

Disadvantages of implant–implant fixed partial dentures

The disadvantages of FPDs on implants are associated with increased difficulty of cleaning and maintaining the prosthesis along with the prosthesis complications associated with conventional tooth-supported FPDs. Based on patient expectations, there is the potential that the patient isn't satisfied with the inability to clean between the retainers and pontic contours. FPDs on implants can also be more difficult to fabricate in the laboratory. In this case there may be issues with the path of insertion on the abutments (necessitating customized abutment) or difficulties in obtaining draw and passive fit between multiple abutments. There is also the danger of mechanical wear and material failure with the completed prosthesis such as abutment loosening, prosthesis fracture or veneer material failure. The use of screw-retained prosthesis may be helpful if retrievability is critical but the screw access hole itself may weaken the strength of the veneering material. Lastly, there is the danger that if one of the supporting implants are lost or the abutment demonstrates recession exposing the transmucosal titanium surface, the entire prosthesis may have to be replaced increasing time and expense to the patient.

In assessing the clinical success of implant-supported FPDs, it is difficult to determine outcomes due to incomplete reporting of the specific types of prosthesis in a range of dental implant studies and yet the primary measure of evidence-based care is the systematic assessment of the clinical question of interest. The literature supporting the use of this type of prosthesis is often retrospective in nature with different outcome measures, end points, duration of recall, etc. This makes comparisons between studies difficult and limited. In the assessment of prosthodontic mechanical complications, the pattern of defects often will vary with a time-dependent pattern. In implant-supported FPDs, early failures (before loading) are often associated with implant loss (Goodacre *et al.* 2003b). As discussed by Pjetursson *et al.* (2004), implant loss prior to restoration can be expected on average to be 2.5% of all implants placed with an additional 2–3% lost over the first 5 years of function. In this systematic assessment of the more recent literature from the 1990s though 2004, 21 studies of 176 reviews were considered based on the inclusion and exclusion criteria. The authors summarized the current literature of five implant systems with 1123 patients, 1336 FPDs on 3578 implants followed for at least 5 years. Implant survival, FPD survival, success, and complications were reported (Table 55-1). The authors outlined that this type of assessment has limitations based on the quality of the studies, their duration, drop-outs, and reliability but in this instance, with the limited dataset, the authors outlined that the most common complication was

Table 55-1 Implant supported fixed partial dentures (FPDs) with an average of 5 years' follow-up (Pjetursson *et al.* 2004: in this review, 90% of the FPDs were screw-retained)

	Average	95% confidence interval
Implant survival	95.6%	93.3–97.2%
FPD prosthesis survival*	95%	92.2–96.8%
FPD success†	61.3%	55.3–66.8%
Complications	38.7%	
• Veneer fracture	13.2%	8.3–20.6%
• Lost occlusal restorations	8.2%	
• Loose screws	5.8%	3.8–8.7%
• Fractured abutments/ occlusal screws	1.5%	0.8–2.8%
• Fractured implants	0.4%	0.1–1.2%

* Survival was defined as retained in function within the mouth. Prosthesis may have had multiple repairs.
† Success was defined as in function with no clinical complications.

Table 55-2 Local features considered in risk assessment for implant-supported fixed partial dentures (FPDs)

FPD location	Anterior locations possess higher esthetic risk Posterior locations may possess higher functional risk
Length of span	Long span increases complexity of prosthesis, mechanical loads and prosthetic complications Short span may increase abutment crowding and restrict hygiene
Occluso-gingival dimension	Increased occluso-gingival dimension results in lower bending moments at abutment and bridge screw connections Reduced occluso-gingival dimension (<6 mm) may limit prosthesis construction and integrity
Excessive vertical residual ridge resorption	Excessive vertical residual ridge resorption results in increased occluso-gingival dimensions of the restoration
Implant malposition	Buccal or lingual malposition creates unintended buccal or lingual cantilever of prosthesis Mesial or distal malposition encroaches on embrasure and hygiene access; both reduce esthetic potential Excessive deep placement increases bending moment at abutment screw, may create anaerobic environment, can lead to bone resorption and esthetic complications
Thin mucosal biotype	Risk of mucosal resorption and unesthetic display of abutment material
History of periodontitis	Elevated risk for peri-implantitis if control is absent. May need multiple staged procedures to replace hard and soft tissue contours

loss of veneering material (often acrylic facings) followed by other mechanical complications inherent in screw-retained style prosthesis. Biologic complications such as peri-implantitis (probing pocket depth >5 mm) with bleeding on probing (BOP) have been reported in one study to average 10% of patients (Pjetursson *et al.* 2004). Pjetursson *et al.* (2004) used a random-effects Poisson modeling approach to determine a pooled cumulative rate of 8.6% for biologic complications (95% CI: 5.1–14.1%) based on a assessment of nine studies providing sufficient information for analysis.

A FPD supported by two or more implants provides a valuable treatment option. It has a role in providing rehabilitation for patients with challenging implant positions and angulation, lost hard and soft tissues, reduced cost, and may allow avoidance of some grafting procedures (e.g. sinus grafting). The selection of a FPD supported by implants often represents the alternative to selecting a much larger FPD supported by many teeth (Table 55-2). While recent reviews suggest there may be little difference in the long-term complication rates for FPDs supported by teeth and implants, it is of practical importance that implant-supported FPDs often are smaller prostheses. On balance, the use of FPDs plays a valuable role in providing multiple tooth replacement therapy.

Tooth–implant fixed partial dentures

The use of dental implants combined with teeth as retainers for FPDs has been advocated by a number of clinicians to restore multiple missing teeth. There are multiple case reports in the literature of prosthesis designs that have either a rigid connection between the natural tooth and implant retainers and or that utilize a non-rigid connection to ostensibly allow individual movement of the implant(s) relative to the greater mobility of the natural teeth (Stanford & Brand 1999). The difference in mobility can be of the order of about one magnitude with mobility on teeth with a healthy PDL being 50–200 μm while an integrated implant will have mobility of <10 μm (Brunski & Hipp 1984; Brunski 1988a,b, 1999, 2003; Rangert *et al.* 1997). The use of implant–tooth FPD does have the potential to reduce costs, time, and morbidity especially if the outcome provides a service to the patient that would be equivalent to implant–implant FPD or single-tooth implant restorations (Fig. 55-7). The advantages must be balanced with the potential complication of pathology associated with the dental retainers or the implant(s). The fate of both is tied together.

Lang *et al.* (2004b) performed a systematic review of the clinical studies that evaluated tooth–implant FPDs over at least 5 years and were able to identify 13 studies using the inclusion/exclusion criteria. Of these, nine were prospective and four retrospective in nature addressing outcomes with five different implant systems in 555 patients (538 FPDs on 1002 implants); the majority (91%) were reported as being screw-retained. The authors assessed the thirteen studies by evaluating those with follow-up from 5–6.5 years. In this group, of the 932 implants installed, 25 were lost prior to restoration and 65 during the recall period. This resulted in a 5-year implant survival proportion of 90.1% (CI: 82.4–94.5%) (Lang *et al.* 2004b). In the second group, followed though 10 years, implant survival was estimated at 82.1% (CI: 55.8–93.6%). Following the same theme, a systematic

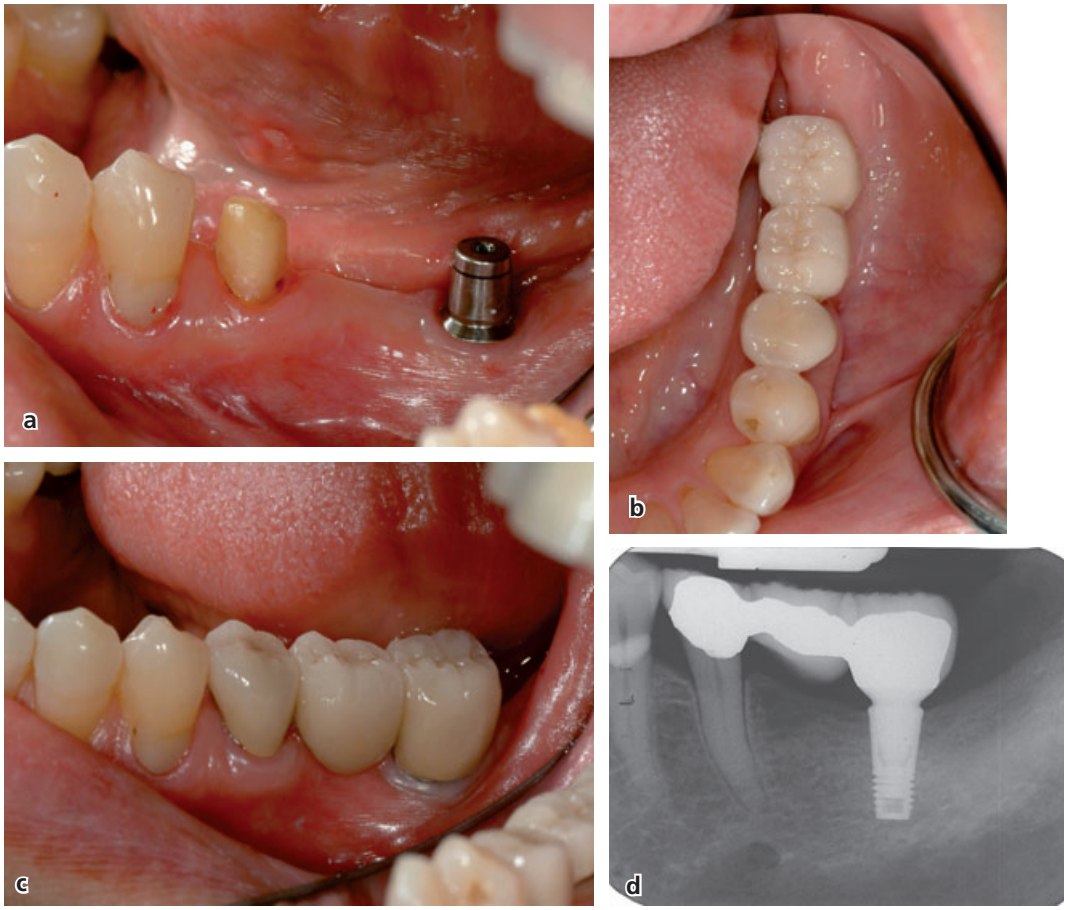

Fig. 55-7 Implant–tooth fixed partial denture. (a) Example demonstrates use of a rigid fixed partial denture (FPD) framework on a three-unit FPD (35–37). (b) A metal–ceramic prosthesis was cemented which has been monitored with frequent recall over 5 years (c). (d) Five-year recall radiograph indicates healthy peri-apical and peri-implant osseous tissues.

review of biologic and technical complications (Berglundh *et al*. 2002) indicated that tooth–implant-borne FPDs were at greater risk for implant loss (irrespective of complications leading to abutment tooth loss) than implant–implant FPDs. In regards to the prosthesis survival, estimates of 94.1% (CI: 90.2–96.5%) at 5 years and 77.8% (CI: 66.4–85.7%) at 10 years were determined (Lang *et al*. 2004). Assessment of dental abutment survival indicated 3.2% were lost by 5 years due to fracture, caries, or endodontic or periodontal complications (Lang 2004) If the patient has the option to restore missing teeth with a conventional removable partial denture combined with implant-fixed prosthodontics it is interesting to assess the long-term outcomes.

There has been a number of concerns raised with connecting teeth to implants with FPDs. Some of these complications are associated with technical complications of the prosthesis. For instance, the prognosis of the FPD can be shortened by veneer fractures and other esthetic issues (Kindberg *et al.* 2001). Loss of retention through fracture of the abutment/prosthetic screws or loss of cement retention are possible. Lang *et al.* (2004b) reported in a systematic review of two studies that assessed lost retention and described an average of 6.2% (CI: 3.7–10.4%) at 5 years (Hosny *et al.* 2000; Naert *et al.* 2001; Lang *et al.* 2004b). Endodontic complications on the abutment teeth can also be a significant concern with a range of 3–28% of teeth needing post-insertion root canal therapy (RCT) (average of 11%) (Goodacre *et al.*). Naert *et al.* (2001) reported on the complications after a mean period of 6.5 (1.5–15) years in a retrospective comparison study of implant–implant to tooth–implant FPDs on 123 patients in each group with tooth-implant FPDs. The authors reported a history of chronic apical periodontitis (3.5%), tooth fracture (0.6%) along with a tooth intrusion (3.4%), and cement failure (8%) (Naert *et al.* 2001).

An interesting and unusual observation is the issue of natural tooth intrusion that has been observed (Pesun 1997). Earlier use of implants combined with teeth advocated the use of non-rigid attachments within the prosthetic design to allow differential movement between the implant and tooth. In some cases, the natural tooth appears to retract away from the prosthesis. This phenomenon has been suggested to be due to the interplay of disuse atrophy, food impaction, rebound memory of the PDL, and/or mechanical binding (Rieder & Parel 1993;

Schlumberger *et al.* 1998; Cordaro *et al.* 2005; Palmer *et al.* 2005). In a multicenter study, Block *et al.* (2002) assessed posterior FPD connected either rigidly or non-rigidly with one type of attachment. Of the 30 subjects followed though 5 years, there was no difference in bone loss between the two types of connections but there was a 66% incidence of measurable intrusion in the non-rigid group versus 44% for the rigid group. The authors concluded that tooth–implant FPD had a higher level of maintenance and post-operative complications. Fugazzotto *et al.* (1999) retrospectively assessed a multi-group practice outcome of 843 patients (1206 implants, 3096 attachments) over a period of 3–14 years and observed nine instances of intrusion (0.3%) associated with fractured or lost lateral set screws (rigid-retention). In a prospective study through 3 years, Palmer *et al.* (2005) evaluated 19 subjects with rigid cemented prostheses between natural teeth and implants. These short-term outcomes at 3 years indicated no greater implant bone loss than would be expected (0.78 ± 0.64 mm) with no signs of intrusion with the rigid tooth–implant FPD designs. These results have led to the clinical recommendation that if the clinician needs to join natural teeth with implants, a rigid connection is advocated with close monitoring for clinical signs of complications (Naert *et al.* 2001; Palmer *et al.* 2005; Stanford 2005a).

Fixed partial dentures joining teeth to implants is a controversial issue. There are times when an assessment of clinical needs, patient desires, costs, time, and risk provide support for the clinician to consider this treatment option. It is critical that the patient be informed of the relative risks associated with this type of prosthesis, the implant, and the abutment tooth in the process of informed consent.

Conclusion

Fixed partial denture therapy for the restoration of multiple missing teeth has a long track record in dental implant care. Connecting two or more implants, or in selected cases, teeth with implants, can provide a stable, esthetic, and predictable outcome. All treatment options need to start with a careful assessment of anatomic, clinical, and patient needs and desires. The patient needs to be informed of the assumptions made and the relative costs and benefits that this treatment approach can provide.

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Chapter 56

Complications Related to Implant-Supported Restorations

Y. Joon Ko, Clark M. Stanford, and Lyndon F. Cooper

Introduction

The quality of dental implants and prosthetic outcomes has significantly improved since their introduction. This has been coupled with the steady increase in the clinical success and/or survival rate (Cochran 1996; Esposito *et al.* 1998; Lindh *et al.*, 1998; Jokstad *et al.* 2003). The biologic aspect, namely osseointegration, has been the particular target of intensive investigation and there have been conspicuous advances. As a part of these developments there have been continuous efforts to improve the characteristics, microtopographies and chemistries of the implant surface. A major change in surface topography can be summarized by the evolution from machined surfaces to a production-based moderately roughened surface. Superior biologic response, or osseointegration, to roughened implant surfaces has been widely documented in the literature (Astrand *et al.* 1999; Rocci *et al.* 2003; Schneider *et al.* 2003). The cumulative effect of all these efforts is reflected in the extremely high biologic success rate of dental implants. With the enhanced predictability of the integration process of implants becoming well documented, an ongoing issue is related to restorative complications of therapy. These complications can be related to both biologic and prosthetic issues. This chapter discusses potential complications of dental implant-supported restorations, particularly focusing on complications related to the prosthetic aspects of therapy.

Clinical complications in conventional fixed restorations

Implant dentistry shares many of the long-term mechanical complications shared with conventional dental restorative therapy. Goodacre *et al.* (2003b) presented data regarding the incidence of clinical complications associated with conventional dental fixed restorations/prostheses including single crowns (all-metal, metal ceramic, resin veneered metal) and fixed partial dentures (all-metal, metal ceramic, resin-veneered metal); all-ceramic crowns; resin-bonded prostheses; and posts and cores. Regarding single crowns, the most common complication was post-cementation endodontic therapy (3%), followed by porcelain fracture (3%), loss of retention (2%), periodontal disease (0.6%), and caries (0.4%). Regarding fixed partial dentures, the most common complications were: caries (18% abutments; 8% prostheses), need for endodontic treatment (11% abutments; 7% prostheses), loss of retention (7%), esthetics (6%), periodontal disease (4%), tooth fracture (3%), prosthesis fracture (2%), and porcelain veneer fracture (2%). In this narrative review, the authors concluded that complication incidence with conventional dental fixed partial dentures was significantly higher than single crowns. In addressing issues related to implant restorations, material failure and wear are common occurrences with both dental and implant-supported restorations (Fig. 56-1). It is likely that the higher

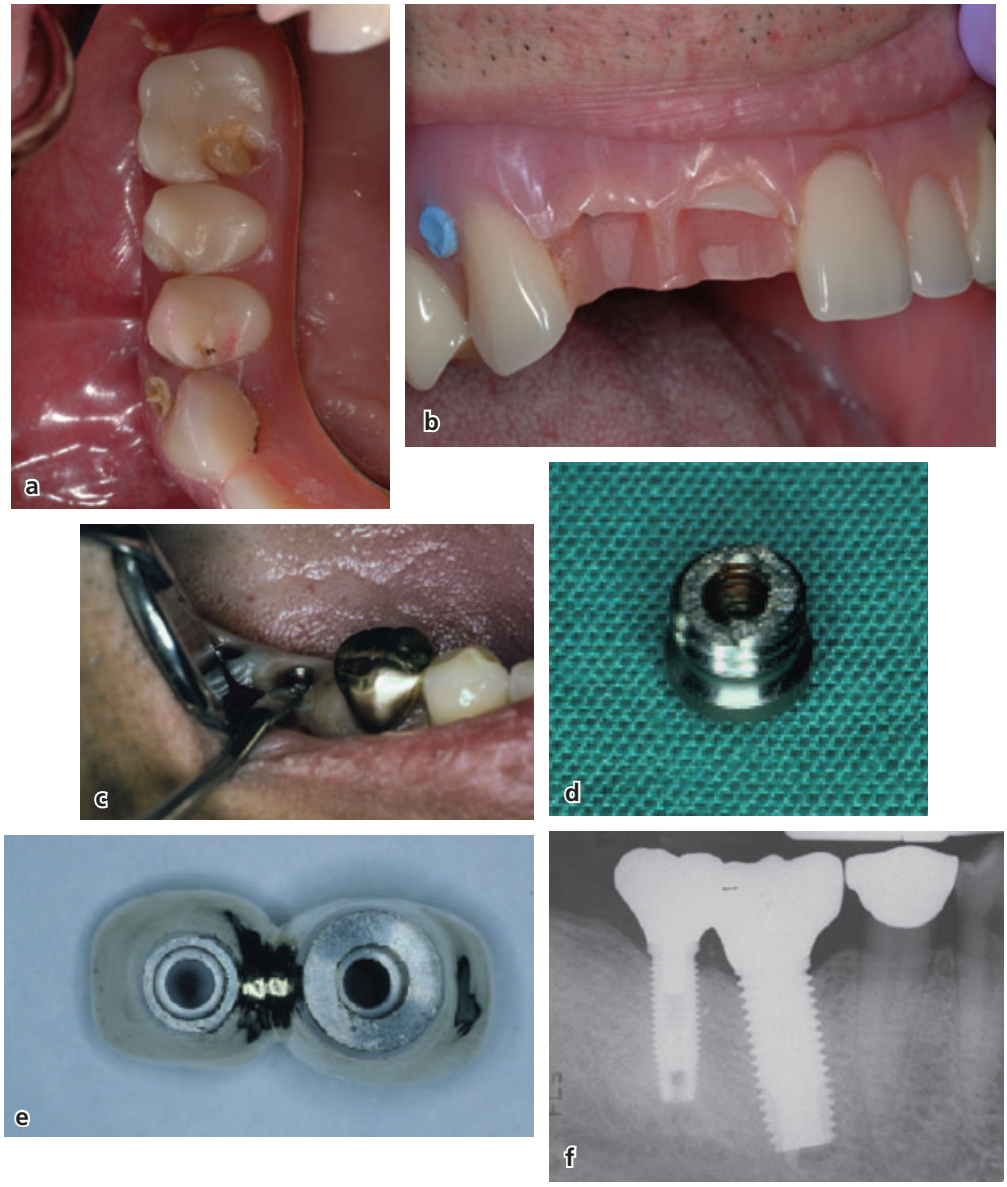

Fig. 56-1 Prosthetic challenges related to wear and component fracture. Wear, fracture, and change in esthetics is a common occurrence with acrylic resin teeth (a) as are fractures of acrylic resin prosthetic teeth on fixed complete denture (b). While implant fractures are rare, the consequences are challenging. (c) Case example of implant that was mobile 2 years after delivery; (d) the prosthesis was removed and the head of the implant was fractured. (e) The implant was replaced with a wide diameter implant in order to increase the wall thickness and provide a greater abutment-to-implant interface. (f) Recall at 10 years.

biomechanical complexity of the design of the prosthesis contributes to higher complication incidence. Among these complications, pulpal complications, periodontal disease, and caries will apply to only tooth-supported restorations.

Tan *et al.* (2004) assessed the long-term success/survival rate of conventional fixed partial dentures (FPDs) and evaluated the failure rates of FPDs due to specific biologic and technical complications. The result of the systematic review based meta-analysis indicated a 10-year survival rate of FPDs was 89.1%. The 10-year success rate of FPDs declined to 71.1%. Success suggests no intervention was needed over the recall period, relative to survival which suggests retention with or without intervention during the recall period. In general in the literature, the mean 10-year survival rate of conventional FPDs was 90%, and success rate 80%. In this study, the most common reasons for dental FPD failure include periodontal disease and secondary caries. Regarding the complications related to caries, the 10-year risk for decay on abutments was 9.5%, but only 2.6% of FPDs were lost as a result of this disease process. In this study, it was clear that loss of vitality of abutment teeth occurred at a later date and so could not be attributed to the trauma from the preparation of the teeth. This may either indicate a slow progressive tissue degeneration induced by the procedure or reflect the increased susceptibility of pulpal infection by dentinal tubules in advanced periodontitis (Bergenholtz & Nyman 1984). The presence of cast post and dowels and non-vital abutments, especially in distal abutments, has been shown to be associated with increased loss of retention and fracture of teeth and cores. This

cautions against over-dependence on non-vital teeth as strategic abutments.

The 10-year risk of loss of FPDs due to recurrent periodontitis was only 0.5%. Overall, there seemed to be no adverse changes in FPDs incorporated into periodontally well-maintained patients even if they presented with a history of advanced periodontal disease. Where the recall or maintenance is less stringent, periodontal breakdown may occur, and may be more pronounced when margins were subgingivally located (Valderhaug & Karlsen 1976). Secondary use of the bridge for removable prosthesis has a detrimental effect on the gingival tissue (Libby *et al.* 1997). The 10-year risk for technical complications, such as loss of retention, loss due to abutment fracture and the occurrence of material complications, were also calculated in this study. An issue in any of these studies is the multifactorial nature of the causes of failure. The highest 10-year risk was for loss of retention, amounting to 6.4%. Far lower was the 10-year risk for the loss of FPD due to abutment tooth fracture. Relatively low 10-year risks were obtained for material complications. These included fractures of the framework, veneers and/or cores and amounted to a 10-year risk of 3.2%. A comparison of the difference in survival between FPDs with acrylic facings and metal–ceramic FPDs showed that over an 18-year period, 38% of FPDs with acrylic facings and 4% with metal ceramic FPDs were replaced (Sundh & Odman 1997). Reasons cited for the increase in failures were the greater incidence of discoloration and fracture after extensive wear of the acrylic resin material.

Clinical complications in implant-supported restorations

Biologic complications

Surgical complications

Surgical complications directly related to implant placement are generally rare. However, due to the surgical nature of implant therapy, it is impossible to avoid surgical sequelae. Recent surgical methods propose excluding tissue flap openings (so called "flapless approaches") which seek to minimize surgical trauma but carry their own risks as well. Goodacre *et al.* (2003a) provided data regarding the types of complications that have been reported in conjunction with endosseous root form implants. The most common surgical complications associated with implant surgery were hemorrhage-related complications (24%), neurosensory disturbance (7%), and mandibular fracture (0.3%).

Implant loss

To date, there is no known single factor that contributes to an implant loss. Some of the factors that are generally accepted as the etiology include infection and/or contamination, patients' physical status, trauma from surgical procedure, excessive and/or premature occlusal loading, unfavorable axial loading, etc. Most of the surgery-related implant losses can be managed by maintaining a strict infection control protocol, meticulous patient screening prior to the surgery, and reducing the amount of time/trauma during surgery. Occlusal loading is a more challenging factor since the operator has more limited control. Premature occlusal loading can be detrimental to the osseointegration when it is combined with excessive load and/or off-axis force. This can happen during the stage of early or immediate provisionalization and illustrates that the patient should be closely monitored during this initial healing period. In the literature, it has been stated that overloading at any stage of osseointegration can lead to bone loss or even complete disintegration of the implant (Isidor 1996, 1997; Brunski *et al.* 2000; Steigenga *et al.* 2003). However, the concept of implant "overload" has recently been questioned with a series of studies indicating bone is highly responsive to dynamic loads and is resistant to bone loss even with high levels of occlusal function (Stanford & Brand 1999; Duyck *et al.* 2000, 2001; Stanford 2005b).

According to the literature, implant loss ranges from a high of 19% with maxillary overdentures to a low of 3% that occurred with both mandibular fixed complete dentures and single crowns (Goodacre *et al.* 2003a). Implant loss is greater with implants 10 mm or less in length compared with implants greater than 10 mm long (ten Bruggenkate *et al.* 1998; Lekholm *et al.* 1999; Friberg *et al.* 2000; Palmer *et al.* 2000). The implant loss is more likely to occur in the presence of type IV bone compared with more favorable typed bones (Stanford, 1999, 2005b; Stanford & Brand, 1999). Other risk factors that have been suggested include smoking and a previous history of radiation therapy (Moy *et al.* 2005). If indeed a loss of implant occurs, approximately half or more of the lost implants were lost prior to functional loading. This result is in agreement with the result from a previous systematic review (Berglundh *et al.* 2002).

Peri-implant complications

Possible peri-implant complications include marginal bone loss, peri-implant mucosal inflammation/proliferation, soft/hard tissue fenestration/dehiscence, fistula, etc. It is widely accepted that continuous marginal bone loss around established implants over time jeopardizes the potential success and/or survival of the implant therapy. Factors that potentially induce marginal bone loss include surgical trauma during implant placement, trauma during repeated abutment insertions and removal, functional load transfer and concentration, micromotion at the implant–abutment junction, and peri-implant gingival inflammation. According to the literature, the mean bone loss occurring during the first year is, on average, around 0.9–1.5 mm, and the subsequent

loss per year after the first year is around 0.1 mm (Albrektsson *et al.* 1986).

Peri-implantitis is defined as an inflammatory reaction associated with the loss of supporting bone in the tissues around a functioning implant (Albrektsson *et al.* 1994). Peri-implantitis could be asymptomatic but it often accompanies bleeding and/or suppuration. Clinically, bony defects are detected by increased probing depth. Radiographically, a saucer-shaped radiolucent lesion may be observed around the implant. From a prosthetic perspective, the onset of peri-mucositis or peri-implantitis (associated with bone loss) can lead to soft tissue recession and unesthetic show of abutment or prosthetic components.

Marginal defects on the facial aspect of the implant complex are not only esthetically compromising, but can jeopardize the stability and long-term success of the implant. These defects, dehiscence or fenestration, are typically caused by the resorption of the buccal/labial plate of the alveolar bone. In order to prevent this type of defect it is important to maintain a minimum of 1 mm thickness of buccal/labial plate (Stanford 2005a). However, in certain areas, this may be difficult to achieve. To reduce the risks of facial marginal defects one can utilize bone augmentation procedures, mainly autogenous, around the marginal alveolar bone in order to maintain the thickness around the implants. In this case, autogenous bone particles derived from the drilling of the osteotomy may be enough for the purpose. In terms of the timing of implant placement after tooth extraction, it is generally accepted that immediate placement has a greater risk of facial marginal defects compared to delayed placement (Nemcovsky *et al.* 2002).

Malpositioned implants

The definition of a 'malpositioned implant' is an implant placed in a position that created restorative and biomechanical challenges for an optimal result. A malpositioned implant could be caused by numerous factors, the most common being deficiency of the osseous housing around the proposed implant site. Bone resorption is observed in osseous remodeling following tooth loss, osteoporosis, orthopedic revisions, craniofacial defects, or post oral cancer ablation associated with surgery/radiation. For the best biologic, biomechanical, and esthetic result of implant rehabilitations, proper implant placement is essential. The placement of an implant into a defective osseous site not only prevents adequate positioning of the final prosthetic restoration, but also results in compromised integration and subsequently a poor prognosis for the therapeutic outcome. In order to place an implant in the optimal prosthetic position for a restoration, augmentation procedures are often necessary. Current approaches in bone reconstruction use biomaterials, autografts or allografts, although restrictions on all these techniques exist. Restrictions include donor site morbidity and donor shortage for autografts (Damien & Parson 1991), as well as immunologic barriers for allografts and the risk of transmitting infectious diseases (Meyer *et al.* 2004). Numerous artificial bone substitutes containing metals, ceramics, and polymers have been introduced to maintain bone function. However, each material has specific disadvantages, and none of these can perfectly substitute for autografts in current clinical dentistry.

If the status of the existing, deficient bone were addressed prior to the surgery and the restorative dentist confirms it will be possible to fabricate the final prosthesis with the implant(s) in the proposed location, generally implant placement can be a straightforward procedure. It is a significant complication for the implant team and the patient when the implants are placed only in the available bone ignoring the optimal desired prosthetic position (Fig. 56-2). Communication between the surgical and restorative team is vital. The best way of communication between the two parties is through use of comprehensive treatment planning, diagnostic wax-up on mounted casts, and fabrication of a surgical guide. The standard protocol for placing implants will start with a treatment plan developed by the restorative dentist. The surgical guide represents the ideal position and angle of the implant determined by a series of diagnostic procedures. The surgical guide should ideally indicate the three dimensions of the proposed implant position – horizontal position, vertical position, and angle (Fig. 56-3). Horizontally, the surgical guide should clearly indicate the bucco-lingual and mesio-distal location of the proposed site. In most cases, this is determined by the morphology and location of the diagnostic wax-up of the missing tooth. Vertically, the surgical guide should indicate how deep the surgeon should place the implant relative to the planned cemento-enamel junction (CEJ). This is particularly important for implants placed in the esthetic zone. As a general rule, the restorative margin for an implant-supported restoration should be located at the vertical height slightly deeper than that of the CEJ of the adjacent teeth. Thus, when an implant system in which the head of the implant represents the restorative margin, the implant should be placed 2–3 mm below the planned CEJ or occasionally on a line connecting the CEJ of adjacent teeth. When an implant system is used which is capable of adjusting the height of the restorative margin through a separate abutment(s), the depth of the implant may be more flexible (Fig. 56-4). Whichever system is used, the surgical guide should have a component that could notify the surgeon of the proposed depth of the implant. The angle of the implant should also be correct to prevent facial or lingual fenestration of the implant as well as penetration into the radicular portions of adjacent teeth or other structures. The angle should be correct for the prosthesis as well. Should the angle of the implant be too facial, the restorative dentist could face significant esthetic challenges, for example, screw access hole position, necessity of the

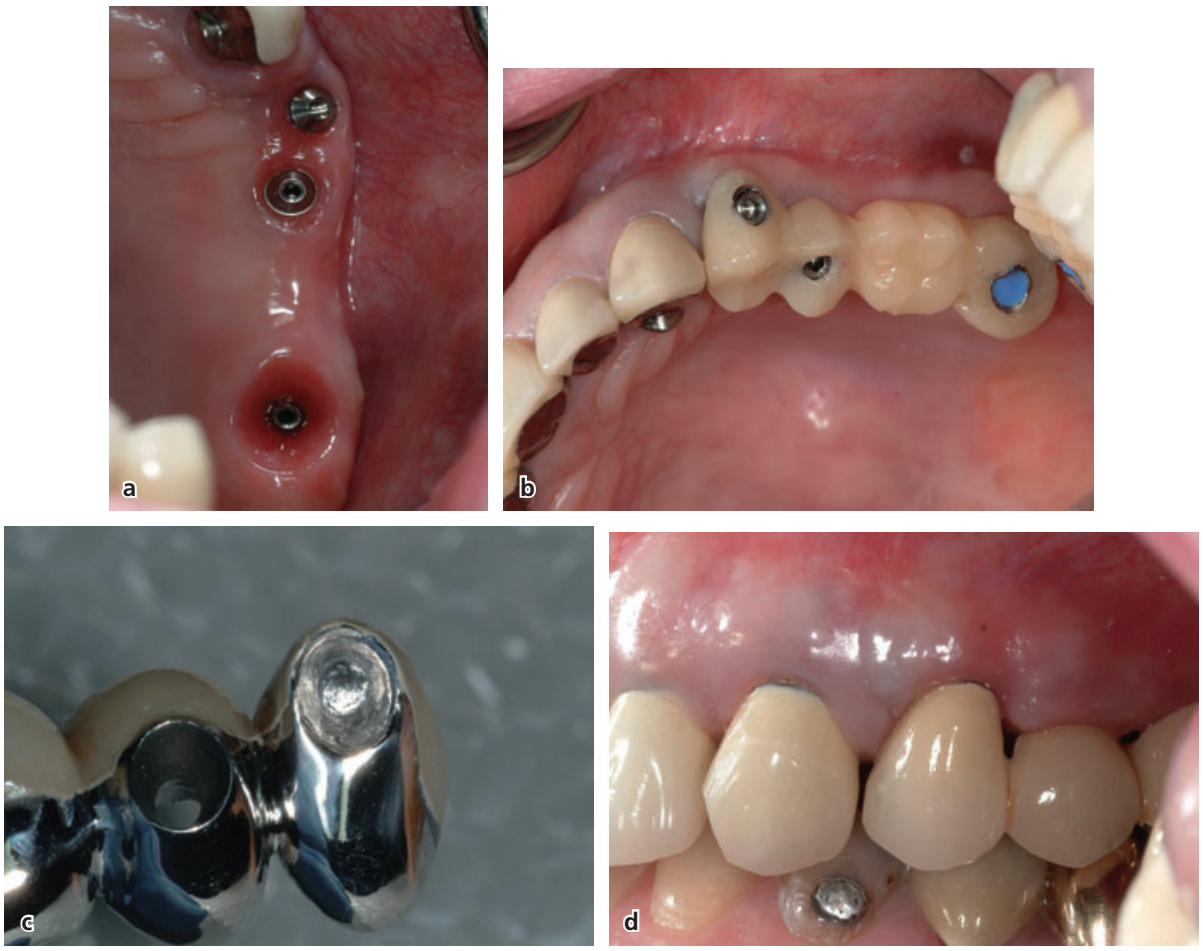

Fig. 56-2 Prosthetic complications with malpositioned implants. (a) Patient had an implant placed in area of 24 with facial angulation. (b) The provisional fixed bridge demonstrated the facial position. Due to the depth and position of the implant, a fixed prosthesis was made that rested on the implant abutment (c) allowing a satisfactory esthetic and functional restoration (d).

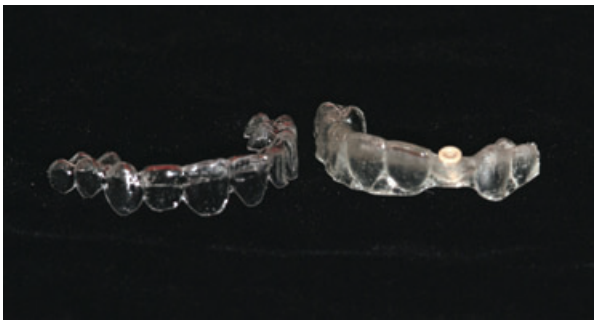

Fig. 56-3 Surgical guides for implant placement. Using a guide with a restrictive channel allows for evaluation in diagnostic imaging studies and during the surgical placement phase.

Fig. 56-4 The restorative margin may be the head of the implant with certain implant designs necessitating the surgeon placing the implant to have a clear idea of where the final margin will be. Other systems use an abutment for cemented restorations that allows variation in the vertical position of the restorative margin.

use of angled abutments, expensive custom abutments, etc. (Fig. 56-5).

Mechanical complications

Overdenture complications

Numerous studies indicate that the use of an acrylic-based implant overdenture has the highest number of post-operative complications (complication being defined as a need for some form of intervention, the degree of which is not necessarily defined). Complications include loss of attachment retention or fracture of the attachment system, fracture of components of the denture, prosthesis-related adjustments, etc.

Fig. 56-5 Innovative use of abutments. (a) Patient presented with a healing abutment indicating placement within the residual ridge. (b) Soft tissue health was adequate though final impression coping (c) indicates angled position relative to remaining teeth. Patient was restored with a cement retained restoration but using a low profile abutment designed for a conventional screw-retained crown (d,e). (Courtesy of Dr. Michael Scalia DDS, and Mr. Henry Husemann CDT (University of Iowa).)

Goodacre *et al.* (2003a) suggested the most common complication in this category was the need for adjustments due to loss of retention and/or attachment system fracture. O-ring systems, Hader-bar and clip-, IMZ-, Ceka-, ERA-, ZAAG-, Locator-attachments all use various forms of plastic components within the anchorage system. Over time, the plastic component tends to wear and distort. Traditional ball attachment systems utilize metal spring matrices and these, too, tend to deform and lose retention with time. Studies that assessed the difference in frequency of maintenance requirement between bar/clip systems and individual attachment systems indicated that individual attachment systems require more frequent adjustments mainly due to loss of retention of the matrix or patrix (van Kampen *et al.* 2003; Walton 2003; MacEntee *et al.* 2005). However, the simplicity and ease of the repair procedure in some individual attachment systems may reduce frequent maintenance and have lead to increasing popularity of these abutment designs. Systems with exchangeable plastic components have especially become popular due to easy maintenance procedures. Further, the conversion of a complete denture patient who rarely returns for maintenance therapy to a routine recall patient (valuable for early

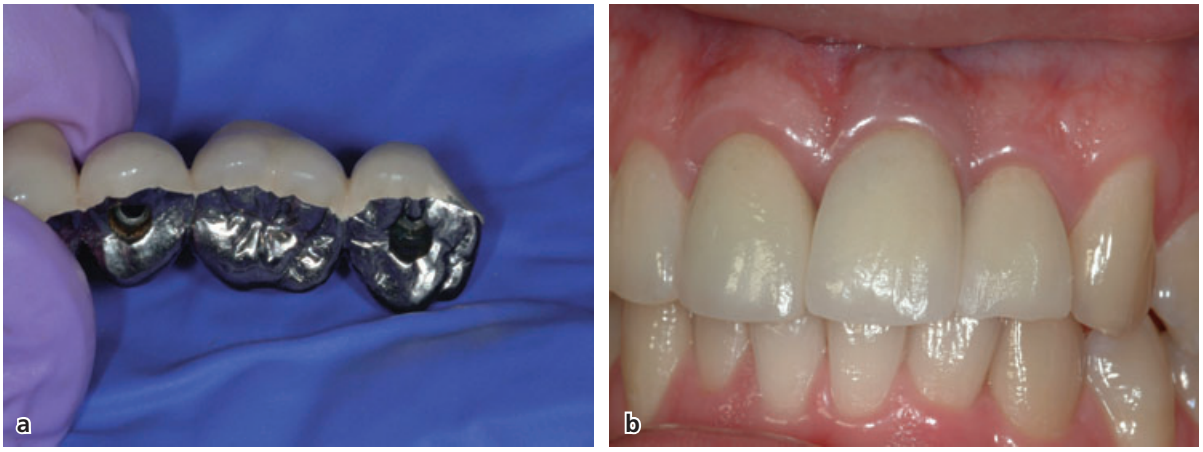

Fig. 56-6 Fractures of veneering ceramic material. (a) Example of facial shear fracture of porcelain on posterior unit. (b) Ceramic shear fracture on facial surface of 22 all-ceramic restoration.

caries detection, oral cancer exams, etc.) by way of their desire to have the attachment system serviced provides a valuable ethical service for the patient.

Because of the housing and attachment components, overdentures typically have a reduced thickness of acrylic resin base in certain areas compared to conventional dentures. It is these thin areas that have a higher risk of fracture. In addition, patients with implant-supported overdentures have a tendency to generate higher masticatory force compared to patients with conventional dentures. The incidence of acrylic base fracture may increase depending on the opposing occlusion. For example, an overdenture opposing an implant-supported fixed complete denture will be at a greater risk of fracture, accelerated wear or prosthetic tooth fracture than one opposing a conventional denture. Overdenture fracture is a relatively common problem according to some studies, and could be as high as 7% of all the mechanical complications related to implant-supported restorations (Carlson & Carlsson 1994; Goodacre *et al.* 2003a).

Prosthesis-related adjustments include reline/rebase of the overdenture, occlusal adjustments, denture adjustment due to soft tissue complications, etc. Normally the hard and soft tissue under the overdenture will remodel with time. Additionally, overdentures only allow limited rotational movements between the abutment and the anchorage system. This means there will be positive vertical and horizontal load on the edentulous ridge, in the area away from the anchorage system. This may increase the rate of resorption and induce the need for denture relines. The change in mucosal adaptation of the prostheses will induce subsequent problems like occlusion changes and soft tissue trauma.

Fracture of fixed restoration veneers/fixed restorations

Without the periodontal ligament (PDL) to provide shock absorption and proprioceptive reflex, dental implants are essentially ankylosed to the surrounding bone. Further, patients tend to generate higher masticatory forces on implant-supported restorations relative to the natural dentition. It has been reported that the maximum bite force generated with conventional dentures is around 50–60 N, whereas implant-supported restorations can generate above 200 N (Carr & Laney 1987; Mericske-Stern *et al.* 1996; Fontijn-Tekamp *et al.* 1998; Morneburg & Proschel 2002; Steigenga *et al.* 2003). As a result, an implant-supported prosthesis is exposed to a risk of higher restorative material failure. Of prosthetic failures, studies suggest the fracture of the restorative veneer material is the most common type of mechanical complication (Fig. 56-6). It includes fracture of the veneering porcelain or resin. Veneer fracture can happen anywhere in the mouth; restorations in the areas of heavy functional forces and higher non-axial forces, such as the occlusal surfaces of mandibular posterior restorations, facial cusps of maxillary posterior restorations, and maxillary anterior restorations, have a greater tendency to shear. To reduce or avoid material failure, especially veneer material fracture, the restoration should have sound supporting structures. The framework that supports the restorative veneer should have sufficient strength and stability to safely support the overlying veneer material. The framework should have minimal flexure even under functional loading – veneer materials usually lack tensile strength and as a result are weak under flexural stress. The framework should be carefully designed so that it will provide maximum support with no unsupported areas of the veneer material (Fig. 56-7). Another important approach to reduce the complication of veneering materials is through control of the occlusion. To reduce or eliminate excessive stress on one particular tooth or restoration, wide distribution of the occlusal force will be better than loads concentrated on a localized area. Also limiting the main occlusal force on to the restoration directly supported by implants may be beneficial: cantilevered restorations may be at higher risk

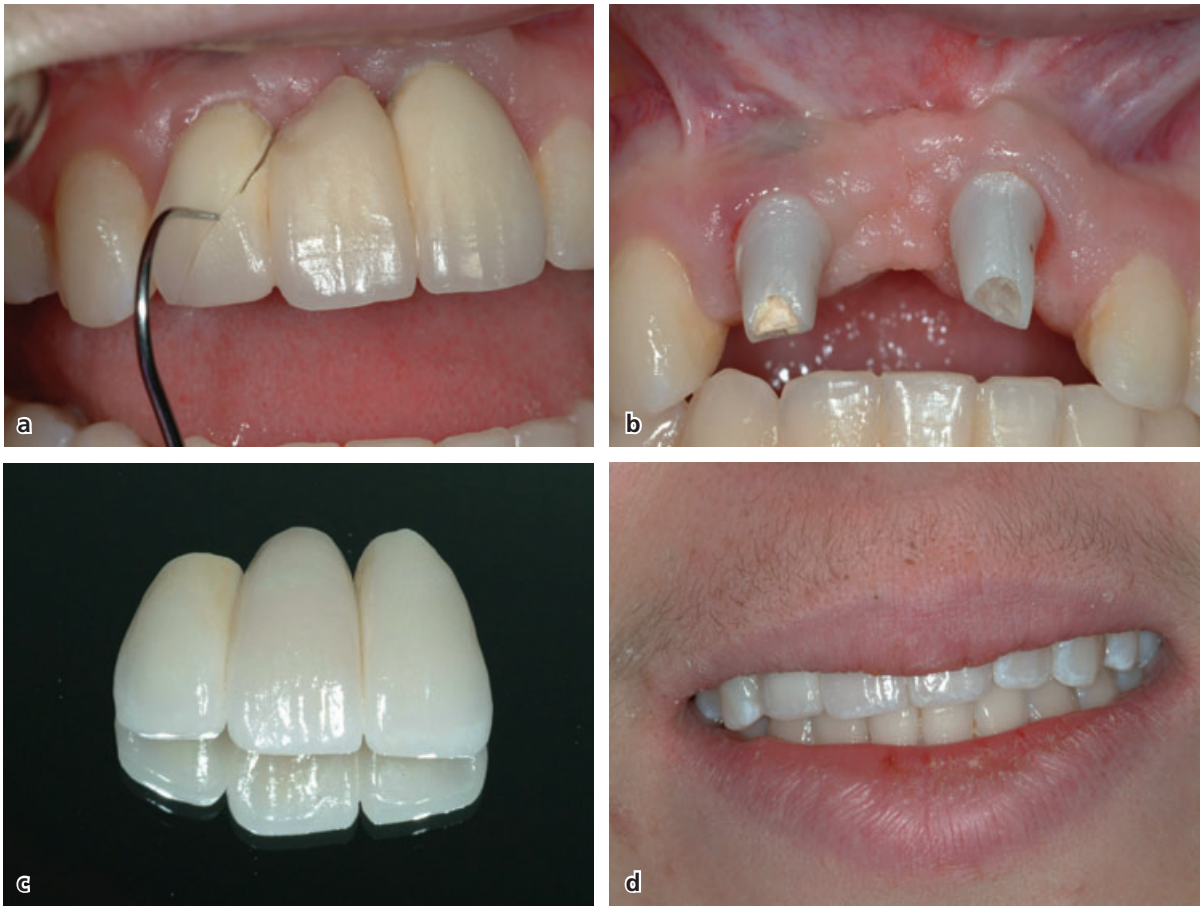

Fig. 56-7 Fractured all-ceramic implant restoration. Patient had a three-unit fixed partial denture (FPD) (12 to 21) with glass-infused ceramic structure. (a) Restoration demonstrated catastrophic rupture 2 years after delivery. Restoration was removed (b), zirconia abutments cleaned and a new Zirconia reinforced FPD fabricated for enhanced strength (c). (d) Final esthetic appearance for the FPD.

of fracture than those supported by the implant/abutment under an identical amount of occlusal load (Becker 2004; Pjetursson *et al.* 2004).

Occlusal wear is more evident in implant-supported restorations for the same reason. When there is a mismatch of opposing restorative materials, the wear could be especially dramatic. Thus one must be prudent in not only selecting the material for the occlusal surface of the restoration but also the status of polishing to avoid serious maintenance issues. It is known that porcelain can be abrasive when opposed with enamel, metal, resin, or even porcelain, especially when it lacks a highly polished surface (Monasky & Taylor 1971). Exposed opaque layer and use of external characterizations with metal oxides all add to the abrasiveness of porcelain and should be used with care.

A rare but possible complication related to prosthesis fracture is the fracture of mandibular implant-supported fixed complete denture at the midline (Fig. 56-8). It is speculated that the flexure of the mandible during function can cause this type of complication. Repeated extreme mouth opening can accumulate fatigue in the metal framework, and once this accumulated fatigue exceeds the fatigue strength of the material, the prosthesis may facture or veneering material delaminate from the framework. Clinically, patients with this type of restoration may feel tightness of the mandible especially during function, and once the restoration fails, they express "relief" from the tightness. To avoid this problem, fabricating a two-piece fixed restoration has been advocated by some, although this has generated its own problem: because of the lack of the bracing effect and rigidity of the framework, these restorations may

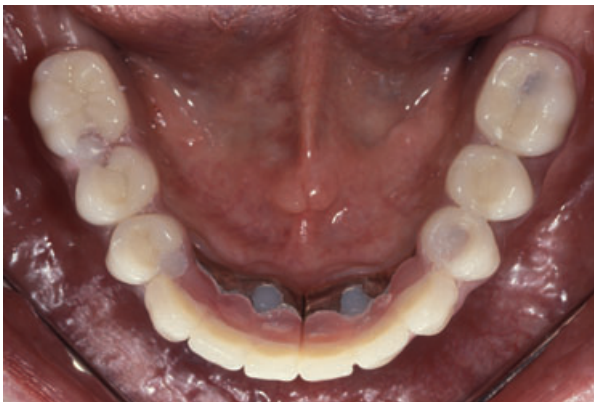

Fig. 56-8 Splitting full-arch ceramometal restoration at the midline to reduce impact of mandibular flexure.

tend to have a higher incidence of screw-related problems.

Implant screw-related complications

Numerous studies indicate that complications related to the screw components of the implant system are very common and require clinical intervention, which could range from simple retightening of the screw(s) to total replacement of the abutment and screw(s). This requires additional time and cost for both dentists and patients. Jemt and Linden (1992) observed with earlier screw abutment designs that screw loosening occurred in 49% of maxillary implant-supported restorations and 20.8% of prostheses in the mandible. They also observed that 57% of the abutment screw loosening occurred within the first year of service and only 37% remained stable over a 3-year period. Goodacre *et al.* (2003a) observed that the frequency of complications related to implant screws like screw loosening or fracture of abutment or prosthetic screws could be as high as 19% of all the potential mechanical complications in implant restorations. Ding *et al.* (2003) reported that the incidence of screw loosening for an external hex system could be as high as 38%. In their systematic review, Pjetursson *et al.* (2004) found that abutment or occlusal screw loosening/fracture was the third most common technical complication, only after restoration veneer fracture and loss of occlusal screw access hole restoration. Its cumulative incidence after 5 years of follow-up was 7.3%.

Theoretically, the lifespan of an abutment or prosthetic screw in an implant restoration needs to last greater than 10^8 cycles of loading or approximately 20 years under the assumption that the system is accurately constructed and the loading conditions are simulating the natural oral environment (Patterson & Johns 1992). However, there are several factors that could drastically reduce the predicted service life resulting in screw loosening and/or fracture. For example, the abutment/implant interface geometry, precision of fit and/or passivity of components, and the amount of preload may lead to reduced service life. In external hexagonal implant system studies, it has been shown that larger implant/abutment contact area provides superior stability of the system and resistance to screw complications and has been one driving force for the use of wider-diameter implant devices (Binon 2000). Additionally, precise anti-rotational features should be present for the joint components to withstand rotational movements that could potentially cause screw loosening (Khraisat 2005). Precise fit of the abutment to the implant interface is highly important. In a study on machining accuracy of several different external hex implant systems, all systems demonstrated rotational movement in excess of four degrees (Binon 1995). Systems that have such "slip-joint" figures such as external hex implant systems are naturally vulnerable to vibration and micromotion during functional loading (Schwarz 2000; Hoyer *et al.* 2001). In the absence of passivity between the implant components, it has been shown that screws accumulate internal stress and this eventually results in metal fatigue failure and screw loosening/fracture (Kano *et al.* 2006). The resulting clamping force exhibited between the abutment and implant generated by the screw is called *preload*. In an external hex system, the preload, along with the frictional force of the abutment/implant joint wall, is the major force resisting functional loads. In most implant systems, a tightening torque is applied and the preload stress in the interface is increased, where this stress should be within the elastic range of the screw material. The screw tightening should result in optimum preload level for the maximum outcome of the implant complex after dynamic loading. Literature indicates that as long as the external loading stress does not exceed the preload stress, the abutment/implant connection can be regarded as safe (Patterson & Johns 1992; Lang *et al.* 2003). Insufficient or excessive preload stress could result in compromised lifespan of the abutment/implant connection.

