David Gillam
Editor

Dentine Hypersensitivity

Advances in Diagnosis, Management, and Treatment

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Foreword

Dentine hypersensitivity has gained increasing interest in recent years due to a number of reasons. For example, the success of caries prevention programs and improved periodontal treatment modalities are factors considered to be responsible for an increased number of patients of all ages with more natural teeth in their mouths than in the past. And these patients apparently suffer more frequently from what they call "sensitive teeth" (dentine hypersensitivity) mainly after exposure to cold and sweet drinks/food or to tactile stimuli. The quality of life of these patients is markedly compromised, and they may ask for pain relief from the clinician.

This is a challenge for both the dental clinician and the dental scientific community. It is reflected, for example, in a constantly increasing number of publications in the scientific literature, of scientific workshops, and of continuing education courses over the recent two decades on the topic.

It is known that patients with dentine hypersensitivity also exhibit gingival recession, sometimes as a sequela of periodontal treatment. They also experience the loss of enamel, e.g., due to the increased consumption of erosive drinks and other acidic food products, extensive tooth brushing with abrasives in the toothpaste, or other factors. This may lead to exposed dentine surfaces, which are a prerequisite for dentine hypersensitivity. However, it should be noted that not all exposed dentine surfaces lead to dentine hypersensitivity.

Further light on the topic was provided by the introduction of the hydrodynamic theory as first proposed by Gysi around 1900 and then further elaborated by Martin Brännström in the middle of the last century. The open dentine tubules on the exposed dentine surface have been considered essential for the fluid shifts in the dentine tubules following thermal, osmotic, or other stimulation subsequently activating mechanoreceptors at the nerve endings associated with the odontoblast processes close to the pulp.

However, not all phenomena can be satisfactorily explained by this theory. For instance, the role of pulp inflammation, tertiary dentine formation, nerve transduction, occlusal stress responsible for cervical abfractions, and periodontal involvement is still being discussed in this context. Thus further research on dentine hypersensitivity needs a multidisciplinary approach involving the classical discipline of operative dentistry but also periodontology, endodontics including pulp biology, immunology, occlusal stress, and the essential aspects of prevention of the condition.

Manufacturers of cosmetics (e.g., toothpaste and mouth rinse products) and dental materials (e.g., dentine adhesives and desensitizing products) quickly responded to the needs of both patients and the profession by the introduction into the consumer market of a large number of products for the treatment of dentine hypersensitivity. Different approaches to reduce dentine hypersensitivity have been developed; most of these products are based on the concept of covering/obturating the tubule openings on the exposed dentine surface. Both the potential effectiveness and clinical efficacy have often been demonstrated by in vitro studies and (mainly) short-term clinical trials, respectively. Again, a number of problems have arisen, for example, the clinical relevance of the in vitro tests used in this context, the mainly limited efficacy of these treatments with the need of constant application, the lack of pain relief in certain cases, or the question of possible pulp damage induced by certain therapies.

Dentine hypersensitivity is a challenge and this book addresses the challenges posed by the condition. Here, all aspects of dentine hypersensitivity are comprehensively covered. The array of topics ranges from the basic research on the aetiology over to the treatment modalities and finally to the preventive aspects including patient communication, motivation, and compliance. A group of well-known authors from both clinical and laboratory research under the wise guidance of David Gillam have not only provided a compilation of the relevant evidence from the published literature but also critically pinpointed the weaknesses of the presently available information and the missing gaps in our understanding of dentine hypersensitivity.

Finally, interesting ideas for the formulation of new products and an innovative design of future studies are presented. Reading this book is certainly a gain not only for researchers but also for the clinician.

Regensburg, Germany Gottfried Schmalz

Acknowledgment

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Introduction and Overview: Statement of the Problem

1

Martin Addy

Aim and Objective

It is more than three decades since dentine hypersensitivity (DH) was described as "an enigma being frequently encountered but ill-understood" (Johnson et al. 1982). Since this time, the "three Rs" of research, writing and review have, considerably but not completely, improved the understanding of DH. A number of surveys in several countries would appear to conclude that DH remains ill-understood by a considerable proportion of dental healthcare professionals (Canadian Advisory Board on Dentine Hypersensitivity 2003; Rao et al. 2010). With respect, it would not seem unreasonable or derogatory to suggest that the topic of DH has received limited attention in both dental undergraduate and postgraduate curricula. Also it would appear that the plethora of literature on the subject, which has grown enormously over relatively recent years, has been read by a minority of dental professionals. The overall aim of this book must be, therefore, to address this imbalance in the understanding of the problem. Specifically using question-based section headings, the aim of this first chapter is to provide a brief overview of DH including current concepts of the condition and possible future innovations in diagnosis, management and treatment. The objective of this chapter, therefore is to provide a basis for the Authors in the subsequent chapters to detail the specific aspects of the diagnosis, management and treatment of DH.

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How Common Is Dentine Hypersensitivity?

There have been a number of surveys of the prevalence and distribution of DH in a variety of subject groups (for reviews, see Addy 2000, 2002; West 2006) (Chap. 3), but whether these surveys used selection protocols based on classical population epidemiological studies is open to question. Indeed, some of these surveys were only from patients attending dental practices or hospitals, some were based on question and answer surveys only and several predated the now agreed definition of the condition and may have included subjects that would be excluded by the said definition. One frequently quoted study was published only as an abstract (Graf and Galasse 1977). However, the average percentage prevalence across studies spanning nearly 35 years that used a dental inspection would suggest that 15 % of adults suffer from DH from one or more teeth at any one time, although much lower, 3 %, and much higher, >50 %, prevalence figures have also been published (for review, see West 2006). A recent review on the burden of DH by Cunhan-Cruz and Wataha (2014) from the published studies would appear to suggest that the best estimate of the prevalence of DH is 10 % with an average of

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33 % across the studies. Despite the fact that DH can be diagnosed in individuals at the extremes of age, teenagers to octogenarians, most commonly it appears to afflict young people between 20 and 40 years old. Females have been reported to be more commonly affected than males and at a younger mean age but not all data reached statistical significance. Available distribution data mostly indicate four features of DH: Canines and first premolars, then incisors and second premolars and finally molars is the order of teeth most commonly affected; left-sided teeth are more frequently afflicted than their right-sided, contralateral counterparts; the site of predilection by far is the buccal cervical region; lesions show little or no plaque (Addy et al. 1987; Fischer et al. 1992).

What is largely missing from the prevalence and distribution data are the numbers of teeth affected and the range of pain scores experienced per individual. This lack of information makes difficult an accurate judgement of how DH impacts on the quality of life of sufferers (see Chap. 9). Thus, although DH is stated to be a common painful condition of the teeth, do 15 % of all populations in developed countries visit the dentist at any one time to report suffering from the condition? Unlikely! Indeed, do 15 % of adults who regularly attend the dentist report voluntarily as suffering from DH? Also, most unlikely! Furthermore, over many years, authors have reported DH to be cyclical, which suggests that lesions "self-heal" through tubule occlusion and then restart by tubule exposure: Is this really the case? Possibly, but other explanations are available, including seasonal variation in aetiological factors and stimuli, stimuli avoidance tactics by sufferers and periodic self-medication with home use desensitising products. All of these would preclude the need for professional intervention. At this early stage of the present chapter, it is apparent that there are important gaps in our knowledge of DH. In summary, prevalence and distribution data associates DH more commonly with younger adults, specific teeth, tooth sides and sites, good oral hygiene and possibly females. Such information must beg the question: Are these associations indicative and even supportive of present-day thoughts on the aetiology of DH? Probably!

Definition and Terminology: Hypersensitivity or Sensitivity?

At an international meeting, DH was defined as: short sharp pain arising from exposed dentine in response to stimuli, typically thermal, evaporative, tactile, osmotic or chemical, and which cannot be ascribed to any other form of dental defect or pathology ('pathology' was subsequently changed to 'disease') (Holland et al. 1997, Canadian Consensus Document 2003). Essentially, the definition is a clinical descriptor of DH as a specific dental condition which needs to be distinguished from other causes of dental pain and calls out for a diagnosis of DH by exclusion (for reviews, see West 2006; Addy and Smith 2010). Moreover, the definition is recommending the continued use of the term DH, perhaps if only because of long-time common usage. This, however, does not end the long-running debate over the accuracy of the term and the conclusion of many authors that the exposed dentine is merely sensitive and therefore lesions should be termed dentine sensitivity. Whilst for many years being sympathetic even supportive of this view, the present author, clearly playing with the semantics of the definition, would like to put forward a counterargument in favour of the term DH. Available evidence indicates that lesions of DH have many more and wider dentine tubules open at the dentine surface and patent to the pulp than nonsensitive dentine (Ishikawa 1969; Absi et al. 1987). According to Poiseuille's law, the potential for fluid flow is therefore increased exponentially in DH lesions. Thus, the affected tooth may be "sensitive" but the exposed dentine is hyper-reactive to appropriate stimuli and thereby "hypersensitive". One condition, within the spectrum of those causing dentine pain, that should be discussed separately is root sensitivity (RS), not least because, until the publication of the definition of DH, it was considered to be the same as DH. The European Federation of Periodontology recommended the term RS to describe short sharp pain from exposed dentine of periodontally involved teeth or following periodontal treatments (Sanz and Addy 2002). Three points need to be made in support of the term: Periodontally involved teeth do not fit the definition of DH; available figures put

the prevalence of RS very much higher than DH (Chabanski et al. 1996); and deep bacterial invasion of the dentine tubules has been reported in periodontally involved teeth (Adriaens et al. 1988) and thus far not in true DH.

Mechanism of Dentine Sensitivity: Does It Apply to Dentine Hypersensitivity?

Three hypotheses have been proposed to explain the sensitivity of dentine: nerves extending to the outer end of the dentine tubules, odontoblast transducer mechanism, and hydrodynamic mechanism. Significant evidence against the first two hypotheses is available but will not be propounded upon further (for reviews, see Pashley 1990; Addy and Smith 2010) (see Chap. 2). Based upon the knowledge that fluid flows outward from the pulp along dentine tubules, Gysi in 1900 proposed the hypothesis of a hydrodynamic mechanism explaining dentine sensitivity. Unfortunately, there was a wait of more than 60 years before the eloquent experiments of Brannstrom and co-workers provided evidence to turn the hypothesis into a theory (for review, see Brannstrom 1963, 1966). Essentially, the hydrodynamic theory of dentine sensitivity postulated that stimuli applied to exposed dentine, such as those listed in the definition of DH, caused an increase in fluid flow in the dentine tubules, the resulting pressure change triggering a mechanoreceptor response in A-beta and A-delta nerve fibres in and around the pulp dentine border. All stimuli applied to dentine were reported to cause an increased outward flow of fluid except heat where there was inward flow. Interestingly, when fluid flow in tubes is increased, a pressure-related streaming potential is triggered suggesting that stimulation of pulp nerves could also be electrical (Anderson and Matthews 1967; Griffiths et al. 1993). For the hydrodynamic theory to apply to DH, lesions would have to exhibit open tubules at the dentine surface and patent to the pulp. Evidence, alluded to already, indeed supports that this is the case. Furthermore, the extensive work of Pashley and co-workers into dentine permeability, including the development and use of the dentine fluid flow cell, provided strong support for a hydrodynamic mechanism explaining the pain mechanism in DH (for reviews, see Pashley 1990, 1992) (Chap. 2). Of note and over the last two to three decades, the flow cell model demonstrated that some DH treatments reduced fluid flow across dentine (Greenhill and Pashley 1981). More recently, albeit indirectly, treatments known to block the dentine tubules in vitro and in situ have been proven to be effective in DH (for review, see Addy and West 2013) (Chaps. 6 and 8).

Aetiology of Dentine Hypersensitivity: Are Lesion Localisation and Initiation Tooth (and Gingival) Wear Phenomena?

The preceding sections indicate that for DH to occur, at any site on a tooth, dentine has to be exposed (lesion localisation) and the tubule system opened (lesion initiation). Evidence concerning the aetiology of these two distinct but interrelated processes unfortunately has been drawn at best from studies in vitro and in situ and epidemiologically derived associations and at worst case reports and clinical anecdote. As no classical randomised controlled trials (RCTs) exist, proving cause and effect, available data are circumstantial albeit quite compelling. Chapter 4 will consider the aetiology in detail and a list of relevant reviews can be found in Addy and Smith (2010), so here, only the salient points will be discussed.

Lesion localisation through dentine exposure can occur by loss of enamel and/or gingival recession (with loss of cementum). Loss of enamel, outside acute trauma, is a tooth wear process involving attrition, abrasion and erosion alone or more usually in combination. Abfraction (cervical tensile stress) has been hypothesised to predispose cervical enamel to abrasion and/or erosion, but opinion is divided (for review, see Grippo 1991). Numerous publications, including a conference report (Addy et al. 2000) and a monograph (Lussi 2006), have considered these wear processes and in particular the combination

of abrasion and erosion acting at buccal cervical tooth surfaces (for review, see Addy and Shellis 2006). There seems to be little doubt that erosion is a major factor in enamel loss, causing dissolution and demineralisation (softening) of this tissue. The most common source of the acid being extrinsic and dietary in nature rather than from an intrinsic source; namely gastric acid. Extensive data, drawn from developed nations, also "implicate" tooth brushing with toothpaste as the main abrasive cause of enamel loss, particularly at buccal cervical areas. Given the resistance of enamel to tooth brushing abrasion, it is further theorised that enamel loss from tooth brushing arises from the abrasion of enamel softened by erosion. Data suggest additive even synergistic effects of the two wear processes (for review, see Addy and Shellis 2006).

Exposure of dentine by gingival recession can be usefully classified as "unhealthy" or "healthy". The aetiology of the former is quite well understood, whereas the latter is poorly explained and as with DH has been described as an enigma (Smith 1997). As dentine exposure, through unhealthy gingival recession, falls outside the definition of DH and is more relevant to RS, it will not be considered further. Reviews on healthy gingival recession using clinical anecdotes, case reports and epidemiological data cite chronic trauma, particularly tooth brushing, as the major aetiological factor (Watson 1984; Smith 1997; Addy and Hunter 2003) (see Chap. 4). RCTs of tooth brushing and "gingival recession" have been conducted but have concentrated only on recording gingival damage (lacerations or excoriations) by different toothbrush characteristics and have been of insufficient duration to measure recession. Interestingly, even surprisingly, the role of toothpaste in gingival damage or recession has rarely been discussed, particularly since toothpaste rather than toothbrushes produces the most wear to dentine. It is probable that exposure of dentine at the buccal cervical area of teeth more commonly occurs through gingival recession than enamel loss, but it has not been studied; indeed, differentiating between the two processes could prove difficult.

Lesion initiation to open the dentine tubule system has mainly been investigated by studies in vitro and in situ. Scanning electron microscopic examination of extracted teeth or replicas reveals that nonsensitive dentine has few if any open tubules at the dentine surface, whereas, and alluded to already, sensitive dentine has large numbers of open tubules (Absi et al. 1987). Assuming, with some degree of caution, that tubules in nonsensitive dentine are covered by a "smear layer" made up of collagen and hydroxyapatite (Pashley 1984), to initiate DH, such a layer has to be removed. Available topographical studies reveal that artificially induced smear layers are very acid labile, thereby implicating again erosion as a major aetiological factor in DH (Absi et al. 1992). Abrasion of dentine as an initiating factor in DH, mainly but not exclusively, has been concerned with the effects of toothbrushes and toothpaste on dentine. Toothbrushes alone are very slow to remove a smear layer and therefore have been discounted as initiating factors; nevertheless brushes, used after an acid challenge, readily open tubules (Absi et al. 1992). Tooth brushing with toothpaste, considered the most common oral hygiene practice in developed countries (Frandsen 1986), has been studied extensively for abrasive effects on the dentine including the propensity to open dentine tubules. The findings are not consistent but appear to depend on the toothpaste formulation. Most toothpaste formulations appear to remove the smear layer and body dentine by an interaction of their abrasive and detergent systems (Moore and Addy 2005). With some toothpaste products however, the loss of the smear layer is followed by tubule occlusion with abrasive particles and/or specific ingredients formulated for such a purpose: Chaps. 6 and 8 will discuss such effects under treatment options for DH. As with brushes alone, erosion appears to promote abrasive effects of toothpaste and also can detach or dissolve some tubule-occluding compounds. In conclusion, is DH a tooth and gingival wear phenomenon? Almost certainly, yes (for review, see Addy 2005)!

Management Strategies for Dentine Hypersensitivity: Logical or Biological?

For decades it has been appreciated that in the condition known as DH, dentine is exposed, usually at the buccal cervical area of teeth. For more than 40 years, it also has been known that tubules are open at such sites. Such pieces of knowledge led to a management strategy that was almost entirely treatment orientated, with formulations being developed to cover the exposed dentine and/or block the tubules. This approach is clearly logical but hardly biological as it does not take into account the aetiology of DH, not unlike the past approach to the management of caries. Two main issues arise with this logical management approach: firstly, the lack of primary and, more particularly, secondary prevention for the condition and, secondly and related, the development of treatments to withstand aetiological impacts. The present-day knowledge of the aetiology of DH, outlined in the previous section, strongly implies that management should have a biological basis with prevention at the core (for review, see Addy and West 2013) (see Chap. 10).

Primary prevention of DH would of course be ideal but at this time is a utopian goal. The removal or limitation of erosive and abrasive factors to prevent exposure of dentine and dentine tubules is made difficult by the fact that this would impact particularly on common if not recommended dietary and oral hygiene practices. Also to date, no agent has been discovered which provides significant protection against erosion of enamel and more particularly dentine that could be used as a dental public health measure (for review, see Ganns et al. 2013). Modification of the erosive potential of beverages has been achieved, but such products are not widely available (for review, see Lussi and Jaeggi 2006). Nevertheless, dental professionals should continue to advise moderation to limit any further erosive/abrasive loss of enamel and abrasive gingival recession and should also be on the lookout for early signs of these conditions. The nature of such professional advice and recommendation has been reviewed (West 2006; Addy and West 2013) and will be considered in Chaps. 4 and 10. In essence, such advice appears sensible rather than scientific as it has yet to be subjected to the rigours of RCTs. In particular, bar anecdotal reports, no information is available to indicate whether such advice motivates a change in behaviour to limit aetiological impacts. Nevertheless, such recommendations are also relevant to the secondary prevention of DH and dovetail well with the treatment planning approach recommended for the condition which can be found in several reviews (Orchardson 2000; West 2006; Addy and Smith 2010; Addy and West 2013) and in Chap. 10. In particular, the treatment plan must include: diagnosis based on the definition, the exclusion and/or management of other causes of dentine pain and identification of aetiological and predisposing factors (see Chaps. 4 and 5).

Treatments for Dentine Hypersensitivity: Are They Proven and Do They Resist Aetiological Insults?

On the one hand, as already alluded to, the logical approach to manage DH is to treat the dentine with an agent that coats the surface and blocks the tubules, thereby stopping the hydrodynamic mechanism; *quod erat demonstrandum*! The biological approach, outlined in the above reviews and on Chaps. 6 and 8, on the other hand, is to first put in place a recommended secondary preventive-based treatment plan to avoid recurrence, where treatment is the last item in the plan (see Chap. 10). Over the past decades, numerous agents and formulations have been used in the treatment of DH. Indeed, the number, range and diversity in apparently effective treatments put DH on a par with treatments for haemorrhoids, with one early review suggesting that some DH clinical studies "belonged in the realms of testimonials" (Addy and Dowell 1983) (see Chap. 8). Of course, it is only in recent decades, as in most if not all branches of medicine and dentistry, that treatments for DH have been tested in RCTs, which conform to the principles of good clinical practice (GCP), large subject areas with texts in

their own right (Holland et al. 1997; International Conference on the Harmonisation for Good Clinical Practice) (see Chap. 7).

At this juncture, however, it is worth raising several issues in respect of "proving" the efficacy of treatments for DH. First and foremost must be the need for caution in extrapolating data drawn from studies in vitro and in situ to outcome in vivo, a problem appreciated many years ago for chemical plaque control agents (for review, see Addy and Moran 2007). Thus, DH studies in vitro and in situ can be supportive, even explanatory, of the results from the RCTs but cannot be taken in isolation. Second, the question must be asked, how close to real life are the testing methods or stimuli used in DH RCTs? This will be discussed in Chap. 7, but clearly some are not, and electrical stimulators based on electrical pulp testers rather stand out! This probably explains why at least two different types of stimuli were recommended for use in DH RCTs (Holland et al. 1997). Third, study outcomes are based almost entirely on statistically significant improvement of the test formulation over control and rarely if ever on numbers of subjects with complete pain relief, raising the difficult question of statistical versus clinical significance. Finally, one pertinent point, relevant to RCTs in DH specifically and painful conditions in general, is the confounding influence of regression to the mode and the placebo response creating considerable improvement in symptoms in the control group: reductions of 40 % having been cited (for reviews, see Curro et al. 2000; West 2006; Addy and West 2013) (see Chap. 7).

Other chapters will consider treatments for DH and only a brief overview will be given here (see Chaps. 8 and 10). Essentially, treatments can be classified by mode of delivery and action. Thus, delivery can be "professional or in-office" or "over the counter or home use", whereas action is either "interruption of pulp nerve response" or "tubule occlusion". There is some overlap in the classifications, as the majority of professionally delivered treatments aim to occlude the dentine tubules, whereas most formulations to interrupt the pulp nerves are home use products. Of course, professional interruption of the pulp nerve response can be achieved through endodontic or extraction procedures, but except in the rare variant of DH where irreversible pulp inflammation is present (Dachi 1965), these approaches are not considered as valid treatment options.

Tubule occlusion using many in-office treatments has been "proven" to occur by clinical observation and by studies in vitro and in situ (for reviews, see Orchardson and Gillam 2006; Pashley 2000; West 2006). Unfortunately, the resistance of the deposited material to aetiological agents, notably abrasion and/or erosion, is rarely tested, and certainly some deposits are very acid labile. Also, given the number of very varied in-office treatments, relatively few have been tested in RCTs. Perhaps, with the exception of in-office treatments which deposit a coating visible to the naked eye, such as adhesive restorative materials, this lack of information makes difficult the recommendations for their use in the management programme for DH. Certainly, there is a great deal of professional anecdote and opinion on their use including efficacy, when to use in the overall treatment plan and frequency of reapplication.

Home use treatments typically use toothpaste as the vehicle, although some mouth rinse formulations are available: Here only toothpaste will be discussed. The "actives" in such products either interrupt the pulp nerve response or occlude the tubules. Various potassium salts have been incorporated into toothpaste to interrupt the pulp nerve response, and many products exist, but few manufacturers have subjected their formulations to RCT and "generic" products appear to "piggyback" any claims of efficacy. This said, there are conflicting scientific opinions and data for the efficacy of potassium toothpaste in DH, which has been reviewed and summarised under "for" and "against" headings and a conclusion of "unproven with the caveat of this not translating to ineffective" (for review, see Addy and West 2013). One rather compelling physiological argument revolves around whether the very water-labile potassium ion can actually pass through dentine fluid in vivo when delivered over the relatively short period of tooth brushing times. If indeed, however, potassium is an effective treatment, one hypothesis propounded by Addy and West (2013)

is the absorption of potassium into the body of the dentine eventually forming a depot at the pulp dentine border, such a proposal would fit with the apparent delayed therapeutic time scale.

Toothpaste formulated to occlude the dentine tubules contain a considerable array of agents and compounds. Here only those for which there are compelling data from RCTs, often supported by studies in vitro and/or in situ, will be elaborated upon (for review, see Addy and West 2013) (see Chaps. 6 and 8).

Strontium chloride and later acetate-containing toothpaste formulations have been available for decades and the product name was perhaps the most well known to dental professionals and lay public. That the strontium ion actually occludes tubules has been questioned, since drawing proof from an autoradiographic study (Kun 1976) is of course flawed and scanning electron microscopy failed to show occlusion (Addy and Dowell 1986). Nevertheless, for those products which formulated the strontium salt with artificial silica abrasive and nonionic detergent systems, tubule occlusion was seen in vitro and in situ: the deposit was largely silica and insoluble in water and mean resistant to dietary acid. Clinical studies have been largely supportive and certainly not negative for efficacy against controls. Interestingly, for many years based on studies in vitro, the present author has recommended not only brushing with these Sr/Si products but topical application with a finger, a regimen recently reinvented by the same manufacturer and others for tubule-occluding toothpaste technologies.

Arginine/calcium carbonate toothpaste has been shown effective in DH, producing a tubule-occluding deposit made up largely of calcium and phosphate (Addy and West 2013; Yan et al. 2013; West and Davies 2014). This deposit as would be expected is soluble in dietary acid however, given the recommended twice daily (and topical) use may not be a factor as any dissolved deposit would be replaced.

Stannous fluoride (chloride) solutions, gels and toothpaste have all been shown to occlude tubules with a stannous containing deposit which is relatively acid resistant (West and Davies 2014). Clinical studies have shown that this effect translates into efficacy.

Calcium sodium phosphosilicate anhydrous toothpaste has also been shown effective in the treatment of DH (West and Davies 2014). As with the previous agents incorporated into toothpaste, studies in vitro show tubule occlusion by calcium, phosphate and silica, together with titanium when the formulation includes titanium dioxide: the deposit appears water and acid resistant (see Chaps. 6 and 11).

The available data on all products that claim to block the dentine tubules is quite compelling even though recent systematic reviews have reported a lack of homogeneity in some of the published clinical studies (Karim and Gillam 2013; Talioti et al. 2014). Nevertheless, this gives the profession choices in recommending a number of toothpaste products as first-line treatments for this common painful condition. All contain a fluoride source, and therefore, users are not disadvantaged in the preventive properties of this ion. Moreover, the promotional material of the manufacturers has provided the profession, even the public, with additional useful education on DH.

What Is Missing in Our Knowledge and Understanding of Dentine Hypersensitivity: A Personal Wish List?