Chronic problems associated with the external hex or butt-joint interface implant systems have been documented. Because of these inherent problems with external hex design, investigators have presented new concepts in implant design, which aim to improve support and reduce the complications associated with external hex design, by means of additional frictional force between the internal wall of the implant and the external wall of a 1-piece abutment/abutment screw. Sutter and colleagues proposed an 8-degree internal-taper connection between the implant and abutment (ten Bruggenkate *et al.* 1998). The original concept of Morse taper comes from engineering, particularly from the area of machine taper. When connecting exchangeable working bits into the work piece, a popular and very effective method is to use frictional forces between the two components, where the pressure of the spindle against the workpiece drives the tapered shank tightly into the tapered hole. The friction across the entire interface surface area provides a surprisingly large amount of torque transmission. The abutment/implant junction can be designed such that an internal connection is utilized with minimal taper (2–15°), while the screw base portion of the abutment will be connected into the receiving portion of the implant. There are numerous studies reporting on the higher mechanical and enhanced clinical behavior of these internal connection designed implants (Binon 2000). Norton (1997, 1999) verified that the internal conical designed systems significantly enhanced the resistance of connection system against external bending forces. Levine *et al.* (1999) found that the internal connection showed significantly lower incidence (3.6–5.3%) of screw-related complications compared to external hex designed systems. The use of the internal interference fit abutment designs has simplified the

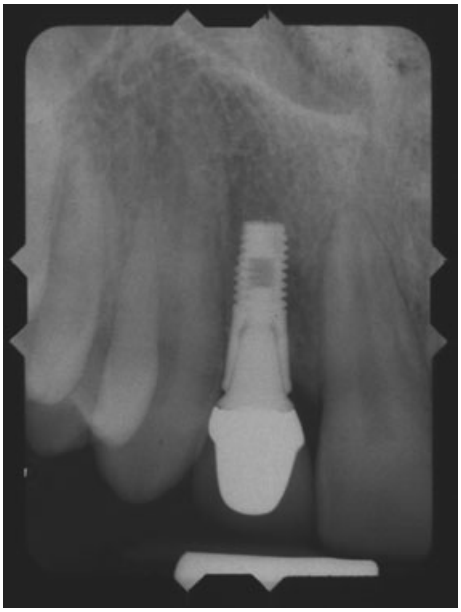

Fig. 56-9 Incomplete seating of abutment in a two-piece implant system. Implant abutment was incompletely seated in implant due to contact on the adjacent osseous contours.

prosthetic phase of therapy and has increased the long-term stability of the screw–joint connections (Stanford & Brand 1999; Brunski 2000, 2003; Jokstad *et al.* 2003).

Abutment-related complications

In positioning an abutment into the implant, there are potential mechanical complications that can arise. One common issue is incomplete seating of the abutment to the implant body (Fig. 56-9). Depending on the implant position and depth, it is also possible that the peri-implant bone may inhibit complete seating of the abutment (giving the dentist the impression that the abutment is fully seated when in fact it is resting on adjacent bone). This may or may not be evident on a radiograph depending on the implant abutment angulation relative to the central beam of the radiographic unit.

Since most prefabricated abutments are produced in standard size and shape, it can be challenging to customize them to individual patients. The modification procedures to a prefabricated abutment may in turn compromise the biomechanical properties of the abutment to achieve an esthetic result. Some systems provide a stock titanium abutment that can be modified by conventional laboratory reshaping or though use of CAD/CAM milling approaches. Depending on the angulation of the implant relative to the prosthesis, the presence of a central abutment screw can sometimes become a complication. This is especially true for narrow-diameter abutments which generally lack sufficient wall thickness for an ideal preparation.

When the head of the implant is placed below the adjacent bone, the architecture of the bone can develop sloped architecture extending from the PDL support of the adjacent teeth down and across to the implant. This often happens in the maxilla area where implants are generally placed deeper to avoid esthetic issues. Periodically this scalloped osseous architecture necessitates the prosthodontist to assess and then modify the abutment and occasionally the implant body in this area (Fig. 56-10). In this case, the mucosal transition zone of the abutment is modified to avoid placing pressure on the bone and soft tissues. It is also helpful to develop a flat or even concave emergence profile of the final restoration to maintain soft tissue dimensions around the restoration (Stanford 2005a).

Other issues related to prosthetic complications

Implant angulation and prosthetic complications

The role of angled implants on clinical outcomes is often of significant concern. Clelland *et al.* (1995) evaluated the stresses and strains generated by an abutment system capable of three angulations (0°, 15°, and 20°). In this study, they observed peak stresses were located in the cortical bone, and the magnitude of these stresses increased with an increase in the abutment angulation. The maximum stress values were generally within the physiologic parameters described for animals, but in one case, the peak compressive stress for the 20° abutment was slightly above this physiologic zone. Peak tensile strains also increased with abutment angulation, but maximum compressive strain values were the same for all three angles. This study suggested that angled abutments were safe to use relative to the bone stability around the implant body.

One approach advocated by some has been to use multiple implants and place a facial–lingual offset between them to enhance the mechanical stability of a connected FPD. Sutpideler *et al.* (2004) evaluated the effect of an offset on the force transmission to bone-supporting implants aligned in either a straight-line configuration or an offset configuration. Also, they addressed the effect of different prosthesis heights and different directions of force application. They observed vertical loading of an implant-supported prosthesis produced the lowest stress to the supporting bone and increasing the angle resulted in greater stress that theoretically simulated surrounding bone. They also observed reducing the height of the prosthesis from 12 mm to 6 mm (crown to implant ratio) or establishing an offset implant location for the middle of three implants can reduce stress, but this reduction did not compensate for the increase in stress found with non-axial loading. This concept has been extended with the recent advocacy for intentionally placing implants at significant

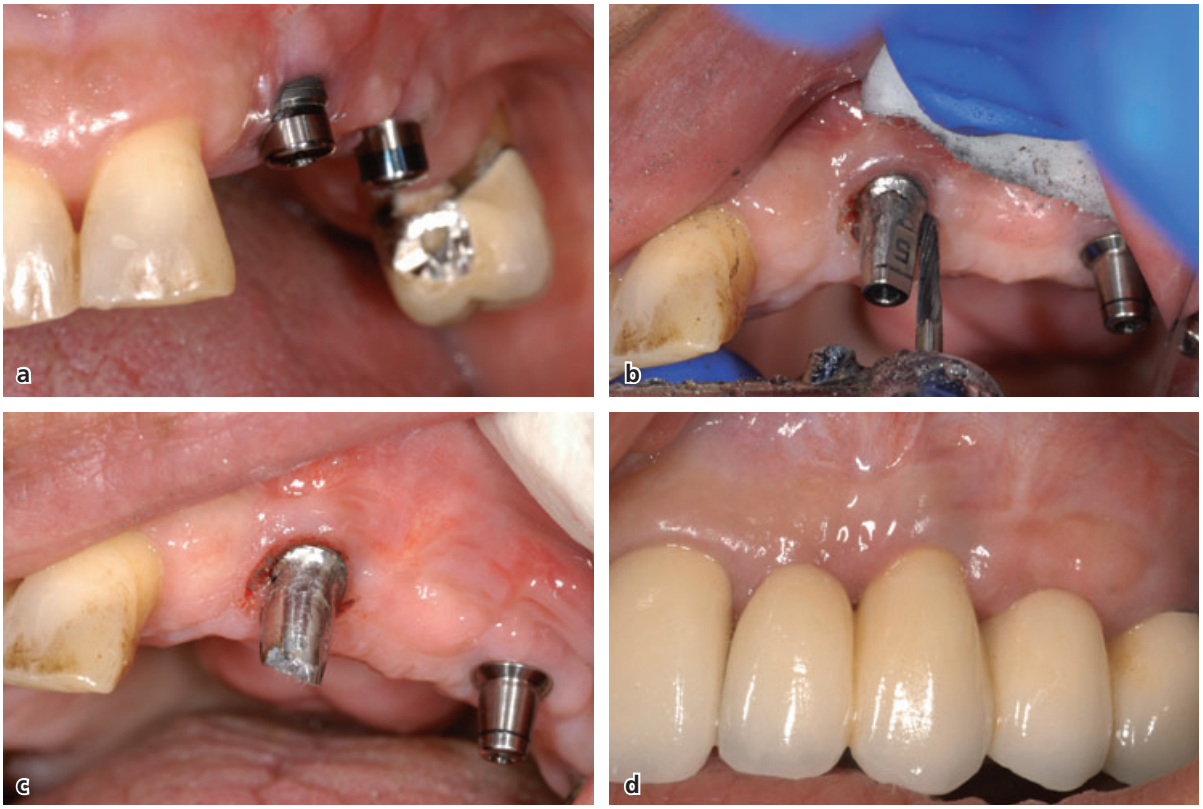

Fig. 56-10 Implant and abutment modification. (a) Patient presented with soft tissue dehiscence on an integrated implant, necessitating placement of an abutment and preparation of the abutment and implant body (b). A fixed partial denture was fabricated using the modified abutment (c) that achieved a reasonable esthetic and functional outcome for this compromised situation (d). Restorative work accomplished by Dr. Manuel Romo DDS (University of Iowa).

angulation relative to each other to avoid vital structures and sinus cavities, and to improve the putative biomechanical position of the implants (Krennmair *et al.* 2005).

Chun *et al.* (2006) investigated the effect of three different abutment types (one-piece, internal-hex, and external-hex) on stress distribution in bone under vertical and inclined loads by finite element analysis. With one-piece implant designs, they observed that the load was transferred evenly into bone as well as within the implant system. However, the maximum stress generated in bone with the one-piece system was always higher than that generated with the internal-hex implant, regardless of load angle inclination. In the case of the internal-hex implant, the contact condition with friction between abutment and implant in the tapered joints and at abutment neck reduced the effect of bending caused by horizontal component of inclined load. The maximum stress in bone was the highest for the external-hex implants.

Erneklint *et al.* (2006) evaluated the load resistance in a conical implant system with two different screw-retained abutment angled designs (20° and 45°) and three different retaining screw materials. They observed that the 20° abutment withstood non-axial forces to a greater extent than a 45° abutment, regardless of retaining screw material. The 45° abutment failed under oblique loads between 450 and 530 N while the 20° abutment failed at 1280–1570 N. Regarding the retaining screw materials, differences were more obvious in a 20° abutment, but not insignificant in the 45° abutment as well. In general, they concluded that abutment taper angles were more important than retaining screw material in determining the assembly strength.

The angulation of the implants can also influence the outcomes of implant overdenture therapy. Gulizio *et al.* (2005) evaluated the retentive capacity of gold and titanium overdenture attachments placed on implants positioned at 0°, 10°, 20°, and 30° from a vertical reference axis. They observed that significant differences in retention of gold matrices were noticed when ball abutments were positioned at 20° and 30°, but not at 0° and 10°. Also they noticed significantly higher variance in retention among the titanium matrices, despite the finding that angle was not a factor affecting retention for titanium matrices. In other words, angle of the implants had an effect on the retention of gold matrices, but not for titanium matrices. This study supports the clinical observation that implant-supported overdentures have higher maintenance needs and may have higher long-term ongoing costs relative to conventional tooth replacement therapies (Naert *et al.* 2004a,b; Krennmair *et al.* 2005; Zitzmann *et al.* 2005; Trakas *et al.* 2006; Visser *et al.* 2006).

Screw-retained vs. cement-retained restorations

The method of attachment of the prosthesis to the implant/abutment can create prosthetic complications. The major advantages of screw-retained implant-supported restorations include their retrievability and freedom from residual cement problems. Thus this type of restoration scheme can be applied when there is a need for future removal, e.g. necessary hygiene maintenance procedures or questionable prognosis of the restoration. It could also be applied when the restorative margin is located too deep for removal of excess cement at the time of restoration delivery. The same advantage applies to provisional restorations as well. However, this type of restoration has inherent disadvantages. Because of the required screw access hole, it not only compromises the esthetics and occlusion, but also has the potential to undermine the strength of the restoration due to the lack of material. The presence of the prosthetic screw also bears the potential of screw complications. Additionally, this type of restoration is more sensitive to the passive fit of the restoration to the supporting implants.

Regarding the clinical performance of each type of restoration, the literature indicates that screw-retained restorations may present more post-operative complications compared to cement-retained restorations. Duncan *et al.* (2003) reported that patients restored with screw-retained restorations had problems with prosthetic screws and screw access hole filling material while no complications were encountered with patients restored with cement-retained restorations after 3 years. Karl *et al.* (2006) found that cement-retained FPDs may result in lower strain levels compared to conventional screw-retained FPDs at the time of either the cementation or screw-tightening procedure. Higher strain level at the time of delivery may reduce the passivity of the fit of the restoration and increase potential future complications. This result is in accordance with other *in vitro* studies (Guichet *et al.* 2000; Taylor *et al.* 2000). However, this study carefully suggests that regardless of the type of restoration, no true passive fit can be achieved. Skalak (1983) theorized that a non-passive fit of the restoration can induce biologic and prosthetic complications. However, Jemt and Book (1996) reported that they could not find a direct association between implant prosthesis misfits with marginal bone loss over 5 years. Vigolo *et al*. (2004) found no evidence of different behavior of the peri-implant marginal bone and soft tissue response around screw-retained or cement-retained single-tooth implant restorations.

Overall, there is no consensus of the superiority of one type over the other – it may be determined by the clinical situation and the operator's preference.

Ceramic abutments

Ceramic implant abutments have recently gained in popularity due to superior esthetic results compared to conventional titanium abutments, especially in thin tissue biotypes (Stanford 2005a). Because of the strength concerns, the current material of choice for ceramic abutments is reinforced ceramic abutment, e.g. alumina (Al_2O_3) or yettria-stabilized Zirconia (ZrO_2) (Fig. 56-7). These abutments were introduced during the 1990s and the first of these abutments consisted of densely sintered aluminum oxide (alumina). Andersson *et al.* (2003) conducted a 5-year multi-center prospective study evaluating the clinical outcome of alumina ceramic abutments. According to this study, the cumulative success rate for alumina ceramic abutments was 98.1% at 5 years compared to 100% for conventional titanium abutments. More recently, zirconia has become popular for ceramic implant abutments. Because ceramic materials are vulnerable to tensile stress, especially around defects or cracks, a ceramic material with higher fracture toughness will be a good material for ceramic abutments. Zirconia is generally known to have higher range of fracture toughness (K_{IC}, ~7–15 $MPam^{-1}$) than that of alumina (K_{IC}, ~4–4.5 $MPam^{-1}$). Its fracture toughness is comparable to that of metal alloys (K_{IC}, ≥20 $MPam^{-1}$) (Piconi & Maccauro 1999; Kelly 2004). Zirconia is known to have the relatively unique property of transformation toughening, where the metastable tetragonal phase can be converted into monoclinic phase with the associated volume expansion (Chevalier 2006). This phenomenon is induced by stress concentration at defect or crack tips, through which the crack is put into compression and its growth retarded. This is the main mechanism for its higher fracture toughness, and it could significantly extend the reliability and lifetime of the restoration. However, there is little evidence if the abutment will still retain this property after being reduced down to less than 1 mm during clinical usage. Further, the hydrolytic properties of water interacting with the material during ageing (hydrolytic ageing) is still an active area of laboratory investigation (Rekow & Thompson 2005). There are outstanding questions relative to the use of this material including long-term fatigue strength, degree of preparation/wall thickness needed, intraoral sites, clinical long-term prognosis, etc. Due to the relatively short period after its introduction, there are few studies that assess the clinical performance of these abutments (Att *et al.* 2006; Denry & Holloway 2006; Deville *et al.* 2006; Itinoche *et al.* 2006; Studart *et al.* 2006).

Esthetic complications

The most frustrating and challenging complication is unacceptable esthetic outcome either at the time of restoration or during long-term follow up. With

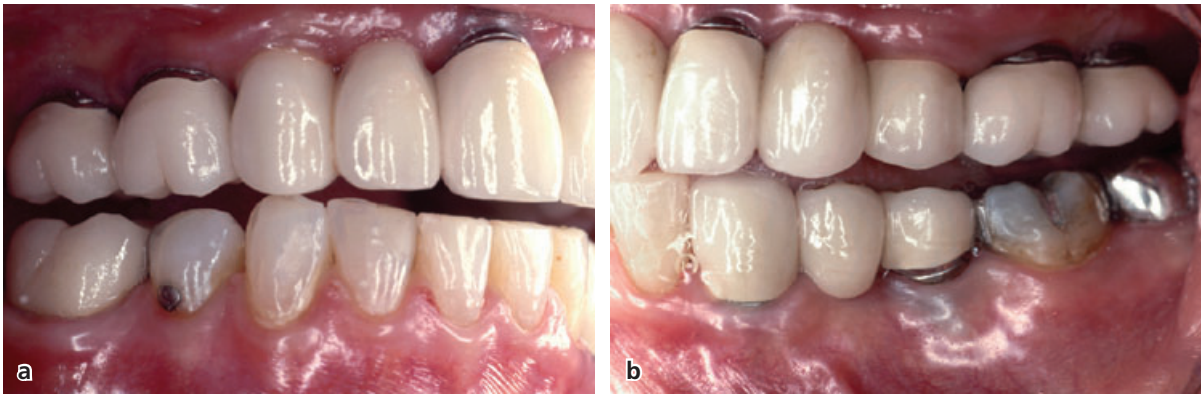

Fig. 56-11 Soft tissue recession on facial aspect of implant supported restoration.

the growing population of esthetically concerned patients, esthetic complications are a serious matter even if the implant team has done its best throughout the procedure. This is an important issue that the implant team and the patient need to be aware of and endeavor to find solutions to prevent or overcome. Common esthetic complications include complications due to malpositioned implants, thin tissue biotypes, and unfavorable soft tissue responses.

The potential cause and impact of malpositioned implants was previously described. A very difficult aspect of implant rehabilitation is that sometimes a slight malpositioning can induce dramatic esthetic compromises which do not become evident until the technician is working with the case. A facially malpositioned implant can become a major challenge for the restorative team (Fig. 56-11). In this case, the restorative dentist may have to address a variety of potential problems, including excessive incisogingival dimensions of the crown, exposed head of the implant, unequal gingival margins, etc. Usually, facially malpositioned implants create greater problems than other malpositioned implants. A 1 mm lingual position to the implant in the maxillary esthetic zone can create a prosthetic challenge to have the final restoration appear even and uniform with the natural dentition. Mesially, or distally malpositioned implants can induce improper anatomy of the restoration as the technician attempts to compensate for implant components in the interproximal space (Fig. 56-12).

Unfavorable soft tissue response can also make the treatment very difficult. It is generally accepted that individuals that have relatively thin attached gingiva, or thin tissue biotype, are more vulnerable to gingival/periodontal disease and subsequent sequelae including gingival recession. Similar findings are reported for the tissue response around implant restorations (Kan *et al.* 2003). Thin biotype tissues tend to show more recessive response to trauma. Restorative procedures, like preparation, impression, repeated abutment/provisional removal, or even toothbrushing, can sometimes cause enough trauma to these thin biotype tissues to result in significant recession and compromise the treatment outcome. It is very important to identify the tissue type early at the treatment planning stage to prevent unfavorable treatment outcome.

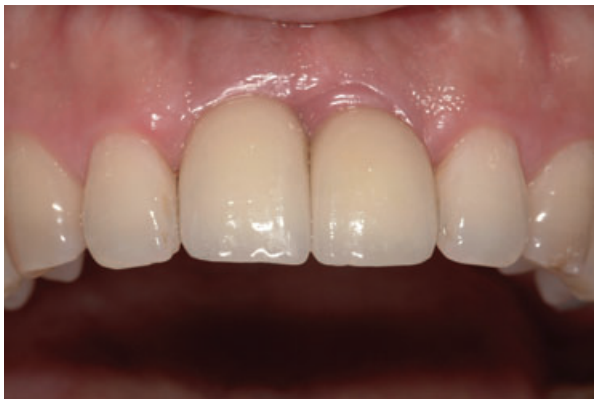

Fig. 56-12 Challenges in creating esthetic outcomes when implants are insufficiently placed. Example demonstrates teeth 11 and 21 with compromised contours due to close proximity of the implants.

Success/survival rate of implant-supported prostheses

As previously described, the biologic success/survival rate is extremely high and has become more predictable even in areas that were considered of high risk (e.g. maxillary posterior region). It may be beneficial to know what the literature indicates regarding the success/survival rate of restorations fabricated on the osseointegrated implants. Pjetursson *et al.* (2004) obtained estimates of the long-term survival/success rates of implant-supported FPDs and of the incidence of technical complications in partially edentulous patients with an observation period of more than 5 years. "FPD survival" was defined as "the FPD remaining *in situ* with or without modification for the observation period", as compared to the definition of "FPD success" being "FPD being free of all complications over the entire obser-

vation period" in this study. The cumulative FPD survival rate was 95% after 5 years and 86.7% after 10 years, respectively. In this study, the authors noted an important fact that most of the prosthetic complications occur after 5 years of clinical service. The underlying issue this illustrates is the problem associated with the rapid rate of manufacturing market changes in implant products and components. By the time the restoration needs repair or replacement, the required components may be difficult if not impossible to obtain. Regarding comparison of different implant systems, there is little evidence of superiority of one system over another in terms of mechanical failure. Implant–abutment joint geometry, design of the restoration, and patient factors like parafunctional habits or heavy occlusal forces tend to have more impact on the outcome of implant-supported restoration than implant surface material or topography (Rangert *et al.* 1995; Astrand *et al.* 1999; Naert *et al.* 2002a,b). Some studies indicate that the cumulative complication rate of prosthetic problems can be as high as 43.1% after 5 years (Jemt *et al.* 2003), compared to other studies finding it to be as low as 19.3% after 5 years (Bragger *et al.* 2001; Pjetursson *et al.* 2004). A summary of these studies indicates that one may expect one out of four implant-supported restorations will require some type of repair whether it be minor, such as screw or abutment tightening, or major, such as entire restoration replacement, after 5 years. This implies that significant chair time may be necessary for the maintenance of these restorations (Pjetursson *et al.* 2004).

Berglundh *et al.* (2002) also noticed the higher mechanical/technical complication rate compared to the lower biologic complication rate. This study observed interesting aspects: the incidence of implant loss prior to functional loading was higher by threefold when multiple implants are placed for larger restorations like overdentures or fixed complete restorations than that of single-tooth restorations; implant loss during function occurred in 2–3% of implants supporting fixed reconstructions, while twice as many implants were lost in overdenture therapy during a 5-year period. In this case, the highest frequencies of implant loss during function occurred in the maxilla.

Conclusions

Implant therapy provides many benefits as a form of tooth replacement therapy. As with any form of prosthetic rehabilitation it has limitations including wear, material fatigue and fracture, soft tissue recession and subsequent complications, increased maintenance and costs. The benefits, though, can be enormous with the enhanced patient quality of life that comes with a definitive replacement of teeth. Patients need to be aware during the treatment planning process that the treatment provided may need to be replaced periodically as normal ageing and wear occurs. Specific patient-based risk factors such as parafunctional habits should be discussed and the patient made aware of the risks to the prosthetic reconstructions.

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Part 17: Orthodontics and Periodontics

Chapter 57

Tooth Movements in the Periodontally Compromised Patient

Björn U. Zachrisson

Orthodontic treatment may be adjunctive to periodontal therapy. The loss of periodontal support or teeth may result in elongation, spacing, and proclination of incisors, rotation, and tipping of premolars and molars with collapse of the posterior occlusion, and decreasing vertical dimension. But orthodontic tooth movement can also facilitate the management of several restorative and esthetic problems in adults. Such difficulties may be related to subgingivally fractured or lost teeth, tipped abutment teeth, excess spacing, inadequate implant or pontic space, supraerupted teeth, narrow alveolar ridges that prevent implant placement, and other conditions (Ong *et al*. 1998). The purpose of this chapter is to discuss how recent basic and clinical information may be used to improve treatment planning, clinical management, and retention for patients in whom different malocclusions are caused or complicated by moderate to advanced periodontal destruction.

Orthodontic tooth movement in adults with periodontal tissue breakdown

Poorly executed orthodontic treatment in periodontal patients can certainly contribute to further periodontal tissue breakdown. In particular, the combination of inflammation, orthodontic forces, and occlusal trauma may produce a more rapid destruction than would occur with inflammation alone (Kessler 1976). However, with properly performed treatment, extensive orthodontic tooth movement can be made in adults with a reduced but healthy periodontium without further periodontal deterioration. Figures 57-1 to 57-6 show the pretreatment and post-treatment conditions in four different adult orthodontic patients with advanced periodontitis. The findings of no significant further periodontal tissue breakdown in these patients were the result of carefully controlled treatment planning considerations.

Only a few well controlled studies have been published on groups of adults with advanced periodontitis, who have received comprehensive orthodontic fixed-appliance treatment. Boyd *et al*. (1989) described ten adults with generalized periodontitis who received pre-orthodontic periodontal treatment including surgery, and then regular maintenance at 3-month intervals during a 2-year orthodontic treatment period. They were compared with ten control adults who had normal periodontal tissues, and 20 adolescent orthodontic patients. The results demonstrated that:

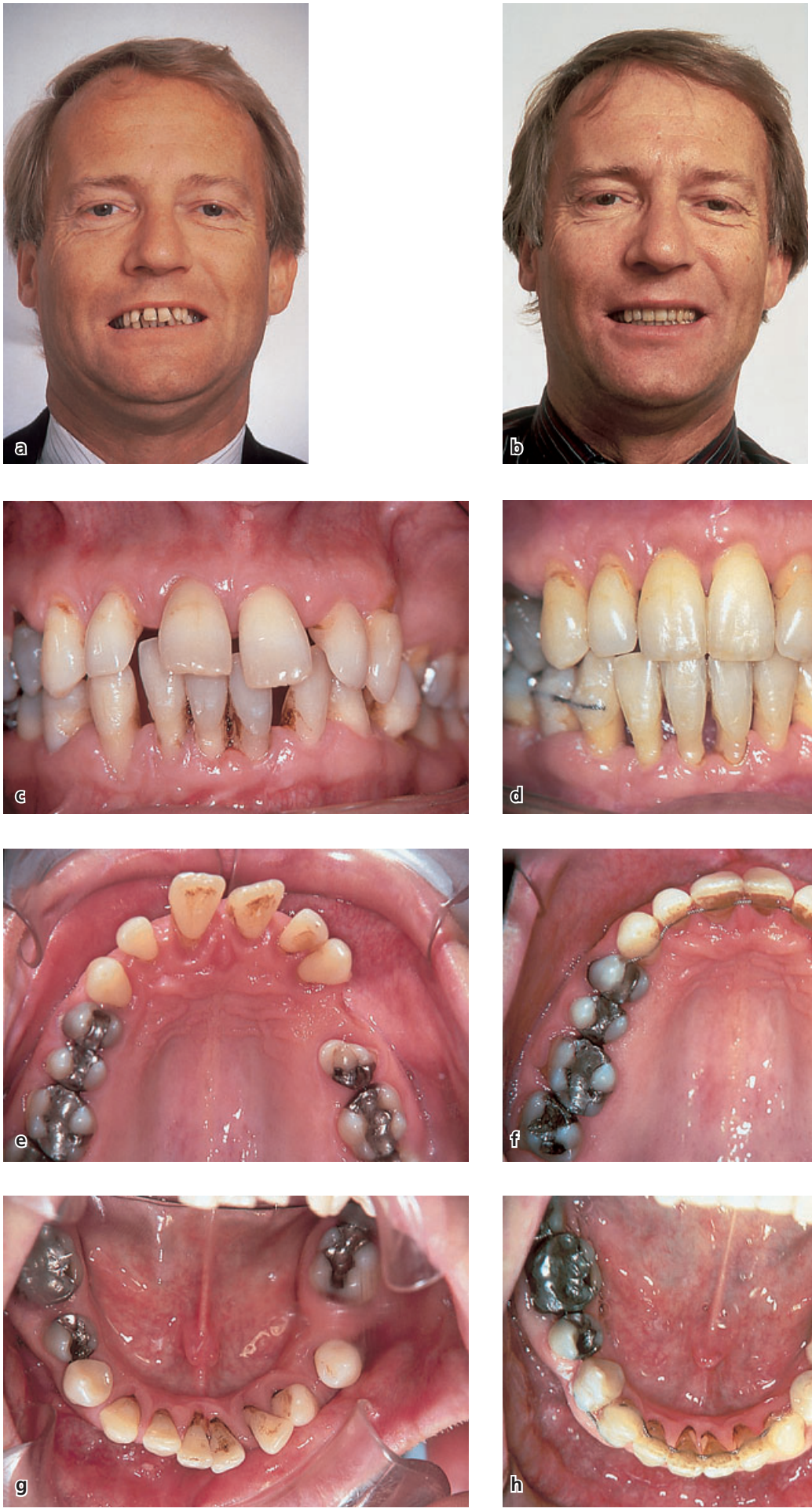


Fig. 57-1 Adult male patient with advanced periodontitis and marked pathologic migration of the anterior teeth before (left column) and after (right column) periodontal and orthodontic fixed-appliance treatment for 2 years. Clinical appearance of the face and dentition are dramatically improved after the combined periodontic/orthodontic treatment. The dental result is maintained by means of bonded lingual retainer wires. A maxillary two-unit and a mandibular three-unit bridge were constructed. Some interdental recession was unavoidable in the mandibular anterior region (d), but it does not show much clinically (b).

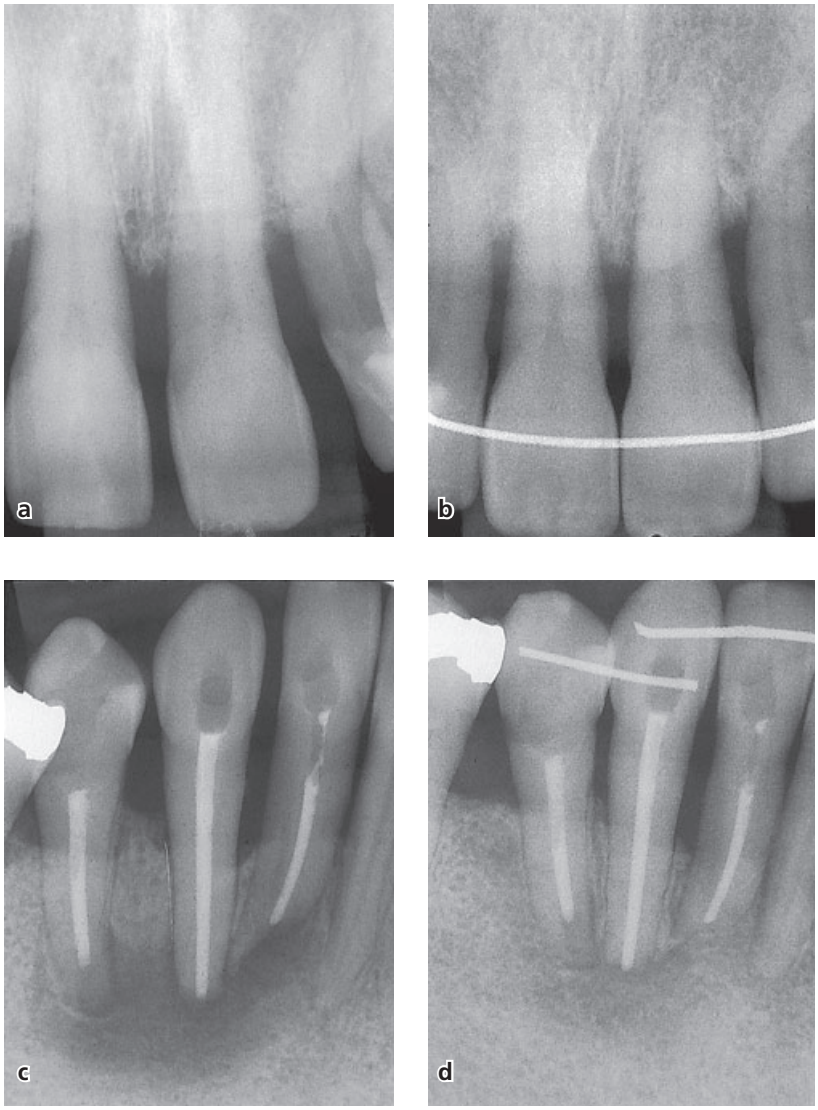


Fig. 57-2 Long-term radiographic follow-up of the same patient as in Fig. 57-1. Radiographs of maxillary and mandibular anterior regions 7 years after the completion of orthodontic therapy (b,d) show reduced but healthy periodontium, with no progression of periodontal tissue destruction compared with the initial situation (a,c).

- Adults were more effective than adolescents in removing plaque, especially late in the orthodontic treatment period.
- Tooth movement in adults with reduced, but healthy, periodontium did not result in significant further loss of attachment (none of the adults had additional mean loss of attachment of more than 0.3 mm).
- Adults with teeth that did *not* have healthy periodontal tissues may experience further breakdown and tooth loss due to abscesses during orthodontic treatment.

In another study by Årtun and Urbye (1988), 24 patients with advanced loss of marginal bone and pathologic tooth migration received active appliance therapy for an average of 7 months, following periodontal treatment. Bone level measurements on radiographs indicated that the majority of sites showed little or no additional loss of bone support. However, a few sites demonstrated pronounced additional bone loss.

More recent studies on much larger groups (350–400 patients) of consecutively treated adult patients from different practices (Nelson & Årtun 1997; Re *et al*. 2000) have confirmed that: (1) pretreatment evidence of periodontal tissue destruction is no contraindication for orthodontics, (2) orthodontic therapy improves the possibilities of saving and restoring a deteriorated dentition, and (3) the risk of recurrence of an active disease process is not increased during appliance therapy. However, these larger samples have indicated that adult orthodontic patients are at a somewhat higher risk than adolescents for tissue breakdown. The mean bone loss on radiographs of the six anterior teeth in the study of Nelson and Årtun (1997) was 0.54 mm (SD 0.62). Only 2.5% of the patients had average bone loss of 2 mm or more, but as many as 36% of these patients had one or more surfaces with bone loss exceeding 2 mm.

Orthodontic treatment considerations

The key element in the orthodontic management of adult patients with periodontal disease is to eliminate, or reduce, plaque accumulation and gingival inflammation. This implies much emphasis on oral hygiene instruction, appliance construction,

Fig. 57-3 Adult female periodontitis patient with pathologic migration of the maxillary incisors before (a,b), during (c–e), and after (f) periodontal and orthodontic treatment. An attempt had been made by the periodontist to grind and splint the overextruded right central incisor with composite resin (b) before orthodontic treatment was started. Due to extensive mesial and distal recontouring of the incisors (stripping) during the treatment (c,d), it was possible to obtain an esthetic final result with almost intact gingival papillae between the incisors in both the maxilla and in the mandible (f).

and periodic check-ups throughout treatment (Zachrisson 1996).

The most appropriate method for tooth movement must be determined in each particular case. Although minor or partial orthodontic treatment with sectional or removable appliances may be possible in some instances, in the majority of cases a fully controlled technique with fixed appliances in both dental arches is preferred in order to carefully control the movement of teeth in three planes.

The orthodontic appliance has to be properly designed. It must provide stable anchorage without causing tissue irritation, and must be esthetically acceptable. For psychologic reasons bonded ceramic brackets are preferred in the most visible regions (Figs. 57-3 to 57-6), generally for the maxillary teeth,

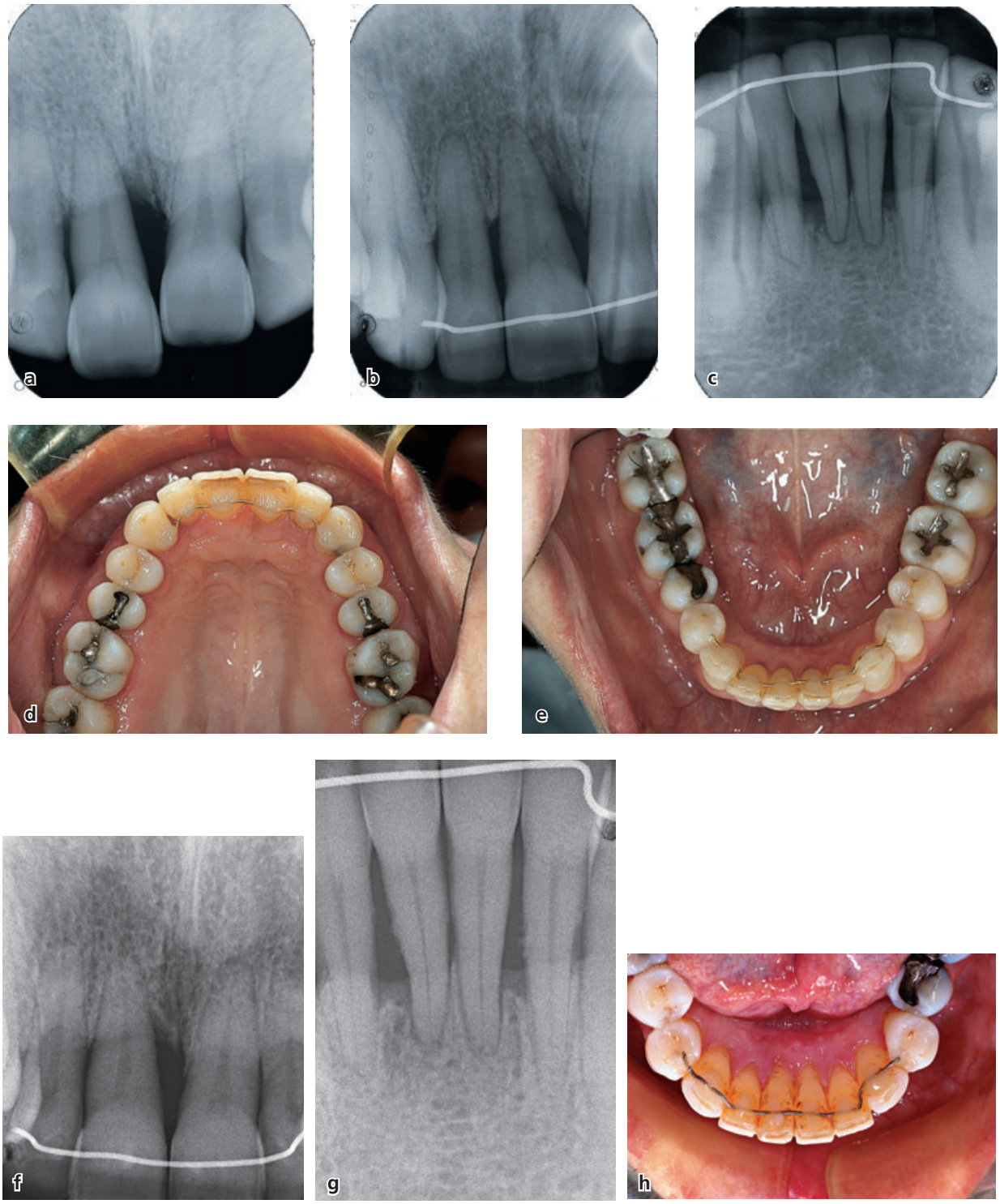


Fig. 57-4 Radiographic and clinical occlusal appearance of the same patient as in Fig. 57-3. No noticeable progression of the periodontal tissue destruction has occurred (compare a and b), and although markedly reduced the periodontium is healthy after the orthodontic therapy (b,c). The treatment result is maintained by means of gold-coated lingual retainers over six maxillary and eight mandibular anterior teeth (d,e).These bonded retainers act as effective orthodontic retainers as well as neat and hygienic periodontal splints. Despite the unfavorable crown–root ratios of particularly the mandibular incisors, the situation is largely unchanged 6 years later (f,g), and the gingival papillae fill in the spaces between the lower anterior teeth nicely (h).

whereas stainless steel or gold-coated attachments are commonly used elsewhere in the mouth (Figs. 57-3, 57-5).

To counteract the tendency of orthodontic appliances to increase the accumulation of plaque on the teeth, attempts should be made to keep the appliances and mechanics simple, and avoid hooks, elastomeric rings, and excess bonding resin outside the bracket bases. The use of steel ligatures is recommended on all brackets (Figs. 57-3 to 57-6), since elastomeric rings have been shown to be significantly more plaque attractive than steel ties (Forsberg *et al*.

Fig. 57-5 Another adult female periodontitis patient with pathologic migration of the maxillary incisors before (a–c), during (d,e), and after (f) periodontal and orthodontic treatment. Despite the advanced periodontal tissue break-down, the case was treated with extraction of two upper first premolars (d). Due to the extensive mesial and distal recontouring of the incisors (stripping) during the treatment (e), it was also possible in this case to obtain an esthetic final result with almost intact gingival papillae between the incisors (h). The clinical and radiographic situation 1.5 years after treatment is shown in g–i. Note gold-coated short labial retainer wires about the closed extraction sites to prevent space reopening (f).

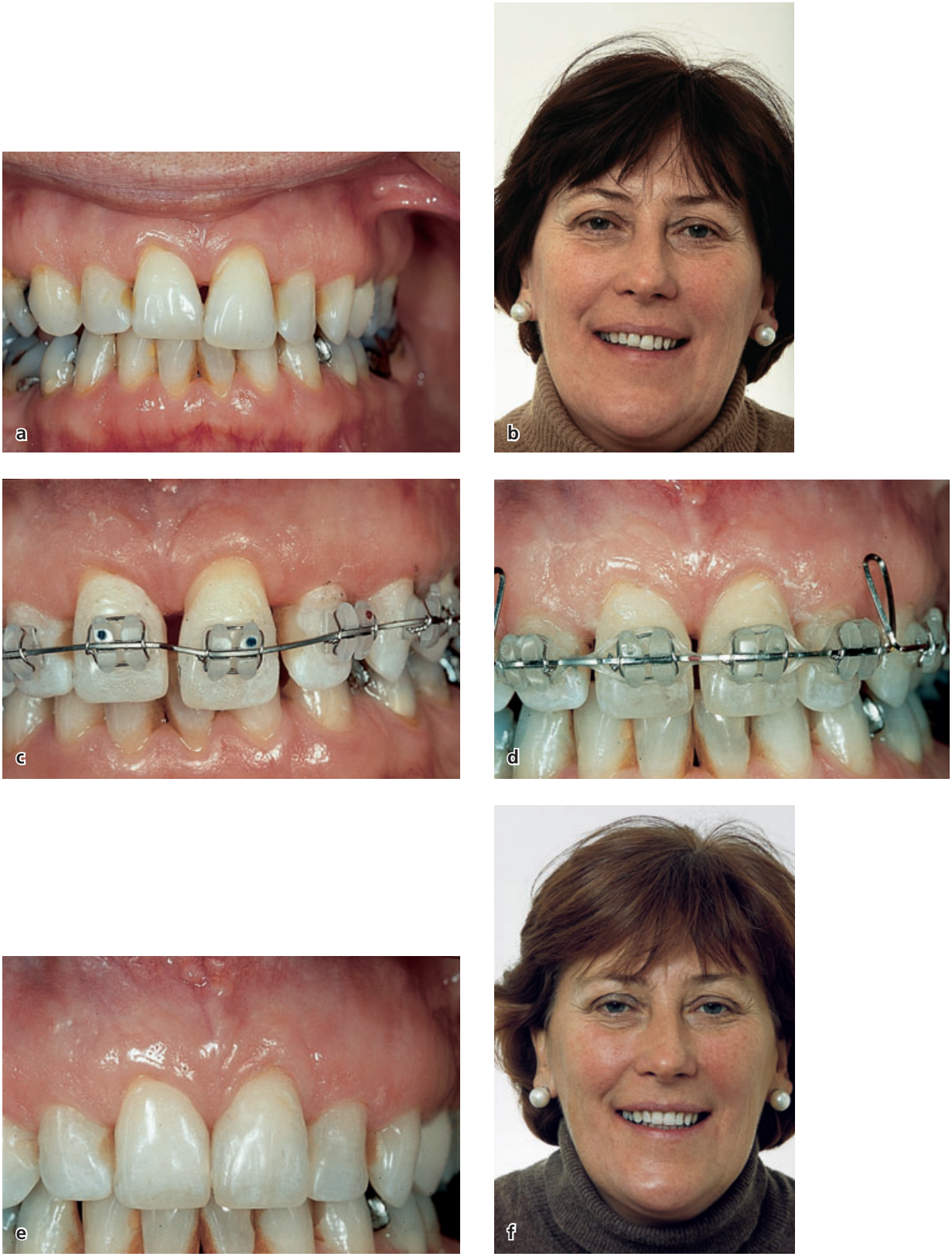


Fig. 57-6 Adult female periodontitis patient with marked loss of the interdental papilla between the maxillary central incisors (a,b). This gap is caused by the "fan-shaped" morphology of the central incisors, which places the interproximal contact too near the incisal edge. To eliminate the unesthetic soft tissue gap, the mesial surfaces of the central incisors were reshaped (c) to lengthen their connector area and move the contact point gingivally (d). After continued orthodontic space closure, a more esthetic final result was achieved (e,f).

1991). Bonds are preferable to bands (Boyd & Baumrind 1992). Bonded molars show less plaque accumulation, gingivitis, and loss of attachment interproximally than banded molars during orthodontic treatment of adults. However, bonding is more complicated in adult patients than in adolescents. Many adults have amalgam restorations and crown-and-bridge restorations made of porcelain or precious metals. Thanks to the introduction of new techniques and materials, it is feasible to bond orthodontic brackets, buccal tubes, and retainer wires to artificial surfaces. Clinical experience with bonding to different artificial tooth surfaces, except gold, is excellent (Zachrisson 2000a,b).

Renewed oral hygiene instruction and motivation is made after placement of the orthodontic appliances. During the treatment period professional tooth cleaning by a dental hygienist or periodontist may be performed at 3-month intervals (Boyd *et al*. 1989; Boyd & Baumrind 1992), or after regular examination updates at 6- and 12-month intervals, depending on the situation. The re-examinations should include recordings of probing depths, mobility, bleeding on probing, suppuration, gingival recessions, bone levels, etc. Professional scaling may be indicated during *active intrusion* of elongated maxillary incisors, since orthodontic intrusion may shift supragingival plaque to a subgingival location (Ericsson *et al*. 1977, 1978). If efforts at maintaining excellent-to-good oral hygiene are unsuccessful, orthodontic treatment should be terminated (Machen 1990).

After appliance removal, reinstruction in oral hygiene measures should be given. Otherwise, subsequent labial gingival recession may be risked due to overzealous toothbrushing, since cleaning is now easier to perform.

Esthetic finishing of treatment results

Adults with a reduced periodontium represent different challenges for orthodontists than adolescents. Worn or abraded teeth, missing papillae and uneven crown lengths are common problems, and it is therefore more difficult to obtain an esthetically optimal appearance of the teeth and gingiva after bracket removal.

Most incisor teeth in adults with malocclusions have more or less worn incisal edges, which represent an adaptation to functional demands. When the axial inclinations and rotations of such incisors are corrected, there is frequently a need for incisal grinding towards a more normal contour. Such grinding can be performed safely as long as the wear is limited, the overbite is adequate, and the patients display enough tooth material in conversation and on smiling. When the abrasion is more significant, however, cooperation with a restorative dentist is generally indicated.

The presence of papillae between the maxillary incisors is a key esthetic factor after orthodontic treatment. Normally, when long-standing crowding with incisor overlap is corrected orthodontically in adults, it is generally not possible to have an intact papilla. This is because the contact point becomes located too far incisally on the triangular crowns that have not had a normal interdental wear pattern. Similarly, in patients with advanced periodontal disease and destruction of the crestal bone between the incisors, the papillae may be absent. This produces unesthetic gaps between the teeth after orthodontics. The best method of correcting this problem is to recontour the mesiodistal surfaces of the incisors during the orthodontic finishing stage (Tuverson 1980). When the diastemata thus created are closed, the roots of the teeth can come closer together. The contact point is lengthened and moved apically, and the papilla can fill out the interdental space more easily (Figs. 57-3, 57-5, 57-6; also see Fig. 57-28).

In patients with high or normal smile lines, the relationship of the gingival margins of the maxillary anterior teeth may be another important factor in the esthetic appearance of the crowns (Kokich 1996a,b). When adult patients have gingival margin discrepancies between adjacent teeth, the orthodontist must determine the proper solution for the problem: orthodontic movement to reposition the gingival margin (see Fig. 57-17) or surgical correction (gingivectomy) to increase the crown length of single or several teeth (see Fig. 57-29).

Retention – problems and solutions; long-term follow-up

Due to the anatomic and biologic differences in tissue reaction between adults and children (Melsen 1991), adults undergoing extensive orthodontic treatment will generally need, at least, a longer period of retention than would an adolescent patient. Also, growth and development no longer take place and cannot aid in changing occlusal levels or in space closure by the eruption of posterior teeth with mesial drift. The space reopening tendency of closed extraction sites in adults can be mitigated by use of labially bonded retainers (Figs. 57-1, 57-5).

The migration of teeth associated with periodontal tissue breakdown around the incisors in adults is usually blamed on inflammatory swelling or the tongue thrust. However, according to Proffit (1978), two major primary factors are involved in the equilibrium which determines the final position of teeth. These are the resting pressures of lip or cheek and tongue, and forces produced by metabolic activity within the periodontal membrane. With an intact periodontium, unbalanced tongue–lip forces are normally counteracted by forces from the periodontal membrane. However, when the periodontium breaks down, its stabilizing function no longer exists and the incisors begin to move. A consequence of this concept would be that persons with advanced periodontal disease and tooth migration would need permanent

retention after the orthodontic correction. For patients with minimum-to-moderate loss of periodontal tissue support, more "normal" retention periods may be sufficient.

The optimal long-term retainer for adults with reduced periodontium is the flexible spiral wire (FSW) retainer bonded lingually on each tooth in a segment. The bonded retainer in the anterior region is generally used together with a maxillary removable plate. The fabrication and long-term evaluation of bonded retainers is described by Dahl and Zachrisson (1991). Figures 57-3, 57-4, 57-5 and 57-20 demonstrate different designs of FSW retainers in the maxilla and the mandible in several patients. At the same time as the FSW retainer works as a reliable, invisible orthodontic retainer, it concomitantly acts as a periodontal splint, which allows the individual teeth within the splint to exert physiologic mobility. As long as the retainer remains intact, small spaces might open up distal to, but not within, the retainer.

Splinting may not be needed for most teeth with increased mobility after periodontal therapy (Ramfjord 1984). However, reduced mobility of teeth after combined periodontal and orthodontic treatment by using a bonded retainer would seem to be of considerable benefit. If a bonded retainer is not used, and instead a removable plate or spring retainer is used at night on a long-term basis, there is a risk for ongoing jiggling of the teeth because of the relapse tendency during the day. Experimental studies in animals indicate that jiggling forces may facilitate the progress of attachment loss in periodontitis, or at least result in more bone resorption. Also, more connective tissue reattachment and bone regeneration may occur around non-jiggled teeth. Monkey experiments have shown that when experimental jiggling of teeth was stopped, a significant gain of alveolar bone occurred (Nyman *et al*. 1982). Similarly, Burgett *et al*. (1992) demonstrated that healing following periodontal therapy may be more advantageous in patients who received occlusal adjustment than in non-adjusted patients.

Long-term follow-up of patients who have received combined periodontal and orthodontic treatment, and have used bonded retainers for several years, demonstrates excellent stability and apparently unchanged, or even improved, periodontal condition (Figs. 57-4, 57-7, 57-8). It should be pointed out, however, that a bonded maxillary retainer must be placed out of occlusion with the mandibular incisors, because biting on a retainer wire will lead to unacceptably high bond failure rates (Årtun & Urbye 1988).

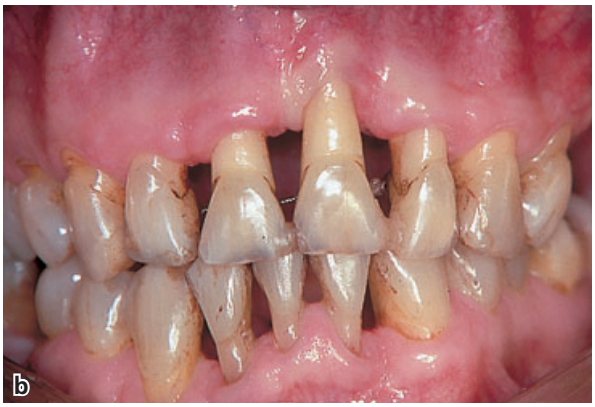
Possibilities and limitations; legal aspects

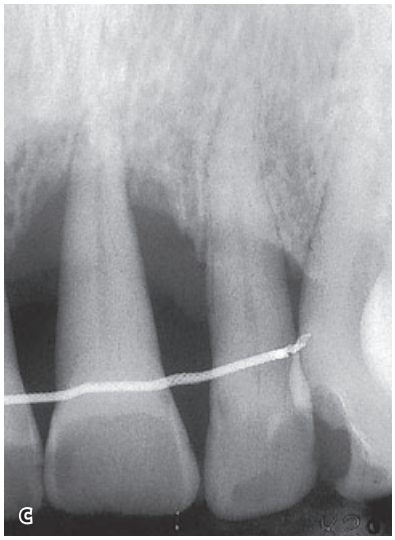
Adult orthodontic patients with marked periodontal destruction may represent potential problems even when optimal treatment is provided. There are, however, no definite metric limits in terms of probing depths or loss of attachment when orthodontic tooth movement can no longer be performed (Diedrich 1999). Each individual treatment plan may depend on a variety of factors and can be limited by biomechanical considerations (force systems, limited anchorage), by periodontal risk factors (tooth/alveolar bone topography, sinus recesses, activity and prognosis of the periodontitis), and by limited patient motivation and poor oral hygiene cooperation.

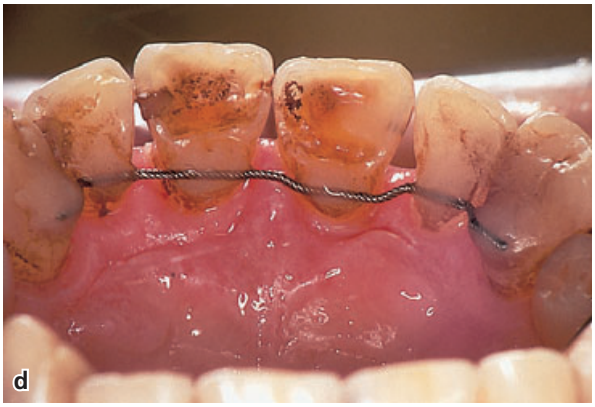
Single case reports have documented successful periodontal–orthodontic treatment with localized juvenile periodontitis (LJP) after conventional periodontal therapy (Harpenau & Boyd 2000), or with continous antiseptic and short-term systemic (Folio *et al*. 1985) or local (Hoerman *et al*. 1985) antibiotic applications, and microbiologic testing during the orthodontic treatment period to reduce the risk of recurrent disease. However, until more evidence is accumulated, it may seem wise to avoid orthodontic treatment in patients with particularly aggressive forms of periodontal disease. Similarly, multi-rooted teeth with questionable prognosis should be moved orthodontically only in exceptional situations.

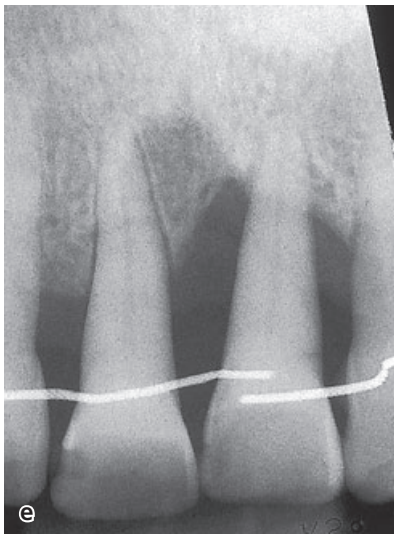
"Hopeless teeth": According to old concepts, the retention of teeth diagnosed as periodontally "hopeless" would accelerate the destruction of the adjacent interproximal periodontium. Such teeth were therefore frequently extracted in the past. However, the theoretic rationale for such extractions would seem unsupported, and recent follow-up studies have demonstrated that retained periodontally "hopeless" teeth do not significantly affect the interproximal periodontium of adjacent teeth following periodontal therapy (Chace & Low 1993). The clinical implication is that these teeth can be useful for orthodontic anchorage, if the periodontal inflammation can be controlled (Fig. 57-9). Occasionally, the hopeless tooth may be so improved after orthodontic treatment that it is retained (Mathews & Kokich 1997). Alternatively, a hopeless molar may be hemisectioned after the orthodontic treatment, and the best root may be used as a bridge abutment (Fig. 57-10). Most of the time, however, the hopeless tooth will be extracted, especially if other restorations are planned in the segment.

For improved patient care, stress reduction, and reduction or elimination of law suits, careful examination protocols, documentation and correspondence techniques, and regular progress evaluations are important. The legal implications of orthodontic risk management concepts may be that it is preferable to terminate treatment for patients who fail to improve oral hygiene care, despite the orthodontist's efforts. In the long term, this will be better for both patient and orthodontist, since termination, if properly handled, will be more easily defended than permitting the condition to worsen (Machen 1990). However, if proper procedures are followed, termination of









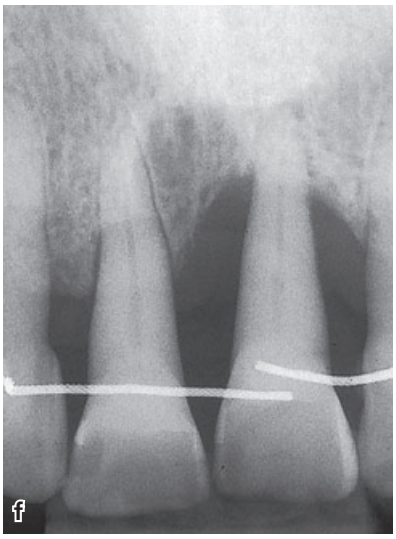


Fig. 57-7 Adult male periodontitis patient after periodontal and orthodontic therapy (a–d). The patient was treated with generalized gingivectomies according to concepts aiming at pocket elimination. The orthodontic result is maintained with a six-unit lingually bonded retainer (d). The bonded wire will act both as an orthodontic retainer and as a periodontal splint, which would appear advantageous in cases where the tissue destruction is as advanced as in this patient. (e) and (f) show the radiographic appearances 7 and 9 years, respectively, after removal of the orthodontic appliances. The left central incisor had so little bone support that if the bonded retainer had not been used, the tooth would probably had been lost over time (see also Fig. 57-8).

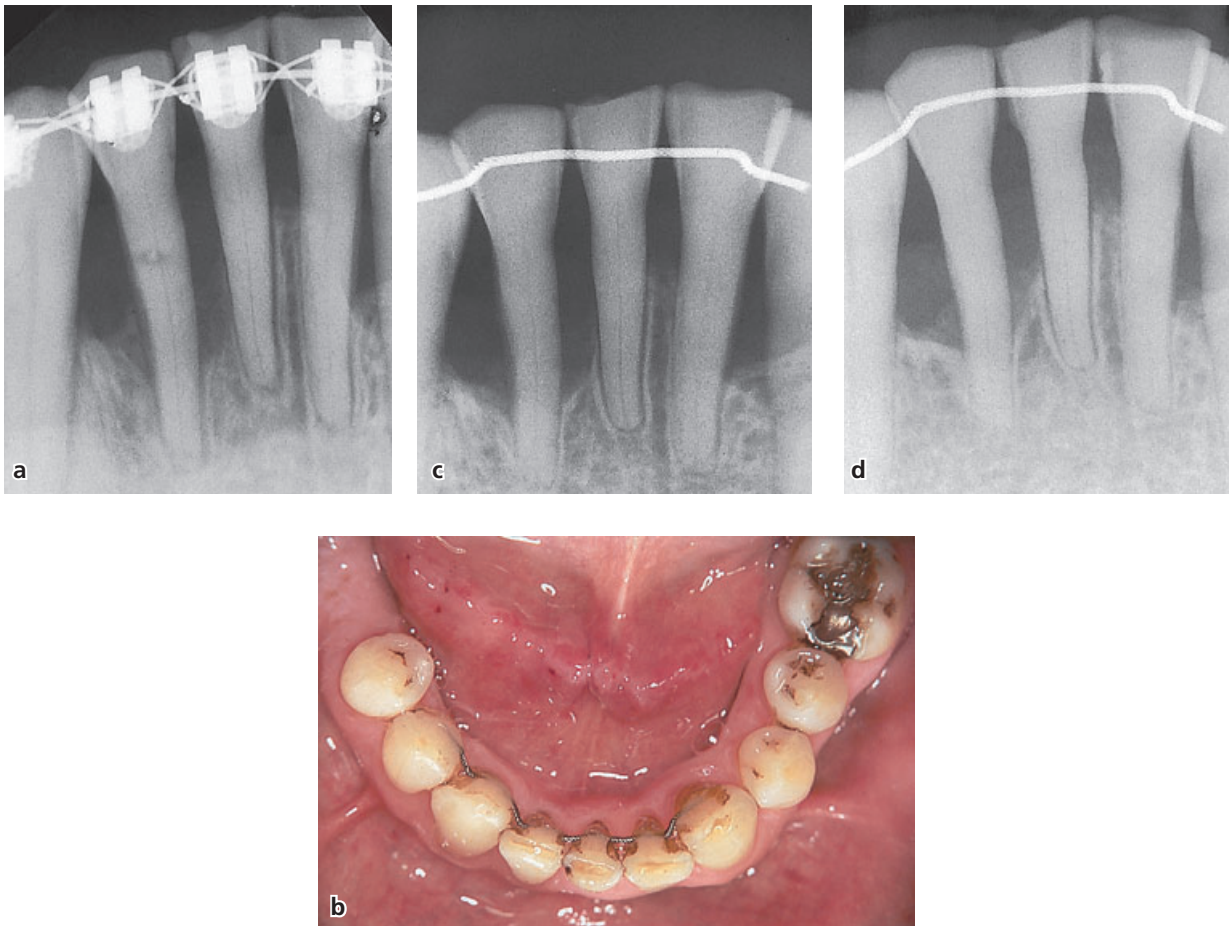


Fig. 57-8 Post-treatment radiographic (a) and clinical (b) appearance of the mandibular dentition in the same patient as in Fig. 57-7 after periodontal and orthodontic treatment. The mandibular six-unit retainer bonded lingual retainer (b) concomitantly acts as a periodontal splint. Note signs of improvement of periodontal condition 7 and 9 years, respectively, after the orthodontic treatment (c,d), with marked crestal lamina dura contours.

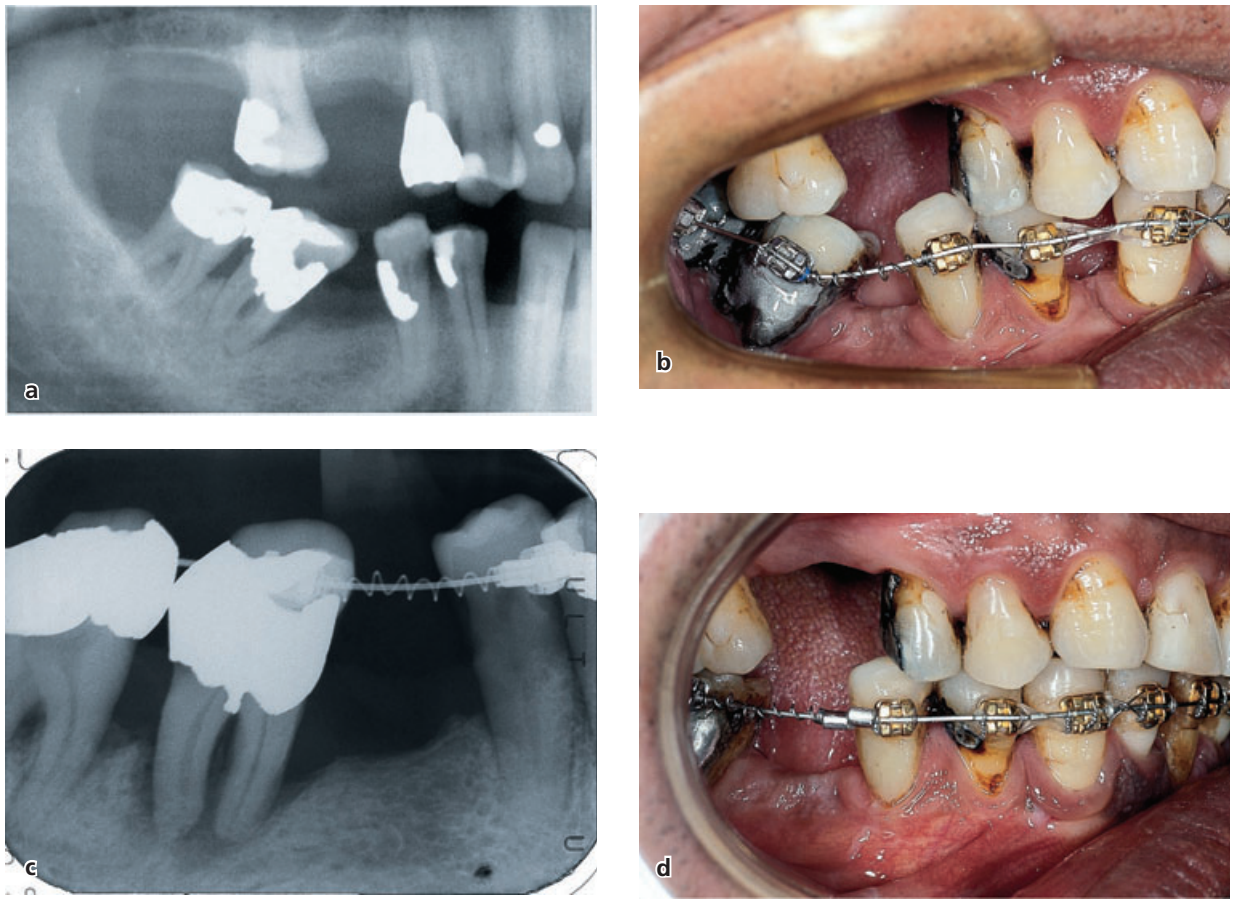


Fig. 57-9 "Hopeless" mandibular right first molar (a) can be used as part of anchorage to move the premolars mesially and upright the second molar (b–d). The first molar may be kept, or extracted, after the orthodontic treatment period.

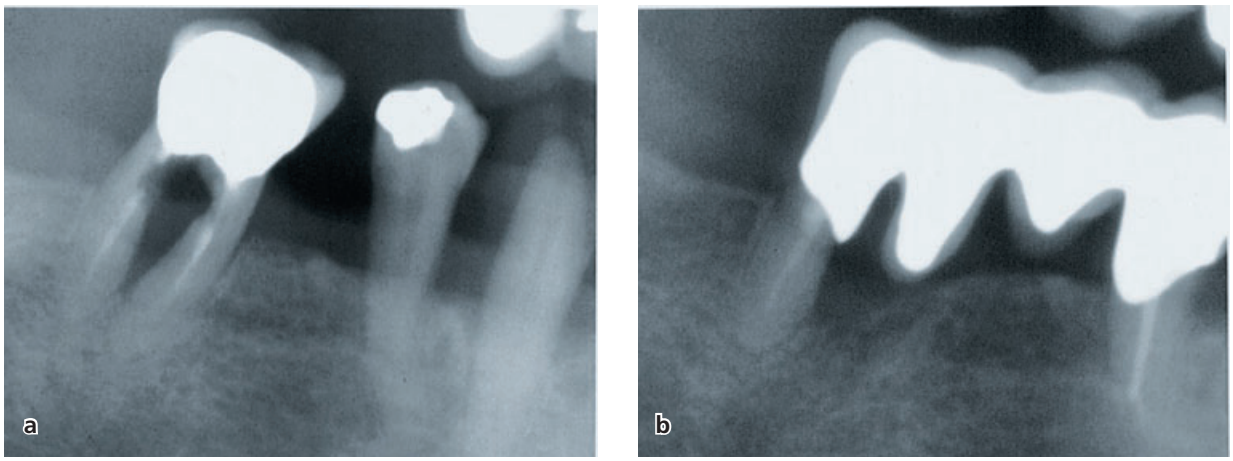


Fig. 57-10 "Hopeless" mandibular right first molar (a) was used as anchorage during orthodontic treatment to close spaces anteriorly, before it was hemisectioned and the distal root employed as a bridge abutment (b).

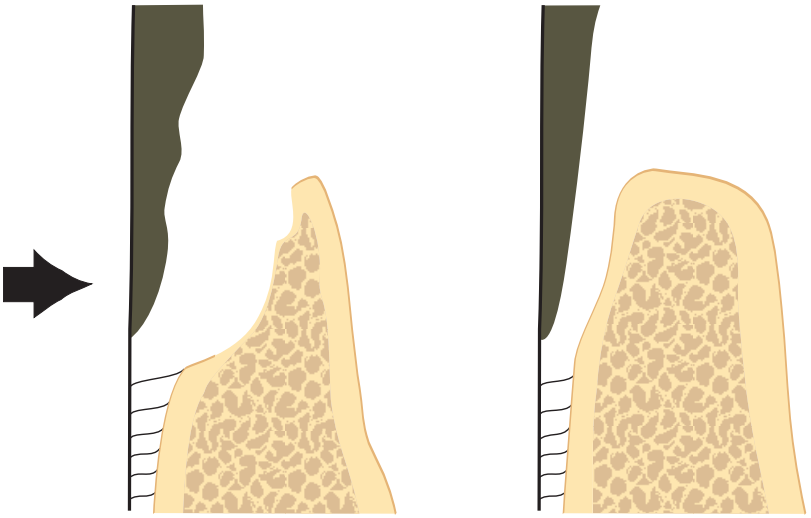


Fig. 57-11 Schematic illustration of persisting junctional epithelium subsequent to orthodontic tooth movement (direction of arrow) into an infrabony pocket.

orthodontic care for periodontal patients will very rarely be needed.

Specific factors associated with orthodontic tooth movement in adults

Tooth movement into infrabony pockets

Orthodontic forces *per se* are unlikely to convert gingivitis into destructive periodontitis. The plaque-induced lesion in gingivitis is confined to the supra-alveolar connective tissue, whereas tissue reactions to orthodontic forces occur in the connective tissue between the root and the alveolar bone. However, infrabony pockets, i.e. angular bony defects with inflamed connective tissue and epithelium apical to the bone crest, may develop as a result of destructive periodontitis. Infrabony pockets may also be created by orthodontic tipping and/or intruding movements of teeth harboring plaque (Ericsson *et al*. 1977). The effect of bodily tooth movement into infrabony defects has been evaluated experimentally in monkeys (Polson *et al*. 1984) and in dogs (Wennström *et al*. 1993). Provided elimination of the subgingival infection was performed before the orthodontic tooth movement was started, no detrimental effects on the attachment level were observed. The angular bony defect was eliminated by the orthodontic treatment, but no coronal gain of attachment was found and a thin epithelial lining covered the root surface corresponding to its pretreatment position (Fig. 57-11). It was therefore concluded that orthodontic tooth movement into infrabony periodontal defects had no favorable effects on the level of connective tissue attachment. However, it was possible to move teeth with reduced *healthy* periodontium without additional attachment loss. If, on the other hand, the orthodontic treatment involved movement of teeth into and through a site with inflammation and angular bone loss, an enhanced rate of periodontal destruction was noted.

Conclusion

Since orthodontic movement of teeth into inflamed infrabony pockets may create a high risk for additional periodontal destruction, and because infrabony pockets are frequently found at teeth that have been tipped and/or elongated as a result of periodontal disease, it is clinically essential that periodontal treatment with elimination of the plaque-induced lesion is performed before orthodontic therapy is begun. It is equally important that excellent oral hygiene is maintained throughout the course of the orthodontic treatment. Following these principles, clinical and radiographic observations confirm that orthodontic treatment can be successfully performed in patients with infrabony pockets resulting from periodontal disease.

Tooth movement into compromised bone areas

Orthodontic tooth movement may sometimes be performed in adults with partially edentulous dentitions (due to agenesis or previous extractions of teeth) and such patients may have a more or less compromised alveolar process. Experimental reports (Lindskog-Stokland *et al*. 1993) and clinical studies (Stepovich 1979; Hom & Turley 1984; Goldberg & Turley 1989; Thilander 1996) have shown that a reduction in vertical bone height is not a contraindication for orthodontic tooth movement towards, or into, the constricted area. Mandibular second molars can be moved mesially through remodeled edentulous first molar areas in adults (Fig. 57-12), with only a limited reduction in vertical bone height, averaging –1.3 mm (Hom & Turley 1984). Space closure is possible also in edentulous maxillary first molar areas, although vertical bone loss and some space reopening can be a complication.

Histologic observations in animal experiments have confirmed that when light forces were applied to move teeth bodily into an area with reduced bone height, a thin bone plate was recreated ahead of the moving tooth (Fig. 57-13) (Lindskog-Stokland *et al*. 1993). The key to moving teeth with bone is direct resorption in the direction of tooth movement, and avoiding hyalinization. Teeth can also be moved with bone into the maxillary sinus (Melsen 1991).

Conclusion

Although the results of clinical experiments and follow-ups are encouraging, provided light forces are used and excellent oral hygiene is maintained, it is probably wise not to stretch the indications for tooth movement into constricted bone areas too far. Marked gingival invaginations are sometimes seen in such areas (Fig. 57-12), and computer tomography analysis and human histologic findings indicate that buccal or lingual bone dehiscences may occur (Diedrich 1996). Such defects are not revealed by conventional radiography. The clinical significance of the gingival clefts and bone dehiscences with regard to relapse tendency and periodontal status is not known. For orthodontic tooth movement into markedly atrophied alveolar ridges, the possibility to acquire new bone by, for example, guided bone regeneration (GBR) procedures should be considered.

Tooth movement through cortical bone

Experimental studies in animals have demonstrated that when a tooth is moved bodily in a labial direction towards and through the cortical plate of the alveolar bone, no bone formation will take place in front of the tooth (Steiner *et al*. 1981; Karring *et al*. 1982). After initial thinning of the bone plate, a labial bone dehiscence is therefore created (Fig. 57-14). Such perforation of the cortical plate can occur during orthodontic treatment either accidentally or because it was considered unavoidable. It may happen, for example, (1) in the mandibular anterior region due to frontal expansion of incisors (Wehrbein *et al*. 1994), (2) in the maxillary posterior region during lateral expansion of cross-bites (Greenbaum & Zachrisson 1982), (3) lingually in the maxilla associated with retraction and lingual root torque of maxillary incisors in patients with large overjets (Ten Hoeve & Mulie 1976), and (4) by pronounced traumatic jiggling of teeth (Nyman *et al*. 1982). The soft tissue reactions accompanying such tooth movements are discussed later in this chapter and in Chapter 51.

Interestingly, however, there is potential for repair when malpositioned teeth are moved back toward their original positions, and bone apposition may take place (Fig. 57-14). Evidently, the soft tissue facial to an orthodontically produced bone dehiscence may contain soft tissue components (vital osteogenic cells) with a capacity for forming bone following repositioning of the tooth into the alveolar process (Nyman *et al*. 1982).

Conclusion

The clinical implication of these observations is encouraging. Bone dehiscences which may occur due to uncontrolled expansion of teeth through the cortical plate may be repaired when the teeth are brought back, or relapse, towards a proper position within the alveolar process, even if this occurs several months later. Similar repair mechanisms may be expected to occur when marked jiggling of teeth is brought under control and stabilized. In the case of buccal cross-bites, the initial discrepancy can apparently be overcorrected with both slow and rapid expansion treatment approaches without causing permanent periodontal injury to the settled occlusion.

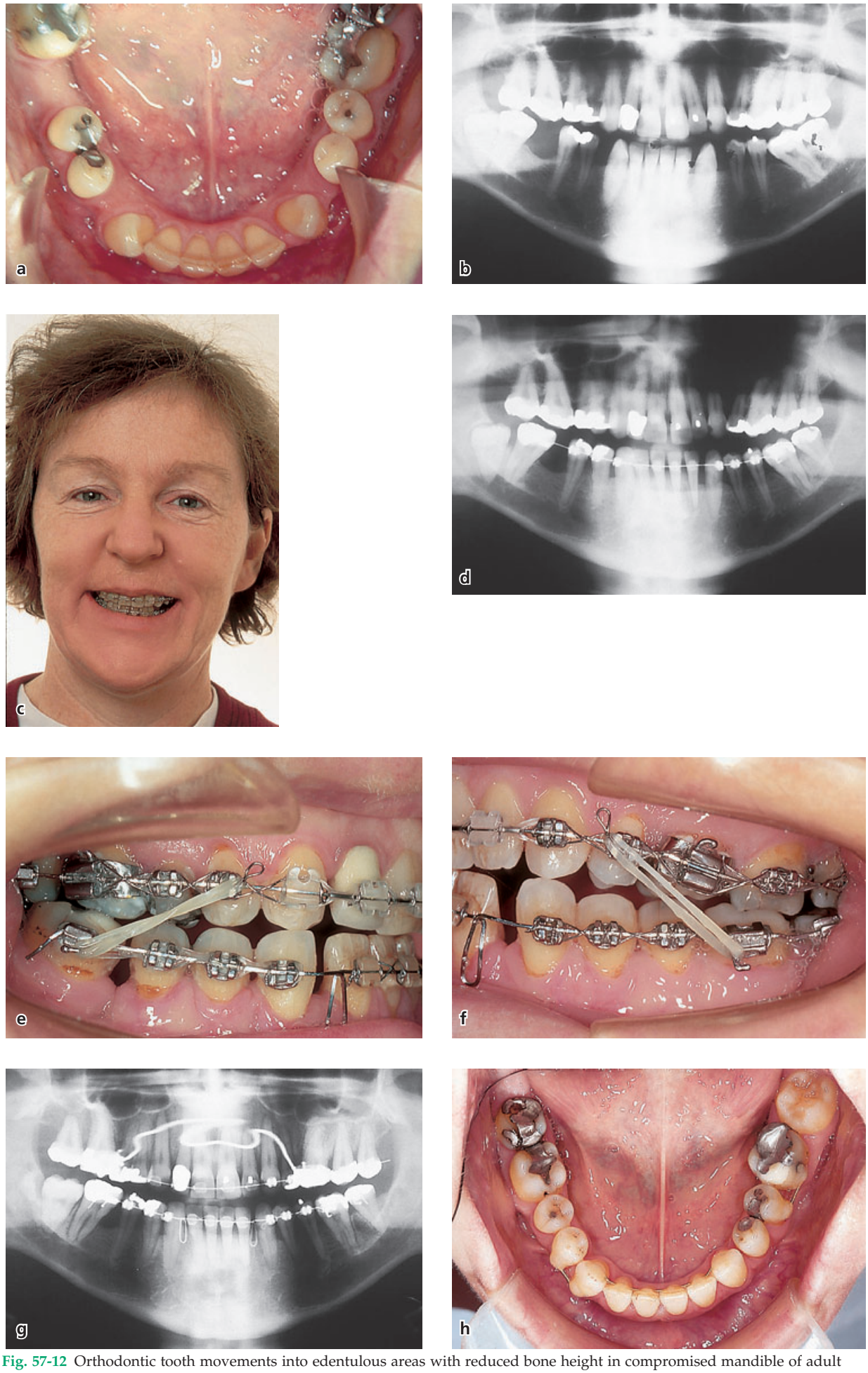


Fig. 57-12 Orthodontic tooth movements into edentulous areas with reduced bone height in compromised mandible of adult female patient. During the orthodontic treatment (c–g), the teeth were moved to close three areas of marked alveolar bone constriction (a,b), most notably in the right first molar area. Note that the impacted third molar erupted spontaneously as the second molar was moved mesially (g). (h) Final result with bonded six-unit lingual and two-unit labial retainers.

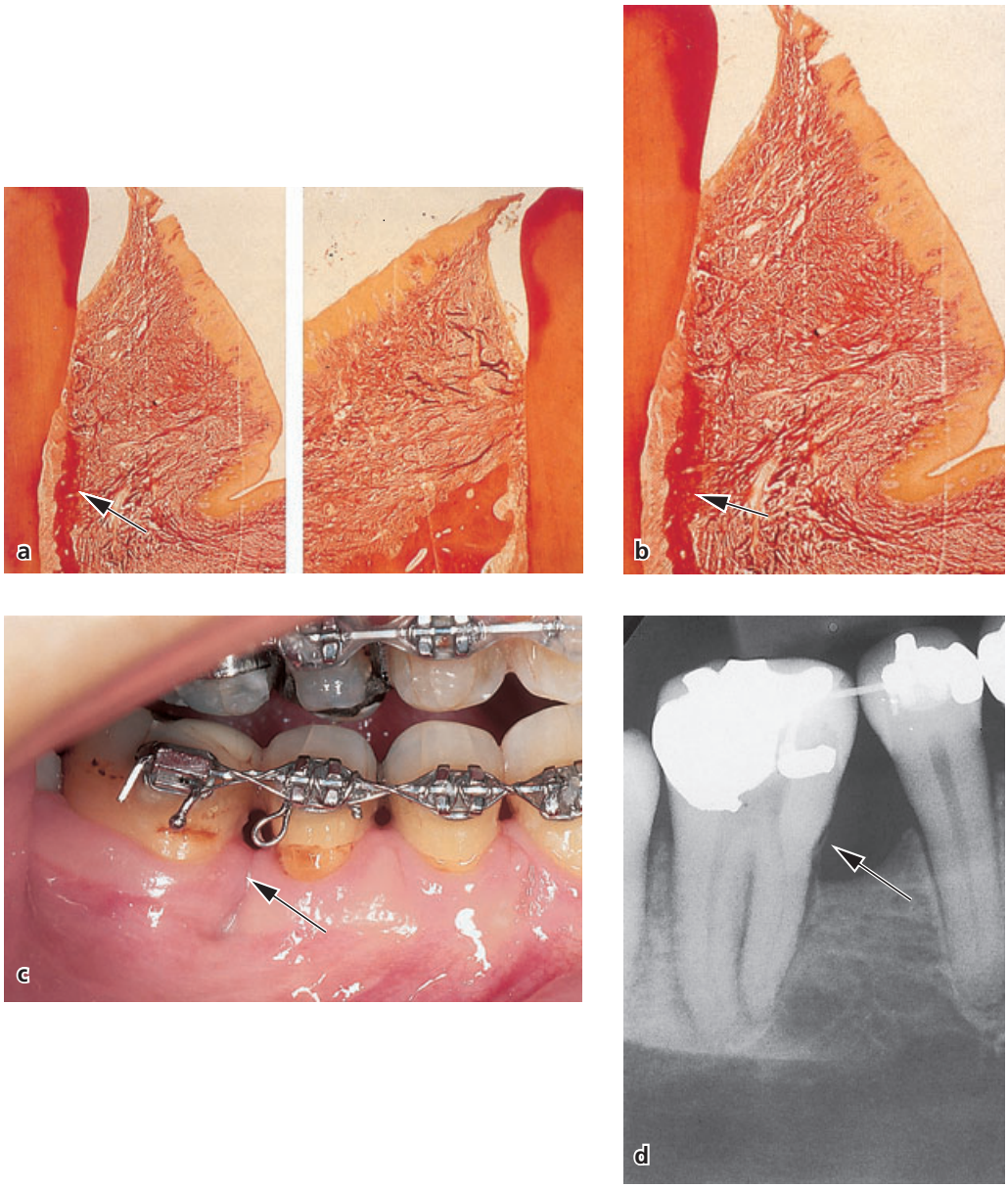


Fig. 57-13 (a,b) Histologic specimens from experimental orthodontic tooth movement into edentulous areas in dogs. The thin bone spicule along the pressure side of the test tooth (b) indicates tooth movement with, and not through, bone. (c,d) The same patient as in Fig. 57-12. Note radiographic visualization of the thin bone spicule on the mesial side of the second molar (arrow in d). Although the molar is moved to contact the second premolar, a marked gingival invagination is present in the area (arrow in c). (a) and (b) from Lindskog-Stokland *et al*. (1993).

Extrusion and intrusion of single teeth – effects on periodontium, clinical crown length, and esthetics

Extrusion

Orthodontic extrusion of teeth, or so-called "forced eruption", may be indicated for (1) shallowing out intraosseous defects and (2) for increasing clinical crown length of single teeth. The forced eruption technique was originally described by Ingber (1974) for treatment of one-wall and two-wall bony pockets that were difficult to handle by conventional therapy alone. The extrusive tooth movement leads to a coronal positioning of intact connective tissue attachment, and the bony defect is shallowed out. This was confirmed in animal experiments (van Venroy & Yukna 1985) and clinical trials. Because of the orthodontic extrusion, the tooth will be in supraocclusion. Hence, the crown of the tooth will need to be shortened, in some cases followed by endodontic treatment.

During the elimination of an intraosseous pocket by means of orthodontic extrusion, the relationship between the CEJ and the bone crest is maintained. This means that the bone follows the tooth during the extrusive movement. This may or may not be beneficial depending on the clinical situation. In other

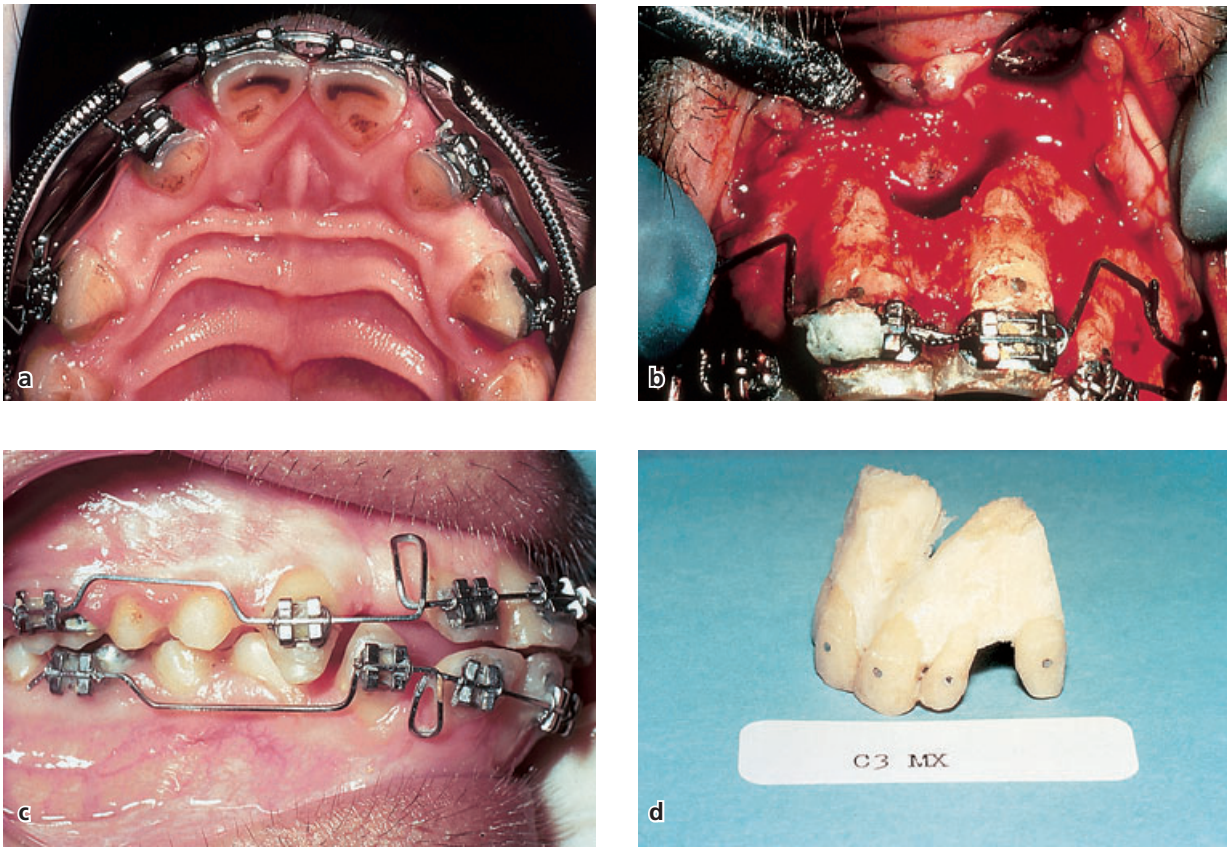


Fig. 57-14 Techniques used by Steiner *et al*. (1981) to advance incisors bodily through the labial bone plate in monkeys (a,b) and by Engelking and Zachrisson (1982) to retract the incisors to their original position (after the teeth had remained in extreme labioversion for 8 months) in a study of periodontal regeneration to such tooth movement. (d) Tissue blocks after tooth repositioning show evident bone regeneration.

words, it is sometimes desirable to have the periodontium follow the tooth and in other situations it is desirable to move a tooth out of the periodontal support. This is further discussed under slow versus rapid eruption of teeth in Chapter 51.

Extrusion with periodontium

Orthodontic extrusion of a single tooth that needs to be extracted is an excellent method for improvement of the marginal bone level before the surgical placement of single implants (Figs. 57-15, 57-21, 57-22). Not only the bone, but also the soft supporting tissues will move vertically with the teeth during orthodontic extrusion. Using tattoo marks in monkeys to indicate the mucogingival junction and clinical sulcus bottom, Kajiyama *et al*. (1993) made a metric evaluation of the gingival movement associated with vertical extrusion of incisors. The results indicated that the free gingiva moved about 90% and the attached gingiva about 80% of the extruded distance. The width of the attached gingiva and the clinical crown length increased significantly, whereas the position of the mucogingival junction was unchanged. Orthodontic extrusion of a "hopeless" incisor is also, therefore, a useful method for esthetic improvement of the marginal gingival level associated with the placement of implants (Fig. 57-22).

Extrusion out of periodontium

In teeth with crown–root fracture, or other subgingival fractures, the goal of treatment may be to extrude the root out of the periodontium (Figs. 57-16, 57-17), and then provide it with an artificial crown. When an increased distance between the CEJ and the alveolar bone crest is aimed at, the forced eruption should be combined with gingival fiberotomy (Pontoriero *et al*. 1987; Kozlowsky *et al*. 1988). In animal experiments, Berglundh *et al*. (1991) showed that when the fiberotomy (i.e. excision of the coronal portion of the fiber attachment around the tooth) was performed frequently (every 2 weeks), the tooth was virtually moved out of the bony periodontium, without affecting the bone heights or level of the marginal gingiva of the neighboring teeth. This procedure is illustrated in Fig. 57-17.

Intrusion

Similar to the indications for extrusion, the orthodontic intrusion of teeth has been recommended (1) for teeth with horizontal bone loss or infrabony pockets, and (2) for increasing the clinical crown length of single teeth. However, the benefits of intrusion for improvement of the periodontal condition around teeth are controversial.

Fig. 57-15 (a,b) Adult female patient with evidence of local severe periodontal tissue breakdown before treatment. The bone loss is particularly pronounced on the mandibular right second premolar (g) and canine (j), whereas the bone support for the first premolar is much better (g,j). The treatment plan included slow orthodontic extrusion of the second premolar and canine to regenerate an improved vertical alveolar bone height prior to the placement of implant-supported restorations. Brackets were placed in a gingival location on the teeth to be extruded (c) and leveling was started with super-elastic rectangular arch-wires. After removal of the pulp, the crowns of the teeth to be extruded were ground with diamond instruments to avoid jiggling with the teeth in the opposing arch (c). A cantilever spring was added for the canine. After 10 months, the leveling was completed (d) and the extruded teeth were extracted with forceps (e). Note the even bone levels (e) and compare with the initial situation (b). A remarkable amount of bone build-up is seen on the radiographs at 10 months of leveling (h,k) before insertion of the implants. A comparison of the final bone heights relative to the cemento-enamel junctions of the neighboring teeth with the initial situation reveals that a significant portion of the bone support for the well integrated implants has been created by the slow vertical tooth movements. The clinical and radiographic situation at the 3-year follow-up is shown in f, i and l.

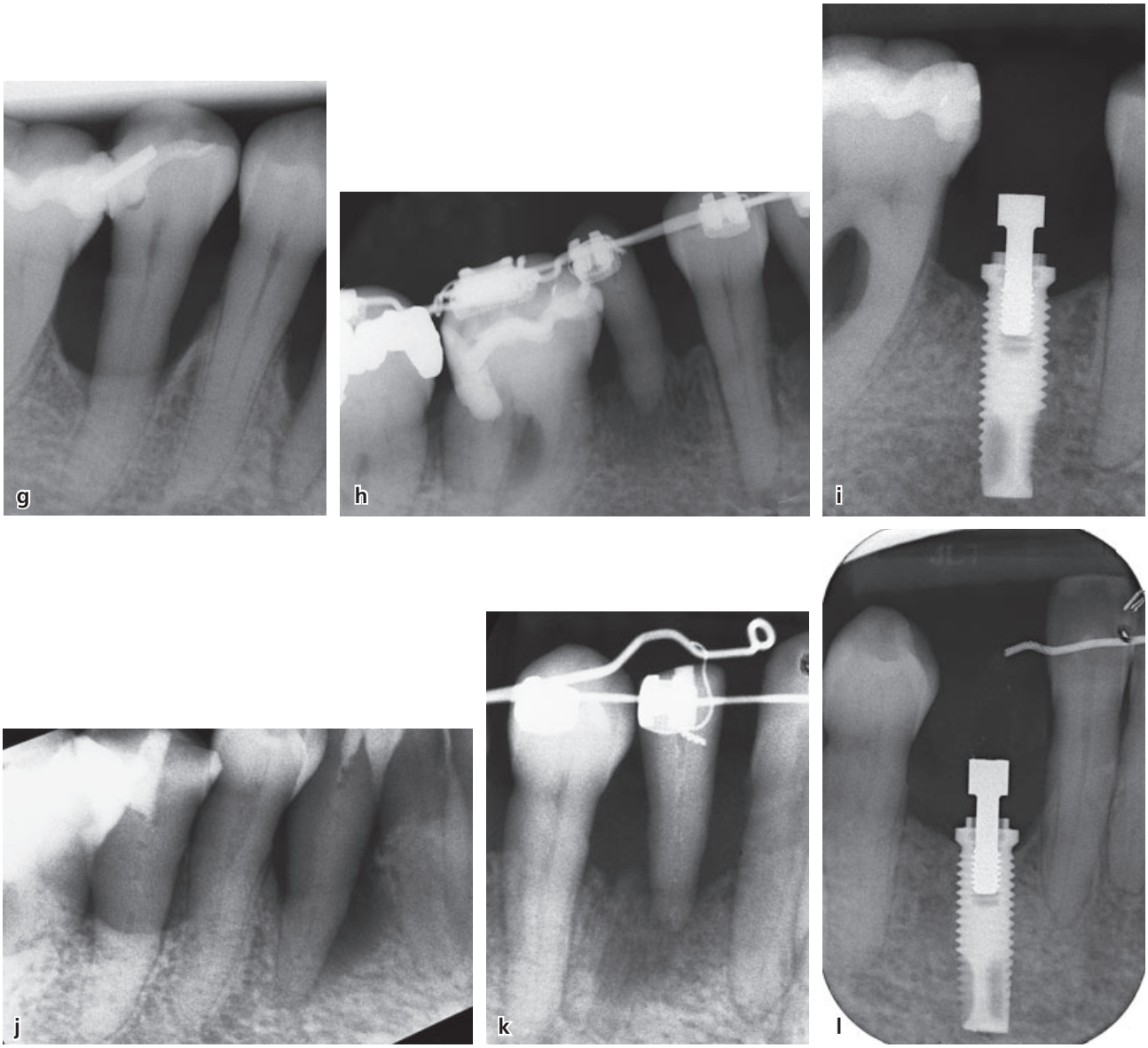


Fig. 57-15 *Continued*

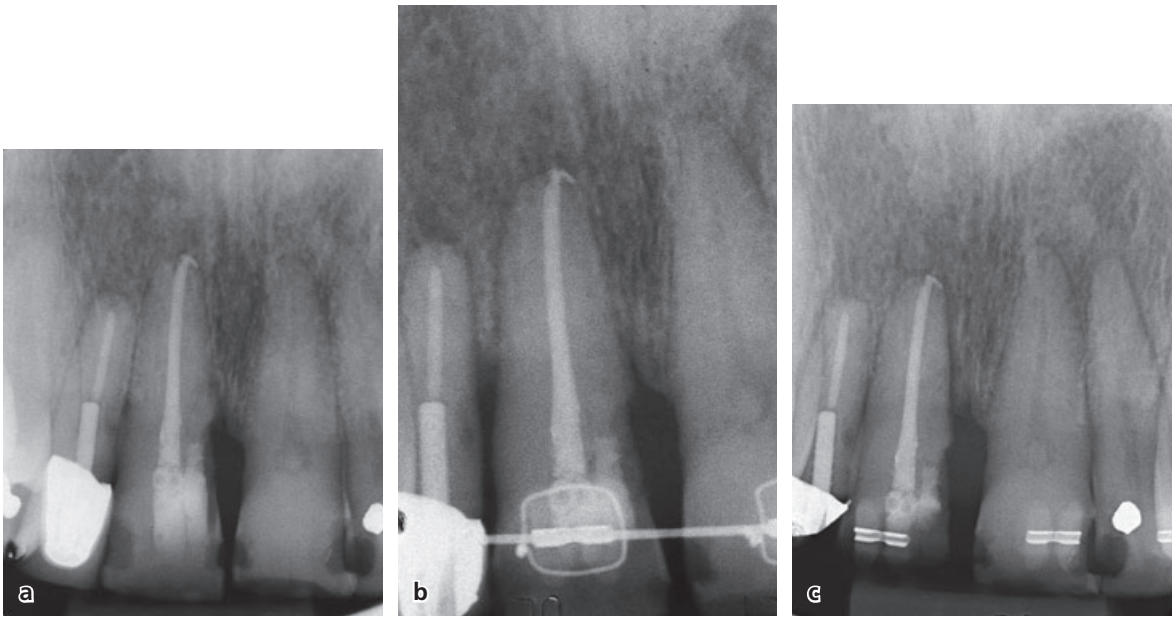


Fig. 57-16 (a) Extrusion out of the periodontium of central incisor with deep crown-root fracture. Rapid extrusion with continuous orthodontic force combined with fiberotomy every 2 weeks. The amount of extrusion can be evaluated by comparing the root ends of the incisors in a–c. (b) The situation after 1.5 months of extrusion. (c) After 4 months, the fracture line was moved from a location below the bone level (a) to a position well above it (c), and the incisor could now be properly restored.

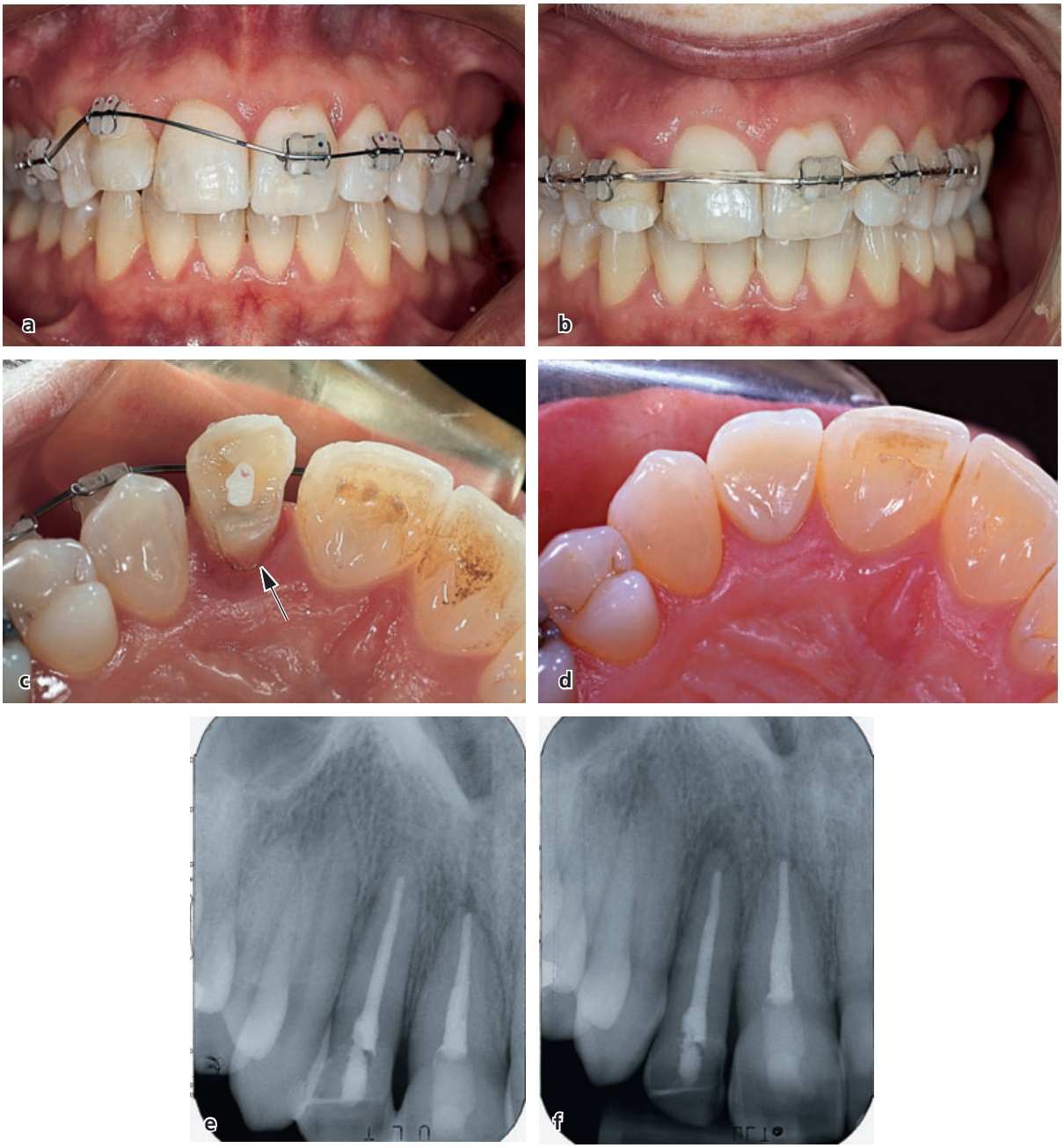


Fig. 57-17 Extrusion out of periodontium. Due to subgingival crown-root fracture on the maxillary right lateral incisor (a,d), this tooth was extruded out of the periodontium with continuous force (a,b) and fiberotomy was performed with 2-week intervals. The amount of extrusion is evident by comparison of the relationship between lateral and central incisor root ends in (e) and (f). Having moved the fracture line to a supragingival position (arrow in c), the tooth could be safely restored. (d) The clinical situation 4 years after treatment.

As mentioned, the intrusion of plaque-infected teeth may lead to the formation of angular bony defects and increased loss of attachment. When oral hygiene is inadequate, tipping and intrusion of the teeth may shift supragingivally located plaque into a subgingival position, resulting in periodontal destruction (Ericsson *et al*. 1977, 1978). This explains why professional subgingival scaling is particularly important during the phase of active intrusion of elongated, tipped, and migrated maxillary incisors commonly occurring in association with advanced periodontal disease. Even in a healthy periodontal environment the question remains as to whether the orthodontic tooth movement intrudes a long epithelial attachment beneath the margin of the alveolar bone or whether the alveolar crest is continously resorbed in front of the intruding tooth.

Histologic (Melsen 1986; Melsen *et al*. 1988) and clinical (Melsen *et al*. 1989) studies indicate that new attachment is possible associated with orthodontic intrusion of teeth. In monkey experiments, periodontal tissue breakdown was induced and intrusion along the axis of the incisors with light forces was initiated following flap surgery. Histologic analysis

showed new cementum formation and connective tissue attachment on the intruded teeth, by an average of 1.5 mm, provided a healthy gingival environment was maintained throughout the tooth movement. The increased activity of periodontal ligament cells and the approximation of formative cells to the tooth surface was suggested to contribute to the new attachment. In the clinical study, the periodontal condition was evaluated following the intrusion of extruded and spaced incisors in patients who had advanced periodontal disease. Judging from clinical probing depths and radiography, there was a beneficial effect on clinical crown lengths and marginal bone levels in many cases, despite large individual variation.

However, the reported clinical and histologic findings associated with a combined orthodontic–periodontal approach must be assessed with great caution, and these findings have not been confirmed by others. Furthermore, new techniques like guided tissue regeneration (GTR) and other regenerative procedures (see below) would appear to be more promising when it comes to creation of new attachment.

Similar to the case with extrusion, metric and histologic studies have been made after experimental intrusion of teeth in monkeys. According to Murakami *et al*. (1989), the gingiva moved only about 60% of the distance when the teeth were intruded with a continuous force of 80–100 g. However, Kokich *et al*. (1984) recommended an interrupted, continuous force for levelling of gingival margins on supraerupted teeth (Fig. 57-18).

The key to understanding why intrusion can be used to increase clinical crown length is related to the subsequent restorative treatment. When orthodontic intrusion is used for levelling of the gingival margins to desired heights, such teeth must then be provided with porcelain laminate veneers or crowns (Fig. 57-18).

Fig. 57-18 (a) Adult female patient in whom the clinical crown length of the maxillary right central incisor was shorter than that of the left central incisor. Because the sulcular depths were normal, the crown lengths were corrected by orthodontic intrusion of the right central incisor (b) and restoring the incisal edge (b) with enamel-bonded ultrathin porcelain laminate veneer (c,d). The alignment and correction of the crown length discrepancy has improved the esthetic appearance of the dentition. Restoration courtesy of Dr. S. Toreskog.

Regenerative procedures and orthodontic tooth movement

The development of barrier membranes to prevent cells of the epithelium and gingival connective tissue from colonizing the decontaminated root surface, as well as the use of Emdogain®, would appear to provide a distinct improvement in orthodontic therapy in the periodontally compromised patient. New supracrestal and periodontal ligament collagen fibers may be gained on the tension side, which can transfer the orthodontic force stimulus to the alveolar bone (Diedrich 1996). In theory, the regenerative techniques would be advantageous associated with both extrusion and intrusion of teeth with infrabony defects, and for uprighting of tipped molars with mesial angular lesions. Moreover, if the epithelium can be prevented from proliferating apically, a bodily tooth movement into or through an intraosseous defect could eliminate the bony pocket more effectively than in the past (Fig. 57-11).