It is probably not unreasonable at this time to promote DH from an enigmatic to a moderately well-understood condition, particularly in respect of aetiology. This said, however, if erosion/abrasion action is involved in the loss of enamel and opening of the dentine tubules, future epidemiological studies usefully could include dietary, tooth brushing and plaque data. Such data could also be drawn from subjects, with and without DH, matched for age, gender and dentine exposure. Protocols for RCTs involving modification of diet and/or oral hygiene practices in an attempt to cause or reduce DH could be devised but are likely to be lengthy and some may skirt close to ethical boundaries.

A wish list, for future research to help further understanding of DH, would include:

1. "Healthy" gingival recession: This very common condition, most frequently seen at buccal

cervical surfaces of teeth, is for many people an aesthetic problem, and potentially the associated exposed dentine can become sensitive. Indeed, a number of "plastic surgical, periodontal procedures" have been developed to deal with the problem (see Chaps. 8 and 10). Yet so little is known about the aetiology and pathogenesis of the condition, and it remains the "poor relation" in respect of dental research. Epidemiological associations, already referred to, implicate tooth brushing as a major causal factor. Perhaps now is the time to try and turn an association into cause and effect, using RCTs. Unfortunately, this author recognises that the time scale and difficulties of such clinical studies would be quite different from those, which, for example, turned the strong association of plaque to gingivitis (Ash et al. 1964) into proof of causation (Loe et al. 1965); protocols for such studies would be gratefully received!

2. Tooth wear: The research interest in this subject area recently has been large and continues to be so. Reviews have identified the historical switch in the main dietary aetiological interactions formally from abrasion/attrition to more recently abrasion/erosion (for review, see Addy and Shellis 2006). Whilst, the monograph entitled *Dental Erosion* (Lussi 2006), soon to have a second edition published, suggests a good understanding of tooth wear processes and their interactions and subsequent management of the worn dentition, however any primary prevention at a public health level appears to be a needed yet distant goal.
3. Treatment effects: Whilst studies in vitro and in situ can show the morphological changes that occur when treatments are applied to dentine with open tubules, it is not necessarily safe to assume that the same happens in vivo; further discussion occurs in the final section of this chapter (see also Chaps. 6 and 11).
4. Management strategies: As alluded to earlier, management strategies for DH have been proposed and are based on biological rather than logical principles but have not been subjected to scientific testing; such evaluation would be perfect!

The above wish list for future research includes the use of RCTs to a greater or lesser degree. Such trials in DH are notoriously difficult with many potential problems. A short second wish list for methods that might overcome some of the problems is as follows:

1. Visualise the dentine surface and tubules: This would aid with diagnosis, treatment effects and possibly even grading severity (tubule numbers and diameters). To some degree, this wish has been granted by using studies in situ and replicas. The former thus far has not modelled for fluid flow in tubules and the latter, from experience, is exacting, clinically difficult and, with respect to those who have tried, clinician sensitive; both methods are also very time consuming and need SEM facilities. Clinical magnification instruments would be ideal but need to visualise structures of less than one micron; could SEM be used in the clinic?
2. Objective criteria for clinical trials: Two main changes can occur when DH is treated by tubule occlusion agents, namely: 1) a reduction in fluid flow in tubules and 2) a reduction in subjective pain scores. To date neither change has so far been measured objectively. Theoretically, a change in fluid flow could be indirectly assessed by measuring the capacitance or impedance of dentine from the exposed surface. Similarly and hypothetically, pain caused by stimuli applied to sensitive dentine could be measured as a central response in the brain using, for example, an electroencephalogram. Also what about lie-detector equipment?

Are these wish lists achievable or just science fiction, even fairy tales? Only time will tell!

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The Physiological Basis of Dentin Hypersensitivity

2

Kenneth Markowitz and David Pashley

Introduction

For over 100 years, dentists have known that enamel is not sensitive to drilling. However, as soon as a bur passes through the dentinoenamel junction (DEJ), patients immediately experience a sharp, well-localized pain. It was clear to dentists and histologists that the dentinoenamel junction represented a boundary between a secreted tissue (the enamel) and dentin, a living tissue possessing the intrinsic biological property of irritability (Verworn 1913). This property of dentin could be readily explained if pulpal nerve fibers extended from pulpal soft tissues and passed through the dentin tubules to the DEJ junction. Histological studies, however, failed to conclusively reveal the presence of nerves in the sensitive, outer portion of the dentin. When present, nerves in the dentin are restricted to the inner half of the tissue, close to the densely innervated dental pulp (Fig. 2.1a) (Byers 1984).

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Odontoblasts, the principal cellular element at the dentin-pulp boarder, have a process extending approximately one-third the distance to the dentinoenamel junction (Byers and Sugaya 1995). Recent physiological and gene expression studies have demonstrated that these dentin-forming cells respond to pain-provoking stimuli in a way that was similar to sensory receptors (Fig. 2.1b) (Magloire et al. 2010; El Karim et al. 2011; Chung et al. 2013). It is not clear, however, whether odontoblasts can activate the intradental nerves, since conventional synaptic structures have not been identified linking these cells. Trauma to the dentin that destroys the odontoblast layer fails to abolish dentin hypersensitivity (DH). Odontoblasts then may play a role but may not be critical to tooth sensitivity (Brännström 1963, 1968; Lundy and Stanley 1969; Lilja et al. 1982).

Gysi (1900) was the first investigator to speculate that the sensitivity of dentin was due to stimulus-evoked fluid shifts in the dentin tubules. Brännström and his colleagues systematically studied fluid movement in dentin in vitro that occurred in response to thermal, evaporative, tactile, and osmotic stimuli (Brännström 1962, 1965, 1966, 1986, 1992; Brännström et al. 1967). In general, stimuli that elicit pain when applied to exposed dentin also induce fluid shifts that can be studied in laboratory experiments. Brännström's theory was referred to as the hydrodynamic hypothesis. Later animal experiments that directly

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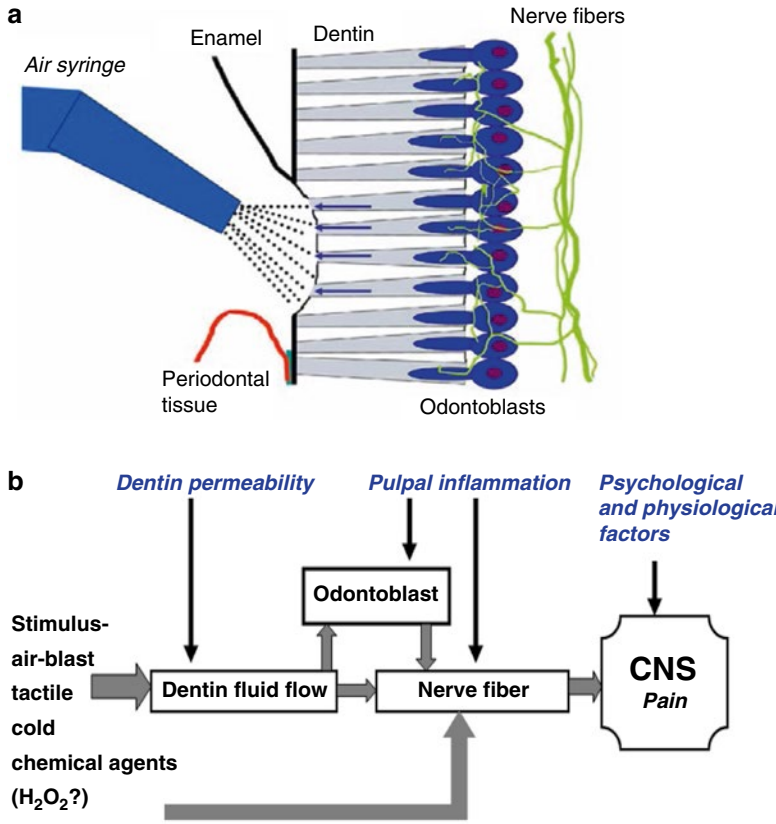

Fig. 2.1 (**a**) Diagram of sensitive dentin showing exposed tubules in an area of dentin erosion or gingival recession. Stimuli, for example, air blasts directed toward the dentin surface, induce outward fluid shifts in the tubules which activate the nerve ending located in the deep dentin and pulp. The odontoblasts respond to various forms of pain-producing stimuli, but it is not clear if these cells can activate the intradental nerve fibers. Treatments for sensitive teeth can act by reducing the dentin permeability or by reducing the excitability of the intradental nerves (Reprinted with permission from Markowitz (2010, 2013)). (**b**) Schematic diagram showing the physiological processes leading to pain-associated DH. Fluid flow in the dentin tubules triggers nerve responses which lead to pain perception in the central nervous system (CNS). The odontoblasts may also respond to certain pain-provoking stimuli. Some stimuli, for example, cold, may also cause pain by directly activating the nerve endings. The relationship between the magnitude of a stimulus applied to the dentin and pain perception is by no means fixed. Dentin permeability, the biological environment of the dental pulp, and central psychological and physiological factors are variables that can alter pain processing (Reprinted with permission from Markowitz (2009))

linked transdentin fluid movements with excitation of the intradental nerves (Matthews and Vongsavan 1994) gave credence to the view that intradental nerves act as mechanoreceptors that are activated by dentin fluid shifts. The hydrodynamic mechanism in teeth represents a novel adaptation of fluid flow-sensing mechanoreceptors to the unique anatomical environment of the dentin pulp complex.

Fluid shifts, however, are not the only way that pain can be evoked. As with the other parts of the body, intradental nerves can respond directly to pain-producing stimuli regardless of the dentin fluid shifts evoked by those stimuli (Chung et al. 2013). Cold foods and beverages may, in part, stimulate nerves directly by activating thermal receptors located on intradental nerve endings (Park et al. 2006). Even where the intensity of the pain response does not correlate with the magnitude of the dentin fluid shifts, the dentin tubules act as conduits whereby the external stimuli reach the pain transduction mechanism (Chidchuangchai et al. 2007).

Although considered "pathological," DH may serve important physiologic functions in humans and other species. The intradental nerves participate in the sensation of biting force and, in this way, may protect the teeth from fracture (Olgart et al. 1988). Dentin sensation arising in the elongated tusk of the narwhal whale appears to contribute to the animal's ability to sense the tonicity in its immediate environment. This tusk has cementum channels connecting dentin tubules to the tooth's surface. This sensory input is important in the Arctic since it helps the animal avoid being trapped by ice (Nweeia et al. 2014).

Understanding pain plasticity is critical to appreciating the impact of disease states, therapy, and host factors in modulating this experience (Pashley 2013). Dentin permeability and intradental nerve excitability are peripheral loci where disease processes can upregulate pain and where therapeutic strategies seek to interrupt the events leading to pain transmission. Analysis of these peripheral factors highlights the relationship of DH to patient behavior and other dental health issues, for example, tooth wear, erosion, caries, and periodontal disease (see Chaps. 4 and 10). Less well understood, but equally important, however is the role of central nervous system plasticity in explaining the large degree of variability observed in the intensity of DH symptoms and the impact of this type of pain on quality of life (Sessle 2000; Bekes and Hirsch 2013; Sixou 2013) (see Chap. 9).

The Anatomical Substrates of Dentin Hypersensitivity (DH)

Intense cold can elicit pain in healthy intact teeth. This form of stimulation is generally used to determine pulp vitality in clinical examinations. Hot foods and beverages can also elicit pain in healthy teeth. Cold, however, has been observed to be a more reliable modality for pulp vitality testing (Fuss et al. 1986). In intact teeth, dentin is covered coronally by enamel and by cementum on the root surfaces. These external coverings seal the tubules so well that there are little intratubular fluid shifts in response to the application of hydrodynamic stimuli (thermal, evaporative, tactile, or osmotic). Once the peripheral coverings of dentin are removed by abrasion, erosion, caries processes, or scaling procedures, dentin becomes hyperconductive, compared to its previous unexposed condition. In this state, hydrodynamic stimuli elicit large fluid shifts that evoke pain (Pashley 2013).

Dentin

Compared to nonsensitive dentin, sensitive areas have exposed patent tubules (Absi et al. 1987, 1989; Yoshiyama et al. 1989). In human subjects, the severity of sensitivity symptoms correlated with the number of open tubules/dentin surface area and the diameters of those tubules (Kontturi-Nahri and Närhi 1993). Root scaling and restorative procedures leave the dentin surface covered by a layer of burnished cutting debris called the smear layer (Pashley 1984) (Fig. 2.2). This cutting debris is actually forced into the tubule orifices for approximately 1 μm and is then cov-

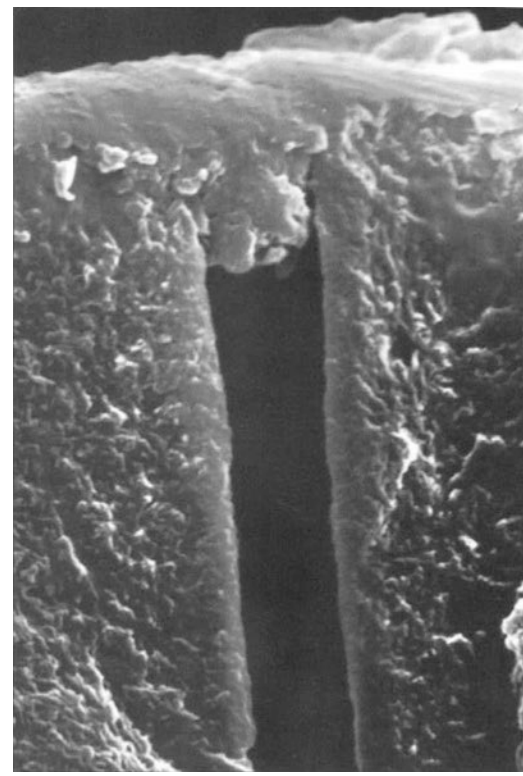

Fig. 2.2 Smear layer covering dentin cut with a high-speed carbide bur. Note that cutting debris extends into the dentin tubule about 1–2 μm. The combination of smear layer/smear plugs reduces fluid flow across dentin by 90 %. Loss of smear layers and smear plugs increases dentin fluid flow and hence DH (Used with permission from Pashley (1992))

ered by a further 1 μm of smear layer. The smear layer reduces the hydraulic conductance (the capacity of dentin for pressure-driven, convective flow), about 10–30 times compared to what it would be in the absence of these surface materials (Pashley et al. 1981; Carrilho et al. 2007). When the smear layer and smear plugs are dissolved by the organic acids present in the diet or produced by plaque microorganisms, the exposed dentin can become sensitive (Pashley 1986).

The dental pulp is surrounded by mineralized dentin. Measurements of the tissue pressure of pulpal soft tissues have shown that its hydrostatic pressure is positive, rather than being negative as is common in the skin (Guyton and Hall 2000). Intraocular, intramedullary, intracranial, and intrapulpal tissue pressures are all positive 14–16 mmHg (Matthews and Vongsavan 1994; Ciucchi et al. 1995; Heyeraas and Berggreen 1999; Guyton and Hall 2000). Positive pulpal tissue pressure is probably the result of the average capillary hydrostatic pressure exceeding the oncotic pressure of plasma proteins and the relative meager lymph drainage of the pulp (Pashley 1992; Heyeraas and Berggreen 1999). This positive tissue pressure in the pulpal soft tissues is responsible for the slow outward seepage of dentin fluid whenever the outer coverings (enamel or cementum) are lost (Ciucchi et al. 1995). The rate of this outward fluid flow that is present in the absence of hydrodynamic stimulation is not sufficient to activate pulpal sensory nerves in the pulp. This was shown definitively in cat teeth by Vongsavan and Matthews (1992) and by Matthews and Vongsavan (1994).

Stimulus-induced fluid shifts occur when the baseline outward convective flow accelerates or reverses in response to probing, air blasts, or thermal changes (Anderson et al. 1967; Matthews et al. 1993; Pashley et al. 1996; Andrew and Matthews 2000; Vongsavan et al. 2000). Experiments using hydrostatic pressure stimuli on human and animal teeth (Fig. 2.3a) demonstrate that the intradental nerves are more sensitive to

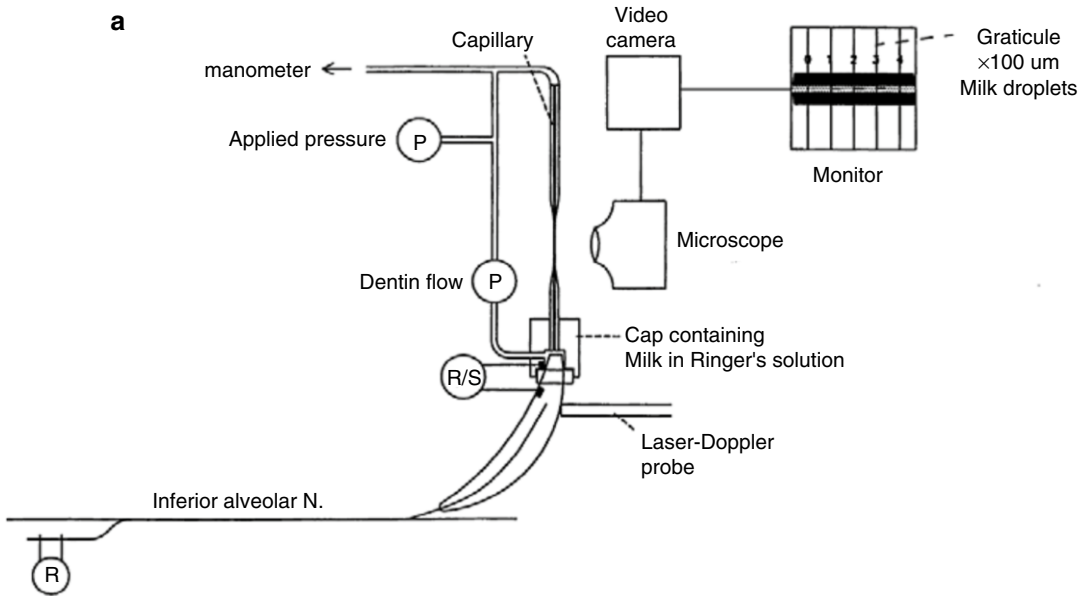

Fig. 2.3 (**a**) Experimental arrangement used to examine the effect of hydrostatic pressure application to an etched dentin surface on transdental fluid flow and intradental nerve activity in animal experiments. Intradental nerve activity was recorded from single fibers isolated from the inferior alveolar nerve and from multiple units in the dentin. (**b**) Following the application of positive pressure to the dentin surface, there is inward dentin fluid flow. This results in little activation of the intradental nerves. In contrast, negative pressure induces outward flow; this is associated with a vigorous nerve response recorded from both the dentin and the single-unit recordings. (**c**) Relationship between transdentin flow rates produced in response to pressure applications, and number of nerve impulse recorded from the dentin. Inward flow evoked little in the way of nerve responses. Outward transdentin flow above approximately 0.75 nl/s/mm^2 evoked nerve responses. The magnitude of the nerve response appeared to be positively associated with the outward flow rate (Vongsavan and Matthews (2007) reproduced with permission)

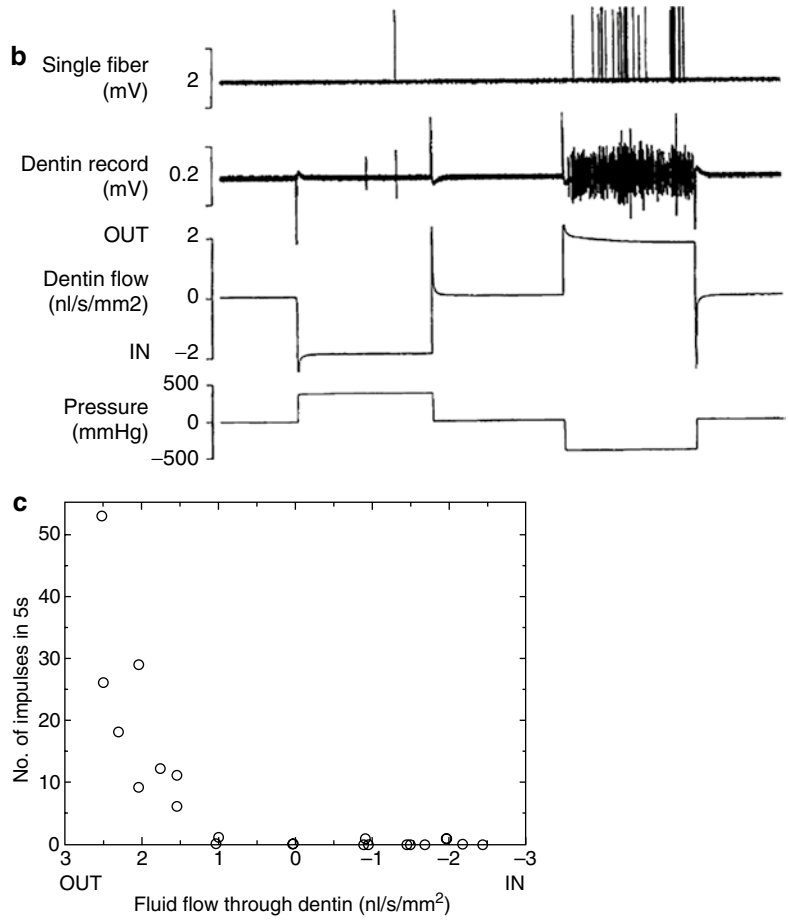

Fig. 2.3 (continued)

outward flow than to inward fluid displacements (Fig. 2.3b, c) (Matthews and Vongsavan 1994; Andrew and Matthews 2000; Charoenlarp et al. 2007; Vongsavan and Matthews 2007).

Both tactile stimulation and air blasts are commonly used stimuli in DH clinical studies (Gillam et al. 2000) (see Chaps. 5 and 7). Intradental nerve responses to these stimuli may also be evoked when the smear layer is removed from dentin, and not in its presence (Hirvonen et al. 1984). Abrading the dentin to form a smear layer or applying agents to the dentin that occlude the dentin tubules abolished these responses.

Pressing the dentin with a sharp explorer induces sufficient inward fluid shift to exceed the pain threshold (Fig. 2.4a). When the pressure is removed, an outward fluid shift occurs due to the elastic recoil of the dentin surface that also activates the intradental nerves (Fig. 2.4b) (Camps et al. 2003).

Air blasting is a very effective provocation of tooth sensitivity pain that acts by inducing rapid outward fluid shifts (Fig. 2.4c) (Matthews et al. 1993; Pashley et al. 1996; Andrew and Matthews 2000). Air blasts evaporate fluid from dentin tubules. This, in turn, produces cooling of the dentin and an outward fluid shift caused by capillary action. Evaporative fluid movement may occur through small or incompletely occluded tubules. It is commonly experienced in clinical practice that superficial dentin as, for instance, in a cavity preparation extending to the dentinoenamel junction (DEJ) is quite sensitive. Superficial dentin has been reported to possess narrow tubules that have a lower hydraulic conductance than deep dentin (Fogel et al. 1988). The dentin tubules do, however, have extensive branching near the DEJ that makes this tissue porous and can sustain evaporative fluid movements (Mjör and Nordahl 1996).

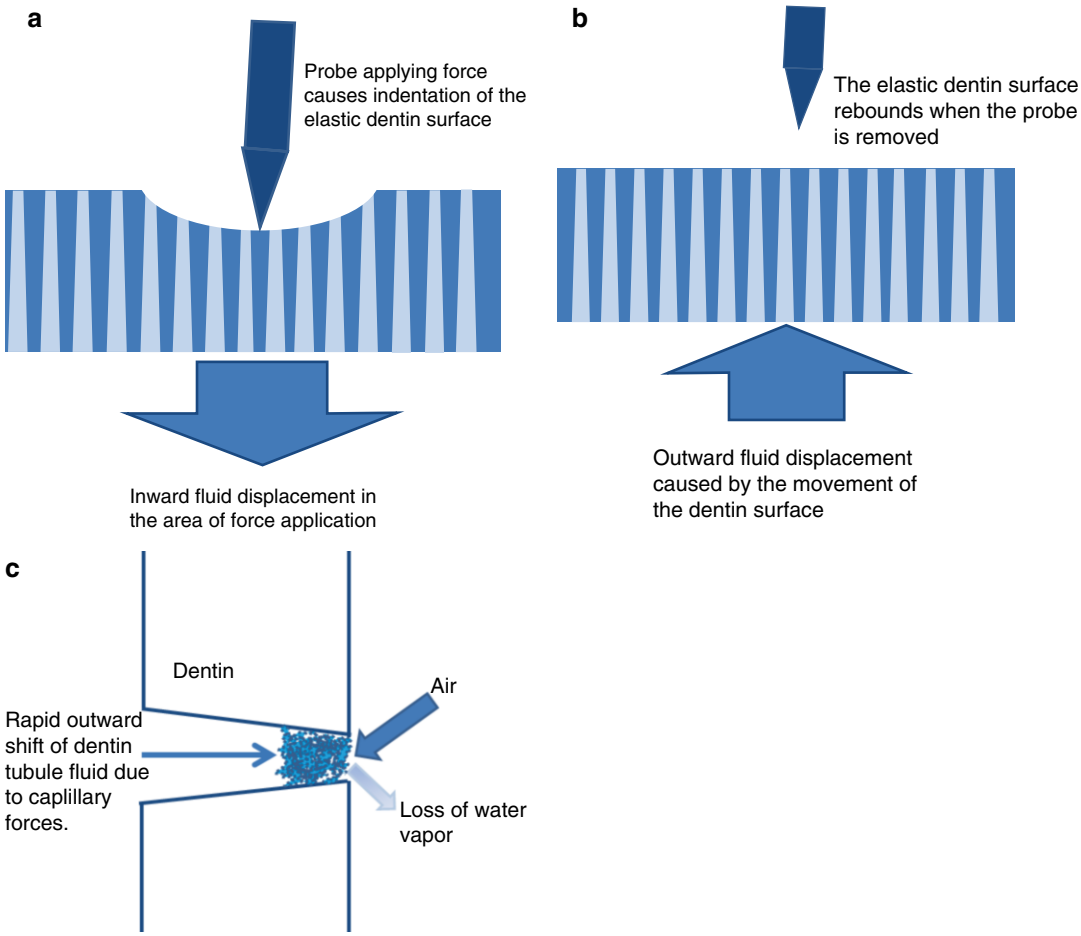

Fig. 2.4 Mechanism by which tactile and air blast stimulations cause pain in sensitive teeth. (**a**) Tactile stimulation with a sharp probe may cause both plastic (scratching) and elastic (reversible) deformation of the exposed, possibly demineralized, dentin surface. When tactile forces are applied with a sharp probe, the dentin surface indents. Since the dentin tubules widen toward the pulp, this causes an inward fluid shift that may be of sufficient magnitude to stimulate the intradental nerves in the deep dentin and pulp (not shown). (**b**) Removal of the probe from the dentin surface causes the surface to recoil. This recoil triggers outward dentin fluid flow that is highly excitatory to the intradental nerves (Camps and Pashley 2003; Camps et al. 2003). (**c**) Air blasts convert fluid in the exposed open ends of the dentin tubules into water vapor that escapes under the influence of the air current. This causes an immediate outward movement of dentin fluid due to capillary forces. The evaporative action of air blasts can also cause cooling of the dentin surface that can induce pain as well. Occlusion of the dentin tubules by a porous substance, such as the smear layer, may result in a near-complete blockage of convective fluid movements but has considerably less impact on fluid shifts induced by air blasts since evaporation of fluid from the tubule orifice will still occur (Matthews et al. 1993)

Physiological Factors Altering Dentin Permeability and Sensitivity

$$Q = \pi \Delta P N r^4 / 8 \eta L$$
$$\left(\text{Hagen-Poiseuille Law for capillary flow}\right) \quad (2.1)$$

where Q = volumetric fluid flow (μL)
N = number of pores (i.e., tubules per unit area)
ΔP = hydrostatic pressure difference across dentin (cm H_2O^{-1})
r = radius of dentin tubules
η = viscosity of fluid
L = length of dentin tubules (cm)

$$\text{Lp} = Q / \Delta P A t \quad (2.2)$$

where Lp = hydraulic conductance (μL cm^{-2} min^{-1} cm H_2O^{-1})
Q = volumetric fluid flow (μL)
ΔP = hydrostatic pressure difference across dentin (cm H_2O^{-1})
A = area of dentin (cm^2)
t = time in min.