So far, however, relatively little clinical information is available about the use of different regenerative procedures in connection with orthodontic treatment. Diedrich (1996) reported an experiment in dogs in which orthodontic intrusion with flap surgery and GTR were compared with flap surgery alone on periodontally affected teeth. In the presence of minimal or no round cell infiltration, the marking notch was located beneath the alveolar margin indicating that new attachment had formed. The potential of the intrusive/regenerative mechanism was most impressive within the inter-radicular area. Some clinical observations (Nemcovsky *et al*. 1996; Stelzel & Flores-de-Jacoby 1998; Rabie *et al*. 2001) confirm that different regenerative procedures may enrich the therapeutic spectrum in combined periodontal/orthodontic approaches (Fig. 57-19). The combined regenerative and periodontal surgical treatments used together with orthodontic tooth movements create new perspectives and should be an interesting field for further experiments on adults with severe loss of periodontal tissues.

However, other clinical trials have demonstrated that treatment results with barrier membranes in the GTR technique may vary between different patients and that the method is operator and technique sensitive (Leknes 1995). The patient's oral hygiene during the healing phase is critical, and inflammation around the membrane, particularly if it becomes exposed and contaminated, may lead to discouraging clinical results with marked gingival retraction.

Since the membrane is covered in the GBR technique, the risk for inflammation is reduced. The possibility for orthodontic movement of teeth into alveolar processes with deficient bone volume may

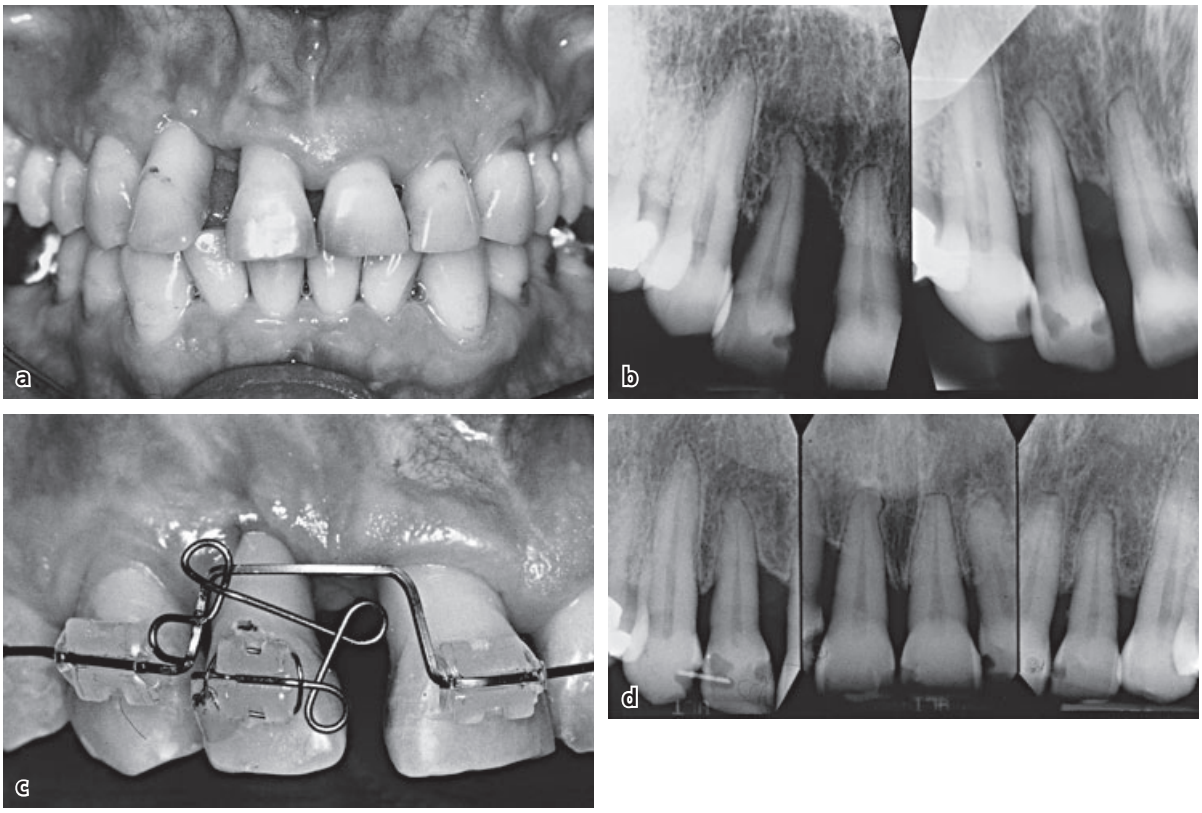


Fig. 57-19 (a) Pathologic tooth migration as a result of an advanced periodontal lesion in adult female patient. (b) Severe intraosseous defect between the right central and lateral incisors. (c) Three months after GTR treatment (GoreTex membrane) partial reossification is evident, possibly with new attachment. (d) Orthodontic leveling with controlled space closure and intrusion of the lateral incisor. (e) Result 6 months after orthodontic tooth movements shows no root resorption and a consolidated alveolar crest. From Diedrich (1996).

thus be improved (Basdra *et al*. 1995). Preorthodontic GBR of markedly constricted alveolar ridges also has the advantage that tooth movement through cancellous bone is easier, and the formation of interfering gingival invaginations can be reduced.

Traumatic occlusion (jiggling) and orthodontic treatment

As discussed in Chapter 14, the role of occlusal trauma in periodontal treatment has not been determined. From an orthodontic perspective, it is of interest that several studies indicate that traumatic occlusion forces (1) do not produce gingival inflammation or loss of attachment in teeth with healthy periodontium, (2) do not aggravate and cause spread of gingivitis or cause loss of attachment in teeth with established gingivitis, (3) may aggravate an active periodontitis lesion, i.e. be a co-destructive factor in an ongoing process of periodontal tissue breakdown (in one way or another favor the apical proliferation of plaque-induced destruction), and (4) may lead to less gain of attachment after periodontal treatment – non-surgical or surgical.

A major problem in this regard is the lack of established and reliable criteria to identify and quantitate different degrees of traumatic occlusion. Various clinical and radiographic indications, such as unfavorable crown/root ratio, increased tooth mobility, widened periodontal ligament space, angular bone loss, alterations in root morphology, etc. are uncertain and insufficient in diagnosis of occlusal trauma, and there have been few scientific clinical reports to evaluate these signs (Jin & Cao 1992).

The extent to which it is necessary to avoid, or reduce, occlusal trauma during orthodontic treatment is controversial and unsupported by scientific evidence. Some orthodontists use bite-planes in virtually every periodontal case with bone deformities, to reduce occlusal trauma and for the purpose of shallowing the bony defects, as teeth supra-erupt. However, independent studies have shown that surgical pocket elimination including bone sculpturing offers no advantage compared with more conservative periodontal treatment (Ramfjord 1984), and apparently there is little need to shallow or eliminate bony deformities. It would still appear sensible to avoid gross interferences, like raising the bite when a maxillary incisor in lingual inversion is moved over the mandibular teeth, and to mitigate evident occlusal interferences on single teeth with markedly increased mobility. However, it may be a futile exercise to try and eliminate all occlusal trauma during active tooth movement, and a more practical solution is to concentrate on controlling the inflammation. After appliance removal, however, occlusal adjustment by selective grinding may be required. Even though good occlusal function is part of the orthodontic treatment goal, correct cusp–fossa relationships cannot always be achieved in adults with orthodontic therapy alone. In general terms, the adjustment should be directed toward obtaining even and stable tooth contacts in centric relation, a straight forward slide from centric relation to centric occlusion without any side shifts or lateral deviation, freedom in centric, smooth gliding contacts in centric and eccentric mandibular motion, and elimination of balancing side interferences (Burgett *et al*. 1992).

The importance of reducing jiggling of teeth *after* orthodontic treatment of patients with moderate to advanced periodontitis may be significant: (1) tooth mobility generally increases with loss of support for the teeth, (2) animal experiments have shown that bone dehiscences produced by jiggling forces will regenerate after elimination of the jiggling trauma, and (3) occlusal adjustment may be a factor in the healing of periodontal defects, especially bony defects, after periodontal treatment. Therefore, the bonded orthodontic retainers, which stabilize the teeth, may secure optimal conditions for improved periodontal healing and bone regeneration after the orthodontic treatment period (Figs. 57-5, 57-7, 57-8). In fact, long-term follow-ups of orthodontic patients with advanced periodontal tissue breakdown may demonstrate better periodontal conditions, with marked crestal lamina dura contours, many years after appliance removal than at the end of the orthodontic treatment (Figs. 57-7, 57-8). If bonded retainers had not been used in many such cases, the most affected teeth would probably have been lost with time.

Molar uprighting, furcation involvement

The problem of mesially tipped mandibular molars because of non-replacement of missing first molars has been the subject of many anecdotal reports over the past 30 years. Tipped molars have been considered a causative or at least an aggravating factor for future periodontal tissue breakdown. However, Lundgren *et al*. (1992) recently observed that 73 molars that had remained in a markedly tipped position for at least 10 years, with most molars having been tipped for as long as 20–30 years, did not constitute an increased risk for initiation or aggravation of moderate periodontal disease at their mesial surface. The study did not consider the potential risk for aggravation of already established advanced periodontitis lesions. This lack of correlation may not exclude other indications for molar uprighting, such as functionally disturbing interferences, paralleling or space problems associated with prosthetic rehabilitation, or traumatic occlusion.

In this context it must be emphasized that the apparent angular bone loss along the mesial surface of tipped molars may be illusive and solely represent an anatomic variation, since lines drawn from the adjacent cemento-enamel junctions appear to parallel the alveolar crest (Ritchey & Orban 1954). While uprighting such a tooth appears to cause a shallow-

ing-out of the angular defect, with new bone forming at the mesial alveolar crest, it may merely reflect the inclination of the molar relative to the alveolar bone, and the attachment level remains unchanged. When there is a definite osseous defect caused by periodontitis on the mesial surface of the inclined molar, uprighting the tooth and tipping it distally will widen the osseous defect. Any coronal position of bone may be due to the extrusion component of the mechanotherapy.

Furcation defects generally remain the same or get worse during orthodontic treatment. For example, if tipped molars have furcation involvement before orthodontic uprighting, simultaneous extrusion may increase the severity of the furcation defects, especially in the presence of inflammation (Burch *et al*. 1992). Hence, initial periodontal therapy and maintenance is essential. The mandibular molar can be split into two roots, one or both of which may be kept and moved orthodontically into new positions. However, this is difficult treatment (Müller *et al*. 1995).

In a thorough study of periodontal conditions around tipped mandibular molars before prosthetic replacement, Lang (1977) reported that after completion of the hygiene phase, significant pocket reduction (mean 1.0 mm) was noted on all surfaces. In addition, a further significant reduction in pocket depth (mean 0.6 mm), associated with a gain of clinical attachment (mean 0.4 mm), was found on the mesial and lingual aspects of the molars as a result of the orthodontic uprighting. He concluded that uprighting of tipped molars is a simple and predictable procedure, provided excellent plaque control is maintained.

Kessler (1976), on the other hand, stated that uprighting of mesially inclined molars is not a panacea, and showed some cases in which evident bone loss and furcation involvement developed during the orthodontic uprighting procedure. Because of the furcation involvement and increased mobility, these teeth were no longer considered suitable as abutments, although they were properly uprighted. Radiographic indications that furcation involvement may develop between the roots at the end of orthodontic molar uprighting is evident also in other studies, even when extrusive movement of the tipped molars has been avoided (Diedrich 1989). However, it is not unlikely that this radiolucent area reflects immature bone.

Conclusion

As risks may be involved in orthodontic uprighting of mesially tipped molars in cases with periodontal lesions along their mesial surface, or with furcation involvement, the indications for molar uprighting must be apparent. Excellent oral hygiene is required during the orthodontic treatment, with careful consideration of the force distribution, and avoiding extrusion as much as possible. The developments of regenerative techniques may make it possible in the future to obtain better outcomes in orthodontic therapy of periodontally compromised patients.

Tooth movement and implant esthetics

Osseointegrated implants may be used (1) to provide anchorage for orthodontic tooth movement and later serve as abutments for restorative treatment, and (2) to replace single missing teeth. The use of implants as anchors for orthodontic treatment is discussed in Chapter 58, and will not be dealt with here.

It is difficult to achieve esthetically satisfactory results with artificial crowns on single-tooth implants, and the orthodontist may play a role in the interdisciplinary treatment planning team of specialists. There are at least three areas where orthodontics may be considered:

- Redistribution of the available space in the dental arch when tooth positions for implant placement are not optimal
- Orthodontic ridge augmentation by vertical tooth movement
- Orthodontic ridge augmentation by horizontal tooth movement.

Redistribution of space

Orthodontic movement of neighboring teeth to optimal positions is often required in association with placement of implants substituting missing maxillary central or lateral incisors (Spear *et al*. 1997). Another common indication is a lack of adequate space for the implant. Figure 57-20 illustrates a typical case with small spaces between the teeth and not enough room to place implants in the maxillary and mandibular first premolar regions.

Ridge augmentation – vertical movement

During selective orthodontic extrusion of one single tooth, both the alveolar bone and the soft periodontal tissues will follow the extruded tooth in an incisal direction, as discussed under forced eruption earlier in this chapter. By this means, it is possible to significantly improve the periodontal tissue esthetics associated with fabrication of prosthetic crowns on single implants (Figs. 57-21, 57-22). The technique of "orthodontic extraction" of a hopeless incisor or molar (Salama & Salama 1993; Zuccati & Bocchieri 2003) may be useful to improve the results for single-tooth implants in patients in whom one or more teeth are to be extracted. Following progressive grinding of the extruded tooth to prevent it from jiggling (Figs. 57-21, 57-22), new periodontal tissues are generated that provide improved conditions for the implant, after extraction of the extruded tooth (Fig. 57-21). Upon extruding a tooth, the periodontal ligaments are pulled away from the bone and thus transfer

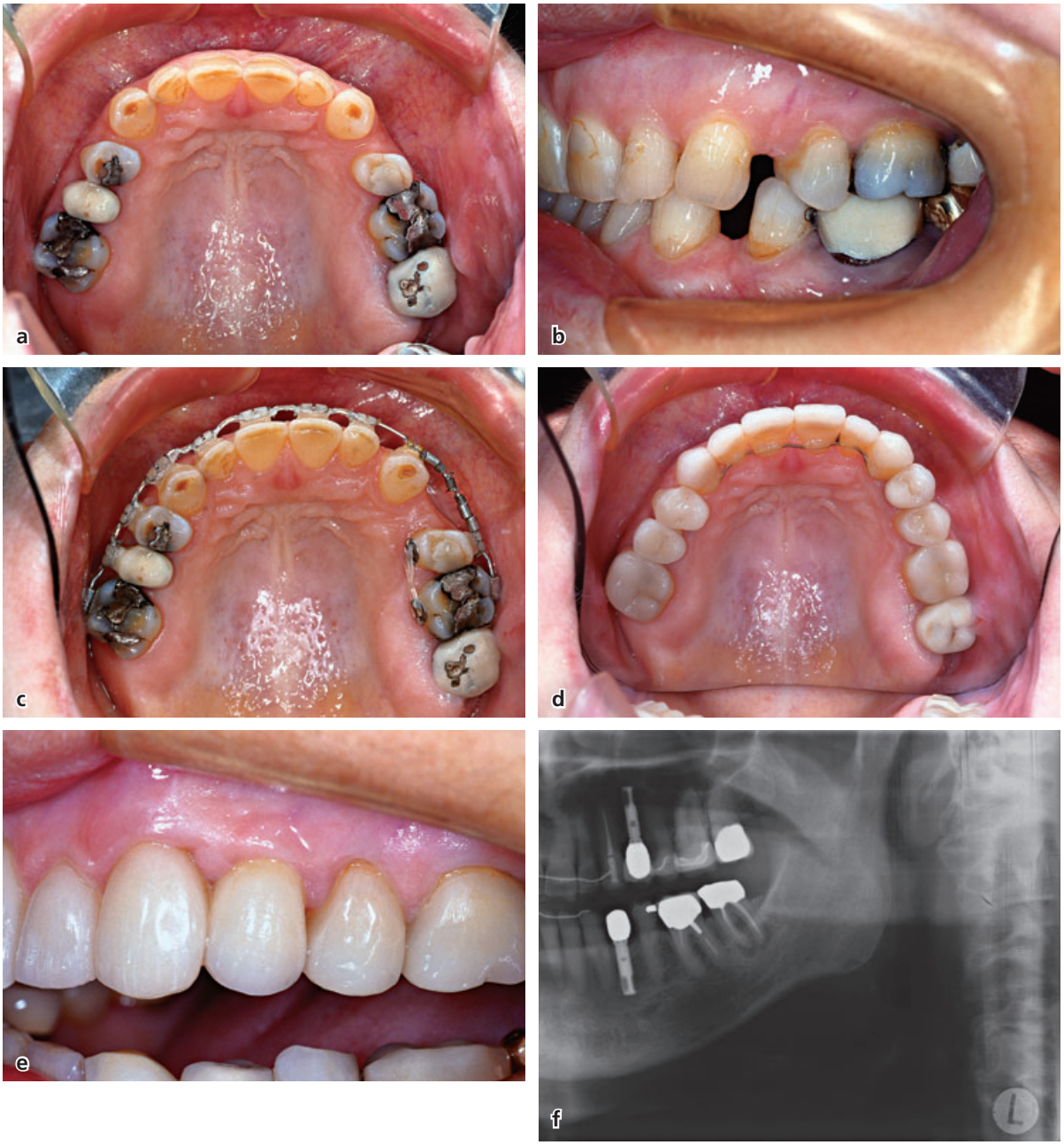


Fig. 57-20 Typical orthodontic space reopening before insertion of two implants in the second and third quadrant in an adult female patient (a–f). Note the lingually tipped maxillary and mandibular incisors and the small spaces before treatment (a,b). Continuous force from push-coils (c) was used to open adequate space for the implants in the first premolar regions in both dental arches (d–f).

mechanical strain to cells in the bone. A series of mechano-transduction mediators (Indian hedgehog), are expressed and lead to bone formation (Tang *et al*. 2004). The type of bone formed initially is the "emergency type of bone" with type III collagen (Chayanupatkul *et al*. 2003; Tang *et al*. 2004). This bone is somewhat weak because the cross-links between the collagen fiber matrix are weak. It takes about 6 months to mature to the more stable type I collagen (Chayanupatkul *et al*. 2003). The stable type of bone may accept an implant without showing relapse. The stability of the newly formed bone can thus be influenced by whether the clinician allows the newly formed bone to remodel to the more stable bone. It is conceivable that the time periods for the extrusion and the observation time before implant insertion should be at least 6 months for the newly formed bone to mature into more stable bone (Figs. 57-21, 57-22). To allow for rest periods in between the activations, an interrupted continuous force is recommended, by using small step bends in the arch-wires (Figs. 57-21b,c, 57-22d).

Ridge augmentation – horizontal movement

If an implant cannot be placed because of reduced bucco-lingual ridge thickness after a previous extraction, one option is to move a premolar into the eden-

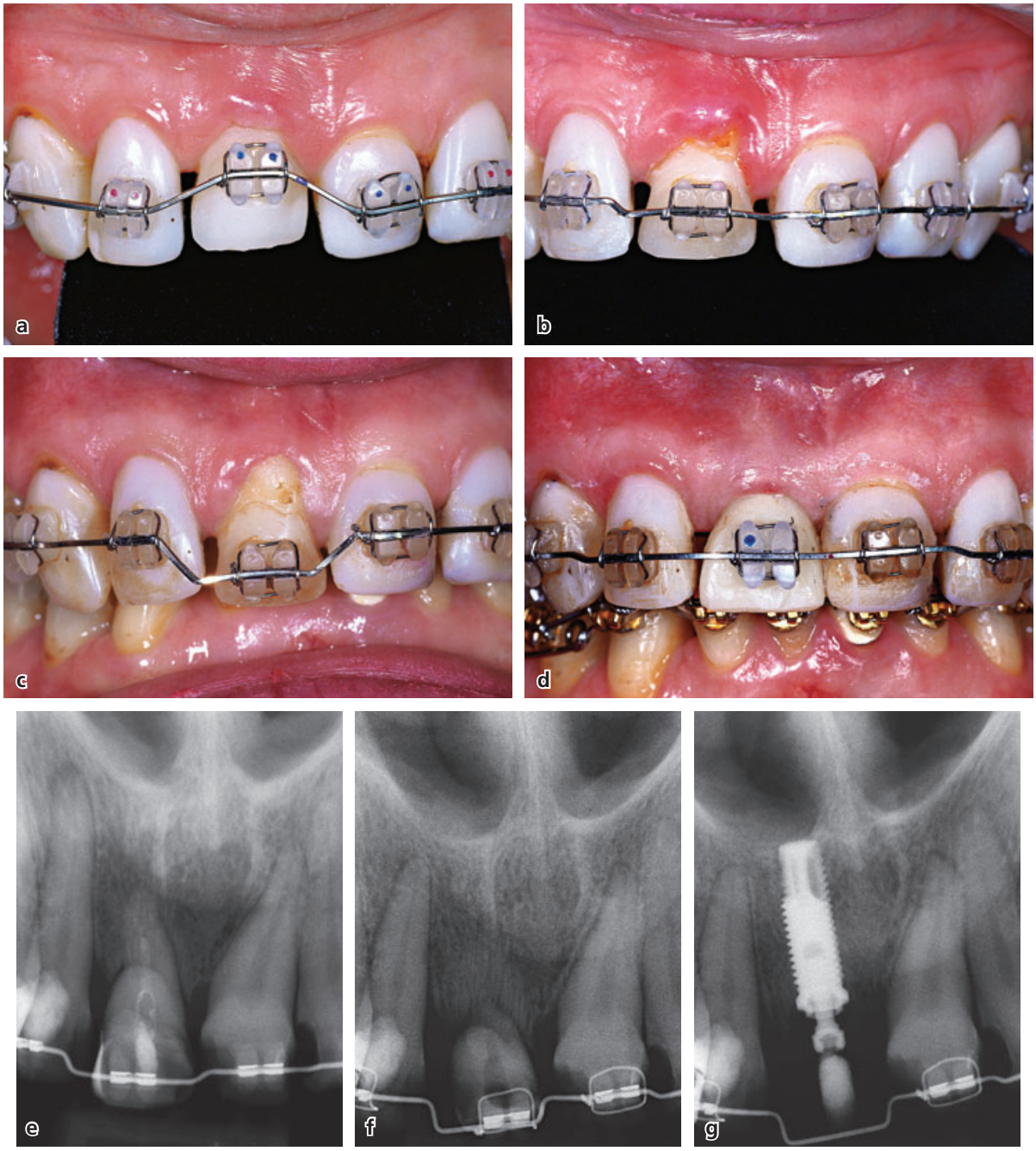


Fig. 57-21 Implant site development by "orthodontic extraction" of maxillary right central incisor with poor prognosis (a,e). The ceramic bracket was positioned in a gingival location on the incisor to be extruded (a), and initial leveling was started with continuous force from a rectangular super-elastic leveling wire. After 1 month, this arch-wire was replaced with a thin rectangular stainless steel wire, using small step-bends for the extrusion (b,e). Such step-bends create an interrupted continuous force which is active for about 2 weeks and then allows 2 weeks of rest before the re-activation at the monthly visits (b,c). The temporary crown on the implant in (d) shows the clinical status at 6 months after implant insertion. The radiographs demonstrate the extensive bone build-up at 10 months (f) and the implant in the regenerated bone at 6 months (g). Note the organization of the bony lamellae reflecting the direction of pull in (f).

tulous space and to place the implant in the position previously occupied by the premolar (Spear *et al*. 1997). The bucco-lingual volume of the new bone on the tension side will be markedly greater than that on the pressure side (Figs. 57-23, 57-24). This is an alternative to surgical ridge augmentation (GBR or bone graft). The situation is similar to that of when a canine is moved distally to open the space for a maxillary lateral incisor implant (Spear *et al*. 1997; Beyer *et al*. 2007). The root of the canine creates an adequate ridge through stretching of the periodontal ligament.

It should be emphasized that there is much less shrinkage of the alveolar bone after horizontal tooth movements than after extractions of teeth. Spear *et al*. (1997) used cast measurements and tomograms through the edentulous ridge to measure the amount of bone loss with time in cases with orthodontic space

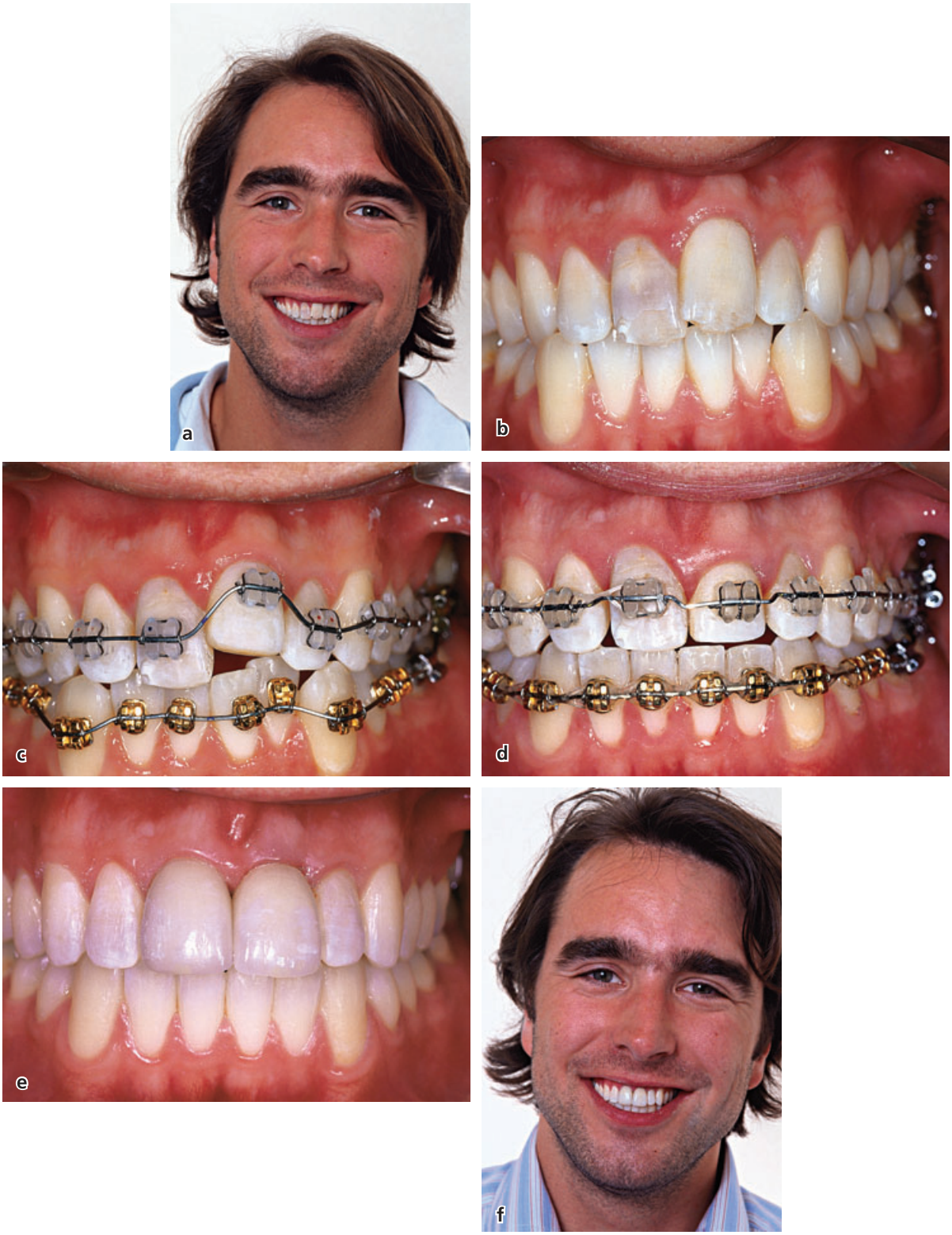


Fig. 57-22 Implant site development in young adult male patient by slow orthodontic extrusion of left central incisor with poor prognosis (a,b). Same procedure as in Fig. 57-21. The ceramic bracket was bonded in a gingival location on the tooth to be extracted. After 1 month of leveling with super-elastic wire, the remaining extrusion for 7 months was made with interrupted continuous force from stainless steel arch-wire, using small step-bends that were reinforced at monthly visits (d). The implant was inserted 4 months after the incisor was extracted. Note the improved gingival margin contour after the orthodontic extrusion (b,d), which permitted an optimal emergence profile of the implant crown (e,f).

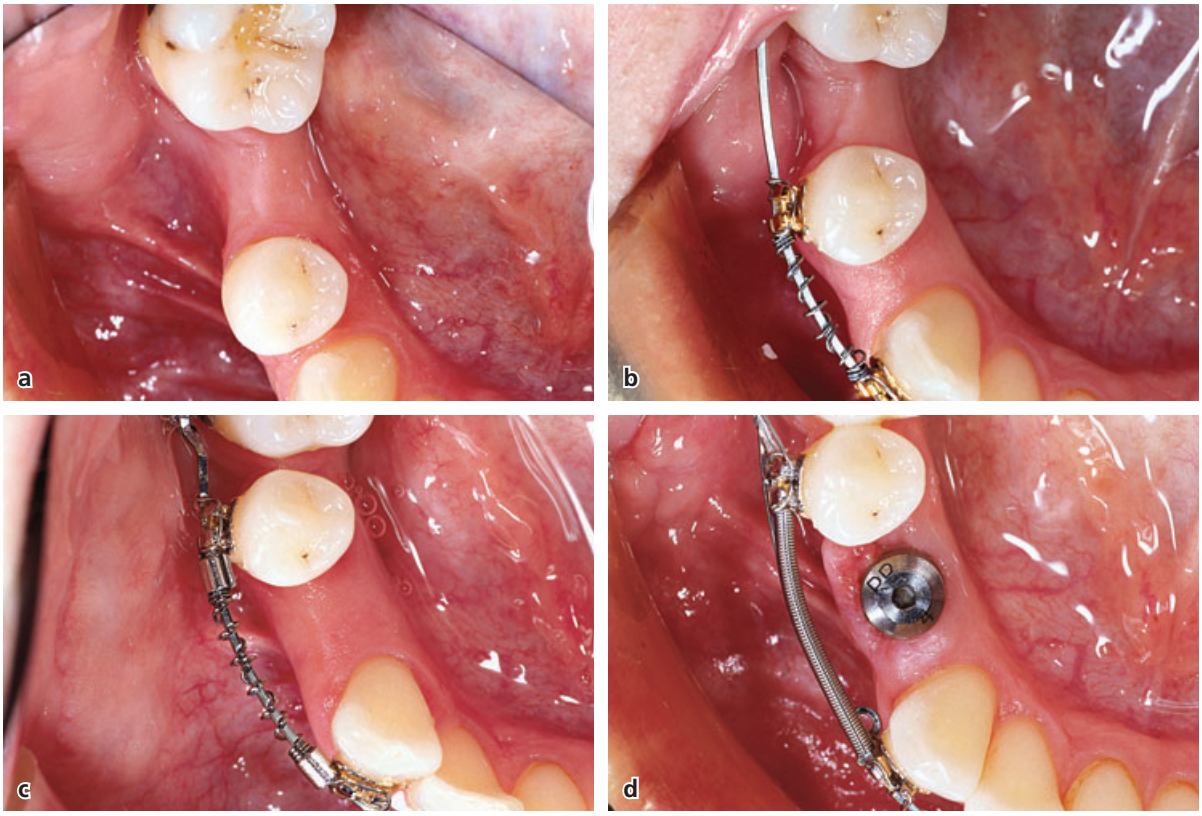


Fig. 57-23 Ridge augmentation by horizontal tooth movement before implant insertion in adult female patient, in whom the alveolar bone in the second premolar area was insufficient to accommodate an implant (a). The first premolar was moved distally with continuous force from a push-coil (b,c). Note wide area of bone regenerated on the tension side of the premolar (b,d) which provided optimal conditions for insertion of the implant (d).

opening for maxillary lateral incisor implants. They found less than 1% alveolar bone shrinkage from the end of treatment up to 4 years later. This contrasts with previous studies showing about 34% reduction of the alveolar ridge over 5 years when anterior teeth are extracted (Carlson 1967).

Figure 57-23 shows a case in which the distal movement of a mandibular first premolar provided new bone of adequate width for implant placement in a previously atrophied alveolar bone area. Similar generation of bone can be obtained in patients who have no molars by moving a terminal premolar distally in the dental arch. Autotransplantation of teeth also represents inherent potential for bone induction and re-establishment of a normal alveolar process after traumatic bone loss (Zachrisson *et al*. 2004).

Gingival recession

Labial recession

"Normal" age changes

Gingival recession, with exposure of cementum on facial surfaces of teeth, may occur on single or multiple teeth. Many factors have been implicated in the etiology, including plaque, position of the tooth in the arch, faulty toothbrushing, traumatic occlusion, high frenum or muscle attachments, lack in dimension of gingiva, lip pressure, etc. (Baker & Seymor 1976). It is difficult to see a single cause of, or a solitary mechanism in the development of, labial gingival recession. Two basic types of recession may occur, one related to periodontal disease, or to factors associated with periodontal disease, and the other relating to mechanical factors, including toothbrushing.

Labial gingival recessions are always accompanied by alveolar bone dehiscences, and there is a direct correlation between the millimetric extension of labial bone dehiscences and the corresponding gingival recessions (Bernimoulin & Curilovic 1977). It has been postulated that a root dehiscence may establish an environment which, for one reason or another, may predispose to gingival recession (Wennström 1990). The position in which a tooth erupts through the alveolar process has a profound influence on the amount of gingiva that will be established around the tooth. When a tooth erupts close to the mucogingival line, only a minimal width, or complete lack, of gingiva may be observed labially, and localized gingival recessions may occur in patients at a young age. Thus the "normal" age changes that will then take place are important. Longitudinal monitoring of labial gingival dimensions during the development of the dentition has shown that provided

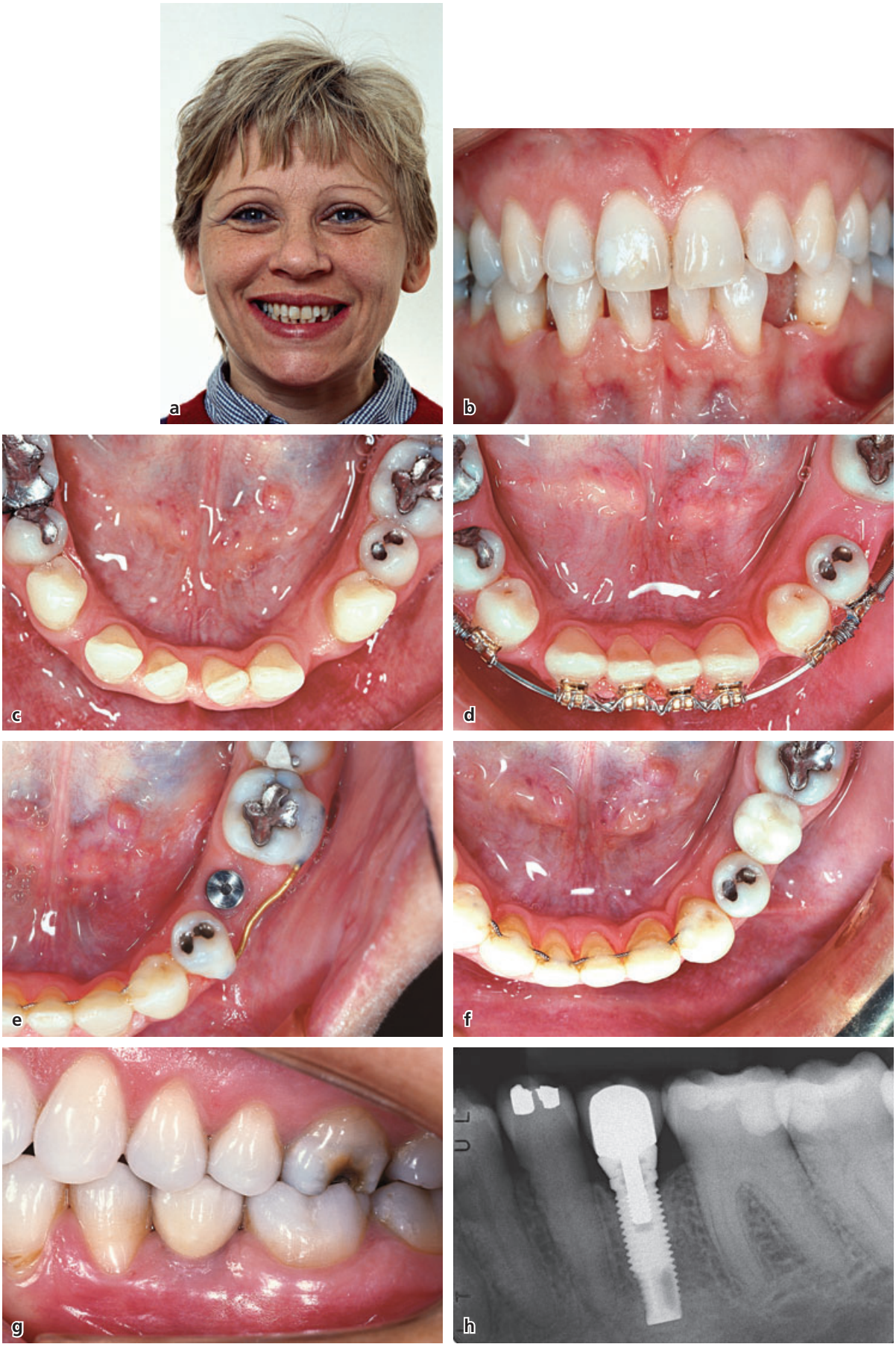


Fig. 57-24 Female patient, 41 years of age, with agenesis of both mandibular central incisors, multiple spacings, thin periodontal tissues, and prominent root topography (a–c). The alveolar bone is too thin labio-lingually to accommodate a titanium implant in the anterior regions (c). The treatment principle was, therefore, to close spaces anteriorly by moving the left first and second premolars mesially (d), and to open up space posteriorly for an implant (e). Note the wide area of alveolar bone on the tension side (d,e), providing ample bucco-lingual space for implant insertion. Permanent implant-supported crown at 3.5 years after treatment (courtesy of Dr. Roy Samuelsson, Oslo, Norway) is shown in f–h.

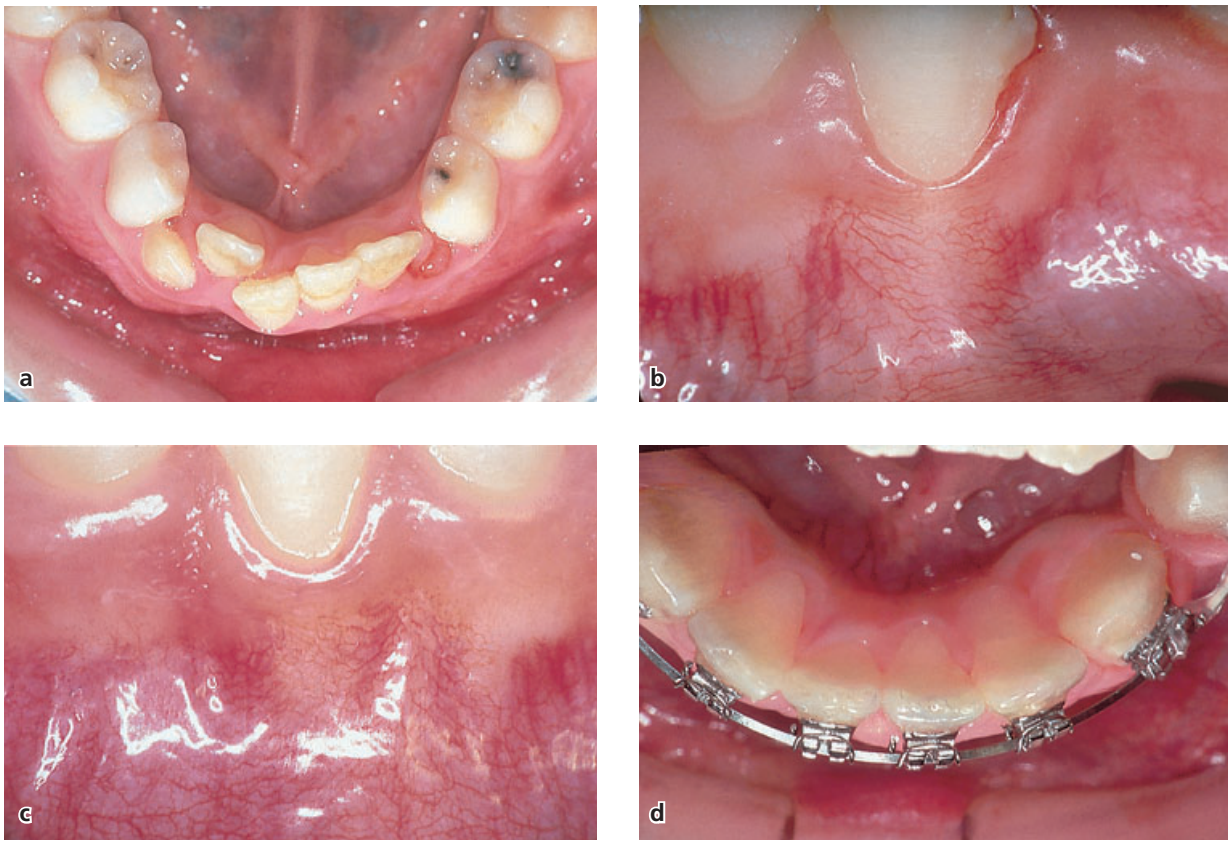


Fig. 57-25 Thin labial gingiva on prominent mandibular right central incisor (a,b) spontaneously became thicker when the incisor was orthodontically moved lingually and aligned (c) after premolar extractions. (d) Condition after appliance removal.

adequate plaque control is established and maintained, a significant increase of the gingival height will generally occur. Spontaneous improvement of localized mandibular labial recessions is the rule rather than the exception, and in some teeth the recessions were totally eliminated during a 3-year observation period (Andlin-Sobocki *et al*. 1991). Also, spontaneous changes of tooth positions in a bucco-lingual direction will affect the gingival dimension. These alterations in gingival dimensions are similar to, albeit less pronounced than, those observed during orthodontic treatment (see below).

Favorable tooth movements, and tissue factors

Alterations of mucogingival dimensions may occur during orthodontic treatment. Contrary to beliefs in the past, these changes are independent of the apico-coronal width of the keratinized and attached gingiva. Wennström *et al*. (1987) found no relationship between the initial width of keratinized gingiva and the tendency for development of gingival recession during orthodontic tooth movements in monkeys. Instead, it is the bucco-lingual thickness (volume), which may be the determining factor for the development of gingival recession and attachment loss at sites with gingivitis during orthodontic treatment.

A tooth that is positioned facially within the alveolar process may show an alveolar bone dehiscence with a thin covering soft tissue. When such a tooth is moved lingually during orthodontic treatment, the gingival dimensions on the labial aspects will increase in thickness (Figs. 57-25, 57-26). Furthermore, because the mucogingival junction is a stable anatomic landmark and the gingiva is anchored to the supracrestal portion of the root, it will follow the tooth during the movement lingually and will consequently get an increase in gingival height (decreased clinical crown height).

Conclusion: It follows that in cases with a thin (delicate) gingiva caused by a prominent position of the teeth, there is no need for a preorthodontic gingival augmentation procedure. In the case of labial gingival recessions a mucogingival surgical procedure should not be performed before orthodontic therapy, when the position of the tooth is improved by the treatment. The recession, as well as the bone dehiscence, will decrease as a consequence of the lingual movement of the tooth into a more proper position within the alveolar bone. If still indicated at the end of orthodontic therapy, the surgical procedure will have a higher predictability of success than if it had been performed before the tooth movement (Wennström 1996).

Unfavorable tooth movements, and tissue factors

Orthodontic movements of teeth *away* from the genetically determined envelope of the alveolar

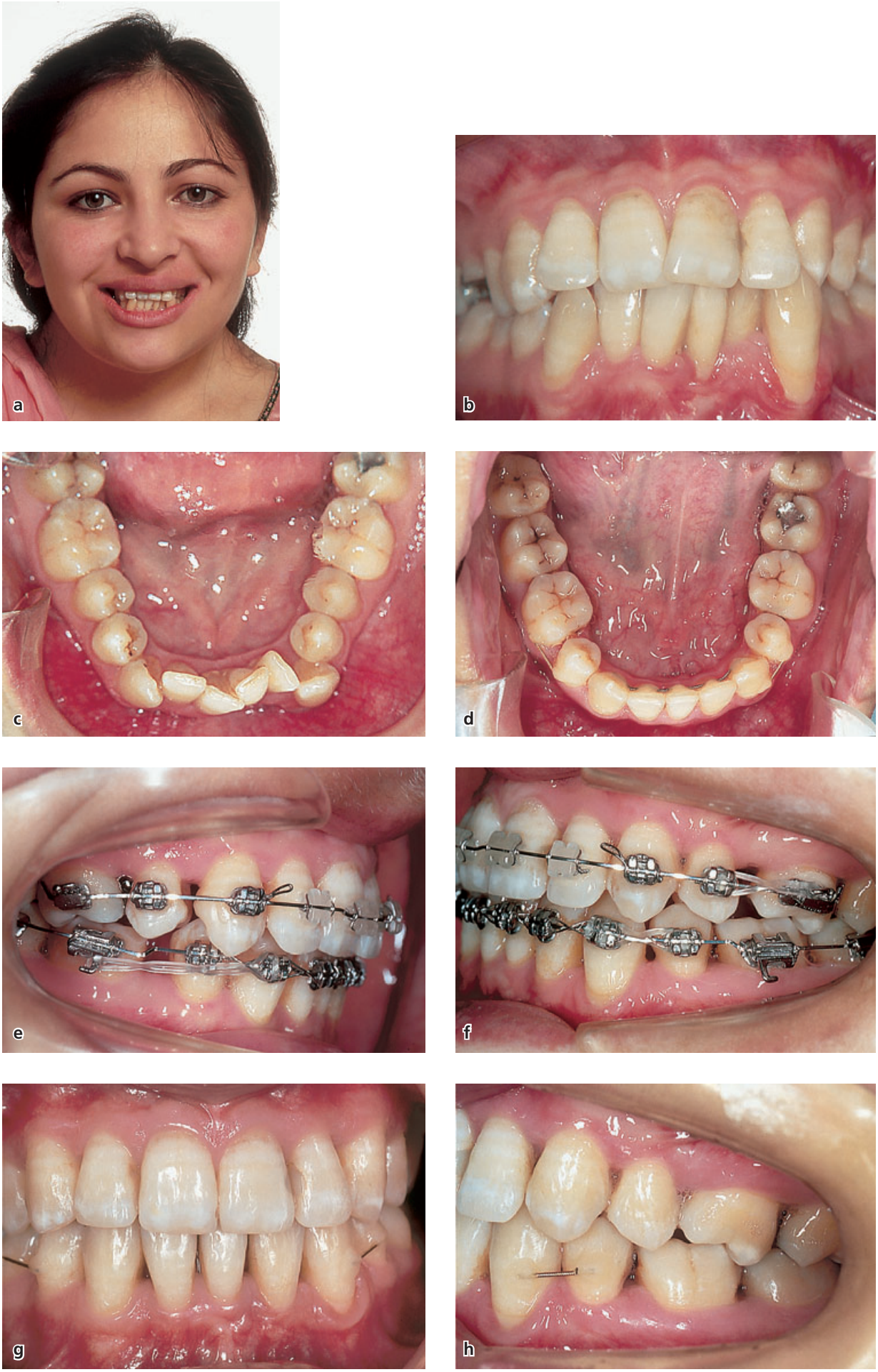


Fig. 57-26 Marked labial gingival recession on prominent left mandibular canine in female young adult patient (a–c). (d) After extraction of two premolars and the left central incisor (sic!), the mandibular arch was leveled orthodontically. (e) and (f) show the clinical condition towards end of orthodontic therapy, and (g,h) at follow-up 1 year after appliance removal. Note spontaneous improvement of gingival recession (f–h).

process are risk movements for development of mucogingival problems, particularly in thin bone and gingival tissues. During frontal and lateral expansion of teeth, tension may develop in the marginal tissues due to the forces applied to the teeth. This stretching may result in thinning of the soft tissues. However, recession-type defects will not develop as long as the tooth is moved within the alveolar bone. If, however, the expansion results in the establishment of a bone dehiscence, the volume (thickness) of the covering soft tissue must be considered as a factor that may influence the development of soft tissue recessions. This may be true both during and after the active orthodontic treatment period. The labial orthodontic tooth movement *per se* will not cause soft tissue recession. However, the thin gingiva that will be the consequence of such movement may serve as a *locus minoris resistentia* to developing soft tissue defects in the presence of bacterial plaque and/or mechanical trauma caused by improper toothbrushing techniques, or orthodontic correction of marked rotations of the incisors.

For stability reasons as well, expansion in the mandibular arch should normally be avoided, if possible. If frontal expansion is still performed in association with orthodontic therapy, the bucco-lingual thickness of the hard and soft tissues should be evaluated. If surgical intervention is considered necessary in order to reduce the risk for development of soft tissue recessions, this should aim at increasing the thickness of the covering tissue (e.g. grafts), and not the apico-coronal width of the gingiva.

Conclusion: Before any kind of orthodontic therapy is started, it is important to check the bucco-lingual thickness of the bone and soft tissues on the pressure side of all teeth, which are to be moved. When tissues are delicate and thin, careful instructions in adequate plaque control measures should be provided, and controlled before and during treatment as well as after removal of the fixed appliances, in order to reduce the risk for development of labial gingival recession.

Interdental recession

Esthetic considerations with regard to defect papillae

Until recently, most clinical emphasis with regard to gingival recession was given to labial defects. If left untreated, most labial gingival recessions will not progress significantly with time, at least if oral hygiene is good, and the main indication for treatment is the esthetic implication for the patient. From an esthetic point of view, however, it would appear that interdental recession, manifest as more or less pronounced empty spaces ("dark triangles") between the teeth, would be equally or more important. Compared with a labial recession, in most patients the loss of interdental papillae would be more visible, both in normal conversation and upon smiling.

Since quality of life (esthetics and lack of pain) has become increasingly important in recent years in selection of periodontal therapies, disfigurement of the gingival papillae during orthodontic treatment of periodontal patients must be avoided, if possible. The development of interdental recession during orthodontic treatment in adults may be caused by one of three factors: (1) advanced periodontal disease, by the tissue destruction or due to pocket elimination by surgery, (2) triangular tooth shape due to abnormal interproximal wear of teeth in crowded positions before the orthodontic treatment, and (3) diverging roots of teeth due to improper bracket placement. To begin with, there is an obvious difference in dental esthetics between patients with advanced periodontitis who have been treated according to "old" and "new" concepts for periodontal therapy. In the past, pocket elimination by gingivectomies frequently resulted in advanced root exposure and complete loss of interdental papillae. However, even with careful non-surgical periodontal therapy in the preparation of patients with advanced periodontal disease for orthodontic treatment, the clinical outcome of the interdisciplinary treatment will normally result in marked interdental recessions, if special precautions are not taken (see below).

Clinical options for treatment

There are only a few options available for the treatment of interdental gingival recession associated with orthodontic treatment in the periodontal patient:

1. Mucogingival surgery, using coronally positioned flaps and GTR techniques (Pini Prato *et al*. 1992)
2. The provision of a gingival prosthesis
3. Orthodontic paralleling of the roots of neighboring teeth
4. Mesio-distal enamel reduction ("stripping").

Of these techniques, the mucogingival surgery aspects are discussed in Chapter 44, and will not be commented on here. A gingival prosthesis may be useful in cases of markedly compromised dentitions, where the psychologic implications of having pronounced retractions are serious. It may be regarded as a last resort. In contrast, the mesio-distal contouring of teeth is a very useful technique to routinely improve the esthetic results achieved by orthodontic treatment in most adult and adolescent patients (Figs. 57-3, 57-5, 57-6, 57-27, 57-28).

Benefits of mesio-distal enamel reduction ("stripping")

Introduced by Tuverson in 1980, mesio-distal recontouring of teeth has now become a routine procedure in orthodontics. It is generally performed on three

Fig. 57-27 Adult female patient with maxillary crowding and large overjet (a,b). After premolar extractions, orthodontic distalization of canines resulted in the development of marked interdental recessions in the anterior region (c). Marked triangular incisor morphology and uneven incisal edges necessitated extensive recontouring (c,d) to allow gingival fill-in after treatment (e,f).

indications: (1) treatment of slight-to-moderate crowding without arch expansion, (2) correction of width discrepancies (so-called TSD, tooth size discrepancies) between maxillary and mandibular teeth, and (3) to prevent interdental recession from developing during orthodontic treatment. The principle involved in stripping is to recontour those teeth which for one reason or another have abnormal morphology, towards an ideal anatomic shape (Figs. 57-6, 57-25). In doing so, the contact points between teeth will be relocated in an apical direction and reduce the contact-to-bone distances (Tarnow *et al*. 1992), and the connector areas (the zone in which two adjacent teeth appear to touch) can be restored towards the optimal 50-40-30 relationships (Morley & Eubank 2001). By this means, normal interdental

Fig. 57-28 Young adult female patient with moderate periodontal tissue breakdown in the anterior region, extruded and irregular maxillary incisors with triangular crown form and incisal wear, and marked interdental gingival recession in the mandibular anterior region (a–c). After 1 month of leveling, the maxillary and mandibular incisors were recontoured by stripping to a more optimal tooth morphology (d). The "new" tooth shapes allowed space closure and leveling and aligning to an esthetic final result (e,f).

gingival papillary contours will be achievable (Figs. 57-3, 57-6, 57-27, 57-28).

In many adult patients with malocclusion, particularly in cases with crowded and overlapping incisors, the crowns of the incisors are much wider at their incisal edges than at the cervical region. As the crowding is unraveled by orthodontic leveling in these instances, the contact point between the incisors will become located in the incisal 1 mm, and a more or less evident space develops above the interproximal contacts of the incisors. Similar, or even more pronounced, loss of the interdental papillae between the maxillary and mandibular incisors, is commonly seen after orthodontic treatment in patients with advanced periodontal destruction.

Short-term (Zachrisson & Mjör 1975) and long-term (>10 years) (Thordarson *et al*. 1991; Zachrisson *et al*. 2007) follow-up studies after extensive grinding of teeth have demonstrated that no harmful side effects are observed subsequent to the procedure, provided adequate cooling is used during the grinding and the prepared surfaces are made smooth and self-cleansing. After the diastema is created, the space between the teeth is closed orthodontically. As this occurs, the roots of neighboring teeth come closer together, the contact area is lengthened, and the reduced papilla can fill out the small space between the teeth (Tarnow *et al*. 1992). In patients with advanced periodontal disease, it is not always possible to restore all papillae in the dentition. Even if it is not possible to eliminate the interdental recession completely after the orthodontic treatment, the esthetic appearance is in most patients substantially improved by stripping, even in cases with extensive periodontal tissue breakdown, such as those in Figs. 57-3 and 57-5.

Minor surgery associated with orthodontic therapy

Several forms of minor periodontal surgery may be used to improve or stabilize the results achieved by orthodontic treatment of malocclusion. More than 30 years ago, Edwards (1970) described clinical techniques to help prevent rotational relapse, reopening of closed extraction spaces (Edwards 1971), and a simple yet effective technique for frenotomy (Edwards 1977). At about the same time, a gingivectomy technique to increase clinical crown length for esthetic improvement of orthodontic results in specific situations was reported (Monefeldt & Zachrisson 1977). Removal of gingival invaginations in extraction sites following orthodontic space closure has also been a subject of considerable interest to orthodontists.

Fiberotomy

The problem of relapse of orthodontically treated teeth in general, and rotated teeth in particular, has been well recognized for years. Methods to reduce the occurrence of rotational relapse may include (1) complete correction, or overcorrection, of rotated teeth, (2) long-term retention with bonded lingual retainers, and (3) the use of fiberotomy.

Two soft-tissue periodontal entities may influence the stability: the principal fibers of the periodontal ligament, and the supra-alveolar fibers. Whereas the fibers of the periodontal ligament and trans-septal groups remodel efficiently and histologically completely in only 2–3 months after orthodontic rotation of teeth, the supra-alveolar fibers are apparently more stable, with a slow turnover. Since the gingival soft tissues are composed primarily of non-elastic collagenous fibers, the exact mechanism by which the gingival soft tissues may apply a force capable of moving the teeth is as yet unknown. From a practical and clinical point of view, however, the supracrestal gingival tissues seemingly do contribute to rotational relapse, as evidenced by the effect of the circumferential supracrestal fiberotomy (CSF) technique.

Basically this technique consists of inserting a scalpel into the gingival sulcus and severing the epithelial attachment surrounding the involved teeth. The blade also transects the trans-septal fibers by interdentally entering the periodontal ligament space. Various modifications of the original CSF technique have been described, in which the scalpel is inserted below the gingival margin, or the cut is reduced to interdental vertical incisions buccally and lingually. In neither case are surgical dressings indicated, and clinical healing is usually complete in 7–10 days. The fiberotomy procedure is not recommended during active tooth movement, or in the presence of gingival inflammation. When performed in healthy tissues after orthodontic therapy, there is negligible loss of attachment (Edwards 1988).

The long-term effectiveness of fiberotomy was evaluated in a prospective follow-up study over a period of 15 years by Edwards (1988). The degree of crowding was examined for CSF and control cases at 4–6 years and at 12–14 years after treatment. A significant effect of the fiberotomy was observed at both time intervals. The surgical procedure was more successful in the maxillary than in the mandibular anterior region; more effective in alleviating rotational than labiolingual relapse; and more useful in reducing relapse in cases with severe rather than mild irregularity of teeth. There was no clinically significant increase in sulcus depth, nor signs of gingival labial recession.

Frenotomy

The contribution of the maxillary labial frenum to the etiology of a persisting midline diastema, and to reopening of diastemas after orthodontic closure, is controversial. The probability for diastema closure in the long run is the same whether or not frenectomy is performed. However, very hyperplastic types of frenum, with a fan-like attachment, may obstruct diastema closure and should be relocated.

In the past, the most common surgical procedure was *frenectomy*, an excision-type operation, which

was often carried over to the palatal aspects. However, a frequently observed complication may be an undesirable loss of the interdental papilla between the maxillary central incisors. For this reason, the *frenotomy*, which represents a more gentle operation, will produce esthetically preferable results. With frenotomy, the attachment of the frenum to gingiva and periosteum is severed, and the insertion of the frenum is relocated several millimeters up on to the alveolar mucosa. If a marked sutural bone cleft is observed in the pretreatment radiographs, the cut is extended to sever the fibers within the coronal part of the midpalatal suture. Tissue healing after a frenotomy procedure is usually uneventful. To further reduce the relapse tendency and/or to increase clinical crown height of single or several teeth, the frenotomy may be combined with fiberotomy and gingivectomy.

Removal of gingival invaginations (clefts)

Incomplete adaptation of supporting structures during orthodontic closure of extraction spaces in adults may result in infolding or invagination of the gingiva. The clinical appearance of such invaginations may range from a minor one-surface crease to deep clefts that extend across the interdental papilla from the buccal to the lingual gingivae. Although gingival invaginations are quite common, the precise cause of the infolding as teeth are moved through an extraction area remains unclear. Since approximated teeth appear to displace the gingival tissue more than move through it, a "piling-up" of gingival tissue is conceivable. There is some resolution of these defects with time, but many invaginations persist for 5 years or more after completion of orthodontic therapy.

Several authors have suggested that compression of trans-septal fibers and alterations of gingival tissue will contribute to extraction-space reopening, but no correlation was found between space reopening and presence and severity of invaginations by Rivera Circuns and Tulloch (1983). They still felt the damage to the gingiva was severe enough to warrant the surgical removal of these defects in selected patients. Edwards (1971) suggested that simple removal of only the excess gingiva in the buccal and lingual area of approximated teeth would be sufficient to alleviate the tendency for the teeth to separate after orthodontic movement. The removal of the gingival papillae in closure sites may enhance the restitution of a more normal connective tissue, although the epithelial hyperplasia, invaginations, and loss of collagen in the underlying gingiva are surprisingly long-standing.

Gingivectomy

The relationship of the gingival margins of the six maxillary anterior teeth plays an important role in the esthetic appearance of the crowns (Kokich 1996a,b). In some instances, it may be necessary to increase clinical crown length of one or several teeth during or after orthodontic treatment. If a gingival margin discrepancy is present, but the patient's lip does not move upward to expose the discrepancy upon smiling, it does not require correction. If the gingival discrepancy is apparent, however, one of four different techniques may be used:

1. Gingivectomy
2. Intrusion + incisal restoration or porcelain laminate veneer (Fig. 57-18)
3. Extrusion + fiberotomy + porcelain crown (Fig. 57-17)
4. Surgical crown lengthening, by flap procedure and ostectomy/ostoplasty of bone (Brägger *et al*. 1992).

Each of these techniques has its specific indications, and whenever gingival margin discrepancies are present, the clinician must determine the proper solution (see also Chapter 44). For example, gingivectomy is not indicated when there is a risk for root exposure, such as when one single incisor has supraerupted (Fig. 57-18).

The gingivectomy technique has proven to be useful in improving orthodontic results, particularly in difficult cases with missing maxillary central or lateral incisors (Fig. 57-29); after premolar autotransplantation to the anterior region; and in some "gummy" smiles. Clinical and histologic examination demonstrated that it was possible to permanently increase clinical crown length after orthodontic treatment by making a labial gingivectomy to the bottom of the clinical pocket. The healing and regeneration of the gingiva was uneventful, provided excellent oral hygiene was maintained in the wound area for 2 months. The result may be explained by one or more of three factors: (1) the effect of the gingivectomy itself, (2) elimination of accumulated hyperplastic gingiva often seen associated with fixed appliance therapy (Fig. 57-29), and (3) elimination of a normally occurring deep pocket. Whatever the reason, the net gain in crown length was close to half the probing depth in all instances (Monefeldt & Zachrisson 1977). The increase in crown length of 1–2 mm may be important to improve the clinical outcome, as shown in Fig. 57-29. Similar long-term results on the position of the marginal soft tissue following periodontal surgery have been reported by others (Lindhe & Nyman 1980). Interestingly, Wennström (1983) demonstrated that even if the gingivectomy is extended into the alveolar mucosa, the regenerated tissue will still be normal gingiva with keratinized epithelium. Thus the human periodontal membrane tissue has the capacity to form a granulation tissue which will prevent the alveolar mucosa from becoming the border tissue against the tooth. When local labial gingivectomies are made in adults, the cut is reduced mesio-distally in order to eliminate the risk for developing interdental recession. Then the incision should not follow the gingival contour all the way, but should be limited by two small vertical cuts towards the interdental papillae.

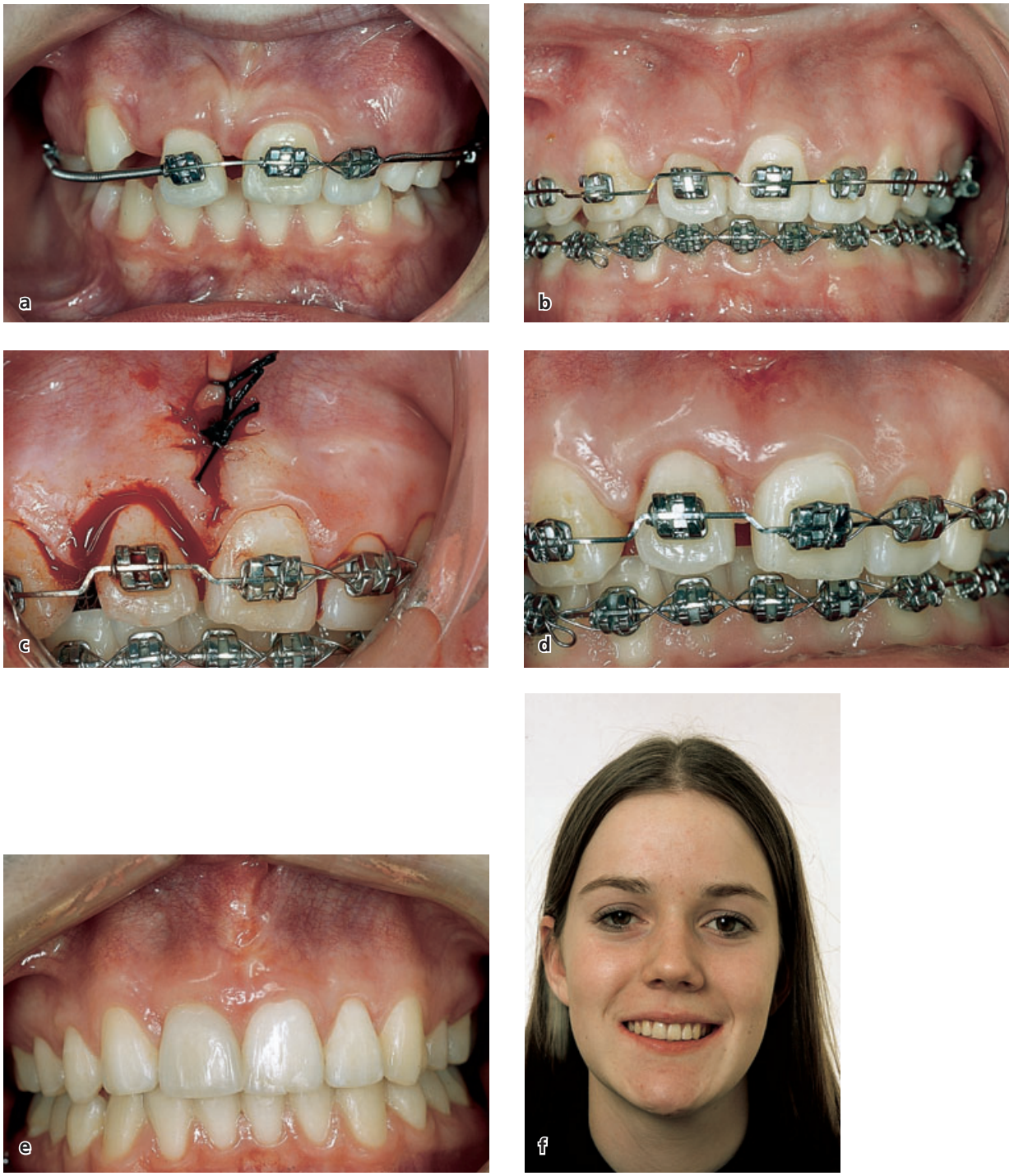


Fig. 57-29 Orthodontic space closure substitution after accidental loss of maxillary right central incisor in young female patient (a). The marginal gingival level on the "new" central incisor was corrected by selective intrusion bends in the arch-wire (b–d) and local gingivectomy and frenotomy (c,d). Local gingivectomies were also performed on the right first premolar in the canine position, and on the left lateral incisor (e). Enamel-bonded ultrathin porcelain veneer on lateral incisor, and vital bleaching of right canine, courtesy of Dr. S. Toreskog. By these means, it was possible to obtain an optimally esthetic result (e,f).

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Chapter 58

Implants Used for Orthodontic Anchorage

Marc A. Schätzle and Niklaus P. Lang

Introduction

Anchorage is one of the limiting factors in orthodontics and its control is essential for successful orthodontic treatment. The term orthodontic anchorage was first introduced by Angle (1907) and later defined by Ottofy (1923). Orthodontic anchorage denoted the nature and degree of resistance to displacement of teeth offered by an anatomic unit when used for the purpose of tooth movement. The principle of orthodontic anchorage was implicitly explained in Newton's third law (1687) according to which an applied force can be divided into an *action* component and an equal and opposite *reaction* moment. In orthodontic treatment, reciprocal effects must be evaluated and controlled. The goal is to maximize desired tooth movement and minimize undesirable effects.

Basically, each tooth has its own anchorage potential as well as a tendency to move when force is applied towards the tooth. When teeth are used as anchorage, inappropriate movements of the anchoring units may result in a prolonged treatment time, and unpredictable or less-than-ideal outcomes.

Orthodontic anchorage is oriented to the quality of the biologic anchorage of the teeth. This is influenced by a number of factors such as the size of the root surfaces available for periodontal attachment, the height of the periodontal attachment, the density and structure of the alveolar bone, the turnover rate of the periodontal tissues, the muscular activity, the occlusal forces, the craniofacial morphology, and the nature of the tooth movement planned for the intended correction (Diedrich 1993). To maximize tooth-related anchorage, techniques such as differential torque (Burstone 1982), placing roots into the cortex of the bone (Ricketts 1976), and distal inclination of the molars (Tweed 1941; Begg & Kesling 1977) may be used. If the periodontal anchorage is inadequate with respect to the intended treatment goal, additional intraoral and/or extraoral anchorage may be needed to avoid negative effects. While the teeth are the most frequent anatomic units used for anchorage in orthodontic therapy, other structures, such as the palate, the lingual mandibular alveolar bone, the occiputal bone, and the neck, are also alternatives.

Additional anchorage such as extraoral and intraoral forces are visible and hence, compliance-dependent, and are associated with the risk of undesirable effects such as tipping of the occlusal plane, protrusion of mandibular incisors, and extrusion of teeth.

Implants, miniscrews and ankylosed teeth, as they are in direct contact with bone, do not possess a normal periodontal ligament. As a consequence, they do not move when orthodontic forces are applied (Melsen & Lang 2001) and hence, can be used for "absolute anchorage" that is independent of the patient's compliance.

The aim of this chapter is to present implants to be integrated into orthodontic treatment as "absolute anchorage", thereby avoiding the disadvantages listed above.

Evolution of implants for orthodontic anchorage

The first attempt to achieve skeletal anchorage was made in 1945. Gainsforth and Higley (1945) placed vitallium screws and stainless steel wires into the ramus of dog mandibles and applied elastics that extended from the screw to the hook of a maxillary arch wire to distally tip/retract the canine by immediate orthodontic loading (Fig. 58-1). Even though the authors did not describe the development of infection, failures encountered may be attributed to infection and the lack of antibiotics at that time, as well as the early dynamic loading of the screws. Although minor tooth movement was accomplished using basal bone anchorage in two animals, an effective orthodontic force could not be maintained for more than 31 days.

A generation later, skeletal anchorage systems have evolved from two directions. One such development originated from orthognatic fixation techniques used in maxillofacial surgery. As pioneers, Creekmore and Eklund (1983) used a vitallium bone screw to treat one patient with a deep impinging overbite. The screw was inserted in the anterior nasal spine to intrude and correct the upper incisors using an elastic thread from the screw to the incisors 10 days after the screw had been placed. Subsequently, Kanomi (1997) described a miniscrew specially designed for orthodontic use.

The second development originated from applications in implant dentistry. Linkow (1969) used blade implants for rubber band anchorage to retract teeth, but never presented long-term outcomes. Later, endosseous implants for orthodontic anchorage were suggested (Ödman *et al*. 1988; Saphiro & Kokich 1988). As indicated in various animal studies, osseointegrated titanium implants remained positionally stable under orthodontic loading and thus could be used for orthodontic anchorage (Sherman 1978; Turley *et al*. 1980, 1988; Roberts *et al*. 1984, 1989; Wehrbein & Dietrich 1993; Wehrbein 1994; Wehrbein *et al*. 1998; De Pauw *et al*. 1999; Majzoub *et al*. 1999) (Figs. 58-2, 58-3). This resulted in the development of specially designed implants in the retromolar area (Roberts *et al*. 1990) and the palatal site of the maxilla

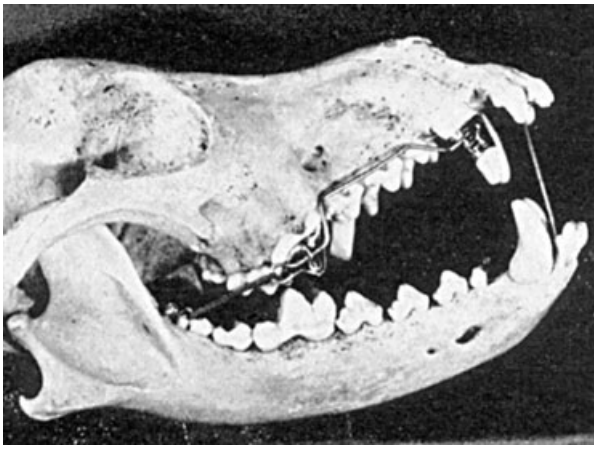


Fig. 58-1 Orthodontic appliance using vitallium screw anchorage. (Courtesy of Gainsforth, B.L. & Higley, L.B. (1945). A study of orthodontic anchorage possibilities in basal bone, *American Journal of Orthodontics and Oral Surgery* **31**, 406–417. Reproduced with permission, copyright © Elsevier.)

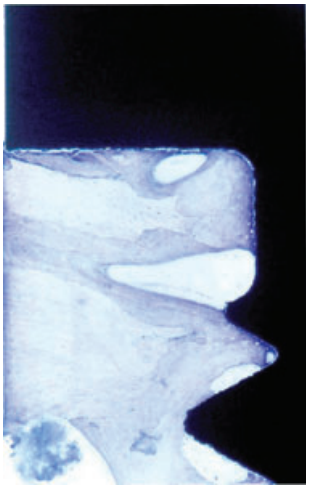


Fig 58-2 Detail of an orthodontic implant 11 months *in situ* in the mandibular retromolar area. Tight contact between the implant shoulder and crestal bone. Signs of remodeling are visible in the peri-implant bone (zones of darker and lighter staining). Toluidine/McNeal stain. Original magnification 20×. From Wehrbein *et al*. (1998) *Clinical Oral Implants Research*.

Fig. 58-3 Longitudinal section of an orthodontic implant after 2 years *in situ*. The implant is well osseointegrated. The shoulder, however, is not in direct contact with the bone surface. Toluidine/McNeal stain. Original magnification 6.6×. From Wehrbein *et al*. (1998) *Clinical Oral Implants Research*.

(Triaca *et al*. 1992). Both applications are used for direct or indirect anchorage (see below).

From a clinical point of view, it is of relevance whether implants are to be used only as temporary anchorage devices (TAD) (Daskalogiannakis 2000) or subsequently to be used as abutment for supporting prosthetic appliances. These aspects determine insertion sites, implant types and dimensions, as well as type of orthodontic anchorage. Moreover, the fact that these devices may have to be placed in a growing patient is of particular importance. Only TADs are suitable for such a purpose.

Prosthetic implants for orthodontic anchorage

The insertion site of prosthetic implants for orthodontic anchorage is determined by the subsequent use of the implant as a prosthetic abutment. The dimensions in length and diameter are dependent on the later prosthetic use. The positions within the alveolar process and the number of implants, however, have to be selected with reference to prospective final tooth position and space after orthodontic treatment.

To determine the location of the prosthetic implants before orthodontic therapy may often be confusing. This is especially true if the teeth are moving towards or away from the implant during orthodontic treatment. In these situations, the presumptive outcomes must be predetermined to achieve the proper implant location and the correct size of the crowns and pontics on the implant-supported prosthesis. In order to use oral implants both for both orthodontic anchorage as well as the subsequent restorative therapy, protocols have been developed for determining the accurate placement of dental implants for prosthetic reconstruction before orthodontic therapy (Smalley 1995; Smalley & Blanco 1995). A plastic placement guide is constructed and used by the clinician to determine proper implant location. The placement guide is based on information derived from a diagnostic wax-up. Therefore, it is necessary to construct the set-up casts from an exact duplicate of the tooth and base portions of the original dental casts. The bases are used as a reference for the proposed position of the implant.

An orthodontic attachment is then either fixed to the provisional crown or to a prefabricated bonding base (Figs. 58-4, 58-5). The orthodontic force acts at the implant suprastructure. The reactive moments and forces are then directly transmitted to the implant and its adjacent bone (direct implant anchorage).

Bone reaction to orthodontic implant loading

Dental implants should not only fulfill prosthetic stability but also withstand the stress and strain applied during orthodontic treatment. There are substantial

Fig. 58-4 Schematic illustration of the assembly of an orthodontic base on a oral implant designated for prosthetic use after the orthodontic treatment.

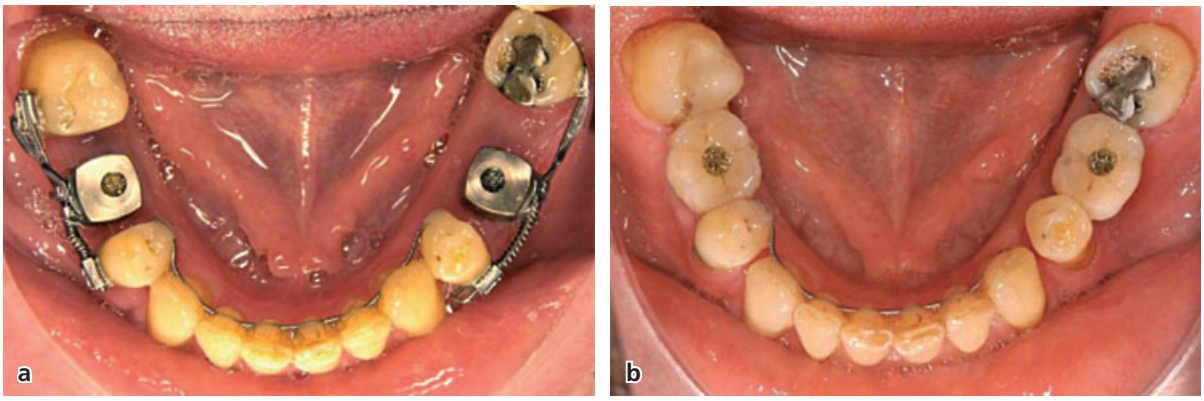


Fig. 58-5 Use of oral implants designated for prosthetic reconstruction as anchorage for orthodontic treatment. (a) Prefabricated orthodontic base as anchorage element. (b) Reconstruction of teeth 35 and 45 on oral implants following orthodontic treatment. (Courtesy of P. Göllner and T. Liechti, Berne, Switzerland.)

Table 58-1 Turnover characteristics of alveolar bone in relation to the magnitude of strain applied (from Melsen & Lang 2001)

Strain values	Bone appositional surface (%)	Resting bone (homeostatic) surface (%)	Bone resorptive surface (%)
>6700 μ strain			
Mean	16.4	21.2	51.5
95% confidence interval	11–22	16–26	42–62
3400–6600 μ strain			
Mean	62.7	16.9	5.0
95% confidence interval	56–70	12–22	1–9
<3300 μ strain			
Mean	20.9	61.9	43.5
95% confidence interval	15–27	56–68	34–53

differences between orthodontic forces and occlusal loading. Orthodontic forces are continuous and horizontal, occlusal loads, in contrast, are discontinuous and mainly in the vertical direction of the implants/teeth.

The effect of orthodontic loading to the adjacent bone of the oral implant is of great interest, because the applied forces should not have a negative impact on the peri-implant bone and therefore, should not impair the long-term prognosis as a prosthetic abutment.

Specially designed oral implants were inserted in monkeys and subjected to well defined continuous loading (Melsen & Lang 2001) (Table 58-1). None of the implants had lost osseointegration after 11 weeks of loading, but loading significantly influenced the turnover of the alveolar bone in the vicinity of the implants. Bone apposition was most frequently found when the calculated strain varied between 3400 and 6600 microstrain. On the other hand, when the strain exceeded 6700 microstrain, the remodeling of the bone resulted in a net loss of bone.

These studies support the theory that apposition of bone around an oral implant is the biologic response to a mechanical stress below a certain threshold, whereas loss of marginal bone or complete loss of osseointegration may be the result of mechanical stress beyond this threshold.

Several other studies where orthodontic forces have been applied confirmed the apposition or increase in bone density rather than loss of bone surrounding an oral implant (Roberts *et al*. 1984; Wehrbein & Diedrich 1993; Asikainen *et al*. 1997; Akin-Nergiz *et al*. 1998).

Indications of prosthetic oral implants for orthodontic anchorage

Orthodontic anchorage provided by prosthetic oral implants may be indicated in partially edentulous adult patients with intra-arch malposition of teeth to correct over-eruption, infra-eruption or tipping of teeth, to retract anteriorly displaced frontal teeth, and intra-arch protraction of teeth that are positioned distally to reduce a multi-tooth gap or improve tooth position in edentulous spaces (Fig. 58-6). Prosthetic oral implants might also be used for the correction of inter-arch malocclusion of single teeth or the whole dentition.

The most important factor of the entire process is interdisciplinary communication and planning. It is critically important for the orthodontist, periodontist, and restorative dentist to work closely as a team during the planning and treatment to achieve the best possible final result (Kokich 1996).

Prosthetic oral implant anchorage in growing orthodontic patients

The use of prosthetic oral implants in growing individuals has been studied in both clinical (Ödman *et al*. 1988; Thilander *et al*. 1994, 1999) and animal studies (Ödman *et al*. 1991; Thilander *et al*. 1992; Sennerby *et al*. 1993). Like ankylosed teeth (Fig. 58-7), oral implants do not follow the developmental changes of the alveolar processes encountered in combination with continuous eruption of adjacent teeth (Fig. 58-8). Moreover, the osseointegrated implants will not be able to be displaced in all dimensions during growth of the jaws (Thilander *et al*. 1994; Iseri & Solow 1996) and hence, would impair the development of the surrounding bony structures and even that of adjacent teeth.

Implant therapy in young individuals with residuous growth potential has been addressed in several studies and yielded major impairment in esthetic outcomes, especially in anterior implant-borne restorations. To assess remaining facial growth potential, hand–wrist radiographs have been proposed for evaluation, but appear not to be specific enough. The best method of evaluating the completion of facial growth is based on the superimposition of sequential cephalometric radiographs. It is, therefore, advisable to await the completion of adolescent body growth in height. At that point, a cephalometric radiograph should be taken. Another radiograph should be taken at least 6 months to a year later. If these radiographs are superimposed with no changes revealed in

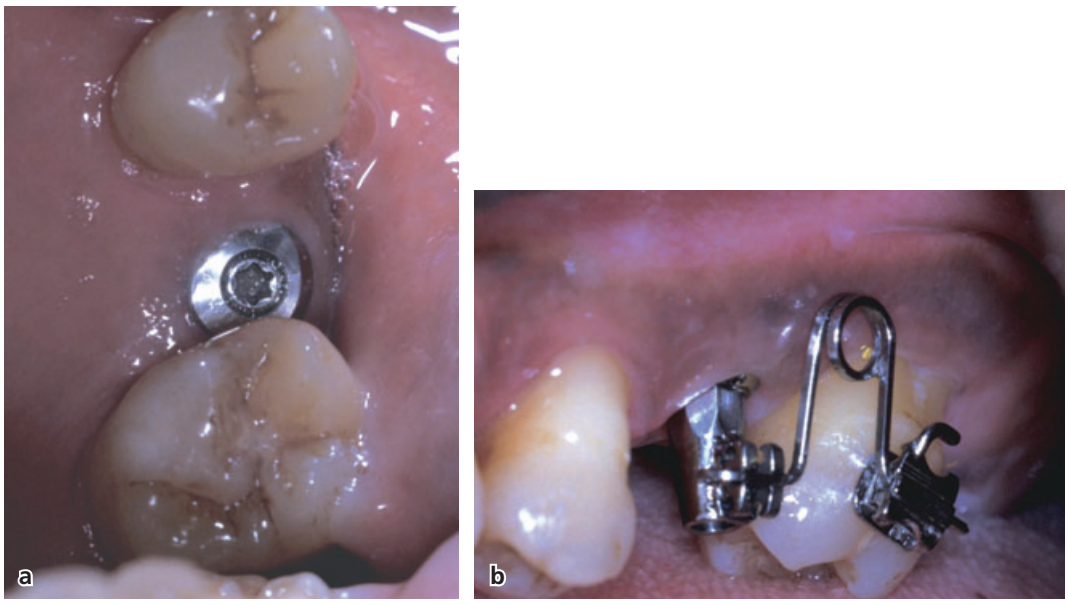


Fig. 58-6 (a) Occlusal view of an oral implant replacing tooth 26, 3 months after installation. Tooth 27 has tipped mesially rendering prosthetic reconstruction of tooth 26 impossible. (b) Following prosthetic abutment connection, the implant is used as anchorage for uprighting tooth 27, hereby providing adequate space for the installation of a single crown.

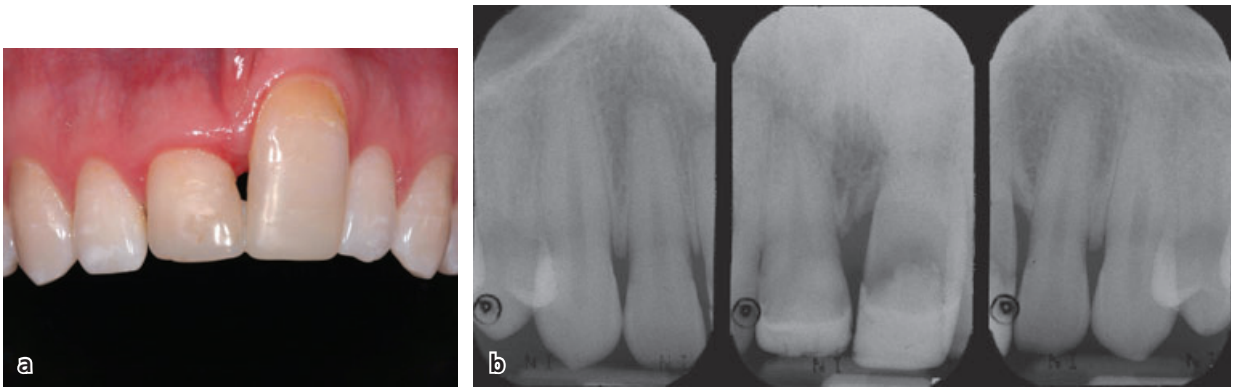


Fig. 58-7 (a) Ankylosed tooth 21 after trauma and on-going composite adaptation over several years. Tooth 21 has not followed the changes associated with alveolar process growth. (b) Radiographic documentation 6 years following trauma of tooth 21 yielding the development of the alveolar process with concomitant ankylosis of tooth 21.

vertical facial height (nasion to menton), the completion of the facial growth may be assumed. The installation of an oral implant at that time may no longer be associated with significant eruption of adjacent teeth (Kokich 2004).

In most adult patients, completion of facial growth is assumed but residual growth and ageing changes affecting the alveolar process may be encountered. This was documented in a retrospective study (Bernard *et al*. 2004) supporting the assumption that mature adults may also exhibit major vertical steps after anterior restorations were inserted on osseointegrated implants.

Orthodontic implants as temporary anchorage devices

Fundamental differences exist with respect to implant dimensions, insertion sites, type of implant anchorage, and intended duration of implant use. The most important difference is that a temporary anchorage device is to be removed after completion of intended orthodontic tooth movement (Daskalogiannakis 2000).

Implant designs and dimensions

As regular orthodontic patients do not display edentulous alveolar bony ridges for the insertion of an implant, implants for orthodontic anchorage must be placed in areas other than the usual topographical locations foreseen for the replacement of missing teeth. Besides the installation of orthodontic anchorage implants into the retromolar area of the mandible (Roberts *et al*. 1990; Higuchi & Slack 1991), the midsagittal palatal region (Triaca *et al*. 1992; Block & Hoffmann 1995; Wehrbein *et al*. 1996a) was initially proposed.

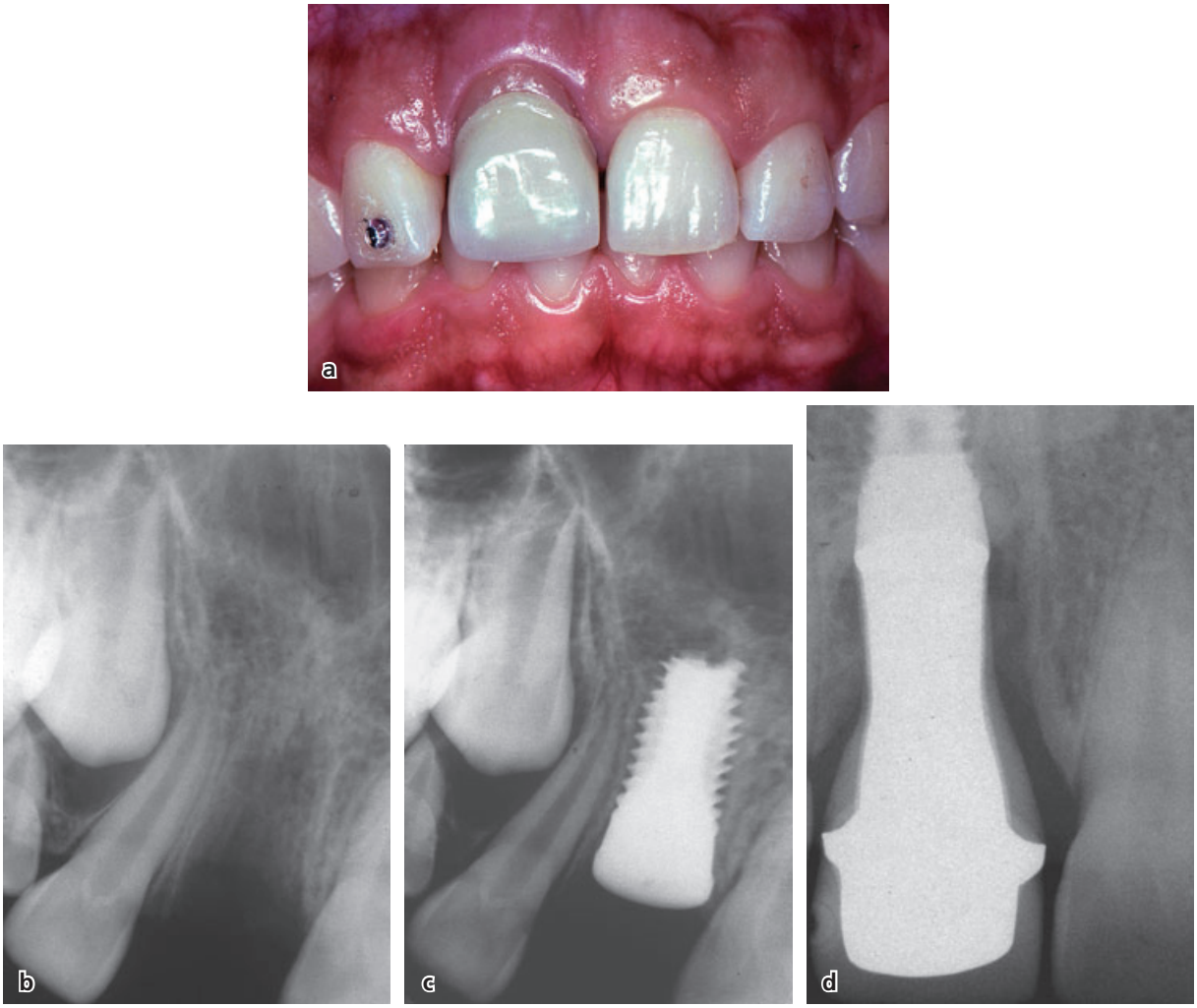


Fig. 58-8 (a) Oral implant placed prematurely (at age 9 years) in a growing patient. The implant did not follow the growth development of the alveolar process resulting in the need for multiple (three times) replacement of the prosthetic reconstruction until adolescence. Unsatisfactory esthetic outcomes persist. Radiographic documentation: (b) Following traumatic loss of tooth 11 at age 9 years. (c) Implant placement in the growing maxilla. (d) Oral implant 9 years after placement and third single tooth crown reconstruction (Courtesy of G.E. Salvi, Berne, Switzerland.)

The introduction of diameter-reduced temporary orthodontic anchorage devices such as miniscrews (<2 mm) in various lengths (Kanomi 1997; Costa *et al*. 1998) and titanium pins (Bousquet *et al*. 1996), as well as L-shaped miniplates with the long arm exposed into the oral cavity (Umemori *et al*. 1999) and the zygomatic anchors (De Clerck *et al*. 2002) both fixed by bone screws, offered new additional insertion sites: (1) the inter-radicular septum (Bousquet *et al*. 1996; Kanomi 1997); (2) the supra-apical and infra-zygomatic area (Kanomi 1997; Costa *et al*. 1998; Umemori *et al*. 1999; De Clerck *et al*. 2002); and (3) the mandibular symphysis (Costa *et al*. 1998). It must be pointed out, however, that the retention of miniscrews and titanium pins constitutes only a mechanical fixation of the devices and, hence, is not based on the principle of osseointegration.

Length-reduced orthodontic anchorage devices, such as titanium flat screws (Triaca *et al*. 1992), resorbable orthodontic implant anchors (Glatzmaier *et al*. 1995), T-shaped orthodontic implants (Wehrbein *et al*. 1996) (Orthosystem®, Institut Straumann, Waldenburg, Switzerland) and the Graz implant-supported pendulum (Byloff *et al*. 2000), were subsequently introduced.

Another device, the Onplant® (Block & Hofmann 1995), placed subperiostally, is a smooth titanium disc with a hydroxyapatite-coated surface that is supposed to connect to the bone. Owing to the submerged installation, monitoring of the healing process of these Onplants® may be troublesome, and their osseointegration may be questioned (Celenza & Hochman 2000).

The most widely used orthodontic anchorage system is the Orthosytem® (Institut Straumann, Basel, Switzerland). This titanium implant consists of three distinct features (Fig. 58-9): (1) the self-tapping endosseous body, 4.2 mm long and either 4.1 mm or 4.8 mm in diameter, designed to be inserted into bone; (2) a smooth neck portion (4.8 mm in diameter and 1.8 mm long) as the transmucosal part; and (3) the trigonal head to serve as the orthodontic appliance fixation.

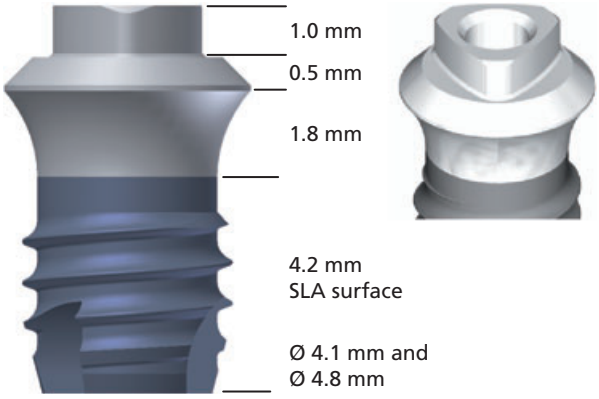


Fig. 58-9 The Orthosystem® (Institut Straumann, Waldenburg, Switzerland) designed for orthodontic anchorage with an intraosseous SLA rough surface, a smooth transmucosal portion, and a trigonal orthodontic fixation base.

Insertion sites of palatal implants

The incomplete closure of the median palatal suture during childhood and early adolescence is a limiting factor for the installation of orthodontic implants in the midsagittal region for fully grown juveniles and adults. Therefore, the paramedian regions of the hard palate (Bernhart *et al*. 2000, 2001) represent a feasible alternative. With respect to the anatomic limitations, sites chosen for palatal orthodontic anchorage device insertion should be carefully evaluated to avoid perforations into the inferior nasal turbinate (Wehrbein *et al*. 1996b). Pre-implantation examinations of the anterior palate have shown that the vertical bone volume decreases from the anterior to the posterior region.

The presence of the palatal suture and the limited bone thickness of the hard palate available may be causes of concern for the achievement of stability of palatal implants. It may be useful to perform imaging diagnosis before palatal implant insertion. Dental computed tomography and/or lateral cephalograms have been recommended for evaluating the vertical bone volume of the hard palate presurgically.

Dental computed tomography of the alveolar process is well established for the evaluation of the alveolar bone volume before implant placement (Lindh *et al*. 1995). It may also be used to assess the vertical bone volume of the hard palate and is currently the most accurate method. The greatest mean thickness was identified to be about 6–9 mm posterior to the incisal foramen in the mid-sagittal plane (Bernhart *et al*. 2000). Avoiding the midpalatal suture, the area suitable for implant placement is, therefore, located 6–9 mm posterior to the incisal foramen and 3–6 mm lateral to the mid-sagittal plane. If the necessary bone volume for an orthodontic implant installation is defined as 4 mm or more (Bernhart *et al*. 2000). In a study, 95% of the patients investigated had adequate vertical bone volume for accommodating palatal implants, 4 mm in length; this is in agreement with other clinical reports (Schiel *et al*. 1996). It must be considered, however, that the patients examined showed a great range of variation of vertical bone volume so a detailed pre-operative diagnostic process is necessary in order to avoid perforation of the lower nasal duct.

Insisting on obtaining precise information for the intended implant sites before placing palatal implants on lateral cephalograms rather than CT examination was proposed (Wehrbein *et al*. 1999). Since the former are used for orthodontic diagnosis and treatment planning, patients are spared from additional radiation exposure. Furthermore, superimposition of structures in CT scans renders this methodology complicated, imprecise, and hazardous for the presurgical assessment of bone volumes for orthodontic anchorage implants.

On wire-marked skulls, the highest bony demarcation of the palatal complex seen radiographically largely coincided with the nasal floor rather than with the mid-sagittal nasal septum, which has additional vertical bone height (Wehrbein *et al*. 1999). Hence, it was suggested that the vertical bone heights in the anterior and middle thirds of the hard palate were at least 2 mm higher vertically than identified on lateral cephalograms. A safety level of at least 2 mm is, therefore, recommended when planning treatment on the basis of lateral cephalograms (Wehrbein *et al*. 1999). It must be realized that even though some implants may project beyond the nasal floor in lateral cephalograms, they may represent false-positive results and may not be related to actual penetrations into the nasal cavity (Crismani *et al*. 2005c). If the palatal complex is perforated, intraoperative probing with a periodontal probe or a sinus probe must be performed for verification.

In addition to the palatal bony morphology, the implant's antero-posterior location and its inclination must also take into account both the pre-treatment and planned final position of the maxillary central incisor, when the implant is placed mid-sagittally (Fig. 58-10).

A distinction has to be made between the vertical bone volume in the mid-sagittal and the paramedian regions, as the indication for implant treatment in the mid-sagittal plane should be limited to adults and fully grown juveniles due to possible developmental disturbances of the palatal suture (Glatzmaier *et al*. 1995; Wehrbein *et al*. 1996b).

Palatal implants and their possible effects in growing patients

During growth, maxillary expansion in a transverse direction is the result of two processes: appositional remodeling of the alveolar process and growth of the palatal suture (Björk & Skieller 1974). While the remodeling process leads to the expansion of the dental arches, the growth in the median suture leads

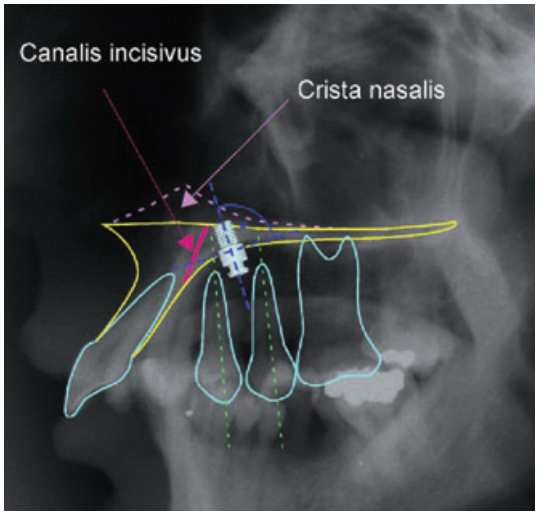
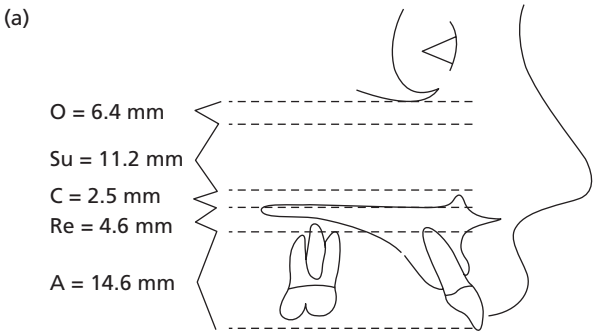


Fig. 58-10 Most palatal implants are installed satisfactorily when the location of entry into the cortical bone is at the antero-posterior level of the maxillary first and second premolars – perpendicular to the palatal surface. From Männchen & Schätzle (2008).



(b)

VERTICAL GROWTH 4 YEARS – ADULT

O	Apposition, floor of orbit
Su	Sutural lowering of maxilla
C	Apposition at the infrazygomatic crest
Re	Amount of resorptive lowering of the nasal floor
A	Apposition, increasing height of the alveolar process

Fig. 58-11 Vertical growth related changes encountered from age 4 years to adulthood. From Björk & Skieller (1977), with permission from the British Orthodontic Society.

to the expansion of the palate that represents the most important factor in the development of the maxillary width. An average growth in maxillary width of 3 mm was demonstrated between the ages of 10 and 18 years (Björk & Skieller 1977). Since the median or paramedian anterior palate may be chosen as insertion sites for palatal implants, the question arises whether or not the implantation of an orthodontic anchorage device may affect normal transverse palatal growth. Palatal implants affected normal transverse growth in an animal study (Asscherickx *et al*. 2005). It could be shown that implant placement resulted in less transverse sutural growth.

Deficient transverse maxillary width may also cause maxillary arch length discrepancies, as demonstrated for canine impaction (McConnell *et al*. 1996). Therefore, all interventions that might cause a restriction in normal transverse maxillary growth should be avoided. Because it has been shown that the insertion of implants in the median palatal suture in adolescent beagle dogs could cause restriction in normal transverse development of the palate (McConnell *et al*. 1996), the installation of the orthodontic palatal implants is better performed in paramedian areas in growing individuals. Moreover, studies have suggested that the installation of orthodontic implants in the midpalatal suture of growing patients is contraindicated because of the questionable quality of bone to provide adequate primary stability (Bernhart *et al*. 2001; Lioubavina-Hack *et al*. 2006). The paramedian region of the anterior palate is largely stable from a growth point of view (Thilander 1995).

The most important vertical growth changes are the result of the displacement of the maxillary complex and surface remodeling processes. The sutural lowering of the maxillary complex as well as the apposition at the orbital floor and at the infrazygomatic crest will not be affected by implant installation in the palate. The resorptive lowering of the nasal floor, however, and the increase of the maxillary alveolar bone height might be influenced. The mean degree of growth from the age of 4 years to adulthood has been identified (Björk & Skieller 1977). The nasal floor appears to drift 4.6 mm caudally, and the height of the maxillary alveolar bone appears to increase 14.6 mm. Assuming that about one third of these growth changes take place from the age of 12 years to adulthood implies a residual vertical growth of about 1.5 mm in the palate and of about 5 mm in maxillary alveolar bone height (Fig. 58-11).

Osseointegrated implants are in direct contact with bone, do not possess a periodontal ligament and hence, behave like ankylosed teeth. Therefore, an osseointegrated palatal implant would remain 1.5 mm behind its surrounding bone, whereas an implant placed in the alveolar bone would produce an infra-occlusion of 5 mm during the same period. Consequently, palatal implants directly or indirectly attached to teeth would lead to an infra-eruption of a single tooth, several teeth or the whole upper dentition, respectively. By influencing the maxillary vertical growth dimension the horizontal displacement of the mandible will also be affected and would, therefore, cause a closing effect on the mandibular plane angle (anterior mandible rotation). It must be considered, however, that palatal implants as temporary orthodontic anchorage devices usually remain 1–2 years *in situ*. Thus, potential vertical and transversal growth impairment are likely to be limited to values of less than 1 mm.

Clinical procedures and loading time schedule for palatal implant installation

Patient stress during implantation and/or explantation and subsequent wound healing may be minimized by applying a minimally traumatic surgical technique. Under palatal local anesthesia, the palatal mucosa is perforated to the cortical bone using a mucosal punch or a system-compatible trephine during explantation and removed with an elevator or a curette (Fig. 58-12a). After smoothing the exposed bone surface to prevent the profile drill from slipping, the centre of the implant site is marked with a round bur (Fig. 58-12b). The implant bed is then prepared to the required depth using a series of pilot and twist drills (Fig. 58-12c). The drilling axis perpendicular to the bone surface is defined based on the presurgical cephalometric analysis. While preparing the insertion site intermediate drilling and cooling of the drilling channel continuously with pre-cooled physiologic saline or Ringer's solution should be performed. The implant is then hand-installed as far as possible, and a ratchet is used to tighten the implant to its final position (Fig. 58-12d). The implant is covered with the healing cap to prevent the inner screw well of the implant from clogging up and from being covered by hyperplastic mucosal tissue (Fig. 58-12e). After insertion, the palatal Orthosystem® implant is allowed to heal *in situ* for 12 weeks during which it should not be loaded.

In some cases, there may be a premature loss of the implant prior to orthodontic load. This loss may be caused by the lack of adequate primary stability. Such insufficient primary stability, causes inappropriate healing and the possible premature loss of the implant (Friberg *et al*. 1991; Lioubavina-Hack *et al*. 2006). Therefore, it is generally recommended to use the 4.1 mm diameter palatal Orthosystem® implant. The 4.8 mm diameter device should only be used if the prerequisite of primary stability cannot be achieved with the smaller (regular 4.1 mm) diameter implant.

Following the placement of an endosseous implant, primary mechanical stability is gradually replaced by biologic bonding. The transition from primary mechanical stability, provided by the implant design, to biologic stability, provided by the osseointegration process, occurs during the first month of wound healing (Berglundh *et al*. 2003). During this critical time, the orthodontic implant should not be used as anchorage.

The installation of implants as absolute anchorage devices facilitates and accelerates orthodontic therapy (Trisi & Rebaudi 2002), even though an inactive waiting time of at least 3 months after insertion (12 week healing time) remains (Wehrbein *et al*. 1996a, 1998; Keles *et al*. 2003; Crismani *et al*. 2005a,b). Especially in adult patients, there is a growing need to reduce this inactive waiting time and to reduce the risk for implant failure during early loading. There are several studies that have reported a successful outcome of early/immediate loaded conventional dental implants placed in the alveolar ridge (Calandriello *et al*. 2003; Rocci *et al*. 2003; Bischof *et al*. 2004; Gallucci *et al*. 2004; Glauser *et al*. 2004; Jaffin *et al*. 2004). However, as of today there is only one study evaluating early loaded palatal orthodontic implants in humans by means of resonance frequency analysis (RFA). On this basis, the possibility of loading palatal orthodontic implants earlier than recommended in the aforementioned literature was suggested with caution (Crismani *et al*. 2006).