Being a system of tubules arrange approximately parallel (in particular in the mid-coronal dentin), flow and diffusion through dentin follows certain physical laws. Fluid flow is generally expressed as the ease with which fluid can flow across dentin or its hydraulic conductance (Lp), (Eqs. 2.1 and 2.2). That is, hydraulic conductance is simply the measure fluid flow rate (Q) divided by the difference in hydrostatic pressure across dentin forcing the fluid through 1 cm^2 of dentin surface area per min (Eq. 2.2). Both convective fluid flow and diffusion are proportional to the number of exposed tubules and inversely proportional to their length. Diffusion across dentin varies with the square of the tubule radius, while convective fluid flow through the dentin tubules varies with the fourth power of the radius (Eq. 2.1). The steep relationship between radius and convective flow is because intratubular fluid flow is laminar (Merchant et al. 1977). That is, concentrically smaller cylinders of fluid slip beneath larger more stationary cylinders adjacent to the walls of the tubules. This causes frictional resistance to fluid flow. If a tubule-occluding agent can reduce tubule radii anywhere throughout the length of the tubule by one-half, the resistance to fluid flow increases not by one-half squared, as in diffusion, but by one-half to the fourth power. Thus, reductions in tubule radius by one-half reduce diffusion to one-fourth of its original value but restrict convective fluid flow to one-sixteenth of its original value. This relationship predicts that dentin tubules need not necessarily be completely sealed in order to reduce DH (Reeder et al. 1978). The dependence of fluid flow on tubule radius, density, and length also explains the anatomic variations that are observed in the permeability of dentin from different sites within a tooth. In general, the deep dentin above a pulp horn of a posterior tooth or above the pulp tip in an anterior tooth has the highest permeability of any area of exposed dentin in that tooth (Pashley et al. 1978, 1987). These areas of dentin also have the highest innervation density (Byers 1984) and tend to be most sensitive.

If one compared the convective flow measured through a dentin specimen of known tubule diameter, thickness, and density with the expected flow calculated for that specimen, the calculated flow is usually an order of magnitude greater than the actual flow (Michelich et al. 1978). Dentin tubules have irregular walls and contain collagen fibers and other structures that partially obstruct flow.

The hydraulic conductance (Lp) of a porous solid is a measure of the ease with which a pressure gradient generates flow through the material (Eq. 2.2). In experiments where dentin flow is measured, hydraulic conductance is a reflection of the dentin's permeability to convective flow (Reeder et al. 1978). As described above, removal of the smear layer and smear plug increases the dentin's hydraulic conductance.

Hydraulic conductance measurements are used to screen the ability of agents to treat DH by reducing dentin permeability.

When solutes are applied to permeable dentin surfaces, they diffuse through the tubules in proportion to their concentration gradient. The physiological outward flow of dentin fluid reduces the inward flux of solutes by its rinsing action (Pashley and Matthews 1993). Due to the different dependencies of diffusion and flow, partial tubule occlusion can reduce this outward rinsing action of flow and enhance inward diffusion (Pashley et al. 2002). The opposing action of outward flow on inward diffusion is an important factor in limiting transdentin drug delivery, the interaction of restorative materials with dentin, and the effect of bacterial toxins on the dental pulp. The outward flow may also transport host-derived proteins, for example, clotting factors (Pashley et al. 1984) and immunoglobulins into the dentin tubules (Hahn and Overton 1997). These macromolecules may interact with one another or the tubules themselves forming obstructions that subsequently reduce fluid flow.

Solutes applied to the dentin surface also initiate outward osmotic water movements. For example, pellets soaked in saturated calcium chloride can draw sufficient fluid through dentin to elicit pain. This may be used as a clinical test to detect defective restoration margins (Pashley et al. 1996). In general, osmotic water movements through dentin are limited since the tubules are permeable to most low molecular weight solutes (Pashley and Whitford 1980). Large molecular weight solutes, for example, proteins, have a limited ability to diffuse into dentin, particularly in the presence of the smear layer. Under conditions where the penetration of the solutes into dentin is restricted, outward osmosis is favored (Pashley et al. 1979).

The dentin tubules provide the pathway that links dentin stimulation with nerve responses. The dentin tubules are also the routes by which pain can be facilitated by bacterial factors or relived by therapeutic agents that either reduce the dentin permeability or inhibit the activation of the intradental nerves (Markowitz and Pashley 2008; Pashley 2013). Although dentin does not remodel in the same way as bone, the formation of smear layers, tertiary dentin, peritubular dentin, and intratubular mineral can reduce dentin permeability and DH (Mjör 2001). The susceptibility of this hard tissue to acid dissolution and abrasion is an important factor in understanding DH etiological factors and designing preventive strategies that are critical to patient management (Addy 1992) (see Chap. 4).

Nerve Activation

The densely innervated teeth give rise to a spectrum of pain experiences ranging from the agony of acute pulpitis to the sensations encountered by DH sufferers. Clinical research, together with evidence from in vivo studies where the nerve responses to dentin stimulation are recorded, has been useful in determining which of the various sensory nerve fiber types present in the pulp respond to dentin stimulation and in determining the role of dentin permeability in altering the capacity of stimuli to evoke nerve responses (Markowitz and Pashley 2008).

Stimulation of exposed dentin in healthy human teeth results in a sharp, well-localized pain that does not last beyond the duration of the stimulus (Anderson et al. 1967; Anderson and Matthews 1976; Ahlquist and Franzén 1994). This corresponds to pain associated with A-fiber type nociceptor activation evident in other parts of the body. The identity of the nerve fiber type responding to dentin stimulation was confirmed in physiological experiments. In these experiments, the nerve units responding to air blasts, probing, and other stimuli applied to etched dentin were observed to have low electrical thresholds and rapid conduction velocities consistent with A-fibers (Närhi et al. 1982, 1992; Närhi 1985). These A-fibers are myelinated throughout most of their course but lose myelination as they reach the superficial pulp and dentin. This loss of myelination has, however, made characterization of the distal portions of the afferents difficult when viewing histological sections. Recently, it has been demonstrated using immunohistochemical markers that most of the unmyelinated nerve

fibers present in the superficial pulp tissue are the extensions of myelinated axons (Henry et al. 2012). In contrast to the intradental A-fibers, slowly conducting pulpal C-fibers are unmyelinated throughout their entire course. These units do not respond to the types of innocuous dentin stimuli that evoke DH pain, but they do respond to direct injurious stimuli, for example, noxious heat, directed to the pulp tissue. Capsaicin, the active ingredient in hot peppers, stimulates C-fibers via the same receptor as is activated by heat but has little effect on the rapidly conducting intradental A-fibers (Närhi et al. 1992; Ikeda et al. 1997).

The relationship between the activation of intradental nerve fiber types and the individual's pain experience was studied in experiments conducted on human volunteers (Ahlquist and Franzén 1994). In these experiments, the electrophysiological responses of the intradental nerves to tooth stimulation were recorded from dentin cavities at the same time as the experimenters recorded the subject's pain rating and description. Cold stimulation evoked pain described as sharp and evoked A-fiber impulses recorded from the dentin (Ahlquist et al. 1984). For a series of cold stimulus applications, the intensity of the pain was proportional to the frequency of the nerve response (Fors et al. 1984). In contrast to cold, the application of several algesic (pain-producing) chemicals to deep dentin or pulp evoked dull aching pain and did not produce nerve responses that could be recorded through dentin cavities (Ahlquist et al. 1994). This type of pain was probably due to small-diameter C-fiber activation. These human and animal studies have established a functional classification of the intradental nerves and relate people's pain experiences to activation of the afferent type and relate tooth sensitivity to other forms of sharp well-localized pain.

Nociceptive afferents may also be classified by histochemical markers, as well as according to types of receptors, ion channels, and transmitters present in the neuron (Chung et al. 2013). Mammalian trigeminal afferents are a heterogeneous population of sensory neurons, most of which convey non-painful mechanosensory information arising in the exquisitely sensitive skin and hairs of the face (Catania 2011), as well as sensation from the mucosa (Sessle and Greenwood 1976). In order to examine the properties of pulpal afferents, histological examination of pulp tissue is performed, or the cell bodies of pulpal afferents are examined in the trigeminal ganglion (Byers et al. 1982, 1987; Pan et al. 2000). Pulpal afferents can be traced to their cell bodies by placing certain rapidly diffusing tracers into dentin cavities, and following a period of time to allow for the transport of these tracers, the cell bodies in the trigeminal ganglion can be visualized (Eckert et al. 1997; Pan et al. 2003). Using the appropriate histochemical technique, these labeled cell bodies can be examined for the presence of various receptors and other markers of neuronal phenotype (Henry and Hargreaves 2007). The labeled pulpal afferent cell bodies can also be isolated, maintained in tissue culture, and harvested for physiological or biochemical analysis (Kim et al. 2011; Chung et al. 2013). Using this approach to isolate pulpal afferent cell bodies, the gene expression of various receptor types and ion channels can be characterized (Chung et al. 2013). Although the electrophysiological responses of isolated cell bodies to various chemicals and thermal stimulation can be recorded, this approach does not allow for the responses of afferents to natural dentin stimuli to be examined (Kim et al. 2011). Because of these limitations, we cannot with certainty assign the various ion channels, transmitters, and receptors observed in pulpal afferents belonging to A- or C-fibers.

The majority of pulpal afferent cell bodies that were isolated in culture were observed to respond to heat and the heat sensation-inducing chemical agent capsaicin. This population of cells also binds the plant isolectin IB4. Electrophysiological recordings revealed that these IB4+ and capsaicin-responsive cells had action potentials having inflections (humps) on their repolarizing phase (Kim et al. 2011). A majority of pulpal afferents also expressed mRNA for TRPV1 (Transient receptor potential cation channel subfamily V member 1) – the heat/capsaicin receptor. This population of neurons probably corresponds to C-fiber nociceptors. In contrast,

approximately 20 % of the pulpal afferent cell bodies examined lacked responses to capsaicin, lacked IB4 binding, and had action potentials that did not have a hump on the repolarizing phase. A similar proportion of afferents were TRPV1 mRNA negative (Kim et al. 2011). Some pulpal afferent cell bodies also respond to cold and cold sensation-inducing chemicals, for example, menthol (Park et al. 2006).

These and other results clearly demonstrate that pulpal afferents possess the ability to respond directly to thermal stimulation. Noxious heat stimulates responses in intradental C-fibers (Närhi et al. 1982; Jyväsjärvi and Kniffki 1992). The sharp abrupt pain responses observed when cold stimuli are applied to teeth are possibly a combined effect of cold-induced dentin fluid flow and direct action of cold on receptors on intradental nerve endings (Jyväsjärvi and Kniffki 1987; Park et al. 2006; Chidchuangchai et al. 2007).

Pulpal afferents also possess purinergic receptors (Cook and McCleskey 2002). When pulpal cells are damaged, cytoplasmic ATP is released into the extracellular fluid. ATP is a potent excitant of nociceptors. The phenomenon of ATP release may contribute to nerve activation by hydrodynamic forces since the odontoblast cell bodies are often aspirated into the tubules and destroyed during air blasting or traumatic restorative procedures (Brännström 1963).

Nitric oxide (NO), an oxidative free radical generated by the enzyme nitric oxide synthetase (NOS), has been implicated in inflammatory processes in the dental pulp. Because NO is rapidly destroyed, investigators examined increases in NOS enzyme activity in normal vs. inflamed rat pulps (Law et al. 1999; Fujita et al. 2004). The exact role of NO in DH remains to be discovered.

When viewed within the intact trigeminal ganglion, a slightly different neuronal pattern emerges. Most pulpal afferents were IB4- and contained the vasoactive neuropeptide – calcitonin gene-related peptide (CGRP) (Fried et al. 2011). Capsaicin stimulation of isolated pulp tissue induces the release of CGRP, indicating that this neuronal population possesses the thermally activated TRPV1 receptor and plays a role in controlling the pulpal vasculature (Fehrenbacher et al. 2009). One population of non-neuropeptide-containing afferents was observed to account for few trigeminal ganglion cell bodies, but formed a dense network of nerve fibers in the superficial pulp, indicating a role in dentin sensation (Chung et al. 2012). This population may include the cell bodies that give rise to the intradental A-fibers since this population is known to be relatively unresponsive to capsaicin (Närhi et al. 1992).

Several characteristics of DH are unique. Pain is the only sensory modality experienced when teeth are stimulated. In conducting experiments using electrical stimulation, human subjects report a tingling (rather than painful) sensation when threshold is reached. This observation suggested that not all tooth stimulation resulted in pain (McGrath et al. 1983). Several lines of evidence also indicate the relationship of this "prepain" sensation to pain. Temporal (increasing the frequency) and spatial (simultaneous administration of the stimulus to adjacent teeth) summation results in this liminal stimulus being perceived as painful, indicating that the tingling sensation was in fact brief, low-amplitude pain (Närhi et al. 1984; Virtanen et al. 1987).

In many respects, the intradental nociceptors resemble low-threshold mechanoreceptors (LTM) known to mediate non-painful mechanosensation in other parts of the body (Fried et al. 2011). The conduction velocities of some of the pulpal afferents classify these units as Aß-fibers (Närhi et al. 1983). This type of afferent is not normally associated with pain but with non-painful mechanosensation. Examination of pulpal afferent cell bodies in the trigeminal ganglion indicated that many express markers and have cytological feature, for example, cell size that resembles LTM rather than typical nociceptors. The stimuli that trigger pain in sensitive teeth are innocuous in that they do not damage tissue without forceful or repeated application. These features of DH have led investigators to consider the intradental nerves responding to hydrodynamic forces – "low-threshold algoneuron" – as opposed to true nociceptors. The reason that activation of these

algoneurons results in pain has to do more with their connections in the central nervous system than to the intrinsic response properties of these cells (Fried et al. 2011).

The transduction of hydrodynamic forces into nerve responses implies that these intradental algoneurons possess receptors that are activated by mechanical forces. The preferential sensitivity of intradental nerves to outward fluid displacements indicates that these mechanoreceptors respond best to a tugging type of force application (Vongsavan and Matthews 2007) (Fig. 2.3).

Mechanosensitive ion channels are found widely in nature and underlie nerve responses to several modalities in addition to touch, including osmotic stimulation and sound. In mechanoreceptors, a transmembrane transduction channel is anchored by intracellular and extracellular elements to the cytoskeleton of the receptor or nerve and to an extracellular structure (Fig. 2.5). The transduction channel responds to tension or shear opening or closing, and it is this action that gates ion conductance (Gillespie and Walker 2001; Tsunozaki and Bautista 2009).

Many ion channels have been proposed as putative mechanoreceptors (Delmas and Coste 2013). Most of these channels also mediate responses to other stimuli such as cold and low pH. It has been difficult to prove a mechanosensory function for several candidate ion channels since genetic knockout animals lacking these channels occasionally appear to retain some mechanically mediated sensations (Kang et al. 2012).

Gene expression of a number of proposed mechanosensory ion channels has been examined in rat trigeminal ganglion cells including labeled pulpal afferents (Hermanstyne et al. 2008).

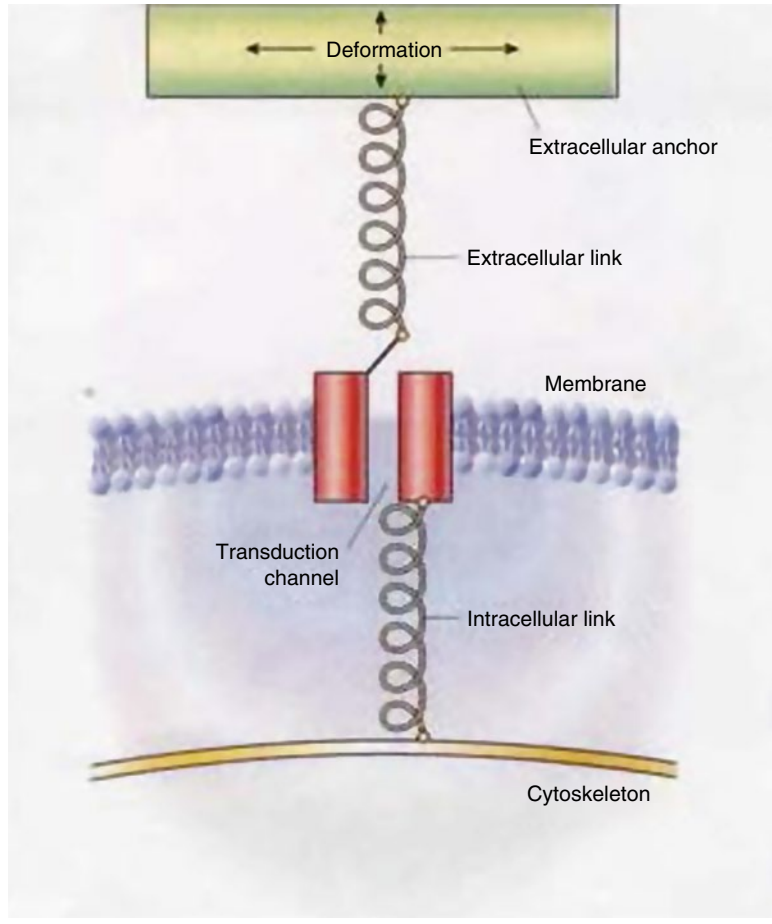

Fig. 2.5 Schematic of a hypothetical mechanosensitive receptor anchored at one end in a nerve membrane and, at the other end, in an extracellular surface. Deformation would open an ion-sensitive channel (Gillespie and Walker (2001) used with permission)

Trigeminal neurons express mRNA for a large number of putative mechanosensory channels, most of which were not expressed in pulpal afferents. Of the mechanosensory channels examined, only one, the acid-sensing ion channel 3 (ASIC3), was expressed in 67 % of the pulpal afferents sampled. In this study, a majority of pulpal afferents also expressed TRPA1, a chemoreceptive channel that may also be activated by cold (McKemy 2005). Based on the observation that TRPA1 is also activated by oxidizing compounds, it has been hypothesized that this receptor is responsible for the pain that accompanies tooth bleaching (Markowitz 2010).

The percentage of neurons expressing ASIC3 was not altered by the induction of pulp inflammation, indicating that ASIC3 is constitutively expressed in the nerve fibers of intact healthy teeth (Hermanstyne et al. 2008). This observation that intradental mechanoreceptors are present in healthy intact teeth was expected since freshly exposed dentin, as would occur in fractured or chipped teeth, is sensitive to both cold air and other stimuli. Physiological experiments examining the nerve responses induced by hydrodynamic stimulation in animals (knockouts) lacking ASIC3 are needed to definitively establish the role of these, and other, ion channels in mediating nerve responses to hydrodynamic stimulation.

In order to activate pain or other forms of conscious sensation, nerves responding to stimuli transmit all-or-none impulses to the central nervous system. In pain fibers, activation of one of the sensory receptors described above depolarizes the nerve cell membrane; if a threshold is reached, voltage-gated ion channels open (Armstrong and Hille 1998), resulting in an action potential that is transmitted to the central nervous system. The pattern and frequency of action potentials encodes information concerning the perceived intensity of the stimulation. Several types of cation-selective ion channels mediate the initiation and termination of the action potential, with voltage-gated sodium channels (VGNa) being responsible for the action potential's rising phase (Amir et al. 2006). In myelinated pulpal afferents, the distribution of VGNa channels is restricted to the nodes of Ranvier in the myelinated segment of the fiber and spreads out in the peripheral unmyelinated portion (Henry et al. 2012).

Dentin overlying a disrupted odontoblast layer may however be still sensitive. This observation challenges the notion that the odontoblasts are a critical cellular participant in DH (Lilja et al. 1982) (Fig. 2.1). However, odontoblasts do possess an assortment of nerve-like receptors that enable these cells to respond to various chemical, thermal, and mechanical stimuli (Magloire et al. 2010; El Karim et al. 2011; Chung et al. 2013; Tsumura et al. 2013). They may also express various VGNa channels depending on the location within the tooth and the tooth's developmental stage (Davidson 1994; Allard et al. 2006; Byers and Westenbroek 2011; Ichikawa et al. 2012).

Although specific intercellular communication mechanisms, for example, synaptic structures linking odontoblasts with the intradental nerves, have not been identified (Byers 1984), sensory transduction by odontoblasts may influence the intradental nerves. The odontoblasts control the environment of the intradental nerve endings, determining the dentin fluid's ionic composition, and they also provide the structural support needed for the mechanosensitive nerve endings to detect dentin fluid flow (Magloire et al. 2010). In response to dentin stimulation, damage to the odontoblasts may also result in prostaglandin formation and, as noted above, release of cytoplasmic ATP or potassium ions into the extracellular fluid (Cook and McCleskey 2002). In experiments where odontoblasts and trigeminal neurons were maintained in culture together, mechanical stimulation of one of the odontoblasts evoked an excitatory calcium conductance in other nearby odontoblasts and neurons. The mechanically stimulated odontoblast released ATP into the extracellular medium through specialized membrane pores. The responses of the neighboring odontoblasts and neurons to this mechanically induced ATP release are mediated by various purinergic receptors (Shibukawa et al. 2014). ATP and other chemical factors released by odontoblasts excite and

sensitize the intradental nerves (Utreras et al. 2013). It has been proposed that odontoblasts participate in mediating the response to hydrodynamic dentin stimulation not by conventional synapses but rather by autocrine/paracrine types of signaling (Shibukawa et al. 2014).

It is also possible that the physiological responses of odontoblasts, like those of osteocytes in bone, have little to do with pain. Osteocytes respond to the mechanical stimulation of bone by boosting their metabolic activity and maintaining the mineralization of the bone matrix (Cowin 2007). In the case of odontoblasts, responses to dentin damage and stimulation may be involved in tertiary dentin formation (Byers and Westenbroek 2011). Further research, however, is needed to determine the sensory function of these versatile cells.

The Physiological Basis of Hypersensitive Dentin

Symptoms including a decrease in the pain threshold and an increase in the intensity of pain accompany inflammation (Park et al. 2001). Pulpal inflammation may be responsible for exposed dentin becoming hypersensitive (Pashley 2013). Inflammation-related plasticity has a major impact on the excitability and pharmacological sensitivity of nociceptors during pathological states (Gold and Flake 2005; Henry and Hargreaves 2007; Chung et al. 2013). Pulp inflammation may also be triggered by trauma to the tooth or bacterial invasion of the pulp or dentin.

Oral microorganisms invade and colonize the dentin tubules when caries spreads into dentin (Love et al. 2000). Bacterial products, enzymes, and antigens diffuse through relatively intact dentin layers into the pulp where they can produce an inflammatory response (Brännström 1962; Lundy and Stanley 1969; Goldberg et al. 2008). In acute pulpitis, inflammatory mediators accumulate in the pulp resulting in sensitization and eventual activation of the nociceptors leading to spontaneous pain (Bowles et al. 2003). This process may also be triggered by bacterial products invading the dentin (Warfvinge et al. 1985; Jontell et al. 1998; Fouad 2012), by chronic dentin exposure, or by the trauma of restorative procedures (Olgart et al. 1991; Mjör 2001).

In caries, the type and intensity of the pulp's inflammatory response are dependent on the depth of bacterial invasion into the dentin (Izumi et al. 1995; Cooper et al. 2011). Considerable variability exists in the symptoms experienced by people with carious teeth. Teeth with deep carious lesions, heavily infected with *Lactobacillus* species, were observed to be relatively asymptomatic. In contrast, teeth with lesions infected with predominantly anaerobic organisms were more likely to present with thermal sensitivity and other symptoms (Hahn et al. 1993).

Various by-products of bacterial metabolism, for example, amines, are highly excitatory to intradental nerves (Panopoulos 1992). Organic acids, the principal metabolic by-product of sugar fermentation by *Lactobacillus* and other caries-associated bacteria, have complex effects on pain. Organic acids have an inhibitory effect on intradental nerve activity induced by chemical stimulation (Panopoulos 1992). Acids also enhance dental pain by activating certain receptors and sensitizing other receptors, e.g., TRPV1, to heat stimulation (Goodis et al. 2006). Variations in the bacterial population of a carious lesion may also influence the type of lesion metabolism and the inflammatory response that develops in the pulp, which in turn may determine the degree to which pain sensitization occurs (Hahn and Liewehr 2007).

Even without directly invading the pulp, bacteria can influence the function of the intradental nerves. Lipopolysaccharide (LPS) is an important toxin released by gram-negative anaerobic bacteria that initiate both local pulpal and systemic inflammatory responses (Okiji et al. 1992; Chattipakorn et al. 2002; Bletsa et al. 2006). This toxin can trigger shock and systemic organ damage (Quan et al. 2001). Direct exposure of the pulp to LPS induces severe inflammation and pain facilitation-associated changes in the central nervous system areas that receive input from pulpal nociceptors (Chattipakorn et al. 2005). LPS may diffuse through dentin and facilitate the

actions of thermally activated ion channels (Nissan et al. 1995; Chung et al. 2011; Diogenes et al. 2011). These changes would be expected to make teeth very sensitive to hot and cold.

There are many links that exist between the activation of the immune system, inflammation, and pain facilitation (Bletsa et al. 2009; Kress 2010). For example, trigeminal neurons possess toll-like receptors and other components of the innate immune system (Byers et al. 1992; Byers and Närhi 1999; Veerayutthwilai et al. 2007; Horst et al. 2009). These receptors are part of the body's early warning system that responds to LPS and other bacterial products. This mechanism may help explain the algesic effect of anaerobic bacteria (Wadachi and Hargreaves 2006). Inflammatory mediators appear to induce phosphorylation of TRPV channels, causing them to become more sensitive than normal to thermal stimulation (Jeske et al. 2006).

Inflammation and pain are intimately linked with nociceptor activation being an initiating factor in triggering inflammation and inflammation sensitizing nociceptors (Kim 1990). Painful stimuli, for example, tooth preparation, result in an increase in pulpal blood flow, as well as increases in intrapulpal pressure and outward dentin fluid flow. These effects can also be evoked by activation of the intradental sensory nerves by electrical, chemical, and hydrodynamic stimuli (Pertl et al. 1993; Heyeraas et al. 1994; Olgart 1996; Andrew and Matthews 2002). Stimulus-evoked release of vasoactive peptides, for example, substance P and CGRP from the pulpal terminals of intradental nerve endings, initiates vasodilatation and increases vascular permeability, the early vascular manifestations of inflammation (Kerezoudis et al. 1993; Fehrenbacher et al. 2009). This phenomenon is referred to as "neurogenic inflammation."

Compared to acute pulpitis, the role of bacteria and pulp inflammation in DH is less clear. Although healthy, freshly exposed dentin can be sensitive and sensitive cervical abrasions are frequently plaque-free (Addy et al. 1987), sensitization of intradental nerve responses can occur due to interactions between the pulp and plaque covering the tooth's root surface (Tammaro et al. 2000). However, bacteria do not pass through the intact dentin boundary separating the pulp from the tooth surface in sensitive teeth (Michelich et al. 1980). Although dentin tubules observed in SEMs appear to have a diameter of about 1 μm, their functional diameter is only about one-twentieth of that value due to the presence of intratubular material such as collagen fibers, mineral concretions, etc. (Michelich et al. 1978). The functional consequence of this restricted tubule diameter is that dentin does not permit bacteria to reach the pulp. That is, the dentin fluid that reaches the pulp chamber is sterile (Michelich et al. 1980). Dentin acts in a similar manner to a 0.2 μm Millipore filter in keeping oral microorganisms from infecting pulpal soft tissue.

Inflammation can exacerbate DH symptoms by making the intradental nerve endings more responsive to dentin fluid flow. Serotonin (5-HT) is an inflammatory mediator that is released by platelets and mast cells into damaged tissue. It is involved in a number of pain conditions including migraine headache (Sommer 2004). 5-HT application to exposed dentin also lowers the threshold of A-fiber units to hydrodynamic dentin stimulation (Ngassapa et al. 1992). Prior to 5-HT application, these units failed to respond to a weak osmotic stimulant – glucose solution application – to exposed etched dentin. Following application of 5-HT to the dentin, glucose application evoked an excitatory response indicting a lowering of the hydrodynamic threshold. This observation may explain the sensitivity to sweets often experienced during pulpitis. Serotonin sensitizes trigeminal nociceptors to both thermal and chemical stimulation and enhances stimulation-evoked CGRP release (Loyd et al. 2013).

Inflammatory mediators frequently act synergistically in potentiating the response to excitation (Hirafuji and Ogura 1987; Bletsa et al. 2009). For example, bradykinin enhances the capsaicin-evoked CGRP release from intradental nerve endings (Goodis et al. 2000). In those experiments, prostaglandin-E application enhanced this action of bradykinin.

There are also structural changes in the intradental nerves that are a consequence of injury and inflammation (Byers and Närhi 1999).

Following traumatic cavity preparation, sprouting of CGRP-containing nerve fiber terminals was observed in the superficial pulp tissue (Taylor et al. 1988). Because of this response, there may be a large increase in the innervation density of the superficial pulp tissue following injury, especially in the normally sparsely innervated cervical and radicular pulp. The timing of sprouting follows the general time course of increases in postoperative DH symptoms encountered following restorative or periodontal procedures. Nerve sprouting is at its maximum 1 week following injury, and then anatomic pattern returns to normal by 3 weeks after injury (Byers 1994; Byers and Närhi 1999; Rodd and Boissonade 2001). Postoperative symptoms tend to be at their worst 1 week after any restorative procedure and generally abate during the following weeks. The nerve sprouting reaction has also been observed in human teeth with deep caries (Rodd and Boissonade 2001).

Injury and inflammation also may initiate the partial demyelination of afferents and changes in the type and spatial pattern of the VGNa channels (Henry et al. 2009). Demyelination can result in abnormal electrical interactions between the axons that allow impulses in one afferent to excite adjacent neurons. These alterations make the afferents more excitable.

The specific type of VGNa channels expressed in nerve fibers may be altered by inflammation and nerve injury (Renton et al. 2005; Henry et al. 2009; Luo et al. 2010). The VGNa channels expressed in neurons exposed to inflammation have altered pharmacological sensitivities compared to neurons innervating healthy tissue (Lai et al. 2004). It is hypothesized that this altered pharmacological susceptibility is responsible for the difficulties encountered obtaining local anesthesia in inflamed teeth (Hargreaves and Keiser 2002).

A mild inflammatory response can be induced in human teeth by preparing dentin cavities and restoring the teeth with defective temporary restorations that allow bacterial leakage. Following 1 week, the inflamed teeth exhibited enhanced pain responses to cold stimulation compared to intact teeth. These changes in thermal sensitivity are not initiated by an increase in dentin permeability (Ajcharanukul et al. 2011). These experiments demonstrate that the pain response in sensitive teeth may be enhanced by inflammation, making the teeth hypersensitive. When sensitive teeth are evaluated clinically, for example, in dental caries, defective restorations and tooth fractures need to be considered in the differential diagnosis and corrected, since in the presence of these conditions, DH is unlikely to resolve with standard topical desensitizing treatments (Fig. 2.6) (Orchardson and Gillam 2006) (see Chaps. 4 and 5).

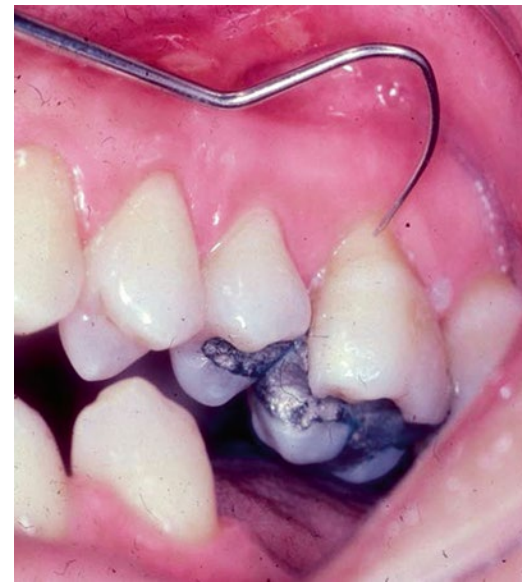

Fig. 2.6 Clinical photograph of a supererupted, sensitive first molar showing the relationship between DH and defective restorations. The tooth was sensitive to cold liquids, air blasts, and probing of the exposed mesial buccal root with a dental explorer as shown. The patient's sensitivity symptoms were long standing and failed to improve following the application of an oxalate-based topical desensitizer to the exposed root surface. Following the replacement of the existing amalgam restoration, the sensitivity symptoms resolved and the tooth remained asymptomatic and vital. Pulpal inflammation caused by bacterial leakage around the restoration is presumed to have sensitized the intradental nerves to stimuli. In this sensitized state, usually effective topical desensitizing agents fail to provide pain relief. Replacement of the defective restoration allows the inflammatory process and the pain sensitization to resolve (From Markowitz K, unpublished photograph (2000))

Using advanced imaging and electrophysiological methods, it is possible to localize the areas of the brain activated by tooth stimulation (Kubo et al. 2008; Meier et al. 2012). Repeated or intense activation of nociceptors may facilitate pain transmission in the central nervous system. Activation of pulpal afferents by noxious heat stimulation has been reported to induce an enhancement of the responses to those same thermal stimuli by second-order neurons in the trigeminal nuclear complex (Ahn et al. 2012). Intense activation of the intradental nerves or the induction of pulpal inflammation by the administration of noxious chemicals may also induce alterations in gene expression in the trigeminal nuclear complex and enhanced nociception in other facial areas, e.g., the lip (Park et al. 2001; Chattipakorn et al. 2005). The role of central plasticity in DH is however unclear at present. It is possible that nociceptor activation accompanying periodontal procedures that precede episodes of DH sensitizes the central pathways, resulting in more pain being triggered by dentin stimulation.

Oral microorganisms also have profound effects on the permeability of exposed dentin. Despite the capacity for excessive toothbrushing to cause tooth surface loss, plaque control has an important role in preventing DH following periodontal therapy (Wallace and Bissada 1990; Tammaro et al. 2000). Plaque-covered exposed dentin surfaces were observed to have widened tubules compared to surfaces that were kept plaque-free (Suge et al. 2006). The acid liability of smear layers is responsible for the frequently observed lack of DH in patients immediately after root scaling and the onset of DH that appeared 7–14 days following scaling procedures (see Chap. 3). This time delay presumably enables the plaque to form on the root surface and the microorganisms to dissolve the smear layer/smear plug combination (Kerns et al. 1991).

Dentin is a biological composite consisting of mineral and an organic phase that is mostly collagen. In addition to collagen, the organic matrix of dentin also contains several non-collagenous proteins that play an important role in dentin mineralization (Tay and Pashley 2008, 2009; Kim et al. 2010). These proteins are highly acidic and contain calcium-binding phosphate groups that pattern mineral formation (Boskey et al. 1990). The odontoblasts trigger mineralization by secreting these proteins into the predentin at the mineralization front (Veis 1993). As with dentin from which it is derived, dentin smear layers also contain mineral and organic components (Pashley 1992).

The composition of dentin influences its susceptibility to damage and its capacity for repair. In order to degrade dentin, both the organic and inorganic phases of the tissue must be attacked (Love 2002). Plaque-derived acids dissolve the mineral component of the smear layer and underlying dentin; bacterial and host-derived enzymes can attack the organic phase of the dentin (Chaussain-Miller et al. 2006). Host-derived collagen-degrading enzymes, for example, the matrix metalloproteinases, (MMPs) originate in the crevicular fluid, the saliva, and the dentin itself. In dentin, these enzymes can be activated by acid exposure, and these enzymes are believed to contribute to erosive tooth structure loss (Buzalaf et al. 2012). In restored teeth, the long-term action of MMPs and other enzymes may weaken the dentin-restoration bond by degrading resin-infiltrated collagen fibrils (Tjäderhane et al. 2013a). Dentin treatment with chlorhexidine or other cationic compounds preserves bond strength by inhibiting these enzymes (Tjäderhane et al. 2013b).

Reducing DH: Natural Processes and Treatment Effects

Desensitization Treatments Targeting the Dentin Permeability

The reduction of dentin permeability via tubule occlusion is an important strategy for treating sensitive teeth (Pashley 1986; Cummins 2009). Reducing dentin permeability acts not only to attenuate stimulus-evoked dentin fluid flow but also to prevent the activation of the intradental nerves by directly acting physical stimuli and by reducing the inward diffusion of irritating chemical agents (Hirvonen et al. 1984; Rifai et al. 2004;

Chidchuangchai et al. 2007). In vitro studies measuring the impact of treatments on the dentin's permeability and microscopic appearance are used to screen the ability of materials and products to reduce dentin fluid flow (see Chap. 6). Treatments that are effective in vitro studies may be considered to be acceptable candidates for more focused research activities including clinical trials. Due to the steep relationship between tubule radius and flow (flow $\propto r^4$), it is expected that dentin may be desensitized by treatments that induce partial tubule occlusion, reducing the stimulus-evoked flow to values that fail to activate a sufficient nerve response to result in a conscious pain sensation. Several clinically tested desensitizing treatments have been reported to demonstrate high reductions in flow when tested in vitro (Pashley et al. 1978). Other desensitizing agents that have been shown to be effective in clinical trials however, have been reported to demonstrate modest (<90 %) reductions in dentin permeability when tested in vitro (Patel et al. 2011) (Fig. 2.7). For some of these treatments, repeated applications are required to achieve near total occlusion (Sharma et al. 2013).

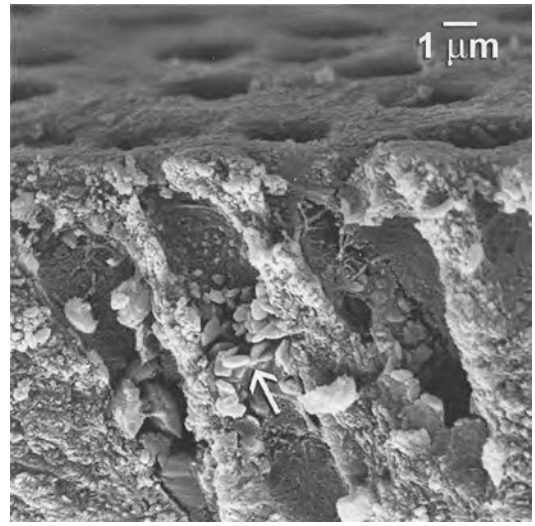

Fig. 2.7 SEM of fracture edge of acid-etched dentin treated with 1.4 wt. % potassium oxalate, pH 4.2 Listerine Advanced Defense Sensitive desensitizing mouthrinse. Because acid etching removes all apatite crystallites from the surface of dentin and from peritubular dentin, potassium oxalate cannot react with any calcium ions until it diffuses down into the tubule about 10 µm. There it can etch Ca^{++} from mineralized peritubular dentin, filling the tubule orifice with calcium oxalate crystals of various sizes (white arrow) that block fluid shifts (From Pashley DH, unpublished micrograph (2013))

In assessing the impact of prospective treatments on dentin permeability, it is important to determine if the dentin flow evoked by pain-producing stimuli is reduced by the treatment (Markowitz and Pashley 2008). Air blasts evaporate fluid at the tubule orifice, displacing the tubule fluid in an outward direction (Fig. 2.4c) (Matthews et al. 1993). Occluding the tubules with a porous material reduces the effective tubule radius and blocks pressure-driven convective flow to a great degree. As observed in Fig. 2.8, treatments, for example, smear layer formation and oxalate application, severely depress convective flow but have more modest effects on air blast-driven flow. These results suggest that very high levels of tubule occlusion may be needed to effectively prevent air blast stimulus-activated flow.

The dentin-pulp complex has the capacity for repair (Smith et al. 2012). However, as is evident from clinical observation, individuals with dentin that is exposed to the oral environment do not necessarily experience DH. Several natural mechanisms are known to exist that may reduce dentin permeability (Daculsi et al. 1987). In animals with continuously erupting teeth, dentin is exposed and the tubules mineralize rapidly. Continuously erupting teeth for example, rat incisors or horse molars wear rapidly. In these teeth, dentin exposure is followed by rapid dentin formation and tubule occlusion (Dimuzio and Veis 1978). In humans, age, chronic exposure to the oral environment, and being subjacent to caries are accompanied by physiological occlusion of dentin tubules (Daculsi et al. 1987; Tagami et al. 1992).

Tertiary and peritubular dentin formations are pulpal processes that reduce dentin permeability and DH (Lundy and Stanley 1969; Senawongse et al. 2008). Growth factors that stimulate tertiary dentin formation are left in the mineralized dentin during development. These growth factors may become exposed and subsequently released by tooth wear, erosion initiated by dietary acids, and dentin etching (Smith et al. 2012). These

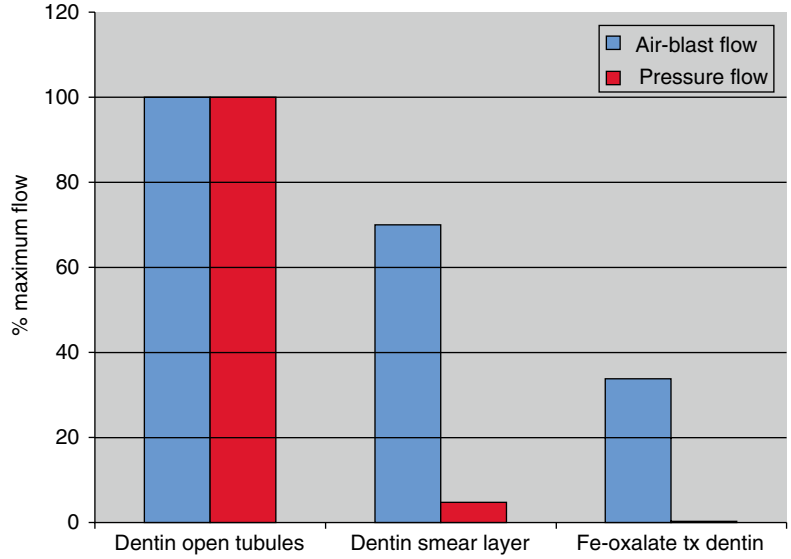

Fig. 2.8 Effects of treatment on fluid flux across deep dentin disks driven by evaporation of water via air blasts or by pressure-induced fluid flow. On the far left, dentin tubules were opened by acid etching. In this condition both pressure and evaporative flow are at their maximal. In the middle section, fluid flux was measured across smear layer-covered dentin. On the far right, acid-etched dentin with open tubules was treated with ferric oxalate to occlude the tubules with calcium oxalate and ferric phosphate crystals. Following the application of ferric oxalate, pressure-driven flow is zero. Creation of porous plugs, for example, smear layers or calcium oxalate crystals, has a greater impact on convective flow than flow induced by air blasts. These results indicate that dentin fluid fluxes induced by natural stimuli may be difficult to eliminate unless the tubules are sealed (Data from Pashley et al. (1996) and Markowitz K, unpublished (2001))

biological and physiochemical processes are natural means by which exposed dentin may become desensitized.

Demineralized dentin matrix retaining acidic proteins has been reported to be capable of remineralization (Clarkson et al. 1991; Bertassoni et al. 2011). This observation has been capitalized on by investigators developing biomimetic analogues of the acidic proteins that would anchor to the appropriate portion of the collagen fibers to facilitate mineral formation in a pattern that replicates the dentin's original structure and restores its physical properties (Tjäderhane et al. 2013). This approach has important applications to the repair of dentin damaged by caries and dietary acid exposure.

Mineralization of the dentin surface can also be achieved by applying materials that adhere to the dentin and interact with saliva to precipitate mineral (Markowitz and Pashley 2008; Cummins 2009). Bioactive glass is an example of a mineralization-promoting material that has been incorporated into dental products (Wang et al. 2011; Lynch et al. 2012) (see Chap. 11). The formation of a mineral-rich surface layer that extends into the dentin tubules, in addition to providing desensitization, may also improve the resistance of the dentin to acid erosion and mechanical wear (Wang et al. 2010; Seong et al. 2013). Several agents that promote the reduction of DH by facilitating the formation of surface mineral also act to prevent or arrest the development of caries (Reynolds 2008; Cummins 2013) (see Chaps. 8 and 10).

Dentin exposure triggers protective host responses that may subsequently reduce dentin permeability. When the dentin in live animals is left exposed, the permeability is reduced in a matter of hours. In contrast, dentin permeability remained high in animals treated with a type of snake venom that caused the depletion of fibrinogen, a soluble blood-clotting factor that is converted into fibrin, a principal insoluble component of blood clots. This experiment demonstrated

that a process related to blood coagulation occurs in the dentin fluid and leads to a reduction in dentin permeability (Pashley et al. 1984). Antibodies reaching the dentin fluid from the pulp have also been demonstrated to reduce dentin permeability in vitro (Hahn and Overton 1997). Large macromolecules similar to those produced in the pulp during defensive reactions move in a peripheral direction through the dentin tubules, transported by outward dentin fluid flow. In the narrower peripheral portion of the tubules, these molecules bind to the tubule walls, reducing dentin permeability. This mechanism protects the pulp from the ingress of bacterial products and would be expected to lead to a decline in DH with time.

Desensitization Treatments Targeting Intradental Nerves

In sensitive teeth, stimuli either activate or reach the intradental nerves by way of the dentin tubules. These tubules can also act as a route of administration for therapeutic agents intended to treat sensitive teeth. Drugs delivered topically to the tooth surface may potentially diffuse through dentin to reach the intradental nerves and other targets located in the deep dentin and pulp (Ciarlone and Pashley 1992). Potassium nitrate (KNO_3) was introduced into clinical use as a desensitizing agent based on empirical observations (Hodosh 1974). Several clinical studies indicate that KNO_3 and other potassium salts reduce sensitivity symptoms over a period of approximately 2 weeks when applied by twice daily brushing (Orchardson and Gillam 2000) (see Chap. 8). These salts have little effect on dentin permeability when tested in vitro (Greenhill and Pashley 1981), suggesting that they alleviate DH symptoms by interfering with the activation of the intradental nerves.

When potassium salt solutions are applied to deep dentin cavities or placed on isolated nerves in concentrations far exceeding their physiological level, they have a profound action on nerve excitability (Orchardson 1978; Markowitz et al. 1991; Peacock and Orchardson 1999). When first applied to deep dentin cavities, or when applied to shallow cavities under positive pressure to drive the solution through the dentin, potassium salts briefly excite the intradental nerves (Markowitz et al. 1991; Wanachantararak et al. 2011). With elevated potassium ion concentration, the intradental nerves become more sensitive to inward flow than they are when exposed to the normal ionic environment (Wanachantararak et al. 2011). Following the initial excitation induced by solutions containing high potassium ion concentrations, the intradental nerves stop firing and their responses to a variety of stimuli are depressed (Markowitz and Kim 1992). In animals, the normally vigorous nerve response evoked by outward dentin flow during the application of negative pressure is transiently inhibited by the positive pressure application of high potassium ion-containing solutions (Wanachantararak et al. 2011).

When solutions containing high potassium ion concentration are applied using positive pressure to test cavities in human teeth, pain is initially evoked (Ajcharanukul et al. 2007). This pain response corresponded to the nerve excitation observed in the animal experiments. When the dentin floor of these test cavities was probed or air blasted after pressure application of a potassium solution, the pain responses were reduced compared to those measured prior to potassium solution application. Solutions containing elevated sodium ion concentration did not share this desensitizing effect. In contrast, when these potassium ion-containing solutions were applied to human dentin cavities without positive pressure, there was no pain. Also the pain-inhibiting action of potassium salts was modest and of short duration when these solutions were applied to human dentin cavities under atmospheric pressure (Noparatkailas et al. 2009). These results indicate that without the assistance of inward pressure, the penetration of potassium ions to the intradental nerve endings by diffusion is limited.

These experiments imply that although potassium salts can inhibit pain induced by clinically relevant stimuli, this effect may be limited when these agents are applied to sensitive teeth in clinical use. In a recent clinical study designed to test an arginine-calcium carbonate-based toothpaste, a commercially available potassium salt-containing

toothpaste was used as a positive control. The potassium salt-based product performed better than the fluoride toothpaste negative control but had an efficacy that was inferior to the arginine compound-containing product (Docimo et al. 2009). Although this and many other clinical studies support the use of potassium salts as a desensitizing agent (Orchardson and Gillam 2000), evidence demonstrating efficacy is considered weak by a number of authors (Poulsen et al. 2006; Karim and Gillam 2013) (see Chap. 8).

Dentin's outward fluid flow acts to oppose and reduce the inward diffusion of solutes such as potassium ions through dentin (Vongsavan et al. 2000). This aspect of dentin physiology accounts for the difficulty clinicians encounter attempting to anesthetize teeth by placing local anesthetic solutions on exposed dentin. Nerve responses can be inhibited if high anesthetic concentrations are applied to dentin or if the solution is administered by inward pressure (Rirattanapong et al. 2013). When applied to the dentin surface in intact teeth, little of the 500 mmol/l potassium ion concentration found in a potassium salt-containing toothpaste diffuses into the innervated inner dentin. The concept that limited transdentinal diffusion hinders the clinical effectiveness of potassium salts as desensitizing agents was based in part on a computer model of potassium diffusion through dentin that takes into account anatomic and physiological parameters (Stead et al. 1996).