There is still a lack of histologic documentation about adequately termed healing periods before loading orthodontic implants in the palatal region and no attempts have been made to document sequential histologic changes of the transition from primary stability to the process of osseointegration. Further studies are needed to define shorter appropriate healing periods.

After the recommended inactive healing period, an impression is taken for the construction of the transpalatal arch (TPA) connection (Fig. 58-12f,g). After integration of the TPA, the implant-related orthodontic treatment is begun. Depending on the treatment goal, schedule, and TPA design, different palatal arches may be necessary during the course of treatment in the same patient.

Direct or indirect orthodontic implant anchorage

Reliable three-dimensional attachment of orthodontic wires to the orthodontic implant is of crucial importance. There are two principles in using implants for orthodontic anchorage:

- Orthodontic forces are applied at anchorage teeth that are not to be moved and are kept in position through a rigid connection (e.g. transpalatal arch, lingual arch) with the implant (*indirect anchorage*) (Wehrbein *et al*. 1996b). The element connected directly to teeth may limit tooth movements and need adaptation or refabrication of the TPA by a dental technician (Fig. 58-12f).
- If force systems act directly between the teeth to be moved and the implant (*direct anchorage*), then the TPA may be adapted more easily by adjusting the active sectional wires (Männchen 1999). It must be considered, however, that the implant should be placed paramedian on the same side in order to keep the torque moments as low as possible, if a direct unilateral sagittal force is applied to the implant (Fig. 58-12g).

The three-dimensional attachment of the orthodontic wire to the implant may be guaranteed by using a clamping cap, a welding or soldering cap or a post cap with a pre-lased wire.

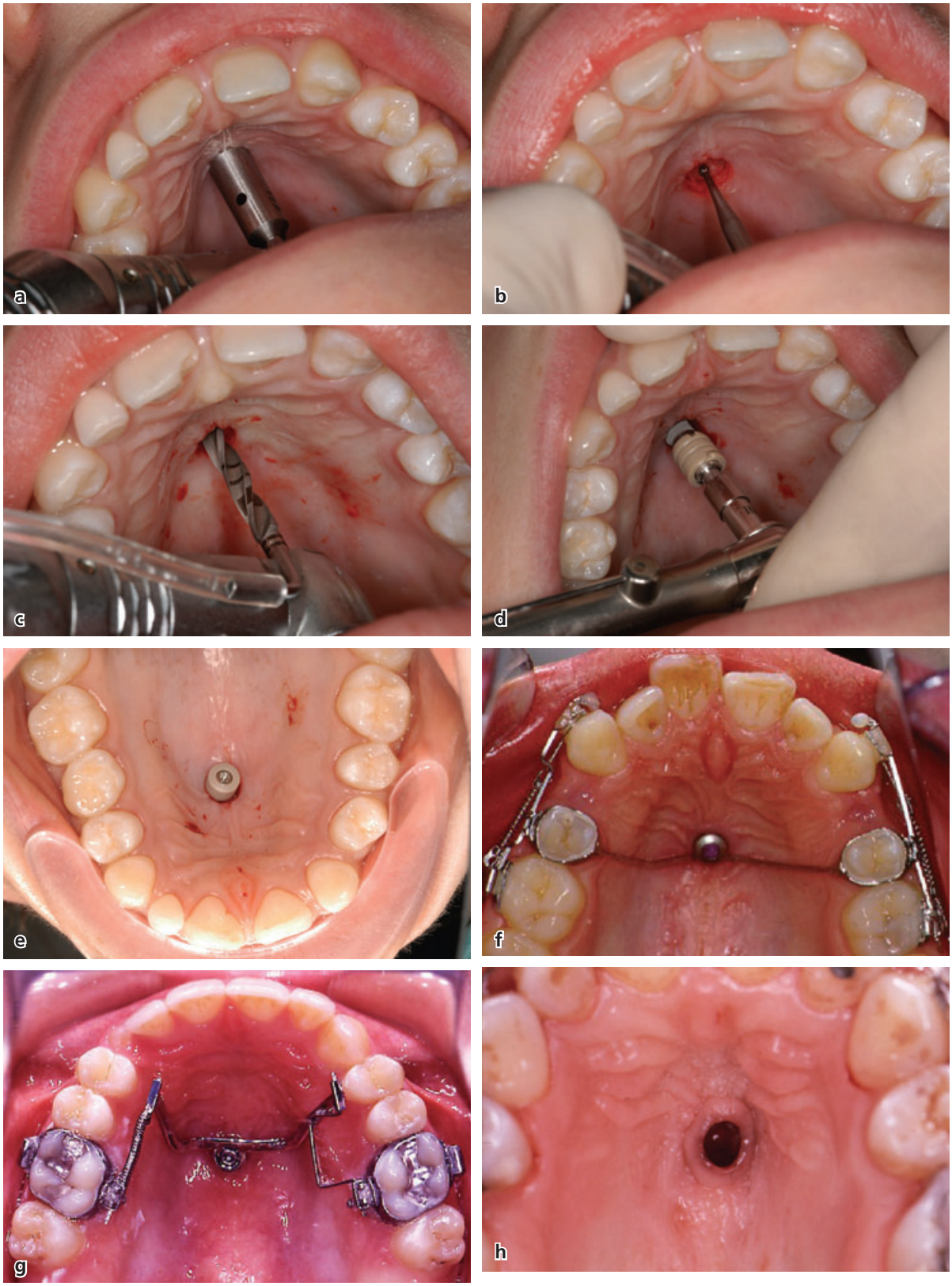


Fig. 58-12 Clinical procedures to install a palatal Orthosystem® (Straumann AG, Basel, Switzerland). (a) Perforation of the palatal mucosa using a system compatible punch or trephine. (b) Marking the center of the intended implant site with a round bur. (c) Preparation of the implant bed at the location determined presurgically and perpendicular to the bone surface. (d) Tightening of the orthodontic implant using a ratchet. (e) Covering the device with a healing cap. (f) Affixation of the transpalatal arch (TPA) for indirect loading (from Wehrbein *et al*. 1998) and (g) for direct loading (according to Männchen 1999). (h) Palatal orthodontic anchorage site after explantation.

Besides offering reliable fixation of the connecting element to the implant abutment, the connecting element must be sufficiently rigid to prevent deflection. A mean loss of anchorage of approximately 1 mm by retracting or torquing of incisors to the buccal segment has been reported (Wehrbein *et al*. 1999a). This contradiction was probably due to deformation of the TPA and/or a slight rotational play of the supraconstruction. Although this anchorage loss might be clinically irrelevant, the pre-activation of the connecting element in the opposite direction may help to avoid this side effect.

It is clear that implant-supported teeth receive continuous loading stimulation. Unfavorable jiggling forces on anchor teeth, as found in compliance-dependent anchorage aids, might be reduced or avoided. This may play a more decisive role in cases with reduced periodontal anchorage.

Stability and success rates

Despite the small dimensions, orthodontic implant anchoring devices must maintain positional stability under orthodontic loading in order to serve as absolute anchorage. As connective tissue encapsulation would initiate implant dislocation, osseointegration is a prerequisite. Histologic examination of explanted human orthodontic implant bone specimens inserted palatally revealed that osseointegration is maintained during long-term orthodontic loading under clinical conditions (Figs. 58-2, 58-3). The percentage of implant-to-bone contact in patients varied between 34% and 93% with an average of 75% (Wehrbein *et al*. 1998), obviously an adequate anchorage to withstand orthodontic loading.

There is only one retrospective cohort study reporting the success rate of a large number of inserted palatal Orthosystem® implants (Männchen & Schätzle 2008). Only three out of 70 inserted palatal implants (4.3%) did not successfully osseointegrate. Of these, two implants were lost due to inadequate primary stability. These were replaced after a short healing period with implants of a greater dimension and osseointegrated successfully thereafter. One implant was placed penetrating the incisal canal and was lost spontaneously. Of the 67 successfully osseointegrated implants loaded actively and/or passively for approximately 19 months, only one implant (1.5%) was lost after 5 months of unilateral heavy active loading (Männchen & Schätzle 2008). This report documented success rates for palatal implants after orthodontic loading comparable to those reported for conventional oral implants (Berglundh *et al*. 2002; Pjetursson *et al*. 2007).

Implant removal

No reports exist on "sleeping orthodontic palatal implants". As a consequence, they have to be removed after completion of the orthodontic treatment. By means of a system-compatible trephine, the peri-implant bone is separated from the device. Then, the implant may be explanted together with the surrounding bone by slow rotations with a extraction forceps. As a variation, the implant–bone contact may be broken by turning the ratchet used for seating the implant counter-clockwise, applying a torque of up to 40 N/cm, and a mechanical torque wrench The implant is then retrieved (Fig. 58-12h). After explantation, possible oro-antral communication must be verified and treated if necessary.

Full recovery at the original anchorage site may be observed 3–4 weeks after implant removal.

Advantages and disadvantages

Even though the orthodontic treatment may be completed faster and with more predictability, patients have to undergo two minor surgical procedures. Additionally, an inactive waiting time after implant installation remains. The extra cost for placing a palatal orthodontic implant must be balanced against other treatment options. Besides cooperation and esthetic aspects to be considered, the costs of orthognathic surgery and/or prosthetic reconstruction may be avoided or reduced by installation of an implant for orthodontic anchorage. In cases in which the palatal implant is directly loaded, bonding of the whole jaw or the entire dentition may not be necessary (Fig. 58-13). The main risks encountered with the use of orthodontic implant anchorage are the development of peri-implant infection, oro-antral connection, and/or implant loss prior to completion of orthodontic treatment.

Conclusions

Osseointegrated implants are providing absolute orthodontic anchorage and hence, are considered to be superior to any orthodontic tooth-borne anchorage device. Indications for orthodontic implant anchorage include: inadequate periodontal anchorage; non-compliant patients for extra- and/or intraoral anchorage aids; prevention of potential side effects of conventional anchorage devices; esthetic aspects; or avoidance of orthognathic surgery after growth completion. Moreover, prosthetic reconstruction may be avoided. The simplicity in use, minimal stress during surgical implant installation and removal, as well as the reliable success rates are prerequisites for the high acceptance of this treatment by orthodontic patients. It must be kept in mind, however, that treatment objectives may be achieved by several treatment plans. Proper orthodontic anchorage should be chosen according to the preceeding diagnosis and to fit the appropriate treatment plan.

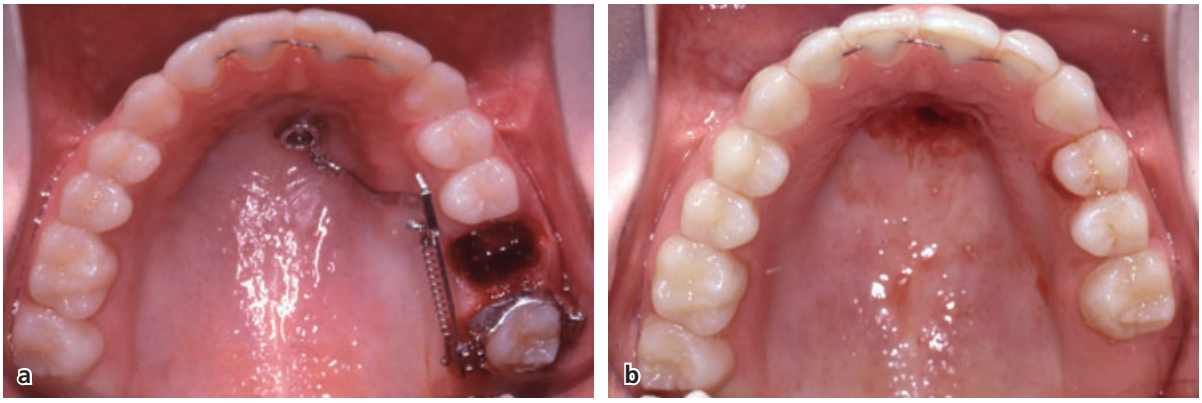


Fig. 58-13 Absolute anchorage by means of a palatal orthodontic implant avoiding the need for bonding the entire maxillary dentition with fixed orthodontic appliances. (a) After the extraction of tooth 26, protraction of tooth 27 was initiated by direct implant loading. (b) At implant and orthodontic appliance removal, the gap between teeth 25 and 27 has been completely closed, thereby avoiding the placement of a fixed partial denture. (Courtesy of R. Männchen, Winterthur, Switzerland.)

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Part 18: Supportive Care

Chapter 59

Supportive Periodontal Therapy (SPT)

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Clinical trials on the long-term effects of treatment of periodontitis have clearly demonstrated that post-therapeutic professional maintenance care is an integral part of the treatment. This also constitutes the only means of assuring the maintenance of long-term beneficial therapeutic effects. Reinfection could be prevented or kept to a minimum in most patients, mainly through rigid surveillance involving professional visits at regular intervals. However, the maintenance systems presented in various studies do not allow the presentation of a clear concept with general validity for the frequency of professional maintenance visits and the mode of maintenance therapy. A danger for supervised neglect of reinfection and recurrent disease in some patients coexists with a tendency for overtreatment in others.

Objective criteria for assessing the patient's individual risk for recurrent disease have been the focus of attention of recent years. However, the evaluation of the patient's individual risk still has to be based on a probability estimation based on the analysis of patient, tooth or tooth site risk assessments.

The purpose of this chapter is to discuss the basics of continuous patient monitoring following active periodontal therapy in order to prevent reinfection and the continued progression of periodontal disease following therapy. The mode and extent of interceptive therapeutic measures needed to achieve this goal will also be evaluated.

Definitions

Periodontal treatment includes:

1. Systemic evaluation of the patient's health
2. A cause-related therapeutic phase with, in some cases
3. A corrective phase involving periodontal surgical procedures
4. Maintenance phase.

The 3rd World Workshop of the American Academy of Periodontology (1989) renamed this treatment phase "supportive periodontal therapy" (SPT). This term expresses the essential need for therapeutic measures to support the patient's own efforts to control periodontal infections and to avoid reinfection. Regular visits to the therapist should serve as a positive feedback mechanism between the patient and the therapist with the purpose of ensuring that patients have the opportunity to maintain their dentitions in a healthy status for the longest possible time. An integral part of SPT is the continuous diagnostic monitoring of the patient in order to intercept with adequate therapy and to optimize the therapeutic interventions tailored to the patient's needs.

Basic paradigms for the prevention of periodontal disease

Periodontal maintenance care, or SPT, follows the paradigms of the etiology and pathogenesis of

periodontal disease and – at present – must consider the fact that these diseases are coping with the result of the host defense on an opportunistic infection.

Almost 40 years ago, a cause–effect relationship between the accumulation of bacterial plaque on teeth and the development of gingivitis was proven (Löe *et al*. 1965). This relationship was also documented by the restoration of gingival health following plaque removal. Ten years later, a corresponding relationship between plaque accumulation and the development of periodontal disease, characterized by loss of connective tissue attachment and resorption of alveolar bone, was shown in laboratory animals (Lindhe *et al*. 1975). Since some of these animals did not develop periodontal disease despite a persistent plaque accumulation for 48 months, it must be considered that the composition of the microbiota or the host's defense mechanisms or susceptibility for disease may vary from individual to individual. Nevertheless, in the study mentioned, the initiation of periodontal disease was always preceded by obvious signs of gingivitis. Hence, it seems reasonable to predict that the elimination of gingival inflammation and the maintenance of healthy gingival tissues will result in the prevention of both the initiation and the recurrence of periodontal disease. In fact, as early as 1746, Fauchard stated that "little or no care as to the cleaning of teeth is ordinarily the cause of all diseases that destroy them" (Fauchard 1746).

From the clinical point of view, the above-mentioned results must be translated into the necessity for proper and regular personal plaque elimination, at least in patients treated for or susceptible to periodontal disease. This simple principle may be difficult to implement in all patients; however, interceptive professional supportive therapy at regular intervals may, to a certain extent, compensate for the lack of personal compliance with regard to oral hygiene standards.

These aspects have been imitated in a beagle dog model with naturally occurring periodontal disease (Morrison *et al*. 1979). Two groups of animals were used. The test group was subjected to initial scaling and root planing and, subsequently, plaque was eliminated by daily toothbrushing and biweekly polishing with rubber cups for a period of 3 years. In the control group, no initial scaling and no oral hygiene practices were performed during the same period of time. Every 6 months, however, the teeth in two diagonally opposed jaw quadrants in both test and control animals were scaled and root planed. The results showed that the reduction of probing depth and the gain of probing attachment, obtained after the initial scaling and root planing in the test animals, were maintained throughout the entire course of the study irrespective of whether or not repeated scaling and root planing had been performed. The control animals, on the other hand, continued to show increasing probing depths and loss of attachment in all quadrants irrespective of whether or not repeated scaling and root planing had been performed. However, in the jaw quadrants where the teeth were repeatedly instrumented every 6 months, the progression of periodontal destruction was significantly less pronounced (Fig. 59-1). These results indicate that professional supportive therapy, performed at regular intervals, may, at least to a certain extent, compensate for a "suboptimal" personal oral hygiene standard. In this respect, it has been demonstrated that following root instrumentation, the subgingival microbiota is significantly altered in quantity and quality (Listgarten *et al*. 1978), and that the re-establishment of a disease-associated, subgingival microbiota may take several months (Listgarten *et al*. 1978; Slots *et al*. 1979; Mousquès *et al*. 1980; Caton *et al*. 1982; Magnusson *et al*. 1984).

In a number of longitudinal, clinical studies on the outcome of periodontal therapy, the crucial role of SPT in maintaining successful results has been documented (Ramfjord *et al*. 1968, 1975; Lindhe & Nyman 1975, 1984; Rosling *et al*. 1976; Nyman *et al*. 1977; Knowles *et al*. 1979, 1980; Badersten *et al*. 1981, 1987; Hill *et al*. 1981; Lindhe *et al*. 1982a,b; Pihlström *et al*. 1983; Westfelt *et al*. 1983a, 1985; Isidor & Karring 1986; Kaldahl *et al*. 1988). In all these studies, probing depths and clinical attachment levels were maintained as a result of a well organized professional maintenance care program (recall intervals varying between 3 and 6 months) irrespective of the initial treatment modality performed. In one of the studies (Nyman *et al*. 1977) an alarming result was that patients treated for advanced periodontal disease involving surgical techniques, but not incorporated in a supervised maintenance care program, exhibited recurrent periodontitis including loss of attachment at a rate three to five times higher than documented for natural progression of periodontal disease in population groups with high disease susceptibility (Löe *et al*. 1978, 1986). Within this area, the effect of negligence in providing adequate supportive maintenance care following periodontal treatment has been studied over a 6-year period by Axelsson and Lindhe (1981a). Following presurgical root instrumentation and instruction in oral hygiene practices, all study patients were subjected to modified Widman flap procedures. During a 2-month healing period, professional toothcleaning was performed every 2 weeks. Following this time period, baseline clinical data were obtained and one out of every three patients was dismissed from the clinic, while the other two were incorporated in a professionally conducted maintenance program with a recall once every 3 months. These patients maintained excellent oral hygiene and consequently yielded a very low frequency of bleeding sites. In addition, probing depths and probing attachment levels were maintained unchanged over the 6-year period. In contrast, the non-recalled patients demonstrated obvious signs of recurrent periodontitis at the 3-year and 6-year

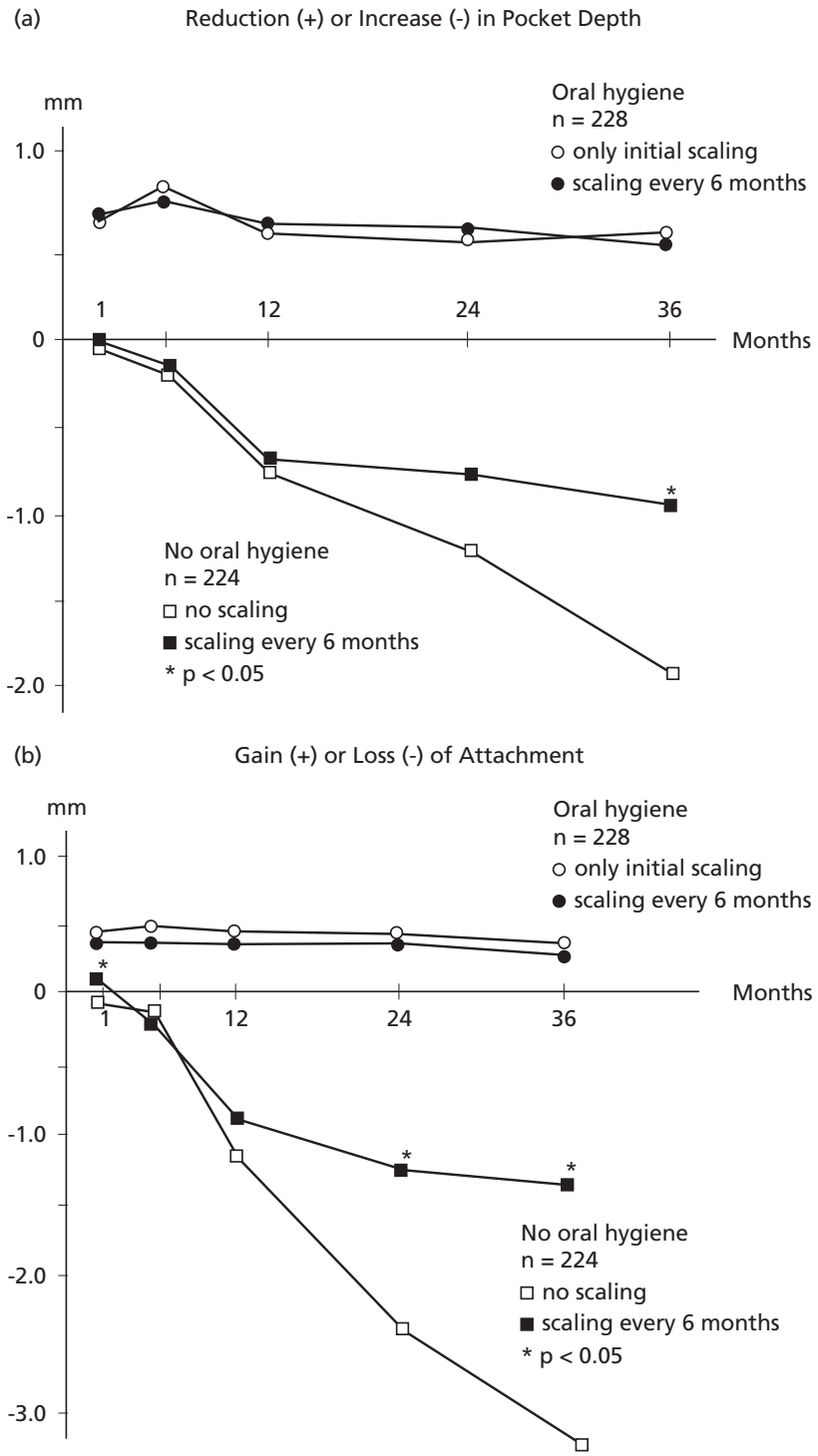

Fig. 59-1 (a) Mean probing depth reduction (+) or increase in probing depth (–) in millimeters with or without repeated scaling and root planing in experimental (oral hygiene) and control (no oral hygiene) animals relative to baseline means. (b) Mean gain (+) or loss (–) of probing attachment with or without repeated scaling and root planing in experimental (oral hygiene) and control (no oral hygiene) animals relative to baseline means. (Data from Morrison *et al*. 1979.)

re-examinations. Further evidence for the likelihood of recurrent disease in patients not subjected to professional maintenance care was presented by Kerr (1981). Five years after successful treatment, 45% of the patients presented with periodontal conditions similar to their status before treatment. Supportive therapy had only been provided at intervals varying between 9 and 18 months.

Similar results have been described for private practice patients who decided not to participate in an organized maintenance care program following active periodontal therapy (Becker *et al*. 1984). Subsequent examinations revealed clear signs of recurrent periodontal disease including increased probing depths and involvements of furcations of multirooted teeth concomitant with tooth loss. Also, loss of alveolar bone observed in radiographs and tooth loss have been reported for a group of patients in whom post-therapeutic supportive maintenance care was provided less frequently than once every 12 months (De Vore *et al*. 1986). From all these studies it is evident that periodontal treatment is ineffective in maintaining periodontal health if supportive maintenance care is neglected, denied or omitted.

Even though the number of well controlled longitudinal clinical trials is rather limited for patients who, in addition to periodontal treatment, have undergone extensive reconstructive therapy, it should be realized that the concept of professional maintenance care has unrestricted validity. In a longitudinal study of combined periodontal and prosthetic treatment of patients with advanced periodontal disease, periodontal health could be maintained over a study period of 5–8 years with regular recall appointments scheduled every 3–6 months (Nyman & Lindhe 1979). Similar results have been presented by Valderhaug and Birkeland (1976) and by Valderhaug (1980) for periods of up to 15 years. Another study of 36 patients who received extensive poly-unit cantilevered bridgework following periodontal therapy, confirmed the maintenance of periodontal health over 5–12 years (Laurell *et al*. 1991). More recent studies on the long-term maintenance over 10 and 11 years of periodontal patients who, following successful treatment of chronic periodontitis, were reconstructed with extensive fixed reconstructions revealed that regularly performed SPT resulted in periodontal stability. Only 1.3% (Hämmerle *et al*. 2000) and 2.0% (Moser *et al*. 2002) of the abutments showed some minor attachment loss during these long periods of observation. In contrast, a report of insurance cases who were not regularly maintained by SPT yielded a recurrence rate for periodontitis of almost 10% after an observation of 6.5 years (Randow *et al*. 1986).

Summary: The etiology of gingivitis and periodontitis is fairly well understood. However, the causative factors, i.e. the microbial challenge which induces and maintains the inflammatory response, may not be completely eliminated from the dentogingival environment for any length of time. This requires the professional removal of all microbial deposits in the supragingival and subgingival areas at regular intervals, since recolonization will occur following the debridement procedures, leading to a reinfection of the ecologic niche and, hence, giving rise to further progression of the disease process. Numerous well controlled clinical trials, however, have documented that such a development can be prevented over very long periods of time only by regular interference with the subgingival environment which aims at removal of the subgingival bacteria.

Patients at risk for periodontitis without SPT

The effect of an omission of SPT in patients with periodontitis may best be studied either in untreated populations or patient groups with poor compliance.

One of the few studies documenting untreated periodontitis-susceptible patients reported on the continuous loss of periodontal attachment as well as teeth in Sri Lankan tea plantation workers receiving no dental therapy (Löe *et al*. 1986). In this – for the western world – rather unique model situation, an average loss of 0.3 mm per tooth surface and year was encountered. Also, the laborers lost between 0.1 and 0.3 teeth per year as a result of periodontitis. In another untreated group in the United States, 0.61 teeth had been lost per year during an observation period of 4 years (Becker *et al*. 1979). This is in dramatic contrast to reports on tooth loss in well maintained patients treated for periodontitis (e.g. Hirschfeld & Wasserman 1978; McFall 1982; Becker *et al*. 1984; Wilson *et al*. 1987). Such patients were either completely stable and lost no teeth during maintenance periods ranging up to 22 years or lost only very little periodontal attachment and only 0.03 teeth (Hirschfeld & Wasserman 1978) or 0.06 teeth (Wilson *et al*. 1987), respectively.

Non-complying, but periodontitis-susceptible patients receiving no SPT following periodontal surgical interventions continued to lose periodontal attachment at a rate of approximately 1 mm per year regardless of the type of surgery chosen (Nyman *et al*. 1977). This is almost three times more than would have to be expected as a result of the "natural" course of periodontal disease progression (Löe *et al*. 1978, 1986).

In a British study of a private practice situation (Kerr 1981) where the patients were referred back to the general dentist after periodontal therapy, 45% of the patients showed complete reinfection after 5 years.

Probably the most impressive documentation of the lack of SPT in disease-susceptible individuals arises from a clinical trial in which one third of the patients had been sent back to the referring general practitioner for maintenance, while two thirds of the patients received SPT in a well organized maintenance system (Axelsson & Lindhe 1981a). The 77 patients were examined before treatment, 2 months after the last surgical procedure and 3 and 6 years later. The 52 patients on the carefully designed SPT system visited the program every 2 months for the first 2 years and every 3 months for the remaining 4 years of the observation period. The results obtained from the second examination (2 months after the last surgery) showed that the effect of the initial treatment was good in both groups. Subsequently, the recall patients were able to maintain proper oral hygiene and unaltered attachment levels. In the non-recall group, plaque scores increased markedly from the baseline values, as did the number of inflamed gingival units (Fig. 59-2a). Concomitantly, there were obvious signs of recurrent periodontitis. The mean values for pocket depth and attachment levels at the 3-year and 6-year examinations were higher than at baseline (Fig. 59-2b). In the recall group, approximately 99% of the tooth surfaces showed either improvement, no change or less than 1 mm loss of attachment, compared to 45% in the non-recall group

(Table 59-1). In the latter patients, 55% of the sites showed a further loss of attachment of 2–5 mm at the 6-year examination, and 20% of the pockets were 4 mm deep or more (Tables 59-1, 59-2).

Summary: Patients susceptible to periodontal disease are at high risk for reinfection and progression of periodontal lesions without meticulously organized and performed SPT. Since all patients who were treated for periodontal diseases belong to this risk category by virtue of their past history, an adequate maintenance care program is of utmost importance for a beneficial long-term treatment outcome. SPT has to be aimed at the regular removal of the subgingival microbiota and must be supplemented by the patient's efforts for optimal supragingival plaque control.

Table 59-1 Percentage of sites showing various changes in probing attachment level between baseline examination, 2 months after completion of active periodontal therapy, and at follow-up examination 6 years later (adapted from Axelsson & Lindhe 1981b)

Change in attachment level	Percentage of surfaces showing change	
	Recall	Non-recall
Attachment level improved	17	1
No change	72	10
Attachment level worse by:		
≥1 mm	10	34
2–5 mm	1	55

Table 59-2 Percentage of various probing depths in recall and non-recall patients at the initial examination, 2 months after active periodontal treatment, and at 3- and 6-year follow-up visits (adapted from Axelsson & Lindhe 1981b)

Examinations	Percentage of pockets of various depths					
	≤3 mm		4–6 mm		≥7 mm	
	Recall	Non-recall	Recall	Non-recall	Recall	Non-recall
Initial	35	50	58	38	8	12
Baseline	99	99	1	1	0	0
3 years	99	91	1	9	0	0
6 years	99	80	1	19	0	1

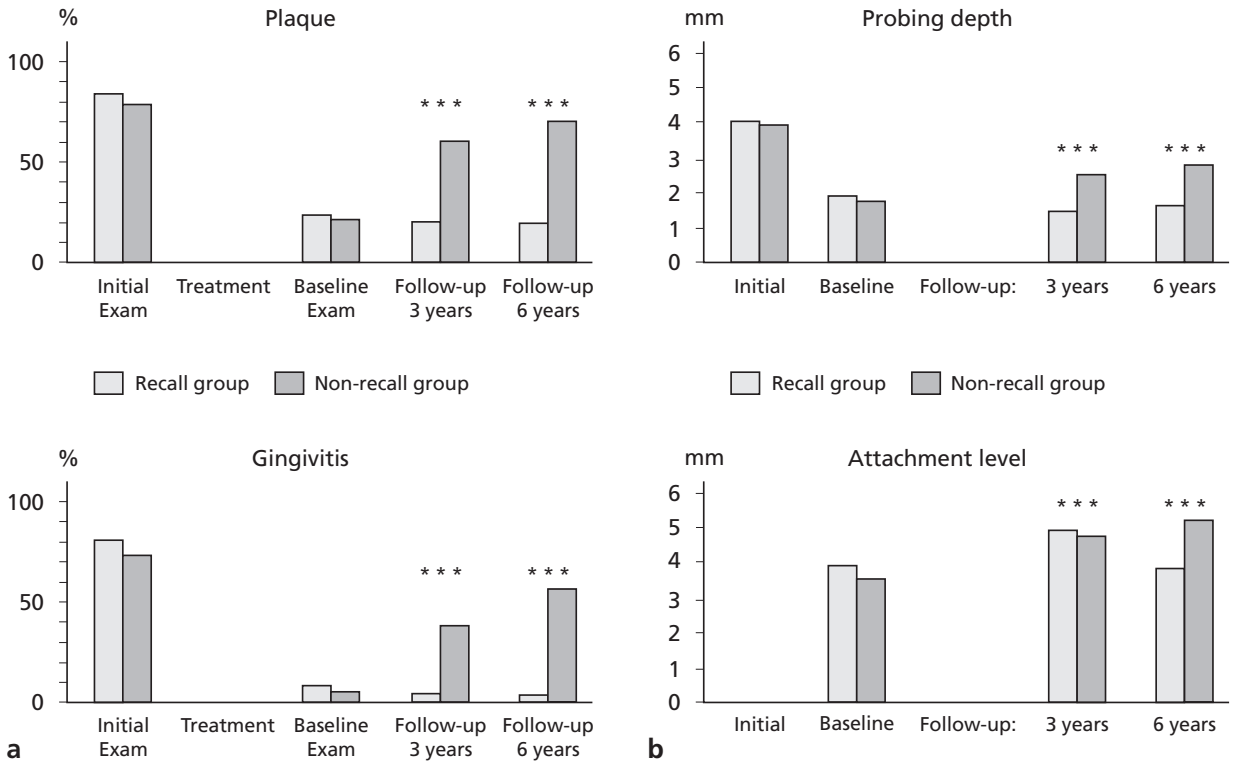

Fig. 59-2 Histograms showing (a) average percentages of tooth surfaces harboring visible plaque (above) and inflamed gingival units (bleeding on probing) (below), and (b) average probing depth (above) and probing attachment levels (below), at initial, baseline and follow-up examinations. (Data from Axelsson & Lindhe 1981b.)

SPT for patients with gingivitis

Several studies, predominantly in children, have documented that periodic professional prophylactic visits in conjunction with reinforcement of personal oral hygiene are effective in controlling gingivitis (Badersten *et al*. 1975; Poulsen *et al*. 1976; Axelsson & Lindhe 1981a,b; Bellini *et al*. 1981). This, however, does not imply that maintenance visits in childhood preclude the development of more severe disease later in life. It is obvious that SPT, therefore, must be a lifelong commitment of both the patient and the profession.

Adults whose effective oral hygiene was combined with periodic professional prophylaxis were clearly healthier periodontally than patients who did not participate in such programs (Lövdal *et al*. 1961; Suomi *et al*. 1971). One particular study of historic significance was performed on 1428 adults from an industrial company in Oslo, Norway (Lövdal *et al*. 1961). Over a 5-year observation period, the subjects were recalled two to four times per year for instruction in oral hygiene and supragingival and subgingival scaling. Gingival conditions improved by approximately 60% and tooth loss was reduced by about 50% of what would be expected without these efforts.

In another study (Suomi *et al*. 1971) loss of periodontal tissue support in young individuals with gingivitis or only loss of small amounts of attachment was followed over 3 years. An experimental group receiving scaling and instruction in oral hygiene every 3 months yielded significantly less plaque and gingival inflammation than the control group in which no special efforts had been made. The mean loss of probing attachment was only 0.08 mm per surface in the experimental as opposed to 0.3 mm in the control group.

When adult patients with gingivitis were treated with scaling and root planing, but did not improve their oral hygiene procedures, the gingival condition did not improve compared with individuals receiving prophylaxes at 6-month intervals (Listgarten & Schifter 1982).

Summary: The available information indicates that the prevention of gingival inflammation and early loss of attachment in patients with gingivitis depends primarily on the level of personal plaque control, but also on further measures to reduce the accumulation of supragingival and subgingival plaque.

SPT for patients with periodontitis

As mentioned previously, a series of longitudinal studies on periodontal therapeutic modalities was performed over the past 25 years, first at the University of Michigan, later at the University of Gothenburg, Sweden, and also at the Universities of Minnesota, Nebraska, and Loma Linda. These studies always incorporated the patients into a well organized maintenance care system with recall visits at regular intervals (generally 3–4 months). Although the patients performed plaque control with various degrees of efficacy, the SPT resulted in excellent maintenance of post-operative attachment levels in most patients (Knowles 1973; Ramfjord *et al*. 1982).

On average, excellent treatment results with maintained reduced probing depths and maintained gains of probing attachment were documented for most of the patients in the longitudinal studies irrespective of the treatment modality chosen (Ramfjord *et al*. 1975; Lindhe & Nyman 1975; Rosling *et al*. 1976; Nyman *et al*. 1977; Knowles *et al*. 1979, 1980; Badersten *et al*. 1981, 1987; Hill *et al*. 1981; Lindhe *et al*. 1982a; Pihlström *et al*. 1983; Westfelt *et al*. 1983a,b, 1985; Isidor & Karring 1986).

In a study on 75 patients with extremely advanced periodontitis, who had been successfully treated for the disease with cause-related therapy and modified Widman flap procedures (Lindhe & Nyman 1984), recurrent infection occurred in only very few sites during a 14-year period of effective SPT. However, it has to be realized that recurrent periodontitis was noticed at completely unpredictable time intervals, but was concentrated in about 25% of the patient population (15 out of 61). This suggests that, in a periodontitis-susceptible risk population, the majority of patients can be "cured" provided an optimally organized SPT is performed, while a relatively small proportion of patients (20–25%) will suffer from occasional episodes of recurrent periodontal reinfection. It is obviously a challenge for the diagnostician to identify such patients with very high disease susceptibility and to monitor the dentitions for recurrent periodontitis on a long-term basis.

As opposed to the study by Lindhe and Nyman (1984) which exclusively involved patients with advanced periodontitis, another study on 52 patients with generalized mild to moderate adult periodontitis addressed the efficacy of SPT 8 years following completion of cause-related periodontal therapy (Brägger *et al*. 1992). Full-mouth intraoral radiographs were used to assess changes in the radiographic alveolar bone height as a percentage of the total tooth length. As a result of cause-related therapy, a gain in probing attachment followed by a loss of 0.5–0.8 mm over the following 8 years was observed. The radiographic loss of alveolar bone height in the same time period was less than 2% and thus clinically insignificant. In this patient group initially presenting with mild to moderate periodontitis, the frequency of SPT rendered per year did not affect the rate of progression of periodontal desease. However, patients seeking SPT less than once per year over 8 years lost further periodontal attachment during the period of observation. From these studies it is evident that patients having experienced periodontitis need some kind of SPT. Obviously, the frequency of SPT visits has to be adapted to the risk of susceptibility for the

disease. Patients with advanced periodontitis may need SPT at a regular and rather short time interval (3–4 months), while for mild to moderate forms of periodontitis, one annual visit may be enough to prevent further loss of attachment.

More recently, the effect of a plaque-control-based maintenance program on tooth mortality, caries, and periodontal disease progression was presented after 30 years of SPT in a private dental office (Axelsson *et al*. 2004). This prospective controlled cohort study initially included 375 test and 180 control patients that received traditional maintenance care (by the referring dentist once to twice a year). After 6 years, the control group was discontinued. The test group was subjected to prophylactic visits every second month for the first 2 years and every 3–12 months (according to their individual needs) during years 3–30. The prophylactic visits to the dental hygienist included plaque disclosure and professional mechanical tooth cleaning, including the use of a fluoride-containing dentifrice. During the 30 years of maintenance, very few teeth were lost (0.4–1.8%), and these were predominately lost because of root fractures. Within 30 years of maintenance, 1.2–2.1 new carious lesions (>80% secondary caries) were found. With the exception of buccal sites, no sites demonstrated any loss of periodontal attachment during this period. On approximal sites, there was even some gain of attachment. This unique study clearly demonstrated that SPT based on plaque control tailored to the individual needs of the patient will result in very low tooth mortality, minimal recurrent caries, and almost complete periodontal stability.

Summary: SPT is an absolute prerequisite to guarantee beneficial treatment outcomes with maintained levels of clinical attachment over long periods of time. The maintenance of treatment results for the majority of patients has been documented up to 14 years, and in a private practice situation even up to 30 years, but it has to be realized that a small proportion of patients will experience recurrent infections with progression of periodontal lesions in a few sites in a completely unpredictable mode. The continuous risk assessment at subject, tooth and tooth site levels, therefore, represents a challenge for the SPT concept.

Continuous multi-level risk assessment

As opposed to an initial periodontal diagnosis which considers the sequelae of the disease process, i.e. documents the net loss of periodontal attachment and the concomitant formation of periodontal pockets and the existence of inflammation, clinical diagnosis during SPT has to be based on the variations of the health status obtained following successful active periodontal treatment. This, in turn, means that a new baseline will have to be established once the treatment goals of active periodontal therapy (i.e. phases 1–3) are reached and periodontal health is restored (Claffey 1991). This baseline includes the level of clinical attachment achieved while the inflammatory parameters are supposed to be under control. Under optimal circumstances, supportive periodontal care would maintain clinical attachment levels obtained after active therapy for the years to come. The relevant question would, therefore, be which clinical parameters may serve as early indicators for a new onset or recurrence of the periodontal disease process, i.e. reinfection and progression of periodontal breakdown of a previously treated periodontal site.

From a clinical point of view the stability of periodontal conditions reflects a dynamic equilibrium between bacterial aggression and effective host response. As such, this homeostasis is prone to sudden changes whenever one of the two factors prevails. Hence, it is evident that the diagnostic process must be based on continuous monitoring of the multi-level risk profile. The intervals between diagnostic assessments must also be chosen based on the overall risk profile and the expected benefit. To schedule patients for supportive periodontal therapy on the basis of an individual risk evaluation for recurrence of disease has been demonstrated to be cost effective (Axelsson & Lindhe 1981a,b; Axelsson *et al*. 1991).

By virtue of their previous disease predisposition, all patients under a periodontal maintenance program represent a population with a moderate to high risk for recurrent periodontal infection. As opposed to the general population without such a history, periodontal patients need to participate in a well organized recall system which should provide both continuous risk assessment and adequate supportive care. Without this, the patients are likely to experience progressive loss of periodontal attachment (Axelsson & Lindhe 1981a; Kerr 1981; Becker *et al*. 1984; Cortellini *et al*. 1994, 1996). On the other hand, it is important to determine the level of risk for progression in each individual patient in order to be able to determine the frequency and extent of professional support necessary to maintain the attachment levels obtained following active therapy. The determination of such risk level would thus prevent undertreatment, and also excessive overtreatment, during SPT (Brägger *et al*. 1992).

Subject risk assessment

The patient's risk assessment for recurrence of periodontitis may be evaluated on the basis of a number of clinical conditions whereby no single parameter displays a more paramount role. The entire spectrum of risk factors and risk indicators ought to be evaluated simultaneously. For this purpose, a functional diagram has been constructed (Fig. 59-3) (Lang & Tonetti 2003) including the following aspects:

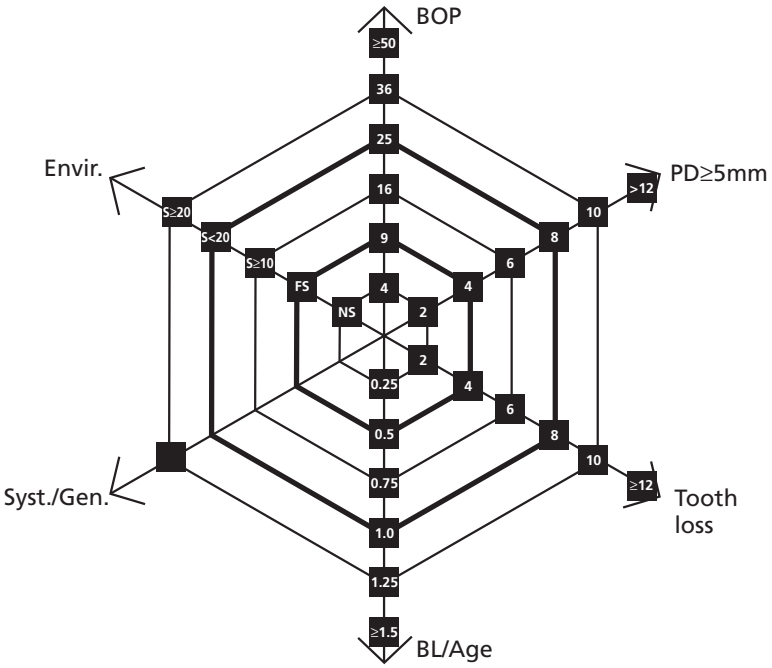

Fig. 59-3a Functional diagram to evaluate the patient's risk for recurrence of periodontitis. Each vector represents one risk factor or indicator with an area of relatively low risk, an area of moderate risk, and an area of high risk for disease progression. All factors have to be evaluated together and hence the area of relatively low risk is found within the center circle of the polygon, while the area of high risk is found outside the periphery of the second polygon in bold. Between the two rings in bold, there is the area of moderate risk.

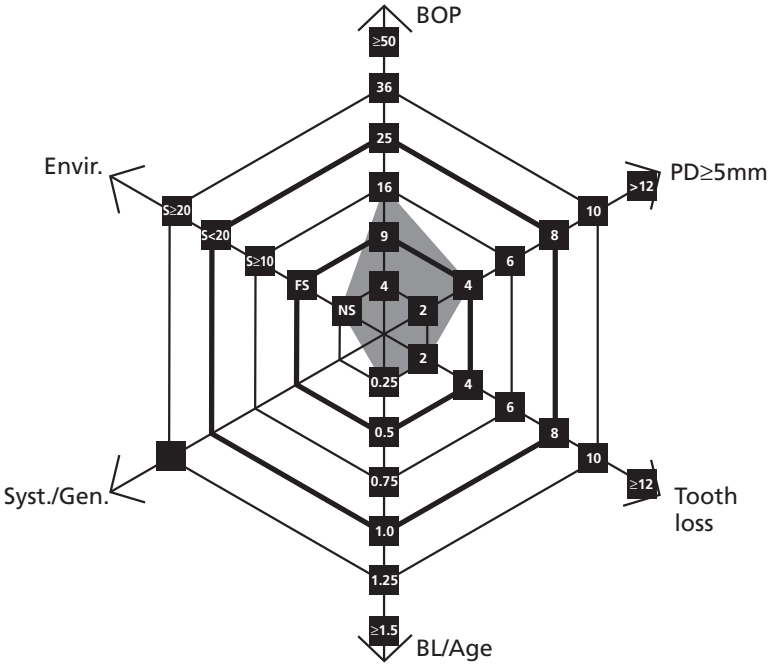

Fig. 59-3b Functional diagram of a low-risk maintenance patient. BOP is 15%, four residual pockets ≥5 mm are diagnosed, two teeth have been lost, the bone factor in relation to the age is 0.25, no systemic factor is known and the patient is a non-smoker.

1. Percentage of bleeding on probing
2. Prevalence of residual pockets greater than 4 mm
3. Loss of teeth from a total of 28 teeth
4. Loss of periodontal support in relation to the patient's age
5. Systemic and genetic conditions
6. Environmental factors such as cigarette smoking.

Each parameter has its own scale for minor, moderate, and high-risk profiles. A comprehensive evaluation, the functional diagram will provide an individualized total risk profile and determine the frequency and complexity of SPT visits. Modifications may be made to the functional diagram if additional factors become important from future evidence.

Compliance with recall system

Several investigations have indicated that only a minority of periodontal patients comply with the prescribed supportive periodontal care (Wilson *et al*. 1984; Mendoza *et al*. 1991; Checchi *et al*. 1994; Demetriou *et al*. 1995). Since it has been clearly established that treated periodontal patients who comply with regular periodontal maintenance appointments have a better prognosis than patients who do not comply (Axelsson & Lindhe 1981a; Becker *et al*. 1984; Cortellini *et al*. 1994, 1996), non-compliant or poorly compliant patients should be considered at higher risk for periodontal disease progression. A report that investigated the personality differences of patients

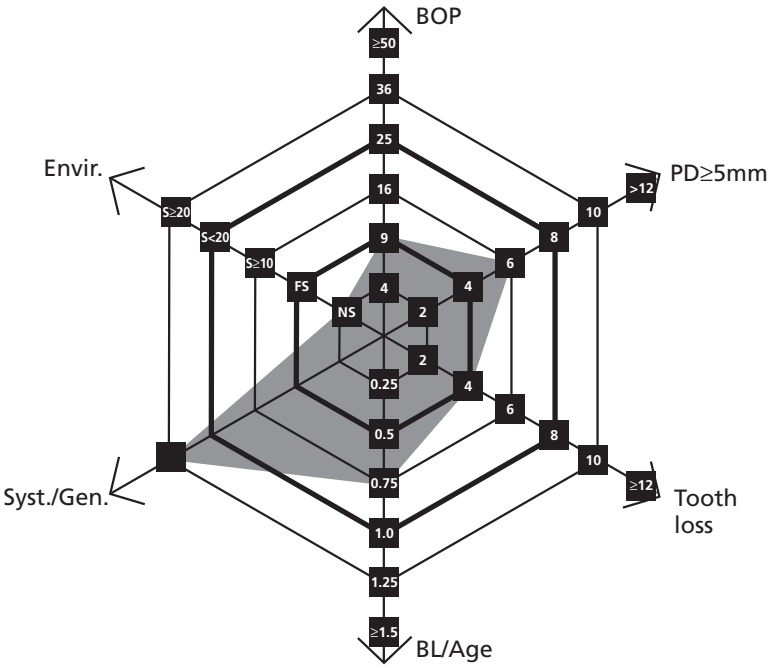

Fig. 59-3c Functional diagram of a medium-risk maintenance patient. BOP is 9%, six residual pockets ≥5 mm are diagnosed, four teeth have been lost, the bone factor in relation to the age is 0.75, the patient is a type I diabetic, but a non-smoker.

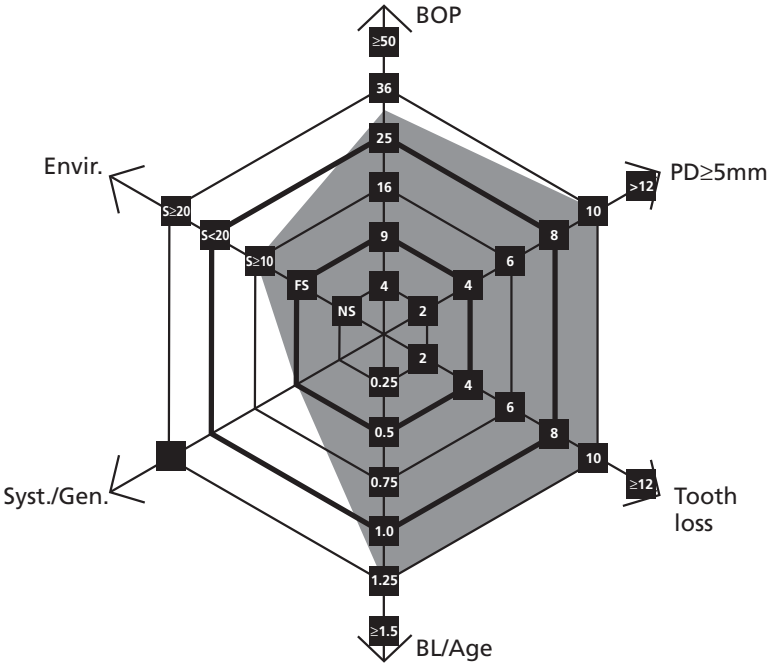

Fig. 59-3d Functional diagram of a high-risk maintenance patient. BOP is 32%, ten residual pockets ≥5 mm are diagnosed, ten teeth have been lost, the bone factor in relation to the age is 1.25, no systemic factor is known, and the patient is an occasional smoker.

participating in a regular recall program as compared to patients who did not, revealed that patients who did not take part in a maintenance program following periodontal therapy had higher incidences of stressful life events and less stable personal relationships in their lives (Becker *et al*. 1988).

Oral hygiene

Since bacterial plaque is by far the most important etiologic agent for the occurrence of periodontal diseases (for review see Kornman and Löe 1993), it is evident that the full-mouth assessment of the bacterial load must have a pivotal impact in the determination of the risk for disease recurrence. It has to be realized, however, that regular interference with the microbial ecosystem during periodontal maintenance will eventually obscure such obvious associations. In patients treated with various surgical and non-surgical modalities, it has been clearly established that plaque-infected dentitions will yield recurrence of periodontal disease in multiple locations, while dentitions under plaque control and regular supportive care maintain periodontal stability for many years (Rosling *et al*. 1976; Axelsson & Lindhe 1981a,b). Studies have thus far not identified a level of plaque infection compatible with maintenance of periodontal health. However, in a clinical set-up, a plaque control record of 20–40% might be tolerable by most patients. It is important to realize that the full-mouth

plaque score has to be related to the host response of the patient, i.e. compared to inflammatory parameters.