In experiments that measured the diffusion of potassium ions or other substances under conditions where there was an opposing transdentinal pressure gradient generating flow, partial tubule occlusion enhanced diffusion across the dentin (Pashley and Matthews 1993; Pashley et al. 2002). Although both convective flow and diffusion are reduced by partial tubule occlusion, occlusion has a greater impact on flow, since flow is $\propto r^4$ (Eq. 2.2) as opposed to diffusion which is $\propto r^2$. Hence partial tubule occlusion greatly reduces the opposing action of flow and has a modest effect on diffusion. Partial tubule occlusion has been examined as a potential method of enhancing toothpaste-derived potassium ion delivery to the inner dentin (Pashley et al. 2002). There is limited clinical evidence however, supporting the idea of using partial tubule occlusion as a means of enhancing the effectiveness of potassium-based toothpaste (Schiff et al. 2000; Sowinski et al. 2001).

The short-term (measured in minutes) actions of potassium salts on the excitability of the intradental nerves that are observed when these agents are placed in dentin cavities can be explained by the role that extracellular potassium ion concentration has in determining the nerve cell's resting membrane potential (Markowitz and Kim 1992; Markowitz and Pashley 2008). Increasing extracellular potassium ion concentration depolarizes the cell; if the depolarized membrane potential exceeds the action potential threshold, the nerve will fire action potentials (Hodgkin and Huxley 1952; Hodgkin and Horowicz 1959). This excitation is recorded in physiological experiments and resulted in pain when potassium solutions are applied to human dentin under pressure (Markowitz et al. 1991; Ajcharanukul et al. 2007; Wanachantararak et al. 2011).

If high extracellular potassium ion concentrations remain, the nerve's action potential threshold adjusts to the depolarization. The maintained depolarization causes the cell's action potential channels to become inactivated and close (Hodgkin and Huxley 1952). When this occurs, the excitation ceases and the nerve cell becomes silent and unresponsive to other stimuli, as was observed in the human and animal experiments described above.

In experiments where isolated nerve fibers were exposed to potassium ion-containing solutions, raising the extracellular K^+ to 10 mmol/l resulted in inhibition of nerve responses (Orchardson 1978; Peacock and Orchardson 1999). These effects are dependent on the extracellular potassium ion concentration and reverse rapidly when the ionic gradients return to physiological levels. It is not clear if these physiological actions of potassium salts on nerve excitability contribute to the clinical effectiveness of potassium salts as desensitizing agents (Markowitz and Pashley 2008; Wanachantararak et al. 2011).

Solutions containing divalent cations, e.g., calcium, magnesium, or strontium, also reduce the excitability of the intradental nerves. Application

of solutions containing these cations blocked the vigorous excitatory response to potassium salt application (Markowitz et al. 1991). Elevated levels of divalent cations in the extracellular environment reduce neuronal excitability (Markowitz and Kim 1992). Strontium salt-containing toothpaste formulations are used to treat sensitive teeth (Hughes et al. 2010). Application of these products to dentin in vitro caused partial tubule occlusion, although the contribution of strontium's effect on nerve excitability to the efficacy of these salts is not clear (Olley et al. 2012; Seong et al. 2013; West et al. 2013).

Pharmacological agents that bind to receptors or have other specific targets are effective at far lower concentrations (have greater potency) and have longer durations of action compared to the effects of potassium ions on intradental nerve activity. For example, the low concentrations of eugenol (0.1 mmol/l) that leach into the dentin fluid from zinc oxide-eugenol fillings have both analgesic and anti-inflammatory effects on the dental pulp (Kozam 1977; Hume 1984; Markowitz et al. 1992). Eugenol has both excitatory and inhibitory actions on nerve cells and interacts with a variety of neuronal receptors (Park et al. 2006, 2009; Chung et al. 2014; Klein et al. 2014). These studies determining the mechanism of action for an old drug lead us to conclude that a more effective targeted treatment of DH and other forms of dental pain is achievable.

One innovative approach is use of the heat/capsaicin receptor (TRPV1) ion channel as a pathway to allow a highly effective but normally impermeant cationic local anesthetic drug to cross cell membranes and block nociceptor activation. This treatment would be accomplished by the simultaneous administration of capsaicin and the cationic local anesthetic. Since many nociceptors (unfortunately not including the neurons responding to dentin stimulation) (Närhi et al. 1992) possess TRPV1 receptors, this approach would selectively target pain without the loss of non-pain sensation (Kim et al. 2010).

Inflammation and inflammatory mediators sensitize the intradental nerves to pain-evoking dentin stimuli (Ngassapa et al. 1992; Olgart 1996; Byers and Närhi 1999; Ajcharanukul et al. 2011). In acute inflammation triggered by tissue injury, prostaglandins sensitize nociceptors and enhance the actions of other mediators (Goodis et al. 2000). These cell lipid-derived mediators contribute to the alterations in neuronal VGNa channels observed in inflammation (Rush and Waxman 2004).

Inhibition of prostaglandin synthesis counteracts some of the effects that acute injury has on intradental nerve function. Systemic administration of nonsteroidal anti-inflammatory drugs (NSAIDS) prevents the activation of the intradental nerves by heat stimulation (Ahlberg 1978). Following tooth injury, systemic administration of NSAIDS reduces pulpal inflammatory mediator production (Chidiac et al. 2009) and prevents central neuroplastic changes that are indicative of enhanced pain perception (Worsley et al. 2008).

Currently, the role of inflammation in DH involving teeth lacking caries or other forms of pathology is not clear. As described above, the pulps of teeth with exposed, patent dentin tubules are susceptible to bacterial insults from overlying plaque. The role of systemic and local anti-inflammatory therapy in the treatment of DH is therefore an open area for investigation (Pashley 2013).

The goal of all DH treatments is to return the dentin and pulp to a state of health. The translation of in vitro results to the clinical arena is complex. As will be discussed in other chapters in this book, the clinical evaluation of tooth sensitivity treatments is complex and presents unique challenges (see Chaps. 4, 5, and 10).

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The Prevalence of Dentine Hypersensitivity

3

Sahar Taha

Methods of Reporting DH Prevalence

Two main methods were reported in the published literature for studying the prevalence of DH, namely, self-reported questionnaires and clinical examination. Higher prevalence values were reported in studies that relied primarily on self-reported questionnaires rather than studies which were combined with clinical examination (Table 3.1). In the self-reported questionnaires, the prevalence values are generally considered to be overestimated due to the complexity of the other diseases or conditions that may present with pain for example, caries, cracks and fractures (Scaramucci et al. 2014; Rees and Addy 2004) (see Chaps. 4 and 5). In addition, patients may not always understand what is required of them by the clinician and may therefore be too embarrassed or not sufficiently concerned to ask for clarification (Clayton et al. 2002).

Moreover, the nature of the questions in the survey may also influence the reported prevalence values. Nonspecific questions that identify pain or sensitivity, relying on the participant's own pain threshold as a trigger for identifying a positive result, will exclude patients who do not perceive their DH to be a problem that requires attention (Cunha-Cruz et al. 2013).

There are relatively few studies that interviewed the subjects and asked them questions related to pain or discomfort before a clinical exam was performed (Costa et al. 2014; Dhaliwal et al. 2012; Kehua et al. 2009; Que et al. 2013). However, this method may also have an interviewer bias effect on the reporting of the condition (Clayton et al. 2002).

The clinical examination for DH generally has focused on two main methods, thermal by air blast or tactile by probing (Chap. 5). Greater numbers of teeth testing positive to the stimulus were usually achieved using the thermal/evaporative technique than other available techniques, e.g. tactile stimulation (Liu et al. 1998). The proposed reason behind the lower values achieved with probing techniques (tactile) was probably due in part to the fact that only a small area of the exposed dentine was sensitive, and if the probe did not touch this area, the subject will not probably respond (Scaramucci et al. 2014).

Other investigators, for example, Flynn et al. (1985), used a cold water mouth rinse to diagnose DH. However, this method does not necessarily provide an accurate response from the teeth affected by this condition as pain arising from other dental conditions may also respond during the rinsing process.

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Table 3.1 Summary of prevalence studies on DH

Study	Country	*n*	Study type	Method of clinical assessment	Setting	Prevalence (%)	Peak of age	M-F ratio	Commonly affected teeth	% with GR[a]
Clayton et al. (2002)	UK	250	Q[b]	NA[j]	GDP[f]	50 %	3rd decade	1:1	Mand right sextant	NA
Gillam et al. (2001)	UK and Korea	557	Q	NA	GDP	52–55.4 %	3rd–4th decades	NA	NA	NA
Gillam et al. (1999)	UK	277	Q	NA	GDP	52 %	3rd decade	1:1.4	NA	NA
Colak et al. (2012a)	Turkey	1,463	Q	NA	University students	8.4 %	NA	1:1.2	NA	NA
Rane et al. (2013)	India	960	Q + CE	AB	Dental hospital	42.5 %	4th decade	1.6:1	Lower anterior teeth	NA
Bamise et al. (2007)	Nigeria	2,165	Q + CE[c]	AB[d]/probing	University	1.34 %	4th decade	1.4:1	Molars	12.8 %
Rees and Addy (2004)	UK	5,477	Q + CE	AB/PDA[e]	GDP	2.8 %	4th decade	1:1.5	Max[g] 1st molars	93 %
Taani and Awartani (2001)	Saudi Arabia	259	Q + CE	AB/PDA	GDP	42.4 %	4th decade	1:4	Max molars and mand anteriors	5 %
Fischer et al. (1992)	Brazil	635	Q + CE	AB/probing	Marine dental clinic	17 %	M, 6th decade; F, 3rd decade	1:1	Incisors and premolars	NA
Flynn et al. (1985)	Scotland	369	Q + CE	CWMR[k]/probing	University	8.7 %	4th decade	1:1	Premolars	NA
Liu et al. (1998)	Taiwan	780	Q + CE	AB/probing	University	32 %	NA	1:1	Premolars and molars	23 %
Amarasena et al. (2011)	Australia	12,692	Q + CE	NA	GDP	9.1 %	4th–5th decades	1:1.5	Max premolars and molars	39 %
Chrysanthakopoulos (2011)	Greece	1,450	Q + CE	AB	GDP	18.2 %	5th decade in Males 7th decade in Females	1:1.25	Premolars	85.9 %
Ye et al. (2012)	China	2,120	Q + CE	AB	GDP	34.1 %	5th decade	1:1.5	Premolars	84.3 %
Tengrungsun et al. (2012)	Thailand	420	Q + CE	AB	University	30.7 %	4th decade	1:2.4	1st molar	NA

Bahsi et al. (2012)	Turkey	1,368	Q + CE	AB/probing	GDP	5.3 %	5th decade	1:2	Max premolars	88.4 %
Colak et al. (2012b)	Turkey	1,169	Q + CE	AB	University	7.6 %	5th decade	1:1.5	Max premolars	95.7 %
Dhaliwal et al. (2012)	Punjab, India	650	Q + CE	AB	Screening participants in villages	25 %	6th decade	1:1.6	Mand incisors	NA
Cunha-Cruz et al. (2013)	USA	787	Q + CE	AB	GDP	12.3 %	18–44	1:2.6	Premolars and molars	85.6 %
Que et al. (2013)	China	1,023	Structure interview + CE	AB	General population	27.1 %	7th decade	1.06:1	Premolars	15.5 % for the age group of 60–69
Scaramucci et al. (2014)	Brazil	300	Q + CE	AB/probing	University	46 %	NA	1:2.56	NA	NA
Al-Khafaji (2013)	UAE	204	Q + CE	AB	GDP	27 %	3rd decade	1.3:1	Lower anterior	15 %

[a]Gingival recession
[b]Questionnaire
[c]Clinical examination
[d]Sensitivity to air blast
[e]Periodontal disease assessment
[f]General dental practice
[g]Maxillary
[h]Periodontal specialty clinic
[i]Mandibular
[j]Not applicable

Contributing and Confounding Factors to the Prevalence of DH

Non-carious Cervical Lesions

In a Chinese population, 1,010 individuals diagnosed with DH, 644 (63.8 %) were also diagnosed to have non-carious cervical lesions (NCCLs) (Que et al. 2013). Erosion was also recognised as a predisposing factor for DH in an Australian population (Amarasena et al. 2011) (see Chap. 4). In the same study, abfraction was the least associated predisposing factor. Similarly, Bamise et al. (2007) reported a 10.9 % prevalence for attrition with DH, 7.4 % abrasion, 3.5 % erosion and 2.7 % abfraction respectively. Abrasion was reported to have the highest prevalence in Emirati patients with DH (27 %), whereas abfraction was the least associated with only a 5 % occurrence in DH patients (Al-Khafaji 2013). The lack of consistency in relating the different NCCL and DH factors may also attribute to the difficulty in diagnosing these lesions.

On the other hand, no association with NCCL was reported in a cohort of 787 Americans (Cunha-Cruz et al. 2013).

Periodontal Disease

As mentioned in Chapter 1 there have been changes to the terminology describing DH and the term Root sensitivity (RS) has been recommended to describe pain associated with and arising from exposed dentine of periodontally involved teeth or following periodontal treatment (Sanz and Addy 2002). Gingival recession has been widely associated with DH (Amarasena et al. 2011). Loss of attachment was a major associative factor leading to an increased incidence of DH in younger age groups (Que et al. 2013). The percentage of DH patients who have gingival recession may be as high as 95.7 % (Colak et al. 2012b).

The incidence of DH has been reported to increase following periodontal treatment (Lin and Gillam 2012; Splieth and Tachou 2012). For example, Al-Sabbagh et al. reported that the incidence increased from 30 % preoperatively to 79 % after 1 week of open-flap periodontal debridement (Al-Sabbagh et al. 2010). Furthermore, Fischer et al. (1992) reported that supragingival and subgingival scaling procedures may also cause a transient occurrence of DH. Lin and Gillam (2012), in their systematic review, reported that the prevalence for DH following nonsurgical therapy was between 62.5 and 90 % 1 day following treatment, decreasing to approximately 52.6–55 % after 1 week. The prevalence of DH following surgical therapy was between 76.8 and 80.4 % 1 day after treatment, subsequently decreasing over time to 36.8 % after 1 week, 33.4 % after 2 weeks, 29.6 % after 4 weeks and 21.7 % after 8 weeks. It was suggested that DH may be relatively mild/moderate in nature and transient in duration following periodontal therapy.

Sample Selection

Studies conducted at hospitals or specialty practices tend to report higher prevalence values (Chabanski et al. 1996); presumably this may be due to the greater risk of root exposure as a result of periodontal attachment loss and gingival recession following periodontal treatment. However, a clear pattern for prevalence values according to the sample selected is still lacking (Table 3.1).

Teeth Location and Surfaces

Various intraoral locations may be affected with DH. The sites of predilection in descending order for DH are canines and first premolars, incisors and second premolars and molars (Dababneh et al. 1999). However, the literature has not been consistent in reporting the intraoral distribution of the condition (Bamise et al. 2007). The buccal surface appears to be the most affected, followed by labial, occlusal, distal and lingual surfaces with the incisal and palatal surfaces which were the least affected (Amarasena et al. 2010; Splieth and Tachou 2012). Interestingly, the occlusal surface was reported to have the highest sensitiv-

ity by 56 %, whereas the buccal surface sensitivity was about 28 % (Bamise et al. 2007), but this may be due to differences in the study populations.

Gender

A number of studies have reported an association between DH and gender. Relatively few studies have reported that females were more affected with the condition (Scaramucci et al. 2014; Rees and Addy 2004; Taani and Awartani 2001; Amarasena et al. 2011). Other studies have, however, failed to find an association (in terms of statistically significant differences) between the two variables (Fischer et al. 1992; Splieth and Tachou 2013; Clayton et al. 2002; Flynn et al. 1985; Liu et al. 1998). The reported slightly higher prevalence in the female population may reflect their better oral hygiene awareness (Dababneh et al. 1999) and their dietary habits in eating more healthy fruity food items which may also be erosive in nature (Splieth and Tachou 2012). Females also tend to visit the dentist more frequently which may result in an over-representation and, therefore, introduce a classical selection bias if the study sample was recruited in dental practices. In addition, females often articulate health problems more willingly than men, which may lead to an added detection bias for females (Splieth and Tachou 2012). Other studies, however, have reported a greater occurrence of DH in males (Rane et al. 2013; Al-Khafaji 2013; Bamise et al. 2007), but again this may be due to differences in the demographics of the study populations.

Age

DH is mostly prevalent among the young population in the third and fourth decades (Table 3.1). This could be linked to the increase in acidic food/drink intake and the influence of greater oral hygiene awareness and measures (Chabanski et al. 1997; Clayton et al. 2002). It would be interesting to speculate that as older individuals in the global population retain more teeth than previously reported, there may be a subsequent increase in the incidence of DH, gingival recession and periodontal disease respectively (Bahsi et al. 2012) (see Chap. 4).

Review of Published DH Prevalence Data

DH is a prevalent clinical condition; however, studies evaluating its prevalence are not abundant and rather contradictory (Splieth and Tachou 2013). A critical review of the published literature on DH clearly demonstrates a wide variation in the reported prevalence values of this condition (Table 3.1). This variation may be attributed to the differences in populations and sample selection, method of investigation and dietary habits (Dababneh et al. 1999; Davari et al. 2013).

Uncertainty regarding the prevalence of DH may also have significant consequences for both patients and dental practitioners. With a vague perception of prevalence comes uncertainty in diagnosis, the appropriate time to treat and how aggressive the treatment should be (Cunha-Cruz et al. 2013). The extreme variation in the prevalence values reported in the published literature may be classified into three categories:

- DH prevalence using surveys (around 50 %)
- DH prevalence diagnosed using combined surveys and clinical exams (1–20 %)
- DH in patients who have periodontal disease or have been receiving periodontal treatment (60–90 %)

The question as to whether DH is a major problem for public health concerns has also been raised, and the consensus in the published literature would appear to be that it is a relatively minor problem (Rees and Addy 2002; Gillam 2013). Although it should be acknowledged that Dentists reported that in 10 % of their patients DH was considered to be a severe problem (Gillam et al. 2002). A recent review on the burden of DH, however, by Cunha-Cruz and Wataha (2014) from the published studies in the literature would appear to suggest that the best estimate of the prevalence of DH was 10 % with an average of 33 % across the published studies accepted in their review.

Future Studies for the Prevalence of DH

DH is a condition with a relatively high prevalence among the different population groups. The presence of national surveys on the condition should help in forming a clear strategy for the prevention and treatment of this condition. Population-based representative samples are now needed (Splieth and Tachou 2012). Furthermore, given the changes in the definition of both DH and RS, investigators should undertake new studies with a view to capture more accurate prevalence values on the two conditions as currently these values are included under the term DH.

Data on the confounding and contributing factors may also need to be collected and analysed more carefully, as some of these factors have previously been disregarded in the reporting of prevalence values. In the future, special attention should be taken in the design of study protocols to include the prevalence of NCCL and in examining its association with DH given the increase in the prevalence of both erosive and abrasive intraoral lesions.

Conclusions

The prevalence reports of DH are not abundant and are somewhat contradictory. The wide variation in the prevalence values reported in the literature may be reduced by dividing the reporting of the condition into three categories: (1) DH prevalence using surveys (around 50 %), (2) DH prevalence diagnosed using combined surveys and clinical exams (1–20 %) and (3) DH in patients who have periodontal disease or have been receiving periodontal treatment (60–90 %). Questionnaires have been commonly used for the evaluation of DH prevalence; however, when combined with clinical examination, these values were significantly reduced. Furthermore, investigators should undertake new studies with a view to capture more accurate prevalence values on both DH and RS. The multiple confounding and contributing factors that are associated with DH should be evaluated more carefully in future research when investigators report on the prevalence of DH.

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Aetiology and Clinical Features of Dentine Hypersensitivity

4

Ryan Olley and David Bartlett

Introduction

Dentine hypersensitivity (DH) is a common oral condition, which is typically short lasting, an intense pain located around teeth and often associated with cold stimuli. An innate problem with DH is that its clinical features are transient and patients do not always present with DH at examination, even though they may suffer from it regularly. Indeed, the nature of DH appears to be cyclic and most sufferers self-medicate and use desensitising toothpaste formulations to control the condition. There are increasing suggestions from the published literature, that DH is transient nature of the condition (Gillam 2013; West 2006; West et al. 2013b). The reasons for this trend, historically, have been unclear. Indeed, the cause/s of DH have been poorly understood and resulted in DH being termed an enigma 32 years ago, and this concept has been revisited on a number of occasions (Johnson et al. 1982; Dababneh et al. 1999; Addy 2002; Markowitz and Pashley 2008). The apparent historical lack in the understanding of the aetiological processes in particular tooth wear often resulted in elusive treatment and preventive strategies which focused on the symptoms of DH rather than its cause/s (Markowitz and Pashley 2008). Nevertheless, our understanding of the condition is somewhat clearer today**.** This chapter therefore focuses attention on the clinical features of DH and in detail on the causes of DH and the associated clinical presentation.

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Clinical Features of DH

DH is a common clinical condition and patients describe it as a short, sharp pain that affects the permanent dentition (Addy 2002). The clinical features are explained in the definition of DH. This was first suggested by Dowell et al. in 1983 (Dowell and Addy 1983), later finalised by an international workshop on the design and conduct of clinical trials for DH (Holland et al. 1997) and most recently modified by the Canadian Advisory Board on Dentin Hypersensitivity (Canadian Advisory Board 2003). The definition stated that DH 'is characterised by short sharp pain arising from exposed dentine in response to stimuli typically thermal, evaporative, tactile, osmotic or chemical and which cannot be ascribed to any other form of defect or disease'. The clinical description of the condition is explained in the first part of this definition. The second part differentiates it from other clinical conditions that might have identical symptoms but different management strategies (Dowell et al. 1985), and these are listed in Table 4.1.

In the definition of DH, the word 'disease' replaced the previously used word 'pathology' following the Canadian consensus. However,

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Table 4.1 Examples of clinical conditions that need to be excluded prior to a definitive diagnosis of DH

Dental caries
Cracked tooth
Fractured restoration
Post-restorative sensitivity
Medication sensitivity
Post-nonsurgical/postsurgical periodontal sensitivity
Palatogingival groove
Non-odontogenic origin

disease relates more to the clinical outcome of the condition, rather than its aetiology or pathology which will be discussed below.

Aetiology

DH can be associated with a number of aetiologies including non-surgical and post surgical treatment of periodontal disease, erosion and gingival recession. These are discussed in turn below together with some other rarer aetiology.

Postsurgical Periodontal Disease (Recession Induced by Management)

DH may occur iatrogenically and it has been reported to affect up to 57 % of the general population in one subject-reported study following scaling or root planning (Irwin and McCusker 1997). Another study of periodontal patients reported a prevalence of 85–95 % (Chabanski et al. 1996). In an early in vitro study, it was reported that after root surface debridement; the dentine surface tubules were exposed following the removal of the surface covering or smear layer (in part). In health, the smear layer reforms and prevents 86 % of fluid movement across the dentine (Pashley et al. 1978). The smear layer may be defined as a thin 'loose' layer consisting of organic collagen and glycosaminoglycans that form an adherent matrix over mineralised tissue arising from saliva and dentine particles that might occlude the dentine tubules (Brannstrom 1966; Pashley 1984). It has also been suggested that in periodontal disease and any treatment that may expose dentine, bacteria may colonise and break down the smear layer and penetrate into the root dentine (Adriaens 1989) which in turn may initiate inflammation in the pulp. Several Investigators have suggested that this may be an alternative explanation for the mechanism associated with DH (Lundy and Stanley 1969; Brannstrom 1982; Dababneh et al. 1999). Although in the light of the changes in the terminology of DH/RS it may be more relevant as a mechanism for RS. It is the bacterial products, however, rather than the bacteria, which are likely to diffuse towards the pulp. Initially, plasma proteins/immunoglobulins from the blood diffuse into the dentine tubules, decreasing permeability (Pashley 1984). Following chronic periodontal disease and ongoing treatment, increases in pulpal pressures, nerve spouting reduction in pain thresholds, scar tissue and reduced plasma proteins may worsen DH (Pashley 1984).

Tooth Whitening Procedures (Unknown or Not Understood Interrelationship)

Tooth whitening procedures often involve carbamide peroxide, which breaks down into hydrogen peroxide and urea and bleach the tooth. This causes dehydration within the tooth and symptoms of DH. However, the symptoms are often temporary and for the duration of treatment (Ferrari et al. 2007). Bleaching may however, involve a different mechanism to that of DH (Gillam et al. 2013) and therefore is not strictly an aetiology factor for DH and may therefore, require alternative management strategies (Markowitz 2010).

Developmental Lesions (Rare Conditions Where Surface Morphology of Teeth Changes)

These can often affect the primary and later permanent dentition and can cause symptoms of DH. They include, for example, amelogenesis and dentinogenesis imperfecta as well as other conditions of the enamel and/or dentine that cause hypomineralisation and hypoplasia. As with bleaching, these symptoms may involve a mechanism different to that of DH.

Dietary Factors (Erosive Diets) and Gingival Recession

DH is most commonly associated with erosive dietary factors and gingival recession, and these will be discussed in more detail in the following sections of this chapter. The largest European clinical study to investigate the presence or otherwise absence of DH in association with its various aetiologies involved 3,187 adults enrolled from general dental practices in France, Spain, Italy, the United Kingdom, Finland, Latvia and Estonia (West et al. 2013b). The proportion of subjects who were examined clinically to have DH on at least one tooth surface was 42 % following an evaporative stimulus in a clinical setting. The proportion of subjects who reported having DH in the previous 12 months was less (27 %), and this might reflect the transient nature of the pain in addition to good coping mechanisms. According to (West et al. 2013b) when the various aetiological factors were investigated, there was a strong progressive relationship between clinically elicited DH and erosive tooth wear caused by dietary factors and gingival recession. 29 % of these subjects had signs of tooth wear recorded using the Basic Erosive Wear Examination (Bartlett et al. 2013). The prevalence figure of DH was relatively high compared to similar studies conducted in general dental practice, 2.8 % (Rees and Addy 2004), 9.1 % (Amarasena et al. 2011) and 5.3 % (Bahsi et al. 2012), but DH has also been reported in other studies and associated with erosive tooth wear (Lussi and Schaffner 2000; Fares et al. 2009) and gingival recession (Bamise et al. 2008) (see Chap. 3). In a population in the United Kingdom, the prevalence of DH examined clinically was observed to be over 40 % and was associated with gingival recession (Olley et al. 2013). An investigation of the same group of patients also indicated that this population had 43 % of tooth surfaces with tooth wear (Olley et al. 2014b). In a prospective study of randomly selected subjects in Switzerland, 34.8 % of subjects reported DH; however, the prevalence of DH in those subjects with tooth wear was 84.6 % (Lussi and Schaffner 2000). In a recent study (Olley et al. 2014b ahead of print), subjects who recently consumed dietary acids were more likely to have DH when examined at their dental appointment. It is therefore not surprising that DH has been described as a tooth wear phenomenon (Addy 2002). It often occurs with intact periodontal tissues when cervical enamel is removed and coronal dentine exposed and in combination with non-carious cervical lesions (NCCLs) or following gingival recession. Therefore, it is important to recognise the clinical features of tooth wear, in particular erosion. These will be discussed in greater detail together with gingival recession and oral hygiene practices below.