Percentage of sites with bleeding on probing

Bleeding on gentle probing represents an objective inflammatory parameter which has been incorporated into index systems for the evaluation of periodontal conditions (Löe & Silness 1963; Mühlemann & Son 1971) and is also used as a parameter by itself. In a patient's risk assessment for recurrence of periodontitis, bleeding on probing (BOP) reflects, at least in part, the patient's compliance and standards of oral hygiene performance. Although there is no established acceptable level of prevalence of BOP in the dentition above which a higher risk for disease recurrence has been established, a BOP prevalence of 25% has been the cut-off point between patients with maintained periodontal stability for 4 years and patients with recurrent disease in the same timeframe in a prospective study in a private practice (Joss *et al*. 1994) (Fig. 59-4). Further evidence of BOP percentages between 20% and 30% determining a higher risk for disease progression originates from studies of Claffey *et al*. (1990) and Badersten *et al*. (1990).

In assessing the patient's risk for disease progression, BOP percentages reflect a summary of the patient's ability to perform proper plaque control, the patient's host response to the bacterial challenge, and the patient's compliance. The percentage of BOP, therefore, is used as the first risk factor in the functional diagram of risk assessment (Fig. 59-3). The scale runs in a quadratic mode with 4, 9, 16, 25, 36, and >49% being the divisions on the vector.

Individuals with low mean BOP percentages (<10% of the surfaces) may be regarded as patients with a low risk for recurrent disease (Lang *et al*. 1990), while patients with mean BOP percentages >25% should be considered to be at high risk for reinfection.

Prevalence of residual pockets greater than 4 mm

The enumeration of the residual pockets with probing depths greater than 4 mm represents, to a certain extent, the degree of success of periodontal treatment rendered. Although this figure *per se* does not make much sense when considered as a sole parameter, the evaluation in conjunction with other parameters, such as BOP and/or suppuration, will reflect existing ecologic niches from and in which reinfection might occur. It is, therefore, conceivable that periodontal stability in a dentition would be reflected in a minimal number of residual pockets. Presence of high fre-

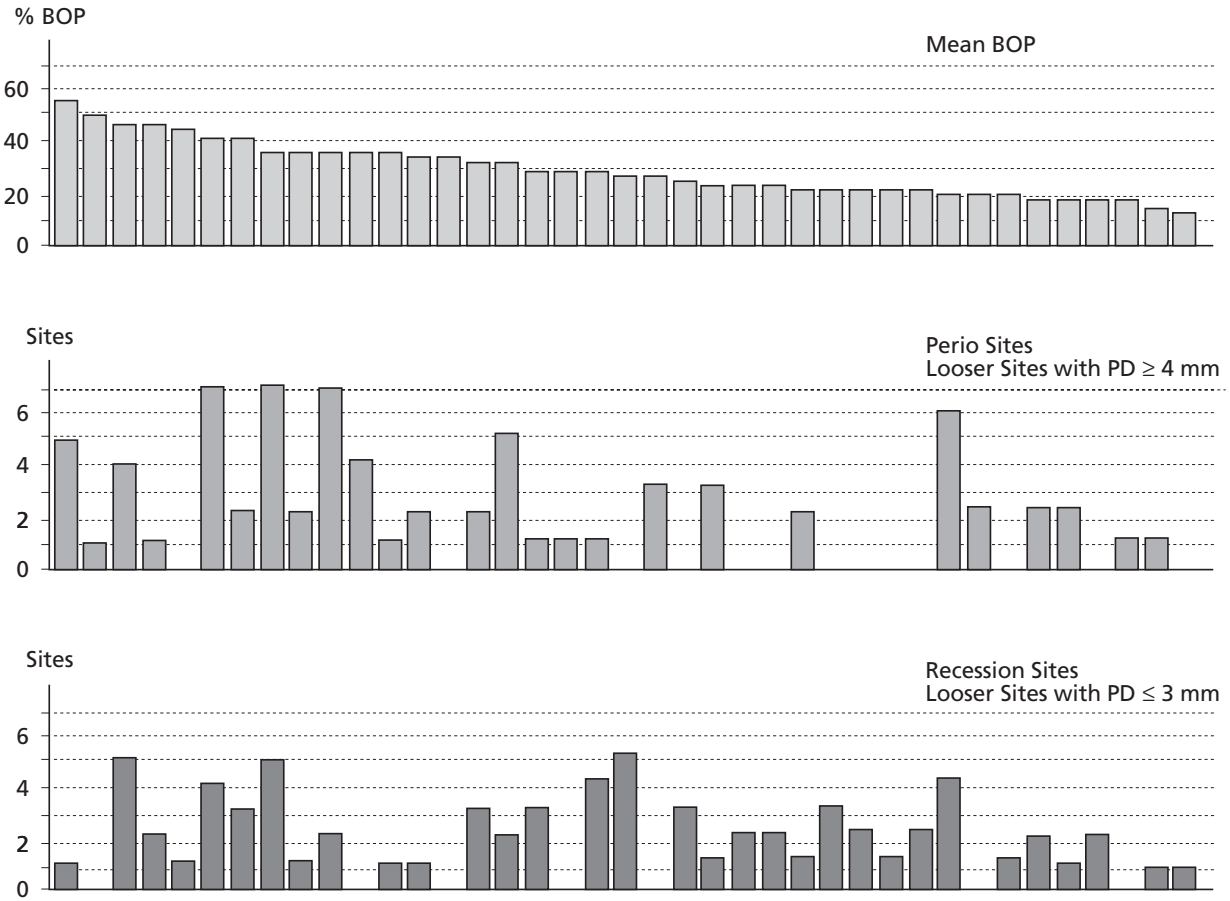

Fig. 59-4 Distribution of "looser" sites (probing depth (PD) ≥4 mm) due to periodontal disease progression with or without concomitant recession, dependent on the mean bleeding on probing (BOP) percentage during an observation period of 4 years. Patients are sorted by decreasing mean BOP percentages. Patients with <20% BOP have a significantly lower risk for disease recurrence. (Data from Joss *et al*. 1994.)

quencies of deep residual pockets and deepening of pockets during supportive periodontal care has, in fact, been associated with high risk for disease progression (Badersten *et al*. 1990; Claffey *et al*. 1990). On the other hand, it has to be realized that an increased number of residual pockets does not necessarily imply an increased risk for reinfection or disease progression, since a number of longitudinal studies have established the fact that, depending on the individual supportive therapy provided, even deeper pockets may be stable without further disease progression for years (e.g. Knowles *et al*. 1979; Lindhe & Nyman 1984).

Nevertheless, in assessing the patient's risk for disease progression, the number of residual pockets with a probing depth of ≥5 mm is assessed as the second risk indicator for recurrent disease in the functional diagram of risk assessment (Fig. 59-3). The scale runs in a linear mode with 2, 4, 6, 8, 10, and ≥12% being the divisions on the vector.

Individuals with up to four residual pockets may be regarded as patients with a relatively low risk, while patients with more than eight residual pockets may be regarded as individuals with high risk for recurrent disease.

Loss of teeth from a total of 28 teeth

Although the reason for tooth loss may not be known, the number of remaining teeth in a dentition reflects the functionality of the dentition. Mandibular stability and individual optimal function may be assured even with a shortened dental arch of premolar to premolar occlusion, i.e. 20 teeth. The shortened dental arch does not seem to predispose the individual to mandibular dysfunction (Witter *et al*. 1990, 1994). However, if more than eight teeth from a total of 28 teeth are lost, oral function is usually impaired (Käyser 1981, 1994, 1996). Since tooth loss also represents a true end-point outcome variable reflecting the patient's history of oral diseases and trauma, it is logical to incorporate this risk indicator as the third parameter in the functional diagram of risk assessment (Fig. 59-3). The number of teeth lost from the dentition without the third molars (28 teeth) is counted, irrespective of their replacement. The scale runs also in a linear mode with 2, 4, 6, 8, 10, and ≥12% being the divisions on the vector.

Individuals with up to four teeth lost may be regarded as patients in low risk, while patients with more than eight teeth lost may be considered as being in high risk.

Loss of periodontal support in relation to the patient's age

The extent and prevalence of periodontal attachment loss (i.e. previous disease experience and susceptibility), as evaluated by the height of the alveolar bone on radiographs, may represent the most obvious indicator of subject risk when related to the patient's age. In light of the present understanding of periodontal disease progression, and the evidence that both onset and rate of progression of periodontitis might vary among individuals and during different timeframes (van der Velden 1991), it has to be realized that previous attachment loss in relation to the patient's age does not rule out the possibility of rapidly progressing lesions. Therefore, the actual risk for further disease progression in a given individual may occasionally be underestimated. Hopefully, the rate of progression of disease has been positively affected by the treatment rendered and, hence, previous attachment loss in relation to patient's age may be a more accurate indicator during SPT than before active periodontal treatment. Given the hypothesis that a dentition may be functional for the most likely life expectancy of the subject in the presence of a reduced height of periodontal support (i.e. 25–50% of the root length), the risk assessment in treated periodontal patients may represent a reliable prognostic indicator for the stability of the overall treatment goal of keeping a functional dentition for a lifetime (Papapanou *et al*. 1988).

The estimation of the loss of alveolar bone is performed in the posterior region on either periapical radiographs, in which the worst site affected is estimated gross as a percentage of the root length, or on bite-wing radiographs in which the worst site affected is estimated in millimeters. One millimeter is equated with 10% bone loss. The percentage is then divided by the patient's age. This results in a factor. As an example, a 40-year-old patient with 20% of bone loss at the worst posterior site affected would be scored BL/Age = 0.5. Another 40-year-old patient with 50% bone loss at the worst posterior site scores BL/Age = 1.25.

In assessing the patient's risk for disease progression, the extent of alveolar bone loss in relation to the patient's age is estimated as the fourth risk indicator for recurrent disease in the functional diagram of risk assessment (Fig. 59-3). The scale runs in increments of 0.25 of the factor BL/Age, with 0.5 being the division between low and moderate risk and 1.0 being the division between moderate and high risk for disease progression. This, in turn, means that a patient who has lost a higher percentage of posterior alveolar bone than his/her own age is at high risk regarding this vector in a multi-factorial assessment of risk.

Systemic conditions

The most substantiated evidence for modification of disease susceptibility and/or progression of periodontal disease arises from studies on type I and type II (insulin-dependent and non-insulin-dependent) diabetes mellitus populations (Gusberti *et al*. 1983; Emrich *et al*. 1991; Genco & Löe 1993).

It has to be realized that the impact of diabetes on periodontal diseases has been documented in patients

with untreated periodontal disease, while, as of today, no clear evidence is available for treated patients. It is reasonable, however, to assume that the influence of systemic conditions may also affect recurrence of disease.

In recent years, genetic markers have become available to determine various genotypes of patients regarding their susceptibility for periodontal diseases. Research on the interleukin-1 (IL-1) polymorphisms has indicated that IL-1 genotype-positive patients show more advanced periodontitis lesions than IL-1 genotype-negative patients of the same age group (Kornman *et al*. 1997). Also, there is a trend to higher tooth loss in the IL-1 genotype-positive subjects (McGuire & Nunn 1999). In a retrospective analysis of over 300 well maintained periodontal patients, the IL-1 genotype-positive patients showed significantly higher BOP percentages and a higher proportion of patients which yielded higher BOP percentages during a 1-year recall period than the IL-1 genotype-negative control patients (Lang *et al*. 2000). Also, the latter group had twice as many patients with improved BOP percentages during the same maintenance period, indicating that IL-1 genotype-positive subjects do indeed represent a group of hyper-reactive subjects even if they are regularly maintained by effective SPT (Lang *et al*. 2000). In a prospective study over 5 years on Australian white collar and blue collar workers on a University campus, the IL-1 genotype-positive age group above 50 years showed significantly deeper probing depth than their IL-1 genotype-negative counterparts, especially when they were non-smokers.

In assessing the patient's risk for disease progression, systemic factors are only considered, if known, as the fifth risk indicator for recurrent disease in the functional diagram of risk assessment (Fig. 59-3). In this case, the area of high risk is marked for this vector. If not known or absent, systemic factors are not taken into account for the overall evaluation of risk.

Research on the association and/or modifying influence in susceptibility and progression of periodontitis of physical or psychologic stress is sparse (Cohen-Cole *et al*. 1981; Green *et al*. 1986; Freeman & Goss 1993). The hormonal changes associated with this condition, however, are well documented (Selye 1950).

Cigarette smoking

Consumption of tobacco, predominantly in the form of smoking or chewing, affects the susceptibility and the treatment outcome of patients with adult periodontitis. Classical explanations for these observations have included the association between smoking habits and poor oral hygiene as well as lack of awareness of general health issues (Pindborg 1949; Rivera-Hidalgo 1986). More recent evidence, however, has established that smoking *per se* represents not only a risk marker, but probably a true risk factor for periodontitis (Ismail *et al*. 1983; Bergström 1989; Bergström *et al*. 1991; Haber *et al*. 1993). In a young population (19–30 years of age), 51–56% of periodontitis was associated with cigarette smoking (Haber *et al*. 1993). The association of smoking and periodontitis has been shown to be dose-dependent (Haber *et al*. 1993). It has also been shown that smoking will affect the treatment outcome after scaling and root planing (Preber & Bergström 1985), modified Widman flap surgery (Preber & Bergström 1990), and regenerative periodontal therapy (Tonetti *et al*. 1995). Furthermore, a high proportion of so-called refractory patients has been identified as consisting of smokers (Bergström & Blomlöf 1992). The impact of cigarette smoking on the long-term effects of periodontal therapy in a population undergoing supportive periodontal care has been reported. Smokers displayed less favorable healing responses both at re-evaluation and during a 6-year period of supportive periodontal care (Baumert-Ah *et al*. 1994). In spite of the paucity of evidence relating cigarette smoking to impaired outcomes during supportive periodontal care, it seems reasonable to incorporate heavy smokers (>20 cigarettes/day) in a higher risk group during maintenance.

In assessing the patient's risk for disease progression, environmental factors such as smoking must be considered as the sixth risk factor for recurrent disease in the functional diagram of risk assessment (Fig. 59-3). While non-smokers (NS) and former smokers (FS) (more than 5 years since cessation) have a relatively low risk for recurrence of periodontitis, the heavy smokers (HS), as defined by smoking more than one pack per day, are definitely at high risk. Occasional (OS; <10 cigarettes a day) and moderate smokers (MS) may be considered at moderate risk for disease progression.

Calculating the patient's individual periodontal risk assessment (PRA)

Based on the six parameters specified above, a multifunctional diagram is constructed for the PRA. In this diagram, the vectors have been constructed on the basis of the scientific evidence available. It is obvious that ongoing validation may result in slight modifications.

- A low periodontal risk (PR) patient has all parameters within the low-risk categories or at the most one parameter in the moderate-risk category (Fig. 59-3b).
- A moderate PR patient has at least two parameters in the moderate category, but at most one parameter in the high-risk category (Fig. 59-3c).
- A high PR patient has at least two parameters in the high-risk category (Fig. 59-3d).

Based on a 4-year prospective cohort study, the application of the multi-functional diagram for the

subject-based PRA was validated (Persson *et al*. 2003) and, indeed, yielded complete periodontal stability after individually tailored recall intervals for all patients with a negative IL-1 gene polymorphism. For the IL-1 genotype-positive patients, however, the PRA resulted only in periodontal stability for 90% of the patients.

Summary: The subject risk assessment may estimate the risk for susceptibility for progression of periodontal disease. It consists of an assessment of the level of infection (full-mouth bleeding scores), the prevalence of residual periodontal pockets, tooth loss, an estimation of the loss of periodontal support in relation to the patient's age, an evaluation of the systemic conditions of the patient, and finally, an evaluation of environmental and behavioral factors such as smoking and stress. All these factors should be contemplated and evaluated together. A functional diagram (Fig. 59-3) may help the clinician in determining the risk for disease progression on the subject level. This may be useful in customizing the frequency and content of SPT visits.

Tooth risk assessment

Tooth position within the dental arch

Early clinical surveys have associated the prevalence and severity of periodontal diseases with malocclusion and irregularities of tooth position (Ditto & Hall 1954; Bilimoria 1963). However, many subsequent studies using clinical evaluation methods could not confirm these conclusions (Beagrie & James 1962; Geiger 1962; Gould & Picton 1966). Although a relationship between crowding and increased plaque retention and gingival inflammation has been established (Ingervall *et al*. 1977; Buckley 1980; Griffith & Addy 1981; Hörup *et al*. 1987), no significant correlation between anterior overjet and overbite (Geiger *et al*. 1973), crowding and spacing (Geiger *et al*. 1974) or axial inclinations and tooth drifts (Geiger & Wasserman 1980) and periodontal destruction, i.e. attachment loss subsequent to gingival inflammation, could be established. It is evident from the literature mentioned that crowding of teeth might eventually affect the amount of plaque mass formed in dentitions with irregular oral hygiene practices, thus contributing to the development of chronic gingivitis, but, as of today, it remains to be demonstrated whether tooth malposition within the dental arch will lead to an increased risk for periodontal attachment loss.

Furcation involvement

It is evident that multi-rooted teeth with periodontal lesions extending into the furcation area have been the subject of intensive therapeutic studies for many years (Kalkwarf & Reinhardt 1988). Retrospective analyses of large patient populations in private periodontal practices of periodontal specialists (Hirschfeld & Wasserman 1978; McFall 1982) have clearly established that multi-rooted teeth appear to be at high risk for tooth loss during the maintenance phase. The most impressive long-term documentation maintained 600 patients for an average duration of 22 years, and 10% of these patients were even maintained for more than 30 years (Hirschfeld & Wasserman 1978). While 83% of the patients could be considered "well maintained" and had lost only 0–3 teeth during the observation period, a patient group of 4% (25) was identified with an extreme risk for disease progression and had lost between 10 and 23 teeth during a regularly scheduled maintenance program. Irrespective of the patient group of low, moderate, and high risk for disease progression during maintenance, the majority of the teeth lost were furcation-involved molars (Hirschfeld & Wasserman 1978). Similar results were obtained in a study on 100 treated periodontal patients maintained for 15 years or longer (McFall 1982).

Prospective studies on periodontal therapy in multi-rooted teeth have also revealed significant differences between non-molar sites and molar flat surfaces on the one hand and molar furcation sites on the other, when looking at the treatment outcomes evaluated as bleeding frequency, probing depth reductions, and levels of attachment (Nordland *et al*. 1987). Again, teeth with furcation involvement and original probing depths >6 mm had reduced treatment outcomes.

The assumption that the prognosis for single-rooted teeth and non-furcation-involved multi-rooted teeth is better than the prognosis for furcation-involved multi-rooted teeth was also confirmed by Ramfjord *et al*. (1987) in a prospective study over 5 years. It has to be realized, however, that these results are not intended to imply that furcation-involved teeth should be extracted, since all the prospective studies have documented a rather good overall prognosis for such teeth if regular supportive care is provided by a well organized maintenance program.

Iatrogenic factors

Overhanging restorations and ill fitting crown margins certainly represent an area for plaque retention, and there is an abundance of association studies documenting increased prevalence of periodontal lesions in the presence of iatrogenic factors (for review see Leon 1977). Depending on the supragingival or subgingival location of such factors, their influence on the risk for disease progression has to be considered. It has been established that slightly subgingivally located overhanging restorations will, indeed, change the ecologic niche, providing more favorable conditions for the establishment of a Gram-negative anaerobic microbiota (Lang *et al*. 1983). There is no doubt that shifts in the subgingival microflora towards a more periodontopathic microbiota, if

unaffected by treatment, represent an increased risk for periodontal breakdown.

Residual periodontal support

Although many clinicians believe that teeth with reduced periodontal support are unable to function alone and should be extracted or splinted, there is clear evidence from longitudinal studies that teeth with severely reduced, but healthy, periodontal support can function either individually or as abutments for many years without any further loss of attachment (Nyman & Lindhe 1979; Nyman & Ericsson 1982; Brägger *et al*. 1990). Hence, successfully periodontally treated teeth can be maintained over decades and function as abutments in fixed bridgework or as individual chewing units irrespective of the amount of residual periodontal support, provided that physiologic masticatory forces do not subject such teeth to a progressive trauma which may lead to spontaneous extraction. Obviously, by virtue of the already reduced support, should disease progression occur in severely compromised teeth, this may lead to spontaneous tooth exfoliation.

Mobility

In light of the discussion of abutment teeth with severely reduced but healthy periodontal support, tooth mobility may be an indicator for progressive traumatic lesions, provided that the mobility is increasing continuously (Nyman & Lang 1994). When assessing tooth mobility, it has to be realized that two factors may contribute to hypermobility: (1) a widening of the periodontal ligament as a result of unidirectional or multidirectional forces to the crown, high and frequent enough to induce resorption of the alveolar bone walls; and (2) the height of the periodontal supporting tissues. If this is reduced due to prior periodontal disease, but the width of the periodontal ligament is unchanged, the amplitude of root mobility within the remaining periodontium is the same as in a tooth with normal height, but the leverage on the tooth following application of forces to the crown is changed. Therefore, it has to be realized that all teeth that have lost periodontal support have increased tooth mobility as defined by crown displacement upon application of a given force. Nevertheless, this hypermobility should be regarded as physiologic (Nyman & Lindhe 1976).

Since tooth mobility is probably more frequently affected by reduced periodontal height rather than unidirectional or multidirectional application of forces on the tooth, its significance for the evaluation of the periodontal conditions has to be questioned. Several studies have indicated that tooth mobility varies greatly before, during, and after periodontal therapy (Persson 1980, 1981a,b). From these studies it can be concluded that periodontally involved teeth show a decrease in mobility following non-surgical and/or surgical periodontal procedures. However, following surgical procedures, tooth mobility may temporarily increase during the healing phase and may resume decreased values later on. Provisional splinting as an adjunct to non-surgical or surgical therapy does not seem to affect the final result of tooth mobility.

Summary: The tooth risk assessment encompasses an estimation of the residual periodontal support, an evaluation of tooth positioning, furcation involvements, presence of iatrogenic factors, and a determination of tooth mobility to evaluate functional stability. A risk assessment at tooth level may be useful in evaluating the prognosis and function of an individual tooth and may indicate the need for specific therapeutic measures during SPT visits.

Site risk assessment

Bleeding on probing

Absence of bleeding on probing (BOP) is a reliable parameter to indicate periodontal stability if the test procedure for assessing BOP has been standardized (Lang *et al*. 1990). Presence of bleeding upon standardized probing will indicate presence of gingival inflammation. Whether or not repeated BOP over time will predict the progression of a lesion is, however, questionable (Lang *et al*. 1986, 1990; Vanooteghem *et al*. 1987). Nevertheless, a 30% probability for attachment loss to occur in the future may be predicted for sites repeatedly positive for BOP (Fig. 59-5) (Badersten *et al*. 1985, 1990; Lang *et al*. 1986; Vanooteghem *et al*. 1987, 1990; Claffey *et al*. 1990).

Obviously, BOP is rather sensitive to different forces applied to the tissues. An almost linear relationship (R = 0.87) existed between the probing force

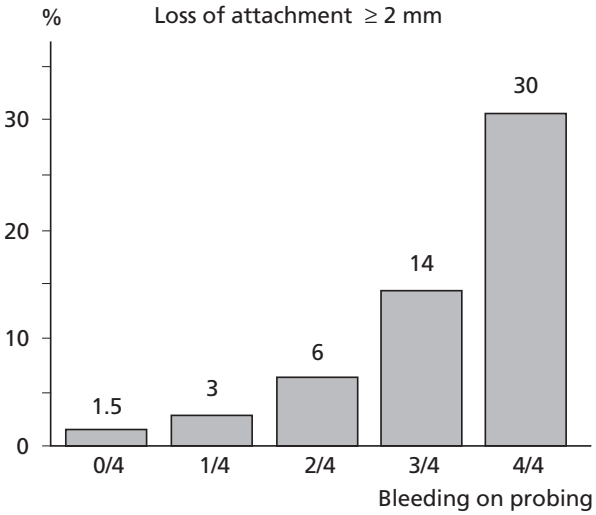

Fig. 59-5 Positive predictive values for loss of probing attachment of ≥2 mm in 2 years in sites which bled on probing 0, 1, 2, 3 or 4 times out of four SPT visits in a total of 48 patients following active periodontal therapy. (Data from Lang *et al*. 1986.)

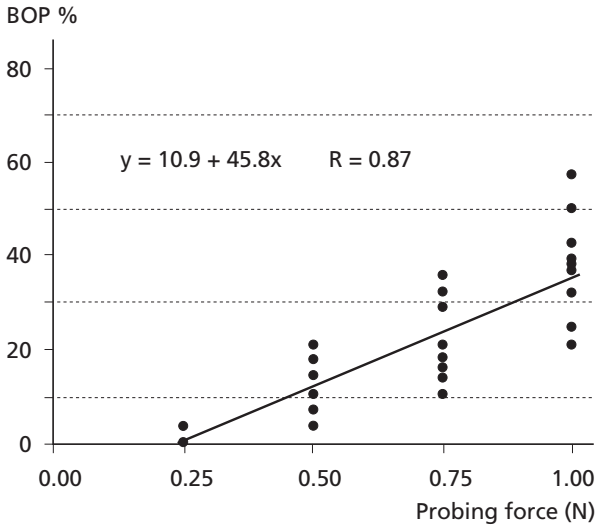

Fig. 59-6 Regression analysis between mean bleeding on probing (BOP) percentage and probing forces applied in young dental hygiene students with a healthy gingiva and normal anatomy. A very high correlation coefficient (R = 0.87) and an almost linear correlation between probing force and BOP percentage was found. (Data from Lang *et al*. 1991.)

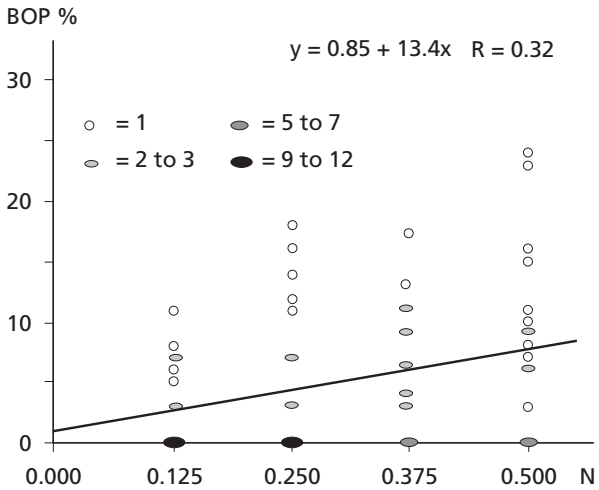

Fig. 59-7 Regression analysis between mean bleeding on probing (BOP) percentage and probing forces applied in subjects with successfully treated periodontitis: a reduced, but healthy, periodontium. (Data from Karayiannis *et al*. 1991.)

applied and the percentage of bleeding sites in a study on healthy young adults (Fig. 59-6) (Lang *et al*. 1991). If the probing force exceeded 0.25 N (25 g), the tissues were traumatized and bleeding was provoked as a result of trauma, rather than as a result of tissue alterations due to inflammation. To assess the "true" percentage of bleeding sites due to inflammation, a probing force of 0.25 N or less should be applied, which clinically means a light probing force. This has also been confirmed for patients who have experienced loss of attachment, i.e. with successfully treated advanced periodontitis (Fig. 59-7) (Karayiannis *et al*. 1991; Lang *et al*. 1991).

Since absence of BOP at 0.25 N indicated periodontal stability with a negative predictive value of 98–99% (Lang *et al*. 1990), this clinical parameter is the most reliable for monitoring patients over time in daily practice. Non-bleeding sites may be considered periodontally stable. On the other hand, bleeding sites seem to have an increased risk for progression of periodontitis, especially when the same site is bleeding at repeated evaluations over time (Lang *et al*. 1986; Claffey *et al*. 1990).

It is, therefore, advisable to register the sites with BOP in a dichotomous way using a constant force of 0.25 N. This allows the calculation of the mean BOP for the patient, and also yields the topographic location of the bleeding site. Repeated scores during maintenance will reveal the surfaces at higher risk for loss of attachment.

Probing depth and loss of attachment

Clinical probing is the most commonly used parameter both to document loss of attachment and to establish a diagnosis of periodontitis. There are, however, some sources of error inherent in this method which contribute to the variability in the measurements. Among these are (1) the dimension of the periodontal probe; (2) the placement of the probe and obtaining a reference point; (3) the crudeness of the measurement scale; (4) the probing force; and (5) the gingival tissue conditions.

In spite of the recognized method errors inherent in clinical probing, this diagnostic procedure has not only been the most commonly used but is also the most reliable parameter for the evaluation of the periodontal tissues. It has to be realized that increased probing depth and loss of probing attachment are parameters which reflect the history of periodontitis rather than its current state of activity. In order to obtain a more realistic assessment of the disease progression or, more commonly, the healing following therapy, multiple evaluations should be performed. Obviously, the first evaluation prior to therapy will yield results confounded by greater measurement error than evaluations following therapy. The reference point (cemento-enamel junction) may be obstructed by calculus or by dental restorations, and the condition of the gingival tissues may allow an easy penetration of the periodontal probe into the tissues, even though the probe position and force applied are standardized. These biologic variables (tissue conditions and calculus) may be minimized following initial periodontal therapy, and hence, repeated periodontal evaluations using probing will improve the metric assessment. The first periodontal evaluation after healing following initial periodontal therapy should, therefore, be taken as the baseline for long-term clinical monitoring (Claffey 1994).

Suppuration

In a proportion of periodontal lesions, pus will develop and may drain through the orifice of a

pocket. This criterion of suppuration may be recognized while clinically probing the lesion, or preferably, by using a ball burnisher (Singh *et al*. 1977). Several longitudinal studies on the results of periodontal therapy have evaluated clinical parameters, including suppuration, for the prediction of future loss of attachment (Badersten *et al*. 1985, 1990; Claffey *et al*. 1990). In all these studies, the presence of suppuration increased the positive predictive value for disease progression in combination with other clinical parameters, such as BOP and increased probing depth. Hence, following therapy a suppurating lesion may provide evidence that the periodontitis site is undergoing a period of exacerbation (Kaldahl *et al*. 1990).

Summary: The tooth site risk assessment includes the registration of BOP, probing depth, loss of attachment, and suppuration. A risk assessment on the site level may be useful in evaluating periodontal disease activity and determining periodontal stability or ongoing inflammation. The site risk assessment is essential for the identification of the sites to be instrumented during SPT.

Radiographic evaluation of periodontal disease progression

As a consequence of the clinical risk assessments the decision may be made to gather radiographic information on the periodontal conditions as well (Hirschmann *et al*. 1994). The task may be related to a generalized pattern of disease progression or a localized monitoring. Not only periodontal aspects, but a comprehensive approach, should influence the choice of the radiographic technique (Rohlin & Akerblom 1992). Periodic radiographic surveys not based on clinical signs and symptoms should not be scheduled simply to confirm health.

Radiographic perception of periodontal changes is characterized by a high specificity, but a low sensitivity, with underestimation of the severity of a periodontal defect (Hämmerle *et al*. 1990; Åkesson *et al*. 1992). Undetectability of minute changes at the alveolar crest is related to overprojections and variations in projection geometry when taking repeated radiographs (Lang & Hill 1977; Goodson *et al*. 1984; Jenkins *et al*. 1992). This may result in mimicked variations in the alveolar bone height, obscured furcation status, etc. In addition, film processing variations may result in unreliable assessments of alveolar bone density changes (Rams *et al*. 1994).

The standard procedure for periodontal evaluations is based on a filmholder system with an alignment for long-cone paralleling technique (Rushton & Horner 1994). With the addition of simple pins to the filmholders as a repositioning reference, the methodologic error was impressively reduced (Carpio *et al*. 1994).

It is a fact that, in general, the standards in oral radiology related to agreement in the choice of a technique, the quality of film processing and the agreement in the diagnosis need to be improved (Brägger 1996).

Clinical implementation

The *three levels* of risk assessment presented represent a logic sequence of clinical evaluation to be performed prior to rendering treatment during maintenance. The information gathered from a stepwise evaluation should not impinge on, but should rather improve, the efficacy of secondary prophylactic periodontal care and treatment. A logical sequence of checks and examinations may be easily obtained in a short period of time and at no extra cost for laboratory tests. The information obtained from clinical monitoring and multi-level risk assessment facilitates an immediate appreciation of the periodontal health status of an individual and the possible risk for further infection and/or disease progression.

Most longitudinal studies published to date have been based on single-level, i.e. site or tooth, risk assessment, rather than accounting for the most evident factor in risk assessment: the patient. Ample evidence indicates that a minority of patients will continue to present problems and hence, differ completely from the maintenance pattern visualized in the majority of the patients. Even in the studies where this fact has been explicitly addressed (Hirschfeld & Wasserman 1978), the factors which determined whether or not a patient belonged to a well maintained group or to a group with continuous loss of periodontal attachment have not been identified.

Summary: It is suggested that patients be evaluated on the *three different levels* mentioned. At the patient level, loss of support in relation to patient age, full mouth plaque and/or bleeding scores, and prevalence of residual pockets are evaluated, together with the presence of systemic conditions or environmental factors, such as smoking, which can influence the prognosis. The clinical utility of this first level of risk assessment influences primarily the determination of the recall frequency and time requirements. It should also provide a perspective for the evaluation of risk assessment conducted at the tooth and site levels.

At the tooth and tooth site levels, residual periodontal support, inflammatory parameters and their persistence, presence of ecologic niches with difficult access such as furcations, and presence of iatrogenic factors have to be put into perspective with the patient overall risk profile (Fig. 59-8). The clinical utility of tooth and site risk assessment relates to rational allocation of the recall time available for therapeutic intervention to the sites with higher risk, and possibly to the selection of different forms of therapeutic intervention.

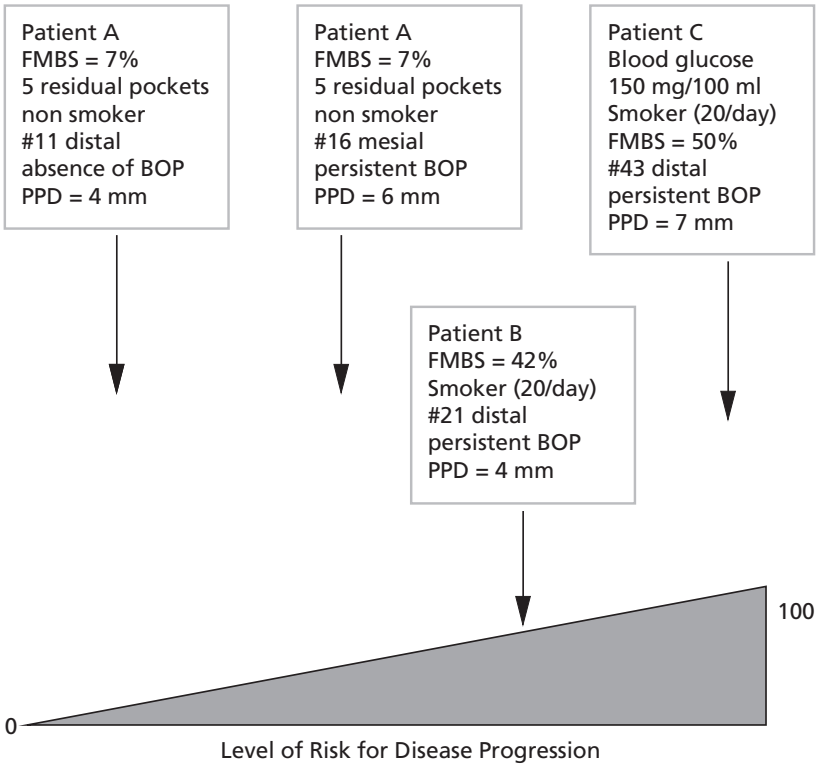

Fig. 59-8 Continuous multiple level risk assessment. Subject, tooth, and site parameters are combined to establish the clinical risk for disease progression. Note that different sites in the same patient may have a different level of risk. Subject-based risk factors are used to put the tooth and/or site risk assessment in perspective.

Objectives for SPT

The objective of maintenance care must be the continued preservation of gingival and periodontal health, obtained as a result of the active periodontal treatment. Irrespective of whether or not additional treatment such as prosthetic reconstructions or placement of implants has been rendered, the regular and adequate removal of supragingival plaque by the patient is, therefore, a prerequisite for a good long-term prognosis. In order to reach these goals, regular clinical re-evaluations with appropriate interceptive treatment, continued psychologic support and encouragement of the patient, and a lifelong commitment by the therapists are required.

General rules regarding frequency of maintenance care visits are difficult to define. However, there are a few aspects to consider in this respect: the patient's individual oral hygiene standard, the prevalence of sites exhibiting bleeding on probing, and the pretherapeutic attachment level and alveolar bone height. This in turn means that patients with suboptimal plaque control and/or concomitant high prevalence of bleeding sites should be recalled more frequently than patients exhibiting excellent plaque control and healthy gingival tissues. Nevertheless, patients with healthy gingival conditions, but with a severely reduced height of periodontal support, should also be recalled with short time intervals (not exceeding 3–4 months) in order to exclude or at least reduce the risk of additional tooth loss. In most of the longitudinal studies referred to above, positive treatment results were maintained with regular maintenance care provided at 3–6-month intervals. It seems reasonable to commence post-therapeutic maintenance with recall visits once every 3–4 months and then shorten or prolong these intervals in accordance with the aspects discussed above.

Since clinical attachment levels are usually stable 6 months following active periodontal therapy, it has been suggested that the first 6 months after completion of therapy be considered a healing phase (Westfelt *et al*. 1983b) during which frequent professional tooth-cleaning has been recommended. Following this healing phase, it is generally agreed to recall patients treated for periodontal disease at intervals of 3–4 months in a well organized system of SPT. It has to be realized that tissue contours may be subjected to remodeling processes despite stable clinical attachment levels and, hence, morphologic changes may still improve the accessibility of all tooth surfaces to oral hygiene practices for months and years. Proper oral hygiene practices appear to be the most important patient factor to guarantee long-term stability of treatment results (Knowles *et al*. 1979; Ramfjord *et al*. 1982, 1987; Lindhe & Nyman 1984). This, in turn, necessitates optimization of the patient's skills and continuous motivation and reinforcement to perform adequate mechanical oral hygiene practices, although chemical agents, such as the potent antiseptic chlorhexidine, may substitute and later complement the patient's efforts during the healing phase, when mechanical practices are difficult (Westfelt *et al*. 1983a). It is obvious that regular recall visits for SPT should be scheduled soon after completion of cause-related therapy, even if periodontal surgical procedures are still to be performed following a careful re-evaluation of the tissue response. To postpone the organization

of a maintenance care program until corrective procedures such as surgery, endodontic, implant, operative or reconstructive therapy have been performed may reinforce a possible misconception of the patient that the professional visits to a therapist or hygienist guarantee positive treatment outcomes and optimal long-term prognosis rather than the patient's own regular performance of individually optimal and adequate oral hygiene practices.

SPT in daily practice

The recall hour should be planned to meet the patient's individual needs. It basically consists of four different sections which may require various amounts of time during a regularly scheduled visit:

1. Examination, re-evaluation, and diagnosis (ERD)
2. Motivation, reinstruction, and instrumentation (MRI)
3. Treatment of reinfected sites (TRS)
4. Polishing of the entire dentition, application of fluorides, and determination of future SPT (PFD).

The SPT recall hour (Fig. 59-9) is generally composed of 10–15 minutes of diagnostic procedures (ERD) followed by 30–40 minutes of motivation, reinstruction, and instrumentation (MRI) during which time the instrumentation is concentrated on the sites diagnosed with persistent inflammation. Treatment of reinfected sites (TRS) may include small surgical corrections, applications of local drug delivery devices or just intensive instrumentation under local anesthesia. Such procedures, if judged necessary, may require an additional appointment. The recall hour is normally concluded with polishing of the entire dentition, application of fluorides and another assessment of the situation, including the determination of future SPT visits (PFD). Approximately 5–10 minutes have to be reserved for this section.

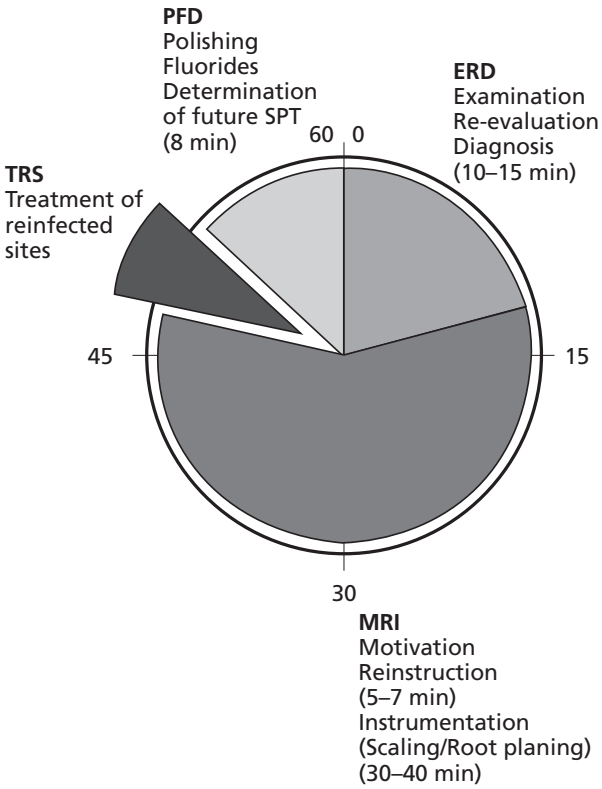

Fig. 59-9 The SPT recall hour is divided into four sections. (1) Examination, re-evaluation and diagnosis (ERD) providing information on stable and inflamed sites. This segment uses 10–15 minutes. (2) Motivation, reinstruction of oral hygiene where indicated, and instrumentation (MRI) will use the bulk of the recall hour (30–40 minutes). Sites which were diagnosed as not stable are instrumented. (3) Treatment of reinfected sites (TRS) may require a second appointment. (4) Polishing all tooth surfaces, application of fluorides and determination of the future recall interval (PFD) conclude the recall hour (5–10 minutes).

Examination, re-evaluation, and diagnosis (ERD)

Since patients on SPT may experience significant changes in their health status and the use of medications, an update of the information on general health issues is appropriate. Changes in health status and medications should be noted. In middle-aged to elderly patients, especially, these aspects might influence the future management of the patient. An extraoral and intraoral soft tissue examination should be performed at any SPT visit to detect any abnormalities and to act as a screening for oral cancer. The lateral borders of the tongue and the floor of the mouth should be inspected in particular. An evaluation of the patient's risk factors will also influence the choice of future SPT and the determination of the recall interval at the end of the maintenance visit. Following the assessment of the subject's risk factors, the tooth site-related risk factors are evaluated. As indicated above, the diagnostic procedure usually includes an assessment of the following:

1. The oral hygiene and plaque situation
2. The determination of sites with bleeding on probing, indicating persistent inflammation
3. The scoring of clinical probing depths and clinical attachment levels. The latter is quite time-consuming and requires the assessment of the location of the cemento-enamel junction as a reference mark on all (six) sites of each root. Therefore, an SPT evaluation usually only includes scoring of clinical probing depths
4. The inspection of reinfected sites with pus formation
5. The evaluation of existing reconstructions, including vitality checks for abutment teeth
6. The exploration for carious lesions.

All these evaluations are performed for both teeth and oral implants. Occasionally, conventional dental radiographs should be obtained at SPT visits. Especially for devitalized teeth, abutment teeth and oral

implants, single periapical films exposed with a parallel and preferably standardized technique are of great value. Bite-wing radiographs are of special interest for caries diagnostic purposes. They also reveal plaque-retentive areas such as overhanging fillings and ill fitting crown margins. Since only approximately 10–15 minutes are available for this section, these assessments have to be performed in a well organized fashion. It is preferable to have a dental assistant available to note all the results of the diagnostic tests unless a voice-activated computer-assisted recording system is used.

Motivation, reinstruction, and instrumentation (MRI)

This aspect uses most of the available time of the SPT visit. When informed about the results of the diagnostic procedures, e.g. the total percentage of the BOP score or the number of pockets exceeding 4 mm, the patient may be motivated either in a confirmatory way in the case of low scores or in a challenging fashion in the case of high scores. Since encouragement usually has a greater impact on future positive developments than negative criticism, every effort should be made to acknowledge the patient's performance.

Patients who have experienced a relapse in their adequate oral hygiene practices need to be further motivated. Especially if the personal life situation has influenced the performance, positive encouragement is appropriate. Standard "lecturing" should be replaced by an individual approach.

Occasionally, patients present with hard tissue lesions (wedge-shaped dental defects) which suggest overzealous and/or faulty mechanical tooth cleaning (Fig. 59-10). Such habits should be broken and the patient reinstructed in toothbrushing techniques which emphasize vibratory rather than scrubbing movements.

Since it appears impossible to instrument 168 tooth sites in a complete dentition in the time allocated, only those sites which exhibit signs of inflammation and/or active disease progression will be re-instrumented during SPT visits. Hence, all the BOP-positive sites and all pockets with a probing depth exceeding 5 mm are carefully rescaled and root planed. Repeated instrumentation of healthy sites will inevitably result in mechanically caused continued loss of attachment (Lindhe *et al*. 1982a).

Similar observations were made in clinical studies by Claffey *et al*. (1988) where loss of clinical attachment levels immediately following instrumentation was observed in 24% of the sites. It is also known from regression analyses of several longitudinal studies (e.g. Lindhe *et al*. 1982b) that probing attachment may be lost following instrumentation of pockets below a "critical probing depth" of approximately 2.9 mm. Instrumentation of shallow sulci is, therefore, not recommended. As it has been shown

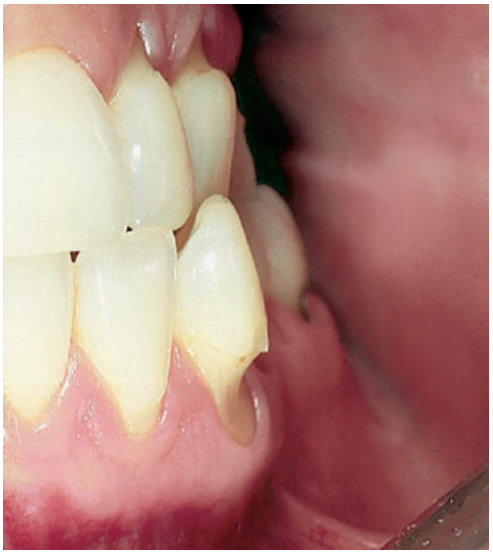

Fig. 59-10 Wedge-shaped defects apical to the cemento-enamel junction following recession of the gingival tissues resulting from overzealous or faulty toothbrushing.

in several studies that non-bleeding on probing sites represent stable sites (Lang *et al*. 1986, 1990; Joss *et al*. 1994), it appears reasonable to leave non-bleeding sites for polishing only and concentrate on periodontal sites with a positive BOP test or probing depths exceeding 5 mm. To protect the hard tissues, root planing should be performed with great caution. The deliberate removal of "contaminated" cementum during SPT is no longer justified (Nyman *et al*. 1986, 1988; Mombelli *et al*. 1995). During SPT visits, root surface instrumentation should be aimed especially at the removal of subgingival plaque rather than "diseased" cementum. This may require a more differentiated approach than hitherto recommended. In this respect, the use of ultrasonics may have to be re-evaluated.

Treatment of reinfected sites (TRS)

Single sites, especially furcation sites or sites with difficult access, may occasionally be reinfected and demonstrate suppuration. Such sites require a thorough instrumentation under anesthesia, the local application of antibiotics in controlled-release devices or even open debridement with surgical access. It is evident that such therapeutic procedures may be too time-consuming to be performed during the routine recall hour, and hence, it may be necessary to reschedule the patient for another appointment. Omission of thorough retreatment of such sites or only performing incomplete root instrumentation during SPT may result in continued loss of probing attachment (Kaldahl *et al*. 1988; Kalkwarf *et al*. 1989).

Treatment choices for reinfected sites should be based on an analysis of the causes most likely responsible for the reinfection.

Generalized reinfections are usually the result of inadequate SPT. Although not all sites positive for

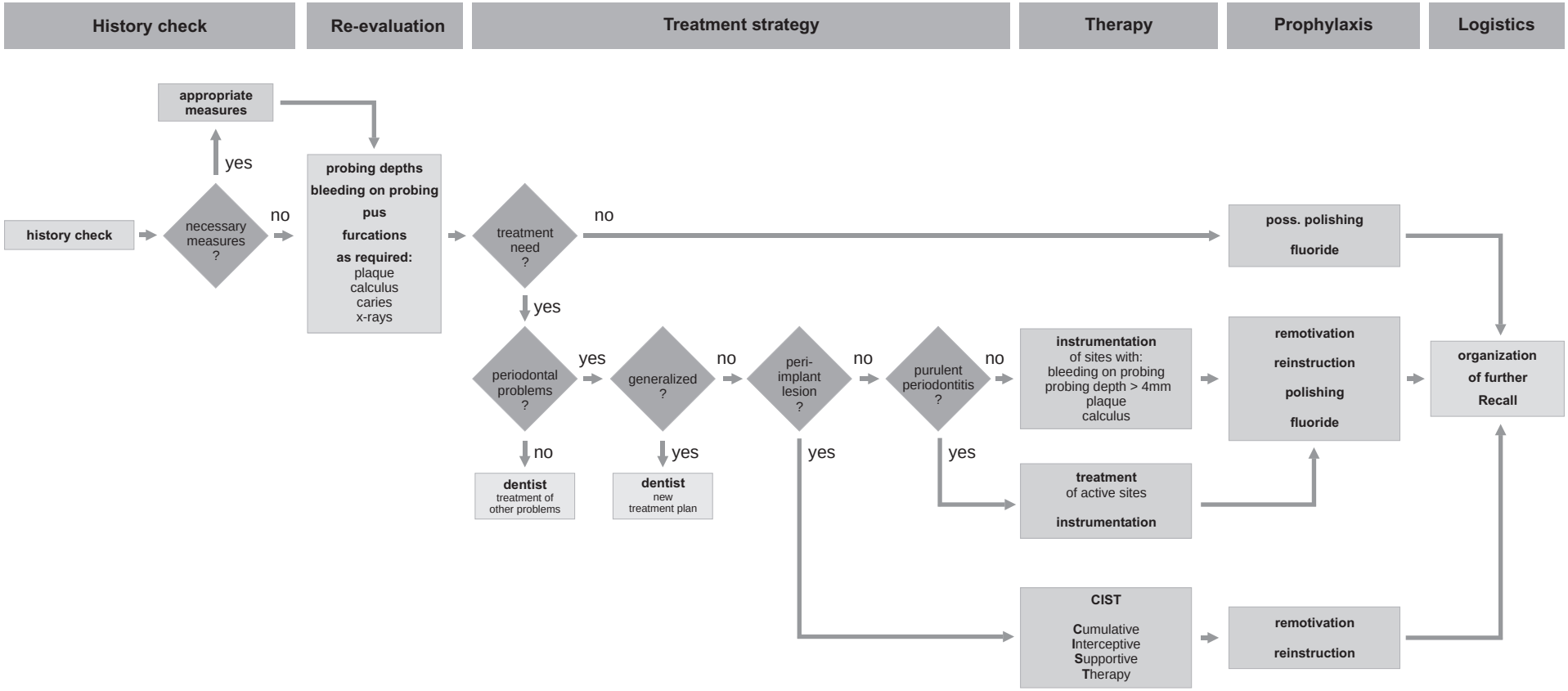

Fig. 59-11 Flow sheet of supportive periodontal therapy (SPT) with strategic decision tree for the recall visit.

BOP may further progress and lose attachment, high BOP percentages call for more intensive care and more frequent SPT visits. Sometimes, a second visit 2–3 weeks after the recall may be indicated to check the patient's performance in oral home care. It is particularly important to supervise patients closely for advanced periodontitis if they have a high subject risk assessment (Westfelt *et al*. 1983b; Ramfjord 1987).

Local reinfections may either be the result of inadequate plaque control in a local area or the formation of ecologic niches conducive to periodontal pathogens. The risk assessment on the tooth level may identify such niches which are inaccessible for regular oral hygiene practices. Furcation involvements often represent special periodontal risk factors which may require additional therapy to be performed following diagnosis in the regular SPT visit.

Polishing, fluorides, determination of recall interval (PFD)

The recall hour is concluded with polishing the entire dentition to remove all remaining soft deposits and stains. This may provide freshness to the patient and facilitates the diagnosis of early carious lesions. Following polishing, fluorides should be applied in high concentration in order to replace the fluorides which might have been removed by instrumentation from the superficial layers of the teeth. Fluoride or chlorhexidine varnishes may also be applied to prevent root surface caries, especially in areas with gingival recession. The determination of future SPT visits must be based on the patient's risk assessment.

Summary: Figure 59-11 provides a flowchart for SPT. The SPT recall hour is divided into four sections. While the first 10–15 minutes are reserved for examination, re-evaluation and diagnosis, the second and most time-consuming section of 30–40 minutes is devoted to reinstruction and instrumentation of sites at risk identified in the diagnostic process. Some reinfected sites may require further treatment, and hence, the patient may have to be rescheduled for an additional appointment. The recall hour is concluded by polishing the dentition, applying fluorides and determining the frequency of future SPT visits.