Tooth Wear and Gingival Recession

Tooth wear is the irreversible, non-traumatic loss of dental hard tissues due to aetiological processes classified as erosion, attrition, abrasion (Bartlett and Smith 2000; Ganss et al. 2006) and abfraction (Lee and Eakle 1984). Tooth wear may be considered a normal part of ageing or a physiological process, from the anthropological perspective (Whittacker 2000). Historically, it has been suggested that the human dentition is designed to wear and that this process is important to optimise the functional capabilities of the dentition (Berry and Poole 1974). Within dentistry, Smith and Knight first distinguished physiological and active or pathological tooth wear (Smith and Knight 1984). Tooth wear may be defined as pathological as opposed to physiological if it appears in relatively younger patients and the rate of progression of tooth wear is fast. Crucially, physiological tooth wear allows time for the pulp to lay down reparative or secondary dentine, which could prevent fluid flow within the dentine tubules and may also reduce DH (Krauser 1986). In contrast, pathological tooth wear may cause DH as well as other aesthetic and functional concerns (Smith and Knight 1984; Al-Omiri et al. 2006). During pathological tooth wear, the symptoms of DH are reported more frequently (Smith and Knight 1984; Absi et al. 1987; Addy and Pearce 1994; Dababneh et al. 1999; Addy 2000, 2002). As pathological tooth wear lesions progress into dentine, the radius of dentine tubules become larger and the distance

to the pulp decreases. As a result, the hydraulic conductance of fluid within dentine would be expected to increase together with an increase in symptoms associated with DH (Pashley 1990). However, exposure of dentine (as a result of tooth wear or gingival recession) will not necessarily lead to the presence of DH per se (Absi et al. 1987; Yoshiyama et al. 1996; Addy 2002). Therefore, tools to measure tooth wear in terms of surface loss alone may not necessarily reflect the presence of DH.

For the purposes of understanding the aetiological processes involved in DH, the names 'lesion localisation' and 'lesion initiation' were proposed (Dababneh et al. 1999; Addy 2002). Lesion localisation involves dentine exposure, which may occur as a result of enamel or dentine wear or gingival recession. Lesion initiation may arise following lesion localisation and involves the exposure of patent or un-occluded dentine tubules from the surface of dentine to the pulp. This often occurs following loss of the smear layer. It should be noted that in addition to the smear layer or other surface occlusions, the degree of sclerosis by peritubular dentine and the extent of occlusion by reparative dentine on the pulpal surface might also affect the capacity for fluid movement within the dentine tubules (Yoshiyama et al. 1996). Dentine exposure will not necessarily lead to DH if the dentine tubule system is not patent. Indeed, clinical observation studies show that DH can be uncommon even in cases where the pulp is visible through a thin bridge of dentine (Bartlett and Ide 1999), which is likely to consist of sclerotic or transparent dentine.

Erosion and DH

Erosion is currently considered to be the most common and important aetiological factor for tooth wear in Europe (Seligman et al. 1988; Deery et al. 2000; Addy and Hunter 2003; Grippo et al. 2004; Lussi 2006). This process is due to the superficial demineralisation of hard tissue and the chemical dissolution of the apatite crystals in enamel by an acid (Bartlett 2005) that is not produced by the oral flora but from intrinsic

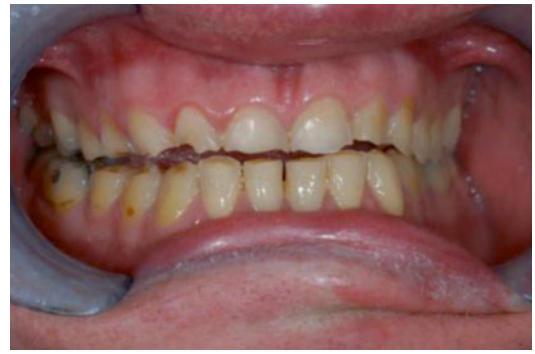

Fig. 4.1 An example of a patient with severe erosion, which has initiated a loss of crown height and an anterior open bite due to gastric erosion

or extrinsic sources (ten Carte et al. 2008), both of which are strongly associated with DH (West et al. 2013a). Typical sources of intrinsic acid are regurgitated stomach acid containing hydrochloric acid (HCL) due to vomiting or gastro-oesophageal reflux (Scheutzel 1996). Typical extrinsic sources are provided below (Zero 1996; Lussi 2006) (Fig. 4.1):

- Diet (e.g. acidic citrus and other fruits, carbonated beverages and sports drinks, beers and herbal teas, vinegars and pickles, candies)
- Medicaments (e.g. non-encapsulated HCL replacement, chewing ascorbic acid tablets (vitamin C) and acetylsalicylic acid tablets (aspirin), iron tablets, salivary stimulants)
- Occupation (e.g. jobs involving wine tasting or working near acidic industrial vapours)
- Sports (e.g. improperly chlorinated swimming pools)

There is an increasing body of literature indicating that acid erosion caused by relatively small acidic challenges will lead to loss of enamel and dentine and expose the dentine tubules and initiate DH. This literature included laboratory research (Addy et al. 1987b; Absi et al. 1992; West et al. 1999; Vanuspong et al. 2002; Gregg et al. 2004; Ganss et al. 2009), review papers (Addy and Hunter 2003; Addy 2005; Zero and Lussi 2005; Lussi 2006), clinical research (Absi et al. 1992; Hughes et al. 1999; Hunter et al. 2000; Olley et al. 2012, 2014a) and prevalence studies (Lussi and Schaffner 2000; Smith et al. 2008; West et al. 2013b).

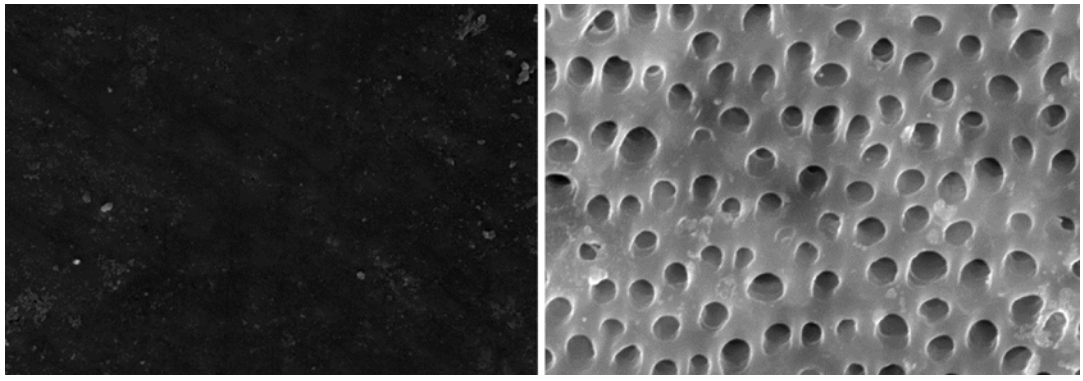

Fig. 4.2 Scanning electron micrograph (SEM) images (×2,000) of untreated root surface (*left*) and root surface following a 1 min 6 % citric acid challenge with gentle agitation (*right*). Scale bar 2 μm

Erosive acid challenges are important in removing the smear layer and pellicle (on the tooth surfaces exposed to saliva) and initiating DH. In two clinical studies, cavities were prepared in dentine and hydrostatic pressures were applied to the exposed dentine. Patients reported sensations of short sharp pain in those lesions in which an acid challenge was used to remove the smear layer from the surface of the prepared cavity but not in lesions in which the smear layer was present (Brannstrom 1965; Ahlquist et al. 1994). This can be easily demonstrated in the laboratory. For example, Figure 4.2 shows a high-powered scanning electron microscopy image of the surface of root dentine taken from the buccal cervical region of a premolar tooth. Following treatment of the surface of the dentine with a 6 % solution of citric acid for one minute under agitation, the smear layer was removed and the dentine tubules become visible. This work is supported elsewhere (Pashley et al. 1981; Addy et al. 1987a). Most of the dentine tubules are greater than 1 μm in diameter post-acid challenge. This is greater than 0.83 μm, the minimum diameter reported as being required to elicit DH at the cervical area of the tooth near the dentino-enamel junction (DEJ) (Absi et al. 1987). The effects of acids are to remove the smear layer and expose patent or un-occluded dentine tubules. It was concluded in these studies that the presence of these patent dentine tubules was related clinically to DH.

There are a number of food products that contain acids which are popular consumables in the United Kingdom. These are summarised, together with pH and pKa values (explained below), in Table 4.2.

Table 4.2 Erosive products (with associated acids) available in the United Kingdom with pKa and pH values

Beverage	Acid	pKa (titratable acidity)	pH
Citric fruits including oranges, lemons, grapefruit	Citric acid	3.14	2.2
Apples, plums and peaches	Malic acid	3.4	2.2
Grapes and wines	Tartaric acid	2.89	2.2
Fermented products and yoghurt	Lactic acid	3.86	2.4
Preservative	Acetic acid	4.76	2.9
Rhubarb	Oxalic acid	4.14	1.3
Cola drink	Phosphoric acid	2.15	1.5

Despite the acidity of these products, not all popular erosive beverages will initiate the exposure of the dentine tubules. This was demonstrated in an early study, which investigated the effect of various dietary beverages on dentine and reported that many of these popular erosive beverages of acidic or 'low' pH would not lead to exposure of the patent dentine tubules (Addy et al. 1987a). These beverages included a low-pH carbonated drink, Coca-Cola and Ribena (a fruit-based soft drink). Instead, consumables, for example, red and white wine, citrus fruit juices, apple juice and yoghurt, produced visible dentine tubules as observed by SEM (Addy et al. 1987a). It should be

pointed out that Addy, Absi et al 1987 examined smear layer removal and not tooth structure loss. Citric acid was described at the time as most detrimental to human enamel (Meurman et al. 1987). Grenby et al. then demonstrated that titratability was likely to be more important than pH in determining the erosive potential of carbonated drinks, fruit juices etc (Grenby et al. 1989). For example, the Coca-Cola drink and Ribena were observed to have substantially lower titratable acidities in contrast to fruit juices (lemon, orange and pineapple), and they were therefore less acidic. Titratable acidity or neutralisable acidity (pKa) is the volume of alkali required (typically 0.1 mol solution of sodium hydroxide) to raise the pH of a standardised volume of beverage (typically 25 ml) to pH 7 (Chadwick 2006). In dental erosion, titratability provides an indication of the actual concentration of hydrogen ions available to interact with a mineralised surface, which provides an indication of the erosive potential of a particular acid challenge (Zero 1996). In addition to a higher titratable acidity and lower pH, the severity of an erosive challenge is also likely to increase with the duration of the acid challenge, temperature and ion concentration, frequency of the acid challenge and the presence of chelating agents (Moss 1998; West et al. 2000; Wiegand et al. 2007). The latter is related to the calcium-binding property of the acid. Acids, for example, citric, malic and tartaric acid, contain more than one carboxyl group in their chemical composition (di and poly carboxylic acids), and this will result to the binding of more than one soluble calcium ion complexes at high pH (Meurman et al. 1987). Calcium binding from the saliva will result in the loss of the ion effect of calcium in saliva, which will lead to more dissolution tendency. Also, if calcium from the saliva is bound, there may be a tendency for more dissolution of the dental tissue in order to replace the calcium lost in saliva (Meurman and tenCate 1996). This will result in further erosion of the surface layer, due to the gradual release of tooth mineral due to a buffering action (Grenby et al. 1989). As a result, fruit juices, for example, orange or pineapple juice, will result in more demineralisation than other popular erosive beverages such as the Coca-Cola and lemonade drinks, which contain phosphate (Grenby et al. 1989). Despite their low pH, the phosphate in Cola drinks raises the degree of saturation of the solution with respect to tooth mineral; Calcium and phosphate. Furthermore, in contrast to most other organic acids, the calcium salt of oxalic acid is insoluble. Foods containing this acid should be therefore less erosive in nature.

The importance of a mature salivary pellicle in providing a protective role during erosion must not however be underestimated; in particular the phosphate, calcium and fluoride content of an erosive challenge may prevent dental wear (Zero and Lussi 2005), and sleeping medications (which may reduce salivary flow) are associated with more reported DH (West et al. 2013a). Currently there is ongoing research in this area, and clinical experiments have demonstrated that the salivary pellicle forms a protective layer against erosion (Moazzez et al. 2014).

Abrasion and DH

Abrasion is a physical process, which occurs as a result of the mechanical wear of dental tissues by foreign bodies. Toothbrushing and toothpaste formulations are common forms of dental abrasion (Addy and Hunter 2003; Addy and West 2013). Toothbrush abrasion is influenced by brushing habits, force applied and the time spent brushing (Hooper et al. 2003). There are additional habits linked to abrasion, for example, onychophagia, clips and other tools, which may come into contact with teeth. Unlike erosion, there are limited data to support the importance of abrasion in causing DH, but toothbrushing with a toothpaste has been previously implicated in the aetiology of DH (Addy and Hunter 2003; Abrahamsen 2005; Bartlett and Shah 2006; Ganss et al. 2009; Addy and West 2013) (Fig. 4.3).

According to Addy (2005), the effects of normal toothbrushing on wear of the enamel are negligible and unlikely to lead to exposure of the underlying dentine alone unless erosion is also occurring. Normal toothbrushing, even for extended periods of time (measured in years), will also cause limited wear of dentine, and the wear may be limited to the smear layer, which would presumably have a subsequent effect on DH (Absi et al. 1992). Increasing the force of

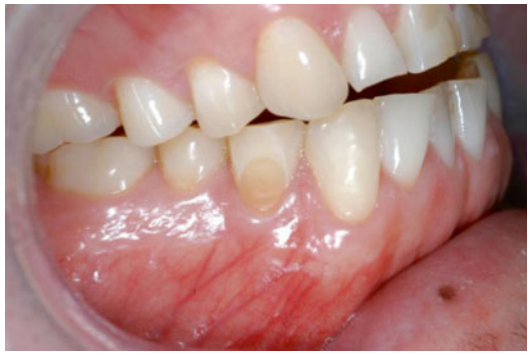

Fig. 4.3 An example of abrasion on the buccal cervical region commonly referred to as a non-carious cervical lesion (*NCCL*)

toothbrushing can, in addition, result in increased tooth surface loss in dentine. Manual, as opposed to electric toothbrushing, has been demonstrated to cause more dentine wear because the force applied with a manual toothbrush was often higher (Knezevic et al. 2010; Van der Weijden et al. 2011). Similarly, prevalence studies have demonstrated that brushing with medium and hard, rather than soft, stiffness toothbrushes will cause more dentine wear (Smith et al. 2008). It has also been reported that when greater forces are applied to healthy dentine using a manual toothbrush, patients are more likely to report pain that resembles DH (Addy 2005).

Toothbrushing with a toothpaste adds an abrasive component. Nonetheless, normal toothbrushing with toothpaste formulations (with the exception of non-hydrated alumina) in the absence of acid is likely to cause little or no wear of enamel and dentine (Hunter et al. 2002; Addy 2005). Abnormal or abusive use (e.g. using excessive toothpaste) can however lead to pathological wear (Hunter et al. 2002; Hooper et al. 2003; Turssi et al. 2010). The filament stiffness of toothbrushes may also be important in dentine wear initiated by a toothpaste. Laboratory studies have demonstrated that smaller filament stiffness (decreasing diameter of filament) initiated more wear in dentine using various abrasives of toothpaste formulations (post-acid erosion) and that the abrasivity of the dentifrice is more important than the filament stiffness (Wiegand et al. 2009). This would suggest that multifilament soft brushes may retain more toothpaste, which in turn might lead to more tooth wear.

Dentifrice (toothpaste) abrasivity is normally measured using the RDA (Relative Dentine Abrasivity), which has a numeric value. The International Organization for Standardization guidelines state that for dentine, the abrasivity of test formulation should not exceed 2.5 times the reference abrasive, e.g. RDA must not exceed 250 (International Organization for Standardization (ISO) 11609, 1995). Interestingly, the allowed pH range for a toothpaste (pH 4–10) might be more a cause for concern as this would suggest that some toothpaste formulations of low pH could intrinsically lead to chemico-physical dental wear. Despite this, ISO standards ensure that all toothpaste products are above a pH that may cause demineralisation (pH 5.5 for enamel and pH 6.5 for dentine) or the contained fluoride balances the low-pH effect (Hunter et al. 2002). Toothpaste formulations saturated with dental mineral and in particular fluoride actively encourages remineralisation due to their buffering capacity and consequently abrasion is less (Betke et al. 2003; Zero and Lussi 2005).

In summary, although toothpaste formulations are unlikely to cause DH lesion localisation, toothpaste formulations of higher abrasivity or overzealous brushing or use of a toothpaste may initiate dentine wear and DH lesion initiation by removal of the smear layer and establishment of patent dentine tubules (Addy and Hunter 2003). Despite this, some toothpaste formulations, especially those containing silica, may have a therapeutic effect in preventing DH by partially occluding the dentine tubules (Addy and Mostafa 1989; West et al. 2002) and may also contain active ingredients capable of increasing this effect (Olley et al. 2012, 2014a).

Attrition and DH

Attrition is the physical wear of dental hard tissues due to tooth-to-tooth contact on occlusal or incisal tooth surfaces. In normal function, the teeth only contact for a short period of time for eating or swallowing. However, when this contact occurs at other times, it is termed parafunction or bruxism. This often occurs nocturnally as a form of stress relief (Bartlett and Smith 2000). Although DH is more common on buccal tooth

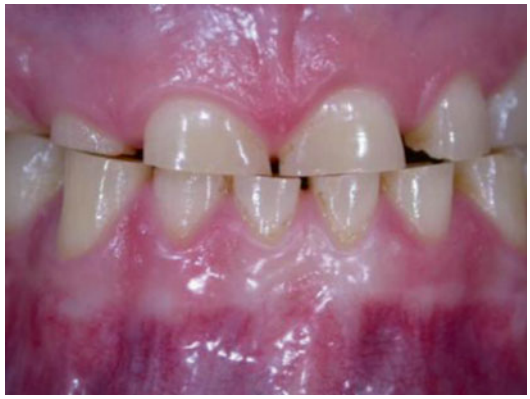

Fig. 4.4 An example of severe attrition associated with bruxism. Note that the incisal surfaces are flattened

surfaces in association with gingival recession, prevalence studies which have also investigated occlusal surfaces show that the occlusal surfaces also demonstrate DH (Bamise et al. 2008; Olley et al. 2013) (Fig. 4.4). The severity of DH on occlusal surfaces is associated with the severity of tooth wear (Olley et al. 2015).

Abfraction and DH

Abfraction (later named in 1991) was first suggested by Lee and Eakle (1984; Grippo 1991). Abfraction was attributed to those tooth wear lesions that could not be explained due to erosion and/or abrasion and which occurred due to occlusal stress often occurring near the cervical margin of teeth (Bevenius et al. 1993). As a cause of NCCLs, they have been associated with DH (Addy 2002). There are limited data however to support the correlation between occlusal stress and NCCLs and the important aetiologies are therefore more likely to be erosion and abrasion (Bartlett and Shah 2006; Smith et al. 2008).

Oral Hygiene, Gingival Recession and DH

Teeth with good oral hygiene and lower plaque scores (e.g. as demonstrated on the surfaces of teeth in the upper left quadrant of patients who are right handed) are more likely to have DH (Addy et al. 1987b, c). Indeed, tooth surfaces with healthy gingiva with no bleeding on probing (and good oral hygiene) are more likely to exhibit DH (Olley et al. 2013). Furthermore, periodontal disease has been linked previously to DH indirectly and/or its treatment through gingival recession (Chabanski et al. 1996; Madhu and Setty 2006). Tobacco is a significant risk factor for periodontal disease throughout Europe (Olley and Gallagher 2010), and European prevalence studies have also demonstrated an association between tobacco usage and DH (West et al. 2013b). Therefore, oral hygiene, periodontal status and tobacco use are all relevant factors in the aetiology of DH. Good oral hygiene and tobacco control must therefore be encouraged by clinicians, but unfortunately the caveat is that patients who have DH may be less likely to brush their teeth due to pain. This increases the level of plaque on their dentine, which may paradoxically reduce DH, but may increase their likelihood of periodontal disease. The evidence for this is however, entirely anecdotal, but it is now known that good oral hygiene is linked to a higher prevalence of DH (Olley et al. 2013), and thus patients with DH are more likely to brush their teeth normally.

Gingival recession and in turn DH may also be initiated iatrogenically due to abnormal oral hygiene procedures (Addy and Hunter 2003). Inappropriate brushing techniques (too hard or frequent) may cause dentine exposure and lesion localisation as a result of gingival recession (Chabanski et al. 1996; Addy and Hunter 2003; Hooper et al. 2003; McCracken et al. 2003; Smith et al. 2008), and there is an association between toothbrushing habits, gingival recession and DH (Addy et al. 1987b, d; Olley et al. 2013).

Multifactorial Aetiologies of Tooth Wear and DH

In tooth wear, it is unusual that attrition, abrasion or erosion occur individually, and it may be more accurate to describe them, as in a previous review, through dental tribology terminology as two-body, three-body and chemico-physical wear,

respectively (Addy 2000, 2005). For patients, these wear processes may include oral hygiene practices, dietary habits, stress and their effects on the occlusion (Bartlett and Shah 2006; Bartold 2006; Shah et al. 2009). Over the last two decades, the predominant aetiologies involved in NCCLs and DH in the published literature have changed. In 1984, a case study and review reported that the predominant aetiologies were more likely to be due to abfraction, erosion and abrasion (Lee and Eakle 1984). Subsequently in 1996, a prevalence study on 1,007 dental hospital patients attributed the main aetiologies as erosion and abrasion (Smith and Robb 1996). More recently, erosion has been described as the predominant aetiology (Addy and Hunter 2003). Overall, the evidence from these studies would suggest that erosion is important in both the exposure of dentine and initiation of a DH lesion. If these aetiologies are to be avoided, then the protection afforded to the dentine by the acquired pellicle and the smear layer must play an important role in the transient nature of DH in both NCCL and postsurgical recession.

For example, dental erosion often works in synergy with abrasion, in the aetiology of NCCLs and DH (Lussi 2006), and toothbrushing will, at the very least, remove the acquired pellicle, which has been shown to offer protection against erosion in vitro (Wetton et al. 2006). A combination of toothbrushing with an erosive acid challenge will also enhance the removal of the smear layer, and it was suggested in an early in vitro study that brushing should therefore be avoided immediately after meals (Absi et al. 1987). Another in vitro study reported that toothbrushing alone may take several years to remove the smear layer and expose the dentine tubule system, but this exposure occurred more readily if followed by an erosive acid challenge (Absi et al. 1992). Clinically, it has also been shown that toothbrushing immediately post-acid challenge can lead to more DH-like symptoms (Ahlquist et al. 1994; Addy 2005). The evidence from the published studies would therefore support the role of multiple factors, in particular erosion and abrasion, in the aetiology of DH, even though one factor may be dominant in the process. The synergy between the various aetiologies is partially reflected in the current clinical suggestion from the dental profession to avoid toothbrushing immediately after acidic food or drink consumption (Dababneh et al. 1999).

Future Trends

This chapter has first recognised the importance of tooth wear and in particular erosion in the aetiology of DH, and it is important that future treatment strategies take into account the importance of the aetiology of the condition. Tooth wear (attrition, abrasion and erosion), unlike DH, are diseases recognised by the WHO. Therefore, the presence of DH could be an important diagnostic indicator of the presence of an active disease process as suggested previously (Dababneh et al. 1999), which if undisturbed may lead to an increase in the frequency and severity of tooth wear lesions (Addy 2002).

The frequency and quantity of an acid challenge may therefore affect the degree of dental erosion, and this may be a concern for the dental profession. For example, there is an increasing trend in the United Kingdom for increasing soft drink consumption as indicated in a report in 1997 which demonstrated that UK soft drink consumption had risen by 56 % in the previous 10 years and was predicted to continue rising 2–3 % each year thereafter (Zenith International Ltd 1997). This predicted increase was subsequently confirmed by a recent report from the British Soft Drinks Association (BSDA 2011). Table 4.3 shows the

Table 4.3 UK soft drink consumption between 2004 and 2010

	Million litres consumed in the United Kingdom	
UK soft drinks	2004	2010
Carbonates	6,195	6,400
Powdered soft drinks and dilutables	3,125	3,500
Bottled water	2,060	2,055
Still and juice drinks	1,090	1,450
Fruit juice	1,040	1,180
Sports and energy drinks	320	600

UK soft drink consumption between 2004 and 2010. Consumption of all beverages, except bottled water, has increased. Of particular concern are the consumed acidic beverages, for example, juice drinks and fruit juices, which have been shown to initiate dental wear and the exposure of the dentine tubules and for which consumption has increased significantly as indicated above. Of particular concern is the fact that both energy and sports drinks have almost doubled in sales and may be common amongst those individuals wishing to follow a healthy lifestyle but, as with the other acidic beverages, are strongly associated with patient-reported DH (West et al. 2013a).