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Part 19: Halitosis

Chapter 60

Halitosis Control

Edwin G. Winkel

Introduction

Offensive body odor is one of the greatest taboos in our society. Conditions that are associated with body odors are bromidrosis, the secretion of foul-smelling sweat, body odor also known as osmidrosis or kakidrosis (Leyden 1981; Lukacs 1991; Guillet *et al*. 2000), flatulence, excessive production of bowel gases (Suarez *et al*. 1999; Bell 2000), and bad breath (Attia & Marshall 1982; Delanghe *et al*. 1997; van Steenberghe 1997). One factor these conditions have in common is that bacteria play an essential role in the etiology.

This chapter will focus on bad breath. Several terms like breath malodor, oral malodor, *fetor ex ore*, *fetor oris*, bad or foul breath, and halitosis are used to prescribe noticeably unpleasant odors exhaled in breathing. Halitosis is a technical term for bad breath and originates from the Latin "halitus" meaning "breath" and the Greek "osis" meaning "abnormal" or "diseased". Knowledge of this condition dates back to ancient cultures. The Talmud, a collection of ancient rabbinical writings dating back more than 2 millennia, states that bad breath is a major disability. The marriage license (the Ketuba) may be legally broken in the case of halitosis of one of the partners (Shifman *et al*. 2002). The theme is also discussed in ancient writings from China, Greek, Roman, early Christian, and Islamic cultures. For example, Islamic theology stresses the importance of the Siwak or Miswak, a stick obtained from a plant called Salvadore Persica, to clean the teeth and the tongue. Prior to the late 1930s, most references pertaining to halitosis consisted mainly of anecdotal statements that have been perpetuated in the literature. In 1934, Fair and Wells developed the osmoscope, an instrument for measuring the intensity of odors. Later, this apparatus was used for breath analysis (Brening *et al*. 1938). During the last 40 years, our scientific knowledge about the source and causes of halitosis has become much greater.

Several non-oral pathologic conditions have been related to oral malodor, including infection of the upper and lower respiratory tracts, the gastrointestinal tract, and some metabolic diseases involving the kidneys and the liver (Manolis 1983). However, clinical surveys have shown that over 90% of all bad breath odors originate in the mouth (Delanghe *et al*. 1997; van Steenberghe 1997).

Epidemiology

Information regarding the prevalence of oral halitosis is scarce due to the lack of epidemiologic studies. An early study from The Netherlands among 11 625 individuals revealed a prevalence of approximately 25% in subjects older than 60 years (de Wit 1966). In subjects under 20 years, the prevalence of oral halitosis was 10%, indicating that the prevalence of this condition increases with age. In Japan the prevalence of individuals with complaints of halitosis is approximately 14% (National Survey 1999). In the USA, it is estimated that 10–30% of the adult population have an appreciable problem with bad breath (Meskin 1996). Recently, in China the incidence of oral halitosis was surveyed in a sample of 2000 individuals aged 15–64 years. Oral halitosis was measured in 27.5% of the subjects with organoleptic measurements

Table 60-1 Breath volatile sulphur compounds and some amines, together with some of their known odor characteristics

Formula	Name	Odor qualification	100% odor recognition concentration (ppb)
H_2S	Hydrogen sulfide	Rotten eggs	1000
CH_3SH	Methyl mercaptan	Pungent, rotten cabbage	35
CH_3SCH_3	Dimethyl sulfide	Unpleasantly sweet	100
CH_3SSCH_3	Dimethyl disulfide	Pungent	7
$CH_2{=}CHCH_2SH$	Allyl mercaptan	Garlic-like	0.05
$CH_2{=}CHCH_2SCH_3$	Allyl methyl sulfide	Garlic-like	Unknown
$CH_3CH_2CH_2SH$	Propyl mercaptan	Unpleasant, pungent	0.7
$CH_3CH_2CH_2SCH_3$	Methyl propyl sulfide		Unknown
CS_2	Carbon disulfide	Slightly pungent	900
NH_3	Ammonia	Pleasantly sweet	55 000
$(CH_3)_2NH$	Dimethylamine	Fishy, ammoniacal	6000
$(CH_3)_3N$	Trimethylamine	Fishy, ammoniacal	4000

24 ppb = 1 nmol/l (at room temperature).
Adapted from Tangerman (2002).

(Liu *et al*. 2006). However, only a few patients visit dental clinics to seek help for this condition.

Odor characteristics

Together with some of their known odor characteristics, the most common odorous volatile sulfur compounds and some amines found in the breath of patients with halitosis of different origin are shown in Table 60-1 (Verschueren 1983; Tangerman 2002). The 100% odor recognition threshold is the concentration at which 100% of the odor panel defined the odor as being representative of the odorant being studied. The unsaturated mercaptans (allyl mercaptan in garlic) and the unsaturated sulfides (allyl methyl sulfide in garlic) are the most odorous, followed by saturated mercaptans (propyl mercaptan in onion, methyl mercaptan in bad breath), disulfides (dimethyl disulfide), and sulfides (methyl propyl sulfide in onion and dimethyl sulfide and hydrogen sulfide in bad breath).

For a proper diagnosis and therapy and/or referral to a physician or specialist, it is important for the general practitioner to clearly differentiate between halitosis from oral and non-oral origin. Therefore, in this chapter the term *intraoral halitosis* (oral malodor) will be used to define halitosis with a cause within the oral cavity, whereas *extraoral halitosis* is used for halitosis of non-oral cause.

Pathogenesis of intraoral halitosis

Intraoral halitosis may be indicative of either oral diseases, such as periodontal diseases, or the presence of excessive bacterial reservoirs on the tongue. The pathogenesis of intraoral halitosis is associated with the bacterial degradation of sulfur-containing amino acids (methionine, cystine, and cysteine) into volatile sulfur compounds (VSCs) of which methyl mercaptan (CH_3SH) and hydrogen sulfide (H_2S) are the major compounds. It appears that methyl mercaptan is the predominant causative factor of malodor (Tangerman 2002; Awano *et al*. 2004; Tangerman & Winkel 2007). Despite the strong evidence that VSCs are the major causative factors in intraoral halitosis, several research groups still suggest that other volatile compounds such as cadaverine, indole, skatole, and butyric acid may influence oral halitosis (Rosenberg & McCulloch 1992; Goldberg *et al*. 1994; Rosenberg 1996; Greenman *et al*. 2004). No data of the presence of smellable concentrations of such volatiles in mouth air have ever been shown. Therefore, no evidence exists of such a relationship. On the contrary, Tonzetich (1977) clearly showed that diamines, such as cadaverine, inhibited odor formation. It was also stated that indole and skatole, although emanating an objectionable odor in pure state, did not impart an odor to saliva under conditions approximating those of the oral cavity. He ascribed this to their extremely low volatility. The same holds for butyric acid. Due to their low volatilities these compounds have a low odor potential. This is in strong contrast with the VSCs which have a very high odor potential (Verschueren *et al*. 1983).

Formation of volatile sulfur compounds

Gram-negative, proteolytic bacteria are believed to play an essential role in the formation of VSCs, although Gram-positive bacteria such as *Peptostreptococcus* species have also shown ability to produce VSCs *in vitro* (McNamara *et al*. 1972; Persson 1989; Claesson 1990; Persson *et al*. 1990). The most active producers of VSCs *in vitro* are shown in Table 60-2. In our clinic we selected over 100 patients with halitosis but without a history of periodontitis. By culturing periodontal pathogens we found meanly *Fusobacterium* species and low levels of *Prevotella intermedia* (unpublished data), which was in accordance with findings of Loesche and Kazor (2002). This

Table 60-2 Microorganisms with a high capability of generating volatile sulfur compounds *in vitro*

H_2S from serum	CH_3SH from serum	H_2S from cysteine	CH_3SH from methionine
Porphyromonas gingivalis	*Porphyromonas gingivalis*	*Bacteroides* spp.	*Bacteroides* spp.
Porphyromonas endodontalis	*Porphyromonas endodontalis*	*Selenomonas* spp.	*Porphyromonas endodontalis*
Prevotella loescheii		*Fusobacterium* spp.	*Fusobacterium* spp.
Treponema denticula		*Peptostreptococcus* spp.	*Eubacterium* spp.
Prevotella intermedia		*Prevotella intermedia*	
		Tannerella forsythensis	
		Eubacterium spp.	
		Centipedia periodontii	

Adapted from Persson *et al*. (1990).

suggested that the indigenous tongue flora is distinct from the periodontal flora. Therefore, microbiologic information about patients with halitosis should clearly differentiate between patients with or without (a history of) periodontitis.

Periodontium

In patients with periodontal disease, methyl mercaptan was found to be the most abundant VSC (Yaegaki & Sanada 1992c). The role of hydrogen sulfide (H_2S) and methyl mercaptan (MM) in the etiology of periodontitis is unclear. VSCs are potentially capable of altering the permeability of the gingival tissues, including inflammatory responses. By modulating the functions of gingival fibroblasts, VSCs may play a role in the pathogenesis of gingivitis and periodontitis (Ratkay *et al*. 1995; Ratcliff & Johnson 1999; Torresyap *et al*. 2003). In an *in vitro* study, it was shown that MM had a more pronounced effect on the permeability of mucosa than a similar concentration of H_2S (Johnson 1992; Ng 1984). MM has also been shown to act synergistically with both lipopolysaccharide (LPS) and interleukin 1-beta (IL-1β) to increase secretion of prostaglandin E_2 and collagenase, important mediators of inflammation and tissue destruction (Ratkay *et al*. 1995). In fact, increased VSCs in mouth air are related to deep periodontal pockets (Coil & Tonzetich 1992; Yaegaki & Sanada 1992a,c). However, it has also become clear that intraoral halitosis may also occur in individuals with a healthy periodontium (Kaizu *et al*. 1978; Bosy *et al*. 1994; Winkel *et al*. 2003). In patients with periodontitis, Yeagaki and Sanada (1992c) found six times more tongue coating than in those who were periodontally healthy.

Tongue

The tongue has the largest bacterial load of any oral tissue and makes the greatest contribution to bacteria found in the saliva. It is believed that the bacterial mass located at the posterior dorsum of the tongue is the principal site where malodorous compounds are produced (Bosy *et al*. 1994; De Boever *et al*. 1994). Individuals that suffer from intraoral halitosis have a significantly higher bacterial load on the dorsum of the tongue in comparison to individuals without intraoral halitosis (De Boever & Loesche 1995; Yaegaki & Sanada 1992a). In addition, the rough surface of the tongue provides an ideal habitat for anaerobic bacteria, which flourish under a continually forming tongue coating of food debris, dead cells, and hundreds of thousands of bacteria, both living and dead.

Pathogenesis of extraoral halitosis

Approximately 10% of cases of halitosis are caused by extraoral halitosis (Delanghe *et al*. 1998; Tangerman & Winkel 2007).

Examples of extraoral halitosis of the upper respiratory tract are chronic sinusitis, nasal obstruction, nasopharyngeal abscess, and carcinoma of the larynx. Examples of the lower respiratory tract are bronchitis, bronchiectasis, pneumonia, pulmonary abscess, and carcinoma of the lungs (Attia & Marshall 1982; Lu 1982; Durham *et al*. 1993; McDowell & Kassebaum 1993).

Extraoral halitosis might also be a manifestation of a serious systemic disease, such as hiatus hernia, hepatic cirrhosis, or diabetes mellitus. These diseases may produce specific smells (Tangerman 2002) (Table 60-3). For example, *fetor hepaticus* in liver cirrhosis is a type of severe bad breath caused by dimethyl sulfide (Tangerman *et al*. 1994). While intraoral halitosis is largely caused by MM and to a lesser extent by H_2S (Tangerman 2002; Awano *et al*. 2004; Tangerman & Winkel 2007), these components cannot be found in blood-borne halitosis (Tangerman 2002). A new finding is outlined in a study by Tangerman and Winkel (2007) where they found that the majority of extraoral blood-borne halitosis was caused by a hitherto unknown metabolic disorder resulting in elevated odorous levels of dimethyl sulfide in blood and breath. Unpleasant odor from the lower gastrointestinal tract is only detectable during belching or vomiting, because the oesophagus is normally collapsed (Attia & Marshall 1982). The stomach is therefore not considered to contribute to halitosis, except in rare circumstances (Rosenberg 1996).

Table 60-3 Odorous volatiles in the breath of patients with extraoral blood-borne halitosis

Causes of blood-borne halitosis	Odorant
Systemic diseases	
Hepatic failure/liver cirrhosis	Dimethyl sulfide
Uremia/kidney failure	Dimethylamine, trimethylamine
Diabetic ketoacidosis, diabetes mellitus	Acetone
Metabolic disorders	
Isolated persistent hypermethioninemia	Dimethyl sulfide
Fish odor syndrome, trimethylaminuria	Trimethylamine
Medication	
Disulfiram	Carbon disulfide
Dimethylsulfoxide	Dimethyl sulfide
Cysteamine	Dimethyl sulfide
Food	
Garlic	Allyl methyl sulfide
Onion	Methyl propyl sulfide

Adapted from Tangerman (2002).

Table 60-4 Organoleptic scoring scale

Score	Category	Description
0	Absence of halitosis	Odor cannot be detected
1	Questionable halitosis	Odor is detectable, although the examiner could not recognize it as halitosis
2	Slight halitosis	Odor is deemed to exceed the threshold of halitosis recognition
3	Moderate halitosis	Halitosis is definitely detected
4	Strong halitosis	Strong halitosis is detected, but can be tolerated by examiner
5	Severe halitosis	Overwhelming halitosis is detected and cannot be tolerated by examiner (examiner instinctively averts the nose)

Adapted from Yaegaki & Coil (2000).

Diagnosis

Flowchart in a halitosis practice

There are no accepted clinical protocols for the diagnosis of patients with halitosis.

In practice, the flowchart in Fig. 60-1 is suggested for patients with complaints of halitosis. The techniques and strategies for diagnosis and treatment that are described below have been drawn from the research methods and results of important workers in the field of halitosis (Tonzetich 1977; Preti *et al*. 1992; Rosenberg 1995; Richter 1996; van Steenberghe & Rosenberg 1996; Yaegaki & Coil 1999; Sanz *et al*. 2001; Coil *et al*. 2002; Quirynen *et al*. 2002b) and from the experience of the author in treating patients with chief complaints of halitosis for more than 10 years.

Before first consultation

Before the first appointment all patients receive detailed medical and halitosis questionnaires as well as written instructions (Fig. 60-2). The general medical questionnaire, which includes questions about e.g. systemic diseases, allergy, asthma, rhinitis, sinusitis, and medication, has to be filled in before the appointment and can be discussed beforehand with the physician if needed. Additionally a specific halitosis questionnaire is given to the patient (Fig. 60-3).

At the first examination

The questionnaires form the basis for the consultation. The various points and their implications are discussed with the patient. These points include the unreliability of the patient's self assessment. One's own breath odor is often undetectable due to habituation. Many patients link bad breath with bad taste (metallic, sour, fecal, etc.). From the start of the consultation it must be made clear to the patient that you are treating *bad breath* and not *bad taste* and that the presence of a bad taste does not mean that the patient also has bad breath. Nor does a fresh taste imply fresh breath. The opinion of the patient about the level of halitosis is thus unreliable.

It is important to start the examination by firstly carrying out both subjective and objective assessment of the degree of halitosis and then start the intraoral examination. In this way, the severity of the halitosis is assessed before any changes in the degree of halitosis can occur.

Organoleptic measurements

Sniffing of expelled air of the patient by using the nose of the examiner, organoleptic scoring, is the usual technique for halitosis examination in daily practice (Schmidt *et al*. 1978; Rosenberg & McCulloch 1992; van Steenberghe 1997). Differentiation between intraoral and extraoral halitosis can easily be done by comparing mouth breath with nose breath (Durham *et al*. 1993; Richter 1996; Rosenberg 1996).

Examination: For the organoleptic evaluation, participants are instructed to close their mouth for 1 minute, then to slowly exhale air out of the mouth at a distance of approximately 10 cm from the nose of the examiner (Fig. 60-4). For evaluation of extraoral halitosis, patients are also asked to slowly exhale air out of the nose, also at a distance of approximately 10 cm from the nose of the examiner. Full mouth and nose organoleptic odor assessments are used, on a scale of 0 to 5 (Table 60-4) (Rosenberg *et al*. 1991b; Yaegaki & Coil 2000).

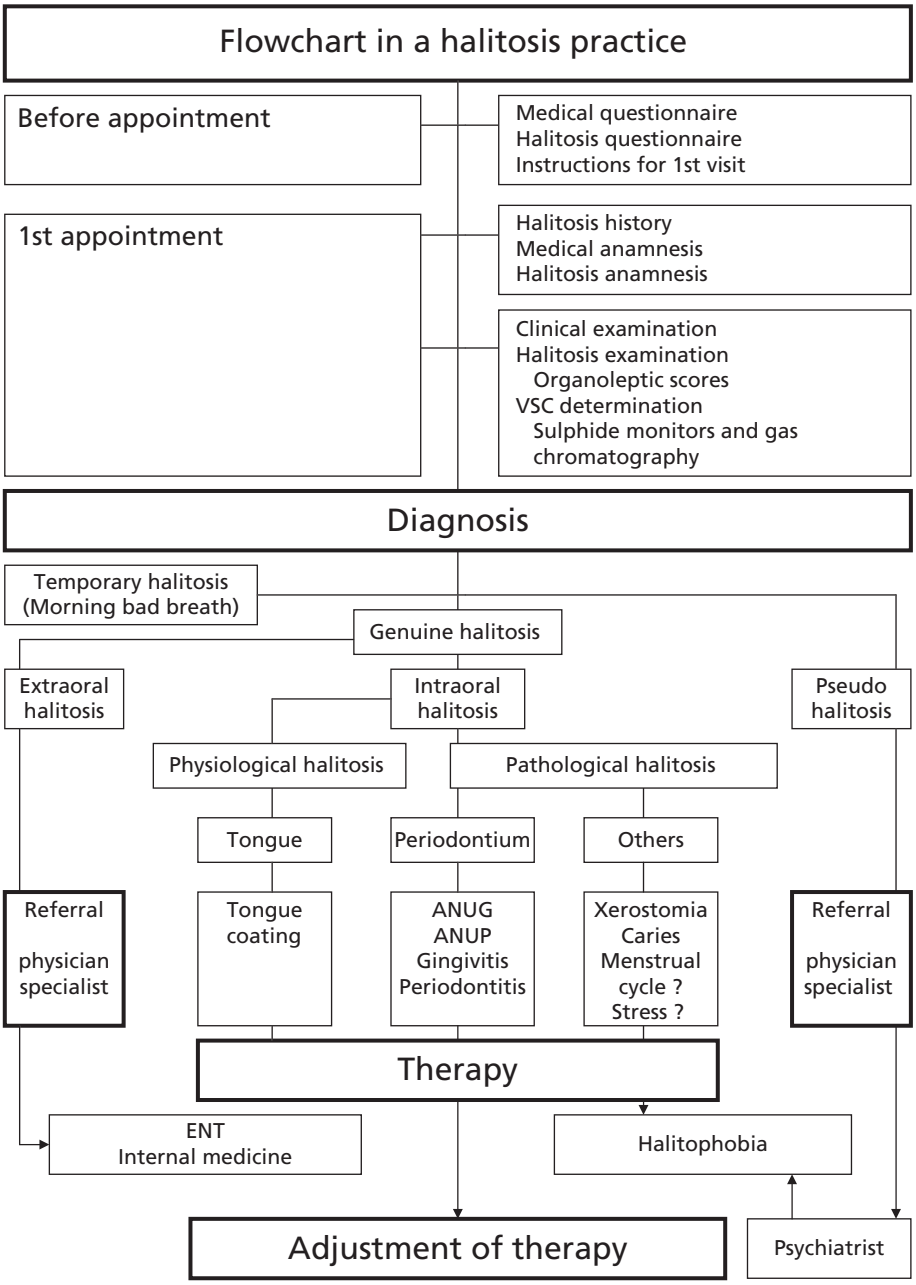


Fig. 60-1 Flowchart in a halitosis practice.

Sulfide monitor

Dental practices and breath clinics now use portable sulfide monitors. For example the Breathtron™ (Sopapornamorn 2006) and the Halimeter™ (Rosenberg *et al*. 1991a) can test the breath air for levels of sulphur emissions. The Halimeter (Fig. 60-5) has a high sensitivity for hydrogen sulfide but a lower sensitivity for methyl mercaptan, which is a significant contributor to halitosis. Certain foods such as garlic and onions produce sulfur in the breath for as long as 48 hours and may result in false readings. The Halimeter is also very sensitive to alcohol, so one should avoid drinking alcohol or using alcohol-containing mouthwashes for at least 12 hours prior to being tested.

The Halimeter is unsuitable for measuring patients with extraoral halitosis from dimethyl sulfide (Tangerman & Winkel 2007).

Examination: The Halimeter needs to be calibrated to zero on ambient air prior to each measurement. First, the disposable straw, connected to the Halimeter, is placed in the opening of the nose of the patient. Then the patient is asked to blow slowly through to the nose. The maximum peak value of VSCs is recorded. Second, the patient is asked to close the mouth for 1 minute. Then the patient is asked to open the mouth and protrude the tongue. The straw is placed at the dorsal posterior mid part of the tongue and fixed until again the maximum peak value of VSCs is recorded. Peak VSC levels are registered in parts per billion (ppb) (Fig. 60-6a). According to

Instructions for 1st visit

In these instructions, subjects are asked **not** to:

1) take antibiotics for 8 weeks before assessment;
2) consume food containing onions, garlic or hot spices for 48 hours before the baseline measurements;
3) drink alcohol or smoke in the previous 12 hours;
4) eat and drink in the previous 8 hours (drinking water up to 3 hours before examinations is allowed);
5) perform oral hygiene, including tooth brushing, interdental and tongue cleaning, and not to use mouthrinses the morning of the examination;
6) use scented cosmetics or after-shave lotions on the morning of the examination.

If the patient has any condition like diabetes, which will be aggravated by fasting for the period of time indicated, please contact the dentist about alternative methods of preparation.

Fig. 60-2 Instructions for first visit.

the manufacturer, human standard ("normal") Halimeter readings range between 80 and 110 ppb (http://www.halimeter.com/halcal.htm). Values over 160 ppb are considered to identify a patient with true halitosis (Fig. 60-6b).

Gas chromatography

Gas chromatography is by far the most appropriate method to detect halitosis of different origins and should be considered as the gold standard. It is an objective means of obtaining exact values for the various odorous volatiles (Tonzetich 1967; Furne *et al*. 2002; Tangerman 2002). New technology is now appearing in the form of portable gas chromatography machines such as the OralChroma™ (Fig. 60-7), which is specifically designed to digitally measure molecular levels of the three major VSCs (hydrogen sulfide, methyl mercaptan, and dimethyl sulfide) in a sample of breath air. It is extremely sensitive and produces visual results in graph form via computer interface (Fig. 60-8a).

Examination: Insert the 1-ml plastic syringe halfway into the oral cavity and ask the patient to hold the syringe between the lips (Fig. 60-8b). Ask the patient not to touch the syringe with the tongue nor the palate. Wait 1 minute, then slowly pull the plunger, push it in again, and pull it for a second time before removing the syringe out of the oral cavity. Avoid saliva in the syringe. If the top of the syringe is wet, wipe it dry with a tissue, attach the needle and eject the air to 0.5 ml and then insert the needle in the injection port of the gas chromatograph (Fig. 60-8c). The apparatus will process the sample in 8 minutes.

Oral inspection

During the first visit, extensive soft tissue, hard tissue, and periodontal examinations are performed in order to determine whether the patient has other oral health problems. Specific attention is paid to the tongue and the presence of tongue debris is noted using a tongue-coating index.

Index systems for tongue coating

A variety of index systems has been developed over the years (Miyazaki *et al*. 1995; Gomez *et al*. 2001; Winkel *et al*. 2003; Lundgren *et al*. 2007). Miyazaki *et al*. (1995) divides the tongue into three sections and the presence or absence of tongue coating is registered as follows: score 0 = none visible; 1 = less than one third of tongue dorsum is covered; 2 = between one and two thirds; 3 = more than two thirds. Gomez *et al*. (2001) divides the tongue into nine different sections, whilst Winkel *et al*. (2003) divides the tongue into six sections, three in the posterior and three in the anterior part of the tongue. Each sextant is categorized as: score 0 = no coating present; 1 = presence of a light coating; 2 = presence of a distinct coating. The resulting Winkel tongue coating index (WTCI) is obtained by adding all six scores (Winkel *et al*. 2003) (Fig. 60-9).

The tongue is normally pink (Fig. 60-10) but a very thin whitish coating can also be considered normal. Having a coating on your tongue does not necessarily mean that you have bad breath (Fig. 60-11), although heavy tongue coatings are usually positively related to halitosis (Fig. 60-12).

Halitosis questionnaire

Do you suffer from a dry mouth?
Do you breathe through your mouth?
How many drinks do you have per day (include **all** beverages)?
How many cups of coffee do you drink per day?
How many units of alcohol do you drink per day?
Do you often have a bad taste in your mouth?
Is this related to your bad breath?
What time of day do you have problems with bad breath?
From who have you heard that you have bad breath?
Over how many years have you had a problem with bad breath?
How would you assess the severity of your bad breath?
How do others assess the severity of your bad breath?
How have you consulted a doctor over this problem?
Do you have problems with phlegm in the back of your throat (post nasal drip)?
Do you think that there is a relationship between your bad breath and stomach troubles?
Do you smoke? If so, how many per day and over how long a period? (pack/years)
Do you ever brush your tongue?
Do you use a tongue scraper?
Do you use a mouthwash? If so, what sort of mouthwash do you use?
Do you move away from other people because of your bad breath? If so what is the minimal distance that you are comfortable with?
Do you use sweets (e.g. mints or chewing gum) to disguise your bad breath?

Fig. 60-3 Halitosis questionnaire.

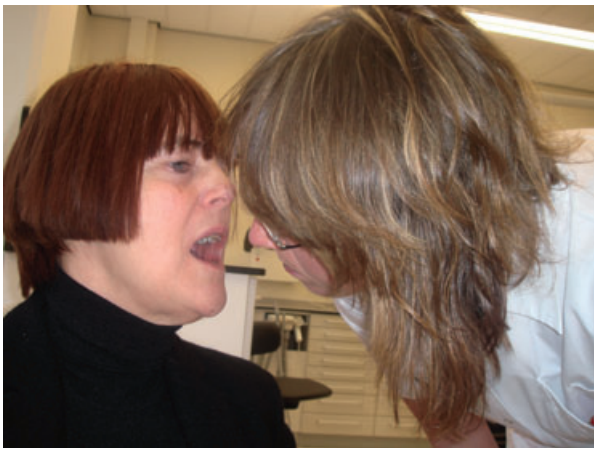


Fig. 60-4 Organoleptic scores. Examiner at 10 cm distance from patient.

Fig. 60-5 Halimeter™.

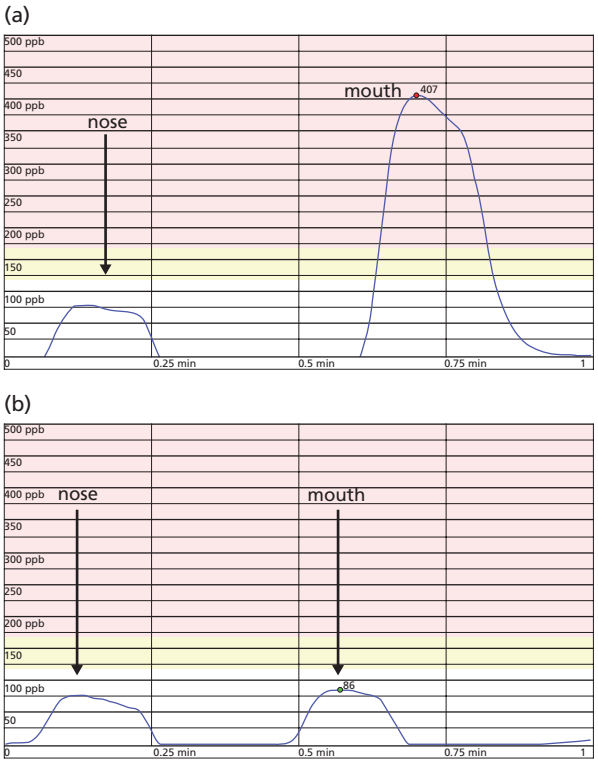


Fig. 60-6 (a) Halimeter computer readout from nose and mouth from patient with intraoral halitosis. (b) Halimeter computer readout from nose and mouth from patient with no halitosis, extraoral halitosis, or after successful therapy or with possible pseudo-halitosis or halitophobia.

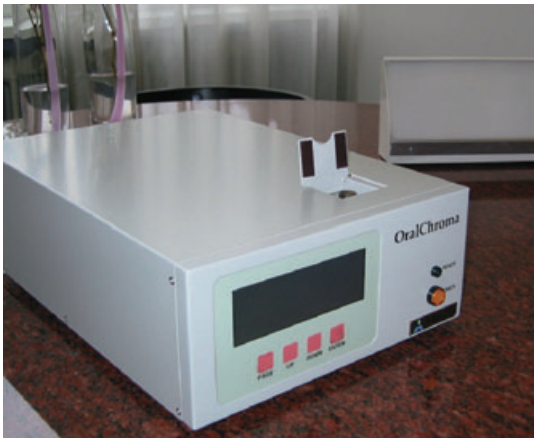
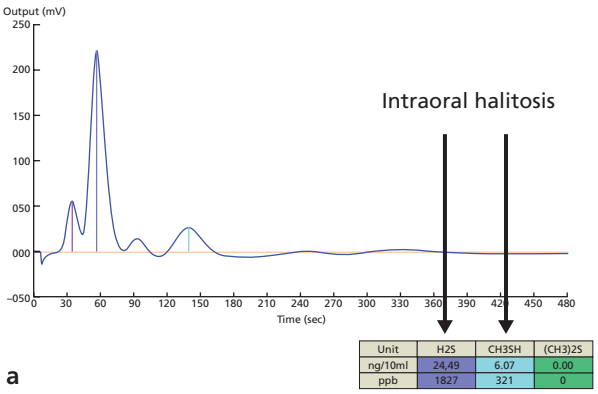


Fig. 60-7 OralChroma™ apparatus.



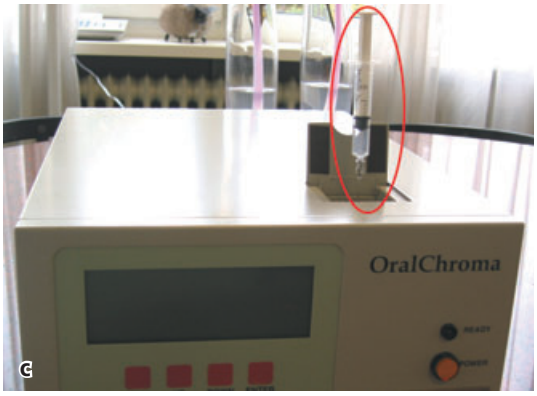


Fig. 60-8 (a) OralChroma graphic from patient with intraoral halitosis. (b) Syringe in mouth for air collection with OralChroma. (c) Syringe in OralChroma.

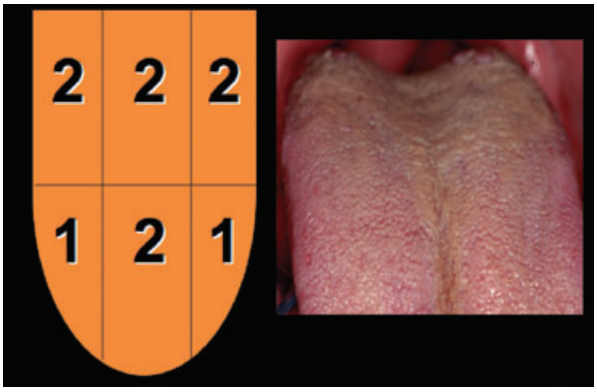


Fig. 60-9 Winkel Tongue Coating Index (WTCI).

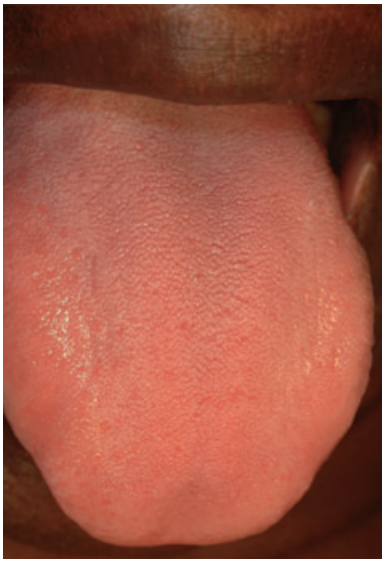


Fig. 60-10 Normal tongue (without coating).

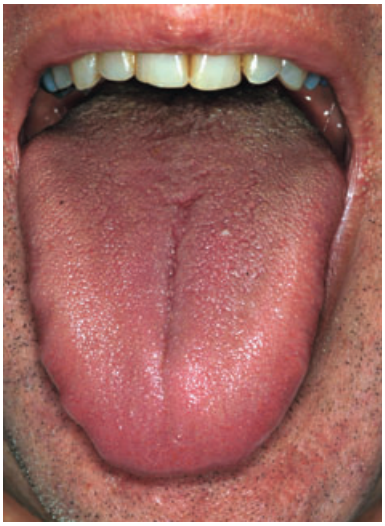


Fig. 60-11 Tongue with light tongue coating.

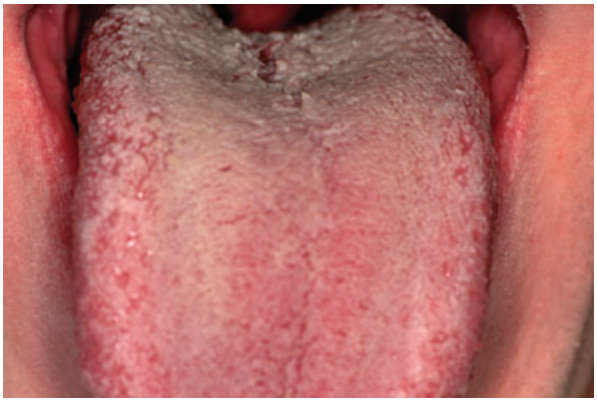


Fig. 60-12 Tongue with heavy tongue coating.

Classification of halitosis

In 1999, Miyazaki and co-workers classified halitosis as "*genuine*" *halitosis*, *pseudo-halitosis*, and *halitophobia* (see Fig. 60-1). One year later genuine halitosis was subclassified as *physiologic halitosis* or *pathologic halitosis*. In physiologic halitosis there is no apparent disease or pathologic condition, whereas pathologic halitosis occurs as a consequence of an infection of the oral tissues. *Pseudo-halitosis* is a condition in which halitosis is non-existent but the patients are convinced that they have halitosis. *Halitophobia* can occur when there is no physical or social confirmation to suggest that halitosis is present, which can persist after therapy for either genuine halitosis or pseudo-halitosis (Yaegaki & Coil 2000).

Temporary or transient halitosis is a term for a very common temporary condition caused by such things as oral dryness, hunger (ketosis), stress, eating certain foods such as garlic (Suarez *et al*. 1999) and onions, smoking, or poor oral hygiene. "*Morning bad breath*" is a common example of temporary halitosis and is attributed to physiologic causes, such as reduced salivary flow during sleep.

Therapy

Pseudo-halitosis and halitophobia

Pseudo-halitosis must be considered if halitosis cannot be detected organoleptically from the patient complaining of bad breath, if higher than normal VSCs cannot be demonstrated instrumentally and if the patient cannot provide reliable third-party verification (confidant) of an odor problem. If after treatment for genuine halitosis or pseudo-halitosis the patient still believes that he or she has halitosis, the diagnosis should be halitophobia (Yaegaki & Coil 2000) and the patient might be referred to a psychiatrist. The therapeutic recommendation is never to advise the patient to use certain products against halitosis, because the patient will think that this therapist has finally found something and the patient may be a constant problem in your practice. Patients with the experience of tonsilloliths also can develop a halitophobia. A tonsillolith, also called *tonsil stone* or *calculus of the tonsil*, is a calcified structure that develops in the tonsillar crypts (Fletcher & Blair 1988;

Tsuneishi *et al*. 2006). These deposits break away from the tonsils and are coughed up as small stones that have an unpleasant smell. Patients often wrongly assume that they have halitosis based on this experience.

Patients with pseudo-halitosis and halitophobia might be advised to visit a clinical psychologist. However, few of these patients are willing to follow this advice. Again, it is very important that such patients are not treated for halitosis because there are no benefits in this course of action.

Temporary halitosis

Temporary halitosis gradually disappears on its own by eating, by not smoking, and not using garlic, onions or spicy food.

Morning bad breath

Morning bad breath in healthy subjects is a cosmetic problem analogous to body malodor. Morning bad breath develops during sleep when the saliva flow rate and the oxygen availability are at their lowest, promoting anaerobic formation of VSCs. This would explain why halitosis is generally most severe upon arising in the morning.

To reduce morning bad breath one could advise the patient to use a tongue scraper in the evening before sleeping (Tonzetich & Ng 1976; Faveri *et al*. 2006). Mouth rinses (Roldan *et al*. 2003a) are also advocated to reduce morning bad breath (see below). After drinking and eating in the morning the halitosis will most likely disappear.

Extraoral halitosis

Nose and throat

Extraoral halitosis associated with respiratory problems, e.g. rhinitis, sinusitis, tonsillitis, pharyngitis or foreign bodies (unilateral), is characterized by bad breath arising from the nose and not or limited from the mouth, i.e. the organoleptic score for nose breath is higher than that for mouth breath. Halimeter and gas chromatographic scores are usually low. Chronic infection of the nasal cavity and paranasal sinuses leads to changes in the cleansing action of the respiratory epithelium, allowing bacterial overgrowth and stasis of the secretions to occur.

These patients should be sent to an ENT specialist. Post-nasal drip may also give rise to unpleasant odors but seems to be difficult to treat. Dental treatment such as root canal therapy and dental extractions may violate the maxillary sinus and cause infections necessitating further dental intervention.

Systemic conditions

Extraoral halitosis associated with pulmonary problems (blood-borne halitosis) is characterized by bad breath arising from both nose and the mouth, i.e. the organoleptic score for nose breath and mouth breath are about the same. The Halimeter readings are low in both cases because H_2S and MM are not present. Gas chromatography may show high dimethyl sulfide (DMS) values and low or zero H_2S and MM levels (Tangerman & Winkel 2007).

Table 60-5 Some drugs associated with halitosis

Tobacco
Alcohol
Chloral hydrate
Nitrites and nitrates
Dimethyl sulfoxide
Disulfiram
Cytotoxic agents
Phenothiazines
Amphetamines

Adapted from Porter & Scully (2006).

Medication

It is important to note that some medications for allergy and high blood pressure, antidepressants, and sinus medication can give rise to blood-borne halitosis (Table 60-5) (Porter & Scully 2006). Metabolites of many drugs have been found to be excreted via the lungs. A good example is disulfiram (Antabuse), a drug used in treating alcoholism, which is metabolized to carbon disulfide (Manolis 1983). Antineoplastic medications may indirectly contribute to halitosis due to mucosites, ulceration, and increased gingival inflammation. Some drugs may induce xerostomia (see below).

Trimethylaminuria: the fish malodor syndrome

The fish malodor syndrome, also known as the fish odor syndrome and trimethylaminuria, is a metabolic disorder characterized by the presence of abnormal amounts of dietary-derived trimethylamine, in the urine, sweat, expired air, and other bodily secretions. Trimethylamine itself has the powerful aroma of rotten fish, resulting in a highly objectionable body odor, which can be destructive to the personal, social, and work life of the affected individual. Therapy for this syndrome is limited. It appears that dietary management might be most effective in mild to moderate forms of fish odor syndrome but not in all cases (Mitchell 2005). Fortunately, cases of trimethylaminuria are very rare.

Treatment planning

Patients with these forms of extra-oral halitosis are referred to the appropriate specialist. Halitosis associated with medication need to be discussed with the patient's physician.

Intraoral halitosis

In a halitosis practice most patients (±90%) have intraoral halitosis (Delanghe *et al*. 1998; Seemann *et al*. 2006). Intraoral halitosis is characterized by a low or non-existant score for nose breath combined with a high organoleptic score for mouth breath. The Halimeter gives similar results. The gas chromatograph shows high levels of H_2S and MM and low levels of DMS. Occasionally, the levels of VSCs registered by the Halimeter are unusually low due to low levels of H_2S whilst the organoleptic scores are high. This is usually associated with halitosis with high levels of MM.

Pathologic halitosis

Periodontium

According to a majority of authors, halitosis is more closely associated with tongue coating than with the severity of periodontal disease (Tonzetich & Ng 1976; Bosy *et al*. 1994). Causes of halitosis such as periodontitis (Sulsur *et al*. 1939; Sato *et al*. 1980; Delanghe *et al*. 1998), pericoronitis, dry socket, necrotizing periodontitis, necrotizing ulcerative gingivitis (NUG), oral infection, and dental caries (Sulsur *et al*. 1939) should be treated accordingly by the dentist and/or periodontist.

Xerostomia

Xerostomia is defined as a subjective complaint of dry mouth that may result from a decrease in the production of saliva (Guggenheimer 2003). Studies have found this condition in approximately 20% of sampled populations (Nederfors 1997). There seems to be a strong correlation between medication (Table 60-6) and dry mouth (Guggenheimer 2003; Nederfors 1997). Dental caries is a major complication of xerostomia. Patients with symptoms associated with a dry mouth and/or medication require further investigation by the appropriate practitioner/specialist.

Table 60-6 Some drugs associated with xerostomia

Anticholinergic agents
Antidepressant agents
Antipsychotic agents
Diuretic agents
Antihypertensive agents
Sedative agents
Muscle relaxant agents
Analgesic agents
Antihistamines
Anticonvulsants
Anorexiants
Anti-incontinence agents
Antiparkinsonian agents
Smoking cessation

Adapted from Guggenheimer (2003).

Menstrual cycles

Elevated VSCs were found in mouth air during mid-cycle and around menstruation (Tonzetich *et al*. 1978; Queiroz 2002).

Stress

Stressful situations can be a predisposing factor for the increase of VSCs in mouth air, but the mechanism cannot be simply explained by the reduction of the salivary flow (Queiroz 2002).

Physiologic halitosis

Tongue coating

It has been shown that mechanical tongue cleaning has a significant reducing effect on the VSC levels in mouth air (Yaegaki & Sanada 1992a; Danser *et al*. 2003). Tongue scraping seems to be the most effective hygienic procedure to reduce morning bad breath in periodontally healthy subjects (Faveri *et al*. 2006), even more than interdental flossing. Tongue scrapers seem to be a little bit more effective than toothbrushes (Seemann *et al*. 2001; Outhouse *et al*. 2006). Cleaning the surface of the tongue with a hard toothbrush wetted with chlorhexidine also seems to be effective in reducing halitosis (Bosy *et al*. 1994; De Boever & Loesche 1995; Cicek *et al*. 2003).

Treatment planning

Tongue scraper

Mechanical cleansing is recommended in patients with tongue coating. Both tongue brushing (Gross *et al*. 1975) and tongue scraping (Fig. 60-13) have been advocated as a means of removing the tongue coating (Quirynen 2004). It is important to clean the back of the tongue as far as possible, because the posterior portion of the tongue is loaded with most coating. A recommended regime for patients with severe halito-

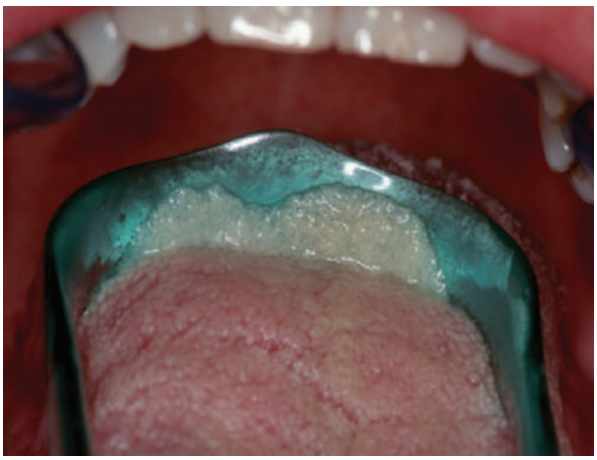


Fig. 60-13 Tongue scraping.

sis is to use five strokes of the tongue scraper twice a day. Care must be taken not to irreversibly damage the tongue. Tongue cleaning reduces the substrate for putrefaction (Gross *et al*. 1975; Quirynen 2004), rather than the bacterial load (Menon & Coykendall 1994; Quirynen 2004). Moreover, tongue scraping improved the taste sensation more than tongue brushing (Quirynen 2004).

Dentifrice

It was shown that brushing the dorso-posterior surface of the tongue with a dentifrice was more effective than brushing the teeth in reducing VSCs (Tonzetich & Ng 1976). In volunteers, dentifrices with triclosan have been shown to reduce organoleptic scores significantly (Gerlach *et al*. 1998; Niles *et al*. 1999; Sharma *et al*. 1999; Nogueira-Filho *et al*. 2002; Hu *et al*. 2003; Vazquez *et al*. 2003; Farrell *et al*. 2006). Also dentifrices with baking soda (Brunette *et al*. 1998), essential oils (Olshan *et al*. 2000), and stannous fluoride (Gerlach *et al*. 1998) seem to be effective. The delivery of an antimicrobial agent via a dentifrice may not be as efficient in reducing intraoral halitosis as the same agent delivered in a mouth rinse (Loesche & Kazor 2002).

Mouth rinses

In addition to tongue scraping, the use of mouth rinses has been advocated (Nachnani 1997; Roldan *et al*. 2003a). Active components in these rinses include antibacterial compounds such as: cetylpyridinium chloride (Yaegaki & Sanada 1992b; Rosenberg *et al*. 1992; Kozlovsky *et al*. 1996; Silwood *et al*. 2001; van Steenberghe *et al*. 2001; Borden *et al*. 2002; Quirynen *et al*. 2002a, 2005; Winkel *et al*. 2003; Carvalho *et al*. 2004; Roldan *et al*. 2004, 2005); chlorhexidine (Rosenberg *et al*. 1992; Bosy *et al*. 1994; De Boever & Loesche 1995; Quirynen *et al*. 1998, 2002a, 2005; van Steenberghe *et al*. 2001; Winkel *et al*. 2003; Roldan *et al*. 2003b, 2004, 2005; Carvalho *et al*. 2004); essential oils (Pitts *et al*. 1981, 1983; Rosenberg *et al*. 1992; Yaegaki & Sanada 1992b; Kozlovsky *et al*. 1996; Silwood *et al*. 2001; Borden *et al*. 2002; Carvalho *et al*. 2004); chlorine dioxide (Frascella *et al*. 1998, 2000; Silwood *et al*. 2001; Borden *et al*. 2002); metal ions, such as zinc lactate and zinc chloride (Schmidt & Tarbet 1978; van Steenberghe *et al*. 2001; Young *et al*. 2001; Borden *et al*. 2002; Quirynen *et al*. 2002a; Winkel *et al*. 2003; Codipilly *et al*. 2004; Roldan *et al*. 2004, 2005); triclosan (Carvalho *et al*. 2004); and hydrogen peroxide (Suarez *et al*. 2000). Most of these studies demonstrated that these products are effective in reducing oral malodor.

Despite the recommendations of the various manufacturers of these oral rinses, the efficacy of these products on intraoral halitosis is not clear. The main reason for this is that the duration and the number of controlled clinical trials is limited. The other problem with the studies which are available is that the patient groups in the studies are rarely patients with a definite diagnosis of intraoral halitosis. The mouth rinses are tested in students (Rosenberg *et al*. 1992; van Steenberghe *et al*. 2001; Quirynen *et al*. 2002a; Carvalho *et al*. 2004) and volunteers (Pitts *et al*. 1981, 1983; Yaegaki & Sanada 1992b; Kozlovsky *et al*. 1996; Suarez *et al*. 2000; Silwood *et al*. 2001; Borden *et al*. 2002; Codipilly *et al*. 2004; Roldan *et al*. 2004; Quirynen *et al*. 2005) without any complaints of halitosis. It is questionable if the results of these studies in "normal" patients and/or patients with Halimeter values within the normal range (80–110 ppb) are applicable for the treatment of patients with real halitosis. Only a limited amount of studies were performed in subjects with a complaint of "bad breath" or with high objectionable levels of VSCs. These are case report studies with 0.2% chlorhexidine (Bosy *et al*. 1994), 0.12% chlorhexidine (De Boever & Loesche 1995), and 0.05% chlorhexidine, 0.05% cetylpyridinium chloride and 0.14% zinc lactate (Roldan *et al*. 2005) with a 3-month follow-up. A dual centre, placebo-controlled, double-blind, randomized controlled clinical trial with 0.05% chlorhexidine, 0.05% cetylpyridinium chloride, and 0.14% zinc lactate was performed by Winkel *et al*. (2003) and Roldan *et al*. (2003). The mouth rinse used in this study (Halita) was specifically formulated to treat halitosis. This mouth rinse contains ingredients with low concentrations of the active components without alcohol and has therefore limited side effects for long-term use. The results indicated significant improvements in organoleptic and VSC scores in the test group.

Quirynen *et al*. (1998) found a reduction in organoleptic scores in periodontitis patients with and without complaints of oral halitosis, after scaling and root planing of all pockets within 24 hours together with the application of chlorhexidine. Despite the demonstrated efficacy of 0.2% and 0.12% chlorhexidine, long-term use of these solutions cannot be recommended because of the side effects (Gagari & Kabani 1995). Some of these adverse effects are lost taste and discoloration of the teeth and the tongue. More suitable agents are mouth rinses with low concentrations of active ingredients. Based on the double-blind placebo-controlled study (Winkel *et al*. 2003) a recommended regime for severe halitosis patients is gargling twice a day for 1 minute with 15 ml of Halita with the tongue out. By gargling, instead of rinsing, the cleansing agents can reach the dorsal surface of the back of the tongue.

Antibiotics

Currently, no research data are available about the use of antibiotics in patients with halitosis. In our clinic some patients with halitosis had used systemic antibiotics for other medical reasons. For a limited

Instructions for recall visit

In these instructions, subjects are asked **not** to:

1) consume food containing onions, garlic or hot spices for 48 hours before recall visit;
2) drink alcohol or smoke in the previous 12 hours;
3) use scented cosmetics or after-shave lotions on the morning of the recall visit.

Patient should perform oral hygiene, including tooth brushing, interdental and tongue cleaning, and use mouthrinses according to the treatment protocol.

Fig. 60-14 Instructions for recall visit.

time there was a reduction of intraoral halitosis but after a few weeks, halitosis recurred. A possible explanation is that patients with intraoral halitosis based on tongue coating have commensal bacteria (Van Winkelhoff & Winkel 1997), e.g. *Fusobacterium nucleatum*. These commensal bacteria are suppressed by the antibiotics for a short period of time but re-colonize up to a normal level after some weeks.

Use of a confidant

Previous research has demonstrated that patients with halitosis are generally unable to rate the intensity of their own halitosis (Rosenberg *et al*. 1995). Therefore, patients cannot reliably assess the effectiveness of the prescribed therapy. The recommended course of action is to ask them to use another person as a confidant. A confidant could be a spouse, a family member or close friend, who is willing to smell the patient's breath and provide straightforward feedback.

Adjustment of therapy

All patients with the diagnosis of intraoral halitosis should come back for a recall visit and adjustment of therapy (Fig. 60-14). At the first visit, patients are seen in the "worst" condition to make a proper diagnosis. At the re-examination patients are asked to present themselves in the "best" condition, meaning proper oral hygiene and correctly following the advised treatment protocol for patients with halitosis. The purpose of the recall visit is to adjust the therapy based on the results of this re-examination. Organoleptic scores, measurement with the sulphide monitor and gas chromatography are performed. The first question to the patient is: "Did the therapy work?" Although, most of the time the therapy for intraoral halitosis is very successful, some patients will answer "No". The reason is that most of these patients still have a bad taste and think that the presence of a bad taste means that they have a bad breath, which is not necessarily the case. A confidant is of paramount importance for this group of patients. Another important question is about the "comfort range". The result is compared with the comfort range from the first examination. If the comfort range is the same and the halitosis is well treated, the patient could develop halitophobia and needs to seek professional help.

Future perspectives

In a preliminary study, Burton *et al*. (2005) showed that replacement of bacteria implicated in halitosis by colonization with competitive bacteria (probiotica) such as *S. salivarius* may provide an effective strategy to reduce the severity of halitosis.

Conclusions

Social relationships are one of the pillars of the quality of life (Elias & Ferriani 2006). In that respect, halitosis can be a crippling social problem and therefore needs to be considered a serious problem. Extraoral halitosis might be a manifestation of a serious disease. It is of paramount importance to differentiate between extra- and intraoral halitosis.

Although there is an effective treatment of intraoral halitosis, many physicians, dentists, and dental hygienists do not recognize intraoral halitosis as a manageable condition. Since in most of the cases of halitosis the oral cavity is *the place of origin*, health professionals in medicine and dentistry should be knowledgeable about diagnosis and therapy of this disorder. In most cases intraoral halitosis can be treated by tongue scraping and the use of chemical solutions with low concentrations of zinc ions, chlorhexidine, and cetylpyridinium chloride. The dental hygienist, dentist, and periodontist are the most appropriate professionals to diagnose and to treat this condition.

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