This data clearly indicates the importance of prevention, counselling and management of DH (see Chap. 10). For example, the progression of tooth wear and associated DH may be measured (at various time points) using clinical photographs or study models for monitoring purposes by the clinician (Bartlett 2003). Furthermore, clinical indices, for example, the Basic Erosive Wear Examination for tooth wear (Bartlett et al. 2008; Olley et al. 2014b) and the Cumulative Hypersensitivity Index (CHI) score, may be used (1) to measure the severity of DH (Olley et al. 2013) and (2) for implementation in clinical studies. The severity of DH has been reported to affect the quality of life (Boiko et al. 2010) (see Chap. 9). Both tooth wear and DH should be identified together with the associated aetiologies as these will also be important in the subsequent management of the condition (Gillam et al. 2013) (see Chap. 10). Although the aetiology of DH is a surface phenomenon, the action of specific desensitising dentifrices that work sub-surface may potentiate their effects for DH management (Olley et al. ahead of print).

In the future, the UK population is projected to continue ageing with the average (median) age rising from 39.7 years in 2010 to 39.9 years in 2020 and 42.2 by 2035. In addition, the population size is projected to increase by 4.9 million from an estimated 62.3 million in 2010 to 67.2 million by 2020 and to 73.2 million over the 25-year period to mid-2035. The numbers of 'older people' (classified as those over 65 years of age) will increase the fastest (Statistical Bulletin: 2010-based National Population Projections, 23 November 2011), and for this section of the population, it is estimated that by 2028, total tooth loss will be eliminated in those under 65 years and significantly reduced in those under 75 years of age (Kelly et al. 1998). In the United Kingdom, with an ageing population retaining their teeth for longer and considering tooth wear, in particular erosion, which has been described as increasing with age (Van't Spijker et al. 2009; Steele and O'Sullivan 2011) together with the predicted increase in consumption of soft drinks; this would suggest that even with a continuing improvement in oral health practice there may be a significant increase in both the prevalence of tooth wear and DH in the future. For example, evidence from the Northwest of the United States has demonstrated that tooth wear was more common in older adults, males, those who use occlusal splints and adults who have periodontal disease (Cunha-Cruz et al. 2010). Recent studies however have reported that the prevalence of DH in the young European population was high (West et al. 2013b) as was the consumption of erosive acidic foods and drinks in young Western adults with NCCLs (Lussi et al. 2004) which may tend to suggest that both tooth wear and DH may start to affect adults at an earlier age than previously reported. This trend may also reverse and affect the younger population and at an earlier age; thus it is important for epidemiological researchers and dentists to be aware that DH may be increasingly prevalent in all age groups.

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Advances in the Diagnosis of Dentine Hypersensitivity

5

Joon Seong and Nicola West

Introduction

The diagnosis of dentine hypersensitivity (DH) is not a straightforward one, as the pain and clinical presentation of the condition is similar to that resulting from other oral conditions that result in tooth-related pain (Addy 2000). For example, following the bleaching of vital teeth, many individuals experience sharp, shooting pain of short duration (Tam 1999; Dahl and Pallesen 2003) which exhibits the characteristics of pain from DH. However, the aetiology of vital tooth bleaching is the result of direct irritation of the vital pulpal tissue by hydrogen peroxide, which from in vitro studies has been shown to penetrate enamel and dentine (Patri et al. 2013; Cooper et al. 1992). This is in contrast to the currently accepted hydrodynamic theory of DH working on the concept that sensitive dentine is based on the stimulus-induced fluid flow in the dentine tubules and consequent nociceptor activation in the pulp/dentine border area (Matthews et al. 2000). Similarly, both DH and pulpitis illicit a sharp pain response following the application of a thermal stimulus (Bender 2000; West et al. 2013a), and other conditions such as caries, marginal leakage of restorations, composite contraction and chipped, cracked, grooved or fractured teeth result in similar pain responses (Porto et al. 2009; Gernhardt 2013; Gillam 2013). These conditions can be differentiated from DH with clinical observation, for example, a cracked cusp will give pain upon release of biting.

Certain clinical features and patient practices, such as exposed dentine as a result of gingival recession or enamel tooth wear, a diet high in acid intake smoking and excessive brushing, are associated with DH (Addy and West 2013), and their presence or history might suggest that DH is the cause of the pain reported. Sufferers from xerostomia not only have a higher risk of erosion and potentially DH but also of caries as a result of reduced saliva flow (Grisius 2001). The effect of overzealous brushing can lead to the exposure of radicular dentine and, when in combination with erosion, coronal dentine exposure, which can result in DH (West et al. 2012), especially in the cervical region.

However, not all individuals with exposed dentine suffer from DH. Often the dentine tubules are occluded, most often due to surface coverage with oral debris creating a smear layer or toothpaste ingredients such as silica or stannous particles (Banfield and Addy 2004; Claydon et al. 2009; White et al. 2007). Alternatively, age-related changes such as the deposition of secondary dentine and fibrosis of the pulpal tissue result in reduced DH (West et al. 2013b).

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Although the term DH is familiar to the dental profession (Addy and West 2013), there is little evidence to indicate that hypersensitive dentine differs in any way from normal dentine and the pain mechanisms are probably the same, sensitive dentine looking clinically the same as nonsensitive dentine. The status of the pulp in DH is not known although symptoms would suggest it unlikely that there is an acute or chronic inflammation due to the length of time symptoms persist. Most investigations report no correlation between pathology and symptoms (Seltzer et al. 1963; Tydesley and Mumford 1970); however, ethically, studies are fraught with difficulty. The term 'dentine hypersensitivity' can be questioned, with perhaps 'dentine sensitivity' being a more accurate description although not used as often (see Chapter 1). Thus, while helpful in diagnosis, the presence of features indicative of DH, such as exposed dentine, alone can only suggest that this might be the cause of a patient's pain.

DH is known to be an episodic condition (Addy 2002), often more prevalent in cold weather and in practicing certain habits, e.g. frequent highly acidic diet. This observation may be as a result of a dynamic equilibrium between the opening and closing of the dentine tubules during daily activity and toothbrushing (Adams et al. 1992). Hence the twice-daily instruction to patients for the use of occluding toothpaste formulations with potential acid-resistant properties (Mason et al. 2010), which may maintain tubule occlusion and reduce or negate any pain symptoms associated with DH (West et al. 2012).

This similarity between the pain and symptoms of DH and the pain initiated by other oral conditions, together with the fact that the oral features suggestive of DH are also common to other oral diseases and complaints, makes the diagnosis of DH problematic. The difficulties in diagnosing DH may account for the lower figures for DH detected clinically than by self-reported questionnaires observed in several studies which used both measures of assessment (Dhaliwal et al. 2012; Ye et al. 2012; Que et al. 2010) (see Chap. 3). Furthermore as it has also been reported that in some instances DH can also adversely affect the quality of life of individuals (Bekes et al. 2008; Boiko et al. 2010), an accurate diagnosis is paramount before any treatment is recommended by the clinician (see Chap. 9). This chapter (5) provides up to date guidance to help with the diagnosis of DH in general dental practice, together with methods of quantification of pain more suited to clinical trials which examine the efficacy of desensitizing products.

Current Approaches to Diagnosing Dentine Hypersensitivity

In the absence of a definitive test for DH, a differential diagnostic approach is utilised whereby other conditions are eliminated by the use of diagnostic tests for other oral conditions, together with the completion of a comprehensive medical history and in particular pain history (Porto et al. 2009; Terry 2011; Gillam 2013). Only once conditions with similar symptoms and presentation have been eliminated is it possible to arrive at a definitive diagnosis of DH.

Several studies have examined the literature and suggested guidelines for the diagnosis of DH (Canadian Advisory Board 2003; Gernhardt 2013); Gillam et al. 2013). As DH is relatively common, with recent studies in Europe, Brazil and India reporting prevalence figures of approximately 42 % in 18–35 year olds, 33 % of over 35 year olds and 42 % of patients attending a dental school, respectively (West et al. 2013a; Costa et al. 2014; Rane et al. 2013), and knowing that the condition may also negatively affect the quality of life (Bekes et al. 2008; Boiko et al. 2010) (see Chap. 9), it is therefore suggested that all patients attending routine dental appointment reviews should be asked whether they have experienced sensitivity on any of their teeth. Screening for DH has however, been reported to be uncommonly undertaken by clinicians (Canadian Advisory Board 2003; Gillam et al. 2013). If pain and sensitivity is reported, the diagnosis of DH should be determined together with a thorough medical and dental history which explores the nature of the pain, sharpness, intensity, duration, how many teeth are involved, stimulating and relieving factors that cause the pain as well as relevant informa-

tion about recent tooth bleaching procedures and dietary habits, which may provide clues to the underlying cause (Terry 2011; Porto et al. 2009) (see Chap. 4). Questions should be phrased in such a way that patients are not led to the answer (Gillam et al. 2013). Classically the pain of DH is short and sharp and of limited duration (Holland et al. 1997). The dull throbbing ache type of pain of long duration is likely to be of pulpal pathology in origin and not due to DH (Addy 2002).

The medical history should be followed by a comprehensive clinical oral examination, in which the clinician looks for obvious defects that might account for the pain reported by the patient and undertakes tests to confirm or reject potential causes (Gillam et al. 2013). Most conditions which result in a pain that is similar to that caused by DH can be diagnosed through the use of diagnostic radiographs or tender tooth testing, and if these tests are negative, then DH may be considered as the potential cause. One of the commonest differential diagnoses to DH is the cracked cusp, determined by pain upon release of biting and usually affecting only one tooth, which is rare in sensitivity where a number of teeth are usually affected (see Chap. 4). It can also be more difficult to diagnose other conditions, for example, atypical odontalgia which occurs in the absence of detectable pathology (Gillam and Orchardson 2006), but if it is demonstrated that the pain is short-lived, is sharp in onset and occurs in response to stimuli known to initiate DH, then DH is indicated as the cause of the patient's pain (Terry 2011).

Assessing the extent and severity of DH is achieved by stimulating the teeth thought to be sensitive with stimuli known to elicit a hypersensitivity response. Such stimulation will inevitably cause the patient pain and this must be taken into account when interpreting a patient's response. People's pain perceptions and expectation of pain also must not be underestimated. In a study by Addy et al. (2007), participants had a number of teeth which exhibited sensitivity to a cold air stimulus. When one of these teeth was stimulated, volunteers described and scored pain, although the teeth were completely shielded and the participant could not have experienced any pain.

The information from such assessments indicates whether pain is localised or more general in nature as well as the intensity of the pain which in turn will determine the treatment planning pathway (Gillam and Orchardson 2006). Although DH can be initiated by a number of stimuli, not all are useful in assessing DH in practice. An osmotic stimulus for example, sugar may give a hypersensitivity response but is hard to control as it diffuses into the dentine fluid making accurate repeat assessments impossible in a short time period as the difference in osmotic potential between the inside and outside of the tubule reduces. The use of electrical stimulation is also not recommended (Holland et al. 1997). Although a benefit of such stimuli is that the amount of stimulus required to achieve a sensory response can be readily measured, nevertheless no correlation was reported between the electrical current threshold and pain scores obtained after stimulation with air blasts or cold (Nahri et al. 1991; Kontturi-Narhi and Narhi 1993). These findings coupled with the fact that electrical stimulation is not really clinically relevant in assessing pain associated with DH would suggest that this approach should not be recommended as a diagnostic tool for assessing DH (Gillam and Newman 1993). Furthermore it should be noted that most of these stimuli would be unsuitable for use in clinical practice apart from the use of an air blast from a cold air syringe and a explorer probe, together with a subjective assessment of the patient's pain score (see below).

To determine the hypersensitivity response to a mechanical stimulus, a conventional or pressure-sensitive sharp dental probe can be employed. The latter provides a measurable, reproducible force (Yates et al. 1998). The Yeaple probe delivers a force which can be increased at 5 g intervals, up to a force of 70 g, stopping when pain is elicited or if no pain is experienced, the tooth being considered not sensitive (Garcia-Godoy 2013). The probe is walked over the area of exposed dentine in incremental horizontal lines. Often only a small area of dentine will respond. However, not all hypersensitive teeth respond to tactile stimulation (Flynn et al. 1985), and has been considered to be a less invasive

procedure than that of a cold air blast (Gillam and Newman 1993). The Yeaple probe technology may however be problematic in that if the force is exceeded, there is no mechanism to detect or highlight this increase in force. Nevertheless, mechanical stimulation is still frequently used as part of the assessment of DH in the clinical trial setting (Gillam and Orchardson 2006; Cunha-Cruz et al. 2010; Costa et al. 2014).

Thermal and evaporative stimuli are also commonly used to assess DH (Gillam and Orchardson 2006; Cunha-Cruz et al. 2010). A short air blast is the most frequently used stimulus challenge in clinical studies seeking to determine the prevalence of DH (West et al. 2013a; Rane et al. 2013; Costa et al. 2014) and is also a practical way to identify sensitive teeth in a diagnostic exam. This stimulus can be perceived as cold if it is applied below room temperature or for a long period of time, so in most clinical studies, if an evaporative stimulus is required, it is applied in a short burst of 1 s, perpendicular to the area of exposed dentine and 10 mm away from the dentine, at approximately 20 °C (West et al. 201a3; Rahiotis et al. 2013). Of the stimuli that provoke DH, the application of cold has been shown to cause a greater pain response than other stimuli (Gillam and Newman 1993), and for this reason, it is not always appropriate to choose this as a stimulus. For clinical trials it is recommended that stimuli should be used in the order of pain evoked. Ideally two stimuli should be applied (Holland et al. 1997; Canadian Advisory Board 2003) (with the least invasive stimulus used before the more invasive stimulus), with an appropriate interval between them such that their effects do not overlap and the pulp has time to recover, about 5 min. Frequently the stimuli chosen are a mechanical stimulus such as an explorer probe, which is recommended to be moved in the mesiodistal direction on the area where dentine is exposed (Oktay et al. 2008; Miglani et al. 2010), followed by an evaporative stimulus such as an air blast (Gillam and Newman 1993; Gillam et al. 2002; Rahiotis et al. 2013; Costa et al. 2014). For a DH diagnosis in clinical practice, however, tactile stimulation of a tooth may be better employed to identify specific areas of sensitivity after an evaporative stimulus such as a blast of air has been used to identify the sensitive tooth provided a suitable time interval has been achieved (see above).

Following a diagnosis of DH an assessment of the patient's pain may be undertaken. This is particularly important in clinical trials of DH where the efficacy of treatments is being tested. Pain assessments are difficult as pain is highly subjective in nature (Gillam et al. 2000), and the response to pain stimuli may be modified by factors such as the situation in which the pain is encountered (Dworkin and Chen 1982) and the anxiety felt by the patient (Oktay et al. 2008). In addition, in the clinical trial setting, pain scores are subject to the placebo effect (West et al. 1997), in which the expectation of receiving an effective pain relief treatment can result in reduced pain scores in all trial participants including those who have been randomised to control products. Trial participants may also temporarily alter their behaviour as a result of taking part in the trial (the Hawthorne effect) although the magnitude of the Hawthorne effect is not clear (McCambridge et al. 2014) (see Chap. 7).

When determining the severity of DH, pain assessments are usually response based, whereby a stimulus is applied and patients are asked to describe how painful it felt in simple terms. Over repeat visits, patients are asked similar questions and whether pain is better or worse, and in this way, the condition and treatment efficacy may be effectively monitored (Gillam et al. 2013). In a clinical trial scenario, more complex response-based pain assessments, for example, visual analogue scale (VAS) in which the patient is asked to mark on a line of length 100 mm how painful a stimulus was, where '0' is not painful and '10' is the worst pain imaginable, are frequently used. The distance to the mark is measured and this represents the pain score. As a continuous variable, the VAS is readily analysed and suitable for use in clinical studies (Clark and Troullos 1990); it may sometimes also be used as part of routine clinical assessment, but patients need to be trained before being assessed using this scale. Given the subjective nature of pain, in addition to patient-scored VAS, clinical studies often employ examiner-assessed pain scales such as the Schiff air evaporative scale (Schiff et al. 2006) in which

the clinician delivering the stimulus assesses patient response on a scale of 0–3. A '0' indicates that the participant does not respond to the stimulus, and '3' indicates that the participant responds to the stimulus, considers it painful and requests it to be discontinued. As an alternative to response-based assessments, stimulus-based assessments may be employed in clinical trials. In such assessments, the threshold of a stimulus required to achieve a response is ascertained, for example, by using a calibrated tactile probe first delivered at a pressure, below the pain threshold, and then at increasing pressures until the participant registers pain (Schiff et al. 2009).

The above protocol should allow dentists to correctly diagnose DH; however, questionnaire-based studies have demonstrated that many dentists do not routinely screen for DH (Canadian Advisory Board 2003; Amarasena et al. 2010; Gillam 2013). It has also been demonstrated that in Canada, less than 50 % of dentists who took part in a questionnaire-based study considered differential diagnosis (Canadian Advisory Board 2003) and that diagnostic tests used in North America vary greatly between dentists (Cunha-Cruz et al. 2010). By contrast, a questionnaire-based study in Australia reported that the majority of dentists would take a differential diagnostic approach if patients reported DH (Amarasena et al. 2010). These findings suggest that there is still a lack of clarity about the best way to diagnose DH, and the difficulties in diagnosis suggest that more work on new tools for this purpose is needed. New regulations in the UK will ensure that tooth wear, one of the major aetiological factors associated with DH, will be assessed on a regular basis, which may help with the management of DH (NHS England 2014).

New Approaches to Diagnosing Dentine Hypersensitivity

A simple test for DH would be the ideal aid for clinicians when diagnosing DH, but at present, no one technique has been developed, although new techniques are being researched.

The Jay sensitivity probe is a new microprocessor-based instrument designed to measure DH. Unlike the Yeaple probe that relies on an electromagnetic device to deliver a controlled amount of force, the Jay sensitivity probe requires daily calibration and it has also been reported that these measurements may be affected by ambient conditions (Garcia-Godoy and Trushkowsky 2013, García-Godoy 2013). The Jay probe delivers force increments that are preset and controlled by the microprocessor. Recently, several studies have been conducted in order to determine the efficacy and accuracy of the Jay probe as compared to the existing Yeaple probe and other measures of DH. In a repeated measures test on a cohort of 12, it was demonstrated that while Yeaple probe scores varied significantly, the Jay probe scores remained consistent (Sowinski et al. 2013). Inter-examiner variation was also reported to be low. Several other studies demonstrated that DH measurements obtained from the Jay probe correlated well with other sensitivity measures (Kakar and Kakar 2013; Hegde et al. 2013; Kakar et al. 2013). Data would appear to suggest that this new probe may be effective in assessing DH, however further studies are required to determine whether this particular probe is any more effective than the other current assessment measures.

A systematic review on the effectiveness of various diagnostic tests in diagnosing DH (Tejaswi and Anand 2014) concluded that the tactile test with the Yeaple probe showed more percentage reduction in DH when compared to other diagnostic tests. These investigators also recommended that tactile testing was a better tool in diagnosing DH when comparing the efficacy of treatment effects than the other diagnostic tests reviewed in the paper.

In addition to improvements in the accuracy of equipment used to illicit DH, improvements in the manner in which DH is measured are also being developed (see below and Chapter7). Currently in clinical trials, the VAS is frequently used as it is easily analysed and participants can be readily taught how to complete the test (Gillam et al. 2000). However, as the labels on the VAS only appear at either end with no reference markers in between, patients may not be consistent when they mark their pain score. Also, as pain from DH generally falls in the lower end of the pain spectrum, scores may be clustered together at the bottom end of the scale

such that it is difficult to determine the spectrum of pain experienced (Heft and Parker 1984). In addition to the VAS test which measures pain intensity, tests that measure pain quality by the use of verbal descriptors may also be used (Turp 2013). The McGill Pain Questionnaire (Melzack 1975) was designed to determine the severities of different characteristics of pain, and it was demonstrated that certain words were more evocative of severe pain than others, for example, the use of the word 'stabbing' indicated a more severe pain than the use of the word 'pricking' (Gillam et al. 2000). However, although verbal descriptors are easy to use, there are only limited words, and different pain intensities may be labelled with the same word (Heaton et al. 2013) (see Chap. 7).

Recently, a series of five studies aimed to develop a pain scale that was sensitive to the differences in the pain experienced by patients with DH (Heaton et al. 2013). The LM scales, either on their own or in combination with a standard VAS, can provide information regarding the intensity, duration, tolerability and description of the pain associated with DH.

The most recent technique to evaluate DH involves taking a replica of the exposed dentine surface with a dental impression material and either observe the impression directly or create a cast of the impression of the dentine. The surface of the replica can be observed under the scanning electron microscope (Absi et al. 1992). Patent dentine tubules can be viewed although one cannot determine if these tubules are open to the pulp. This is an interesting concept and worthy of further exploration to detect DH clinically.

Summary

In conclusion, in the clinical environment DH is diagnosed by the exclusion of other oral pain conditions. Although there are a number of diagnostic tests that have been recommended for both clinical practice and research purposes in the published literature, there does not currently appear to be one test that is confirmatory for a definitive diagnosis of DH.

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Advances in In Vitro Testing Techniques for Dentine Hypersensitivity

6

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Introduction

Dentine hypersensitivity (DH) is a common clinical condition that is responsible for pain and/or discomfort in response to various stimuli – typically thermal, tactile, osmotic or chemical – not ascribed to any other tooth or oral disease (Charoenlarp et al. 2007) (Chap. 1). The frequent use of acidic beverage and foods is considered one of the typical conditions improving discomfort and pain. Moreover, restorative procedures including periodontal therapy and hygienic professional procedures may also induce mild to moderate discomfort (see review from Lin and Gillam 2012) that require the use of desensitising products to reduce and remove the symptoms. It was also evident from both prevalence studies and clinical practice that DH was identified in two population groups, namely, those individuals with good oral hygiene and those with periodontal disease (or DH following periodontal therapy) (see Chaps. 1, 3 and 4). As a result of recent changes in the definitions of DH and root sensitivity (RS) (Canadian Advisory Board on Dentin Hypersensitivity 2003; we may discuss DH in the following manner: (1) a *primary* dentine hypersensitivity (DH) when (cervical) dentine surface is exposed as a consequence of enamel erosion and abrasion and after appearance of gingival recession and retraction and (2) a *secondary* dentine hypersensitivity (RS) when certain clinical periodontal procedures have been performed and the root surface has been altered with possible smear layer removal, thereby exposing a number of dentine tubules to the oral cavity (see Chap. 1).

From a historical perspective, it has been recognised that there are several possible mechanisms for the transmission of various stimuli (e.g. mechanical, thermal, chemical, etc.) across dentine to the pulp (see Chap. 2). Microscopic examination of teeth from patients complaining of DH appears to demonstrate that open dentine tubules are more numerous and wider in sensitive dentine than in nonsensitive dentine (Absi et al. 1987; Yoshiyama et al. 1990). These observations would therefore appear to be consistent with the hypothesis proposed by Brännström (1963) that pain may be mediated by a hydrodynamic mechanism. According to Gillam (2014), the hydrodynamic theory therefore promotes two basic approaches for treating DH, namely, (1) dentine blocking agents that occlude patent (open) tubules (e.g. fluoride, strontium salts,

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oxalate, calcium phosphate, restorative materials, etc.) and as a consequence reduce any stimulus-evoked fluid movements within the dentine tubule and (2) nerve desensitisation agents that reduce intradental nerve excitability (e.g. potassium ions, guanethidine) in order to prevent a response from intradental nerves to the stimulus-evoked fluid movements within the dentine tubules.

A number of both professionally applied in-office treatments and over-the-counter (OTC) products have been used by clinicians with varying degrees of success in order to relieve DH and RS; however, despite the claims of efficacy for these desensitising agents, there does not appear to be a universally agreed gold standard for treating DH (Gillam 1997; Gillam et al. 2013).

The main purpose of this chapter therefore is to review and discuss the recommended in vitro testing techniques in order to evaluate the morphological aspect of both primary and secondary DH (and some aspects of the so-called supersensitive dentine as suggested by Pashley 2013) and to test in vitro the efficacy of (new) products designed to reduce DH. The chapter will also discuss the methods currently used in the laboratory in order to detect the reduction of the functional diameter of dentine tubules and the subsequent effect on dentine fluid flow (dentine permeability).

Concepts for Dentine Hypersensitivity Treatment

The main concept of both treatment strategies is the permanent and stable occlusion of the exposed and open dentine tubules (Markowitz and Pashley 2007). The occlusion of tubules must therefore be permanent and not be affected or modified by acidic fluids, for example, soft drinks (Prati et al. 2002, 2003), or acidic plaque. The occlusion of dentine tubules may also maintain the status quo of the hydraulic conductance (e.g. permeability) of dentine. On the other hand, the opening or reopening of the dentine tubules increases the permeability within the dentine tubules and thereby creates the conditions conducive for DH (see Chap. 2).

Furthermore, strategies involving new treatments for DH must ideally initiate a new and continuous intratubular remineralisation associated with an intertubular remineralisation. Novel remineralising agents are in progress to create the conditions for an ideal intratubular remineralisation product and for the creation of new apatite deposits into the deeper aspects of the dentine tubules (Suge et al. 2008; Gandolfi et al. 2012; Brauer et al. 2013; Vollenweider et al. 2007; Gandolfi et al. 2011) (see Chap. 11).

It is important to note that the exposed dentine is a "dynamic" surface morphology where a number of chemical and mechanical stresses create a number of morphological alterations, for example, the removal of smear layer, the removal of mineralised sound dentine, the erosion of dentine tubules and the enlargement of their diameter. A smear layer is usually created by toothpaste formulations and brushing procedures (and other mechanical stresses) and subsequently invaded by the plaque bacteria. These bacteria may create a number of biofilm layers and reduce DH due in part to a dynamic tubule occlusion process. According to Pashley (2013), the biofilm and bacteria may also produce sufficient organic acids to solubilise the smear layer in 7–10 days. Acid soft drinks and other acidic foods have also been demonstrated to remove the smear layer (Prati et al. 2002, 2003) and affect the biofilm. A limited or reduced buffer capacity of saliva may also play a negative role in inducing fast dentine erosion and smear layer removal.

The above description is therefore a useful scenario in which to discuss the influences of the normal oral condition, the influences of acidic solutions and the various in-office and OTC products that may interact with the exposed dentine surface and the conditions that may induce DH. It is important however to realise that it may be impossible to fully replicate this dynamic substrate in an in vitro environment; nevertheless, despite the limitations of using dentine sections from human (or bovine) teeth, the model may provide the investigator with information with regard to the potential ability of a desensitising agent to occlude the dentine tubules and reduce the fluid flow through dentine. Care however must be taken not to extrapolate the in vitro findings into the

clinical environment. Prior to the introduction of desensitising agents (products) into the clinical environment, these materials are generally evaluated in the laboratory to determine their suitability for clinical use. For example, professionally applied products include resins, varnishes and dentine bonding agents which have been reported to occlude the dentine tubules through the precipitation of their active substances (Pashley 1986, 1989; Pashley et al. 1996). As indicated above, it is often difficult to completely mimic the conditions in the oral environment, for example, the application of a dentine bonding agent (resin) in the clinical environment may be difficult due to the saliva or blood contamination on the dentine surface due to both these constituents have been reported to reduce the contact of the agent with the dentine surface and thereby reduce the effectiveness of the proposed treatment (Prati et al. 2001; Tay and Pashley 2004). Recently, calcium phosphate agents, CCP-based mousse and bioactive hydraulic calcium silicate cements derived from MTA root-end filling materials have been proposed as novel treatments for DH (Gandolfi et al. 2008). Bioactive cements, for example, calcium silicates, have been reported to overcome the problems associated with the "wet" dentine surface by its ability to set and leach calcium hydroxide and silica into the solution during the hydration reaction (Tay and Pashley 2008; Gandolfi et al. 2010). At-home (OTC) treatment which involve the application of toothpaste, paste and mousse or mouthrinse formulations by the consumer has also been reported to occlude the dentine tubules in the in vitro model and has the potential to protect the dentine surface from the impact of an acid environment (Gillam et al. 2001).

In Vitro Laboratory Testing Techniques

The recommended laboratory tests are listed in Table 6.1.

A dynamic method to measure fluid flow rate (dentine permeability) through the dentine tubules was first proposed by Pashley (1986, 1989). It was postulated (in accordance with the hydrodynamic theory) that the larger the area and numbers of open dentine tubules, the higher the fluid flow rates through the dentine tubules, as demonstrated by Pashley (1986). The calculation of the in vitro dentine permeability and its variation over time represents an interesting method that offered the possibility to quantitatively determine the effectiveness of a specific treatment (Chap. 2). It should be noted however that there was a wide variation in the flow rates across the dentine disc when using this model. For example, flow rates may be higher in mid- to deep coronal dentine close to the pulp chamber than in superficial dentine (e.g., root dentine). As mentioned in Chap. 2, the importance of the radius of the open dentine tubule as implicated in the Hagen-Poiseuille equation is important when considering the impact of tubular occlusion of dentine permeability. Following these initial investigations by the Pashley group, other investigators have validated the methodology which has been extensively documented (Gillam et al. 1997). According to Prati et al. (2003), the advantage of this system was represented by the possibility to make repeated measurements over time and following storage in saliva or simulated body fluids and following acid exposure from, for example, Coca-Cola or citric acid. The method is extremely sensitive and offers

Table 6.1 Recommended laboratory methodologies used to evaluate the effectiveness of prospective agents for the treatment of DH

Dentine permeability evaluation – fluid flow rate (hydraulic conductance model)
Scanning electron microscopy (SEM)
Environmental scanning electron microscopy (ESEM)
Energy-dispersive X-ray spectroscopy (EDS, EDX or XEDS) also called energy-dispersive X-ray analysis (EDXA) or energy-dispersive X-ray microanalysis (EDXMA)
Atomic force microscopy (AFM)
Raman and micro-Raman spectroscopy
Fourier transform infrared spectroscopy (FTIR)
Confocal laser scanning microscopy (CLSM)
Focused ion beam scanning electron microscopy (FIB SEM)
Solid-state nuclear magnetic resonance (NMR) spectroscopy
^{27}Al, ^{29}Si, ^{19}F and ^{31}P magic angle spinning nuclear magnetic resonance (MAS-NMR)

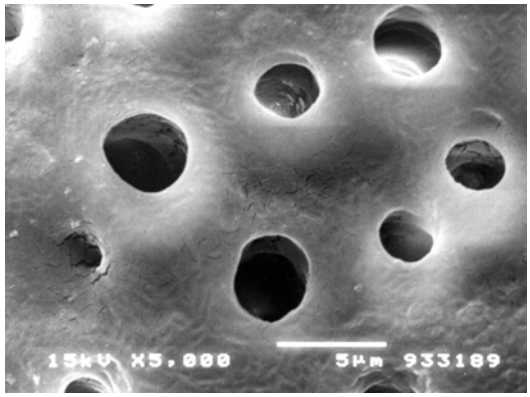


Fig. 6.1 Laboratory preparation of a dentine disc from a human third molar tooth. SEM observation of the occlusal surface following the removal of enamel, and after treatment with EDTA solution for 3 min, SEM observation confirmed the absence of the created smear layer and smear plugs and the presence of open dentine tubules

Table 6.2a Dentine permeability (Lp) of dentine surfaces soaked in artificial saliva, citric acid and DPBS or HBSS used as simulated body fluids (SBFs)

Treatment	After EDTA	After 10′ treatment	After 24 h
Intact new smear layer	100 ± 0.1	99.4 ± 0.5	102.7 ± 3.2
Citric acid 10 %	100 ± 0.1	32.2 ± 7.9	37.3 ± 9.5
Artificial saliva (pH 5.4)	100 ± 0.1	94.7 ± 1.6	94.0 ± 2.2
DPBS	100 ± 0.1	98.7 ± 7.3	98.4 ± 8.7
HBSS	100 ± 0.1	98.1 ± 2.1	80.6 ± 12.4

many advantages that represent a fundamental step in the evaluation of any new and experimental treatment. Furthermore it represents a sophisticated yet practical method to evaluate the mechanisms associated with fluid flow in DH. It should be noted however as discussed above that there are limitations with using both human and bovine dentine discs with respect to anatomical differences as well as variations in the flow rates between extracted teeth (already in the oral cavity) and extracted unerupted third molars.

The treatment of dentine surface with EDTA (a chelating agent) or with etching agents (phosphoric acid, citric acid, etc.) has been demonstrated to remove all the smear layer present on the dentine surface and provides the possibility to create a standardised dentine surface with open dentine tubules representative (characteristics) of a tooth surface with DH (Reeder et al. 1978; Pashley et al. 1996; Gandolfi et al. 2008) (Fig. 6.1).

A number of investigators have reported that the presence of a smear layer on the dentine consistently reduces or abolishes the fluid flow rate (Table 6.2a). The initial studies by Pashley (1986, 1989) clearly demonstrated the correlation between the fluid flow rate and the number of open dentine tubules with the formation of the precipitation of a surface deposit on top of dentine tubules which artificially created an environment conducive to reducing and/or stopping the fluid flow rate (Pashley 1989). According to Prati (1994), both toothpaste formulations and varnishes may play a temporary role in reducing these fluid movements; however, many of these precipitates are easily removed by saliva and drinking, rinsing, chewing movement, acidic soft drinks, etc.

One should however be aware of the differences in the fluid flow rates between the superficial and deep layers of dentine, for example, superficial dentine contains lower numbers of relatively small-diameter tubules that is relatively less permeable than that of the mid- to deep coronal dentine with a higher number of dentine tubules which is more permeable. Furthermore, it is also important to note that most of the investigations evaluating the effectiveness of potential desensitising products use mid-coronal dentine sections rather than cervical dentine sections which are probably more representative of DH in the clinical environment. This was often for practical reasons as the cutting of mid-coronal sections was relatively easier to perform rather than sectioning the cervical dentine of the crown/root area. Furthermore, the dentine tubules of the mid-coronal dentine were more numerous, wider in diameter and parallel compared to the dentine tubules in the cervical area of the tooth. The combination of both fluid flow rate measurement and SEM observation has also established that a thick smear layer may completely close all the dentine tubules and maintain over time reduced fluid flow rates (Fig. 6.1, Table 6.2a). The partial or the complete exposure of dentine tubules has also been reported to increase the fluid flow rate

following the removal of the smear layer with citric acid (a common component of commercial acidic soft drinks and juices) (Prati et al. 2002) (Tables 6.2b and 6.2c).

The use of SEM is however important to detect the morphology of dentine surface before and following the application of some treatment and to test the resistance/stability of the treatment on the dentine surface. The main scope of this methodology is the quantification of changes in the dentine tubule parameters and the detection of the closed/open dentine tubules following the application of different agents, for example, solutions, toothpaste formulations, professionally administered polishing pastes, etc. (Pashley 1989; Gillam et al. 2001; Ahmed et al. 2005; Burnett et al. 2013). The analysis of the longitudinal sections of dentine discs may also offer the ability of mapping the dentine tubule morphology (Pashley 1989). Smear plugs created by a smear layer or by toothpaste formulations may (as previously mentioned) occlude the dentine tubules for more than 10 μm or occlude the dentine tubule by a deposition in the middle part of the tubules (Figs. 6.2 and 6.3).

SEM observation in combination with fluid flow rate measurement has also demonstrated that the application of a mild to strong acid (acidic soft drinks, e.g. Coca-Cola, juices, etc.) may completely remove the smear layer and open dentine tubules with a subsequent increase in the fluid flow rate. Phosphoric, citric, pyruvic, maleic, tannic and acetic acids and other acids present in wine and beverages may also strongly increase dentine permeability and remove all the smear layer, as demonstrated by SEM observation

Table 6.2b Dentine permeability (Lp) values following the application of selected commercial toothpaste formulations

Treatment	After EDTA (Lp 100 %)	After 10′ treatment ($t=0$)	After 24 h in HBSS
Colgate Pro-Gum Health	100 ± 0.1	34.6 ± 5,9	39.9 ± 10.3
Elmex Sensitive Professional (toothpaste)	100 ± 0.1	26.7 ± 12.9	22.3 ± 15.9

Table 6.2c Dentine permeability (Lp) following the application of selected professional treatments

	After EDTA (Lp 100 %)	After 10′ treatment ($t=0$)	After 24 h in HBSS
Voco Admira Protect	100 ± 0.1	30.7 ± 9.4	45.3 ± 14.7
Alfa TC-MTA	100 ± 0.1	37.7 ± 12.5	49.2 ± 25.0
Gluma	100 ± 0.1	38.61 ± 12.1	79.7 ± 32.4

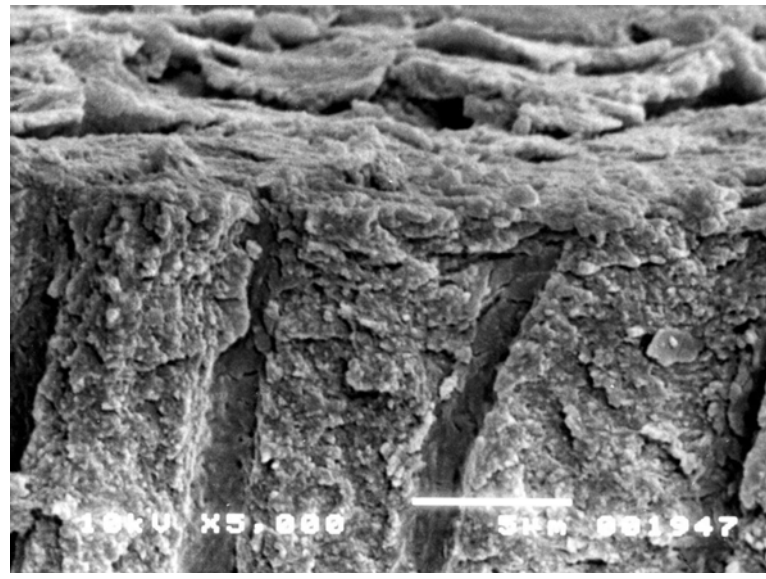


Fig. 6.2 Cross section of a dentine disc sample. The smear layer is visible on the surface of the dentine. The cobblestone morphology of the smear layer observed in this section may be due to the desiccation of the sample. The dentine tubules are partially covered (and occluded) by a number of smear plugs

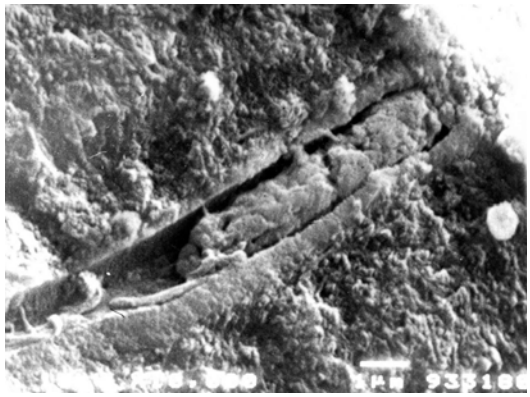


Fig. 6.3 Cross section of a dentine disc sample where the smear plug is visible in the occluded dentine tubule. The brushing procedures may create fine debris (smear layer) and together with the toothpaste components may be burnished or forced into the open dentine tubules creating a smear layer plug. Interestingly, there are small gaps visible around the plug, but this may probably be related to the desiccation of the sample. In this condition the recorded dentine fluid flow rate was very low. The observation that when the majority of the dentine tubules or either partially or completed occluded with a subsequent reduction in fluid flow may therefore have relevance according to the hydrodynamic theory in potentially reducing DH in the in vivo environment

(Prati et al. 1989; 2002), resulting in the dentine surface being completely depleted from any smear layer protection and a subsequent increase in dentine permeability. One of the added advantages of using the SEM methodology is its ability to provide details of the dentine surface, dentine plugs and collagen fibril, although the methodology does have its limitations, for example, the time taken in the preparation of the specimen, the preparation of the specimen which limits any further investigation, artefacts in the form of fractures of the dentine structure or associated smear layers due to the desiccation of the sample prior to imaging, etc.

For example, toothpaste formulations create a deposition or precipitate that may cover the entire surface and obscure a number of the dentine tubules as demonstrated by the SEM pictures (Figs. 6.4, 6.5 and 6.6). Each toothpaste may present a typical morphology, suggesting that the different compositions of both the active ingredient(s) and excipients may be sufficient to have a chemical interaction on "a so active" substrate as in dentine and smear layer (Prati et al. 2003). A number of these toothpaste

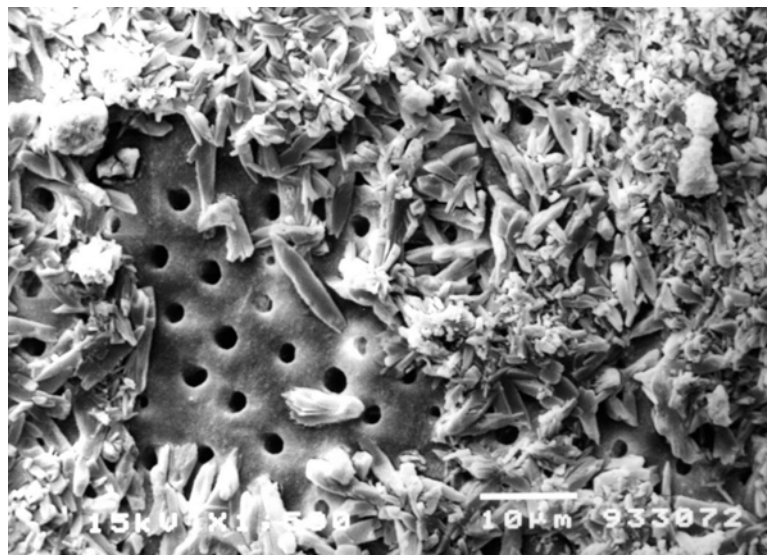


Fig. 6.4 The occlusal surface of a dentine disc. The application of toothpaste and the subsequent immersion in water/saliva created a newly constituted smear layer, mainly composed of toothpaste crystals and deposits. In this sample the dimension of the toothpaste deposits prevented their penetration into the dentine tubules. The effectiveness of the toothpaste to occlude the dentine tubules and subsequently reduce dentine permeability may be affected by a number of factors within the oral environment, for example the deposit may be 'washed out' by the brushing of the teeth, the impact of saliva and acidic components within the diet (e.g., acidic soft drinks)

formulations create a layer of cuboidal crystals of 0.5–2 μm diameters with associated fine debris that appears to be partially immersed in a deeper collagen matrix. It is evident that the application of toothpaste to the dentine surface may create a new artificial smear layer mainly composed of toothpaste ingredients, for example, silica. This artificial smear layer may however be susceptible to removal by saliva or by a gentle washout with water which may reopen the dentine tubules and affect the fluid flow rate. As previously mentioned, the application of acidic soft drinks may partially remove the surface deposition as in the example of calcium oxalate crystal deposits. Potassium oxalate has however been reported to be acid resistant reducing the risk of their removal. Furthermore, potassium oxalate has the ability to create very fine deposits inside the dentine tubules (Gillam et al. 2001, Mongiorgi and Prati 1994, Pereira et al. 2005, Markowitz and Pashley 2007) which may effectively reduce the functional diameter of the dentine tubules and affect the fluid flow rate.

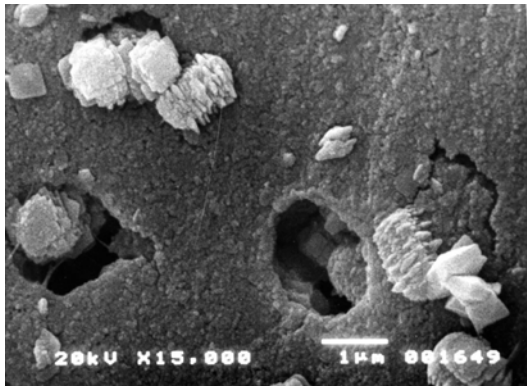
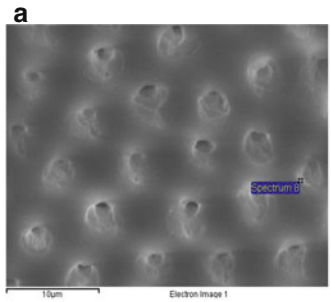
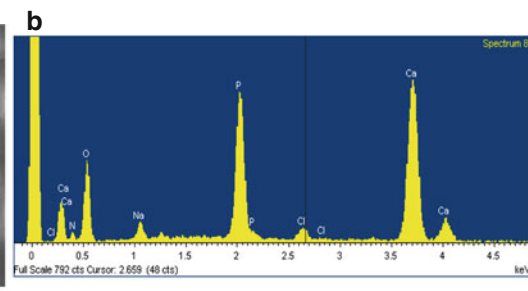


Fig. 6.5 The occlusal surface of a dentine disc. Higher magnification of the dentine surface following treatment with a commercial toothpaste and in vitro brushing procedures. In this sample we can observe some cuboidal deposits (component of toothpaste) that occlude the dentine tubules and are still in place following brushing. It was also observed that while only partially occluded tubules were present in this dentine specimen, the dentine permeability values were reduced to very low values, as the deposits in the partially occluded tubules appeared to reduce the functional diameter of the dentine tubules and subsequently reduce the (fluid) flow rate

SEM techniques may also be utilised to evaluate a replica of the dentine (and enamel) surface following a dental impression of both sensitive and nonsensitive teeth. A epoxy resin cast is made from the dental impression material prior to SEM observation in order to detect the differences of the presence of any open/closed dentine tubules appearing on dentine surface (Pashley 2013). A further extension of this methodology would be to take impressions (and replica moulds) before and after treatment during a clinical trial. According to a number of investigators, the combination of SEM and EDX observation would be a vital step in the evaluation of the effectiveness of desensitising agents (Prati et al. 1999; Gandolfi et al. 2008). For example, EDX may confirm the presence of the various compounds deposited on the dentine surface, for example, zinc, silica and strontium,





c

Elem	Weight	Atomic
N K	13.97	19.77
O K	46.58	57.72
Na K	2.51	2.16
P K	13.70	8.77
Cl K	1.36	0.76
Ca K	21.88	10.82
Totals	100.00	

Fig. 6.6 The dentine surface following EDTA treatment for 3 min, copiously washed with water and left in simulated body fluid (DPBS) for 24 h. (**a**) ESEM micrograph at 1,000× magnification. Dentine with no visible smear layer and with open dentine tubules. (**b**) EDS spectrum peaks of Ca and P and traces of Na and Cl. (**c**) Table of element analysis

which are frequently included in the toothpaste formulations. For example, the presence of silica on the dentine surface may confirm the ability of the toothpaste ingredients to react with the dentine surface and/or penetrate deeply into the dentine tubules.

According to Gandolfi et al. (2009), the ESEM (environmental scanning electron microscopy) may be a more appropriate technique to use than SEM. For example, ESEM allows for the use of wet dentine samples and prevents any surface alterations and artefacts due to the desiccation and metal/gold coating. The versatility of the ESEM over SEM techniques when investigating the morphology of humid or wet samples, for example, dentine and hydraulic cements, may have a number of advantages as there is no need to remove any water or requirement to metal coat the samples prior to observation and therefore the frequency of artefacts may be relatively low.

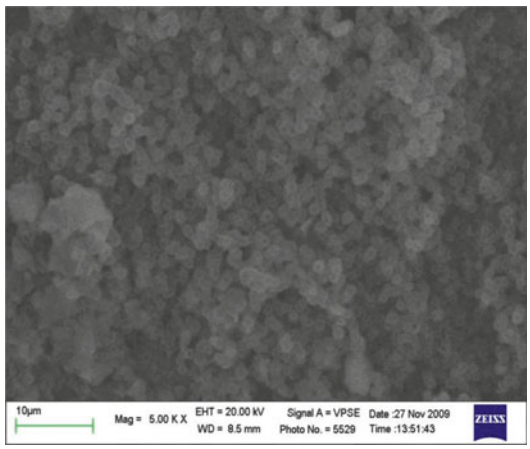


Fig. 6.7 The dentine surface was completely depleted by the smear layer (following EDTA treatment) and subsequently treated with an alfa TCP calcium silicate experimental agent for 3 min and left in DPBS for 24 h. ESEM micrograph at high magnification (10,000×) of a layer of small needle-like crystals spread all over the dentine surface. Discrete clusters of spherical crystals were also observed (original magnification 10,000×)

The use of EDX/EDS connected with ESEM is a perfect combination of methods to detect the surface (morphological and chemical surface modifications) of the dentine samples (Gandolfi et al. 2012). For example, the application of a reactive calcium silicate bioactive cement has been demonstrated to induce the formation of calcium phosphate deposits as apatite precursors and the creation of micro-calcium phosphate deposits able to occlude the dentine tubules and to remineralise the surface (Gandolfi et al. 2008, 2012) (Figs. 6.7 and 6.8). In this respect the ESEM/EDX would appear to be a suitable tool to investigate desensitising agents, cements, etc. (e.g. bioactive glasses) that may require a humid dentine surface (Gandolfi et al. 2011).

The use of confocal optical microscopy and confocal laser scanning microscopy can introduce the application of fluorescent dye solutions (e.g. rhodamine B, calcein, etc.) to trace the deposit

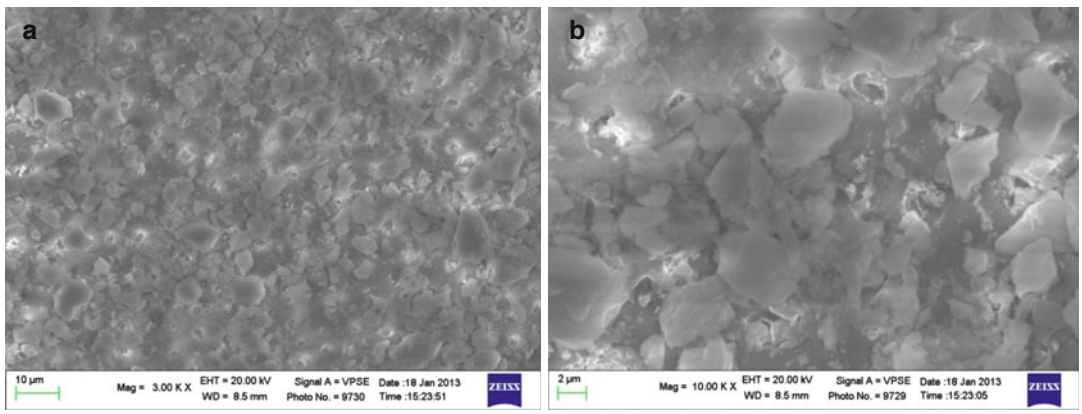


Fig. 6.8 (**a**) Dentine surface treated with a commercial toothpaste and soaked for 24 h in simulated body fluid (ESEM analysis 3,000×). (**b**) At higher magnification (10,000×), the surface appears to be coated by precipitates covering the surface with no dentine visible

formation (e.g. after the application of a desensitising agent) and to analyse the penetration of agents into the depth of dentine tubules following the preparation of longitudinal sections of treated dentine sample (Fig. 6.9). Precipitates from both toothpaste and mouthwash ingredients may penetrate deeply into the dentine tubules and subsequently reduce the functional diameter of the tubule and the fluid flow rate through the tubule. In other words, the application of a flowable paste into the dentine tubules may prevent the washout and the removal of materials from the dentine tubules. Many paste/toothpaste formulations may be labelled by a dye solution in order to obtain more detailed information on the penetration and distribution of deposits/precipitation into the dentine tubules and whether these deposits can withstand an acid challenge or cold water rinse (Fig. 6.10). Furthermore these techniques may be extended to investigate dentine bonding agents, glass-ionomer cements and other materials. The use of CLSM to inspect the hydrated dentine samples may also reduce any artefacts associated with the other techniques that have been recommended (Burnett 2013; Burnett et al. 2013) and may also offer distinct advantages in the evaluation of the dentine surface in order to observe the presence of an intact or modified smear layer.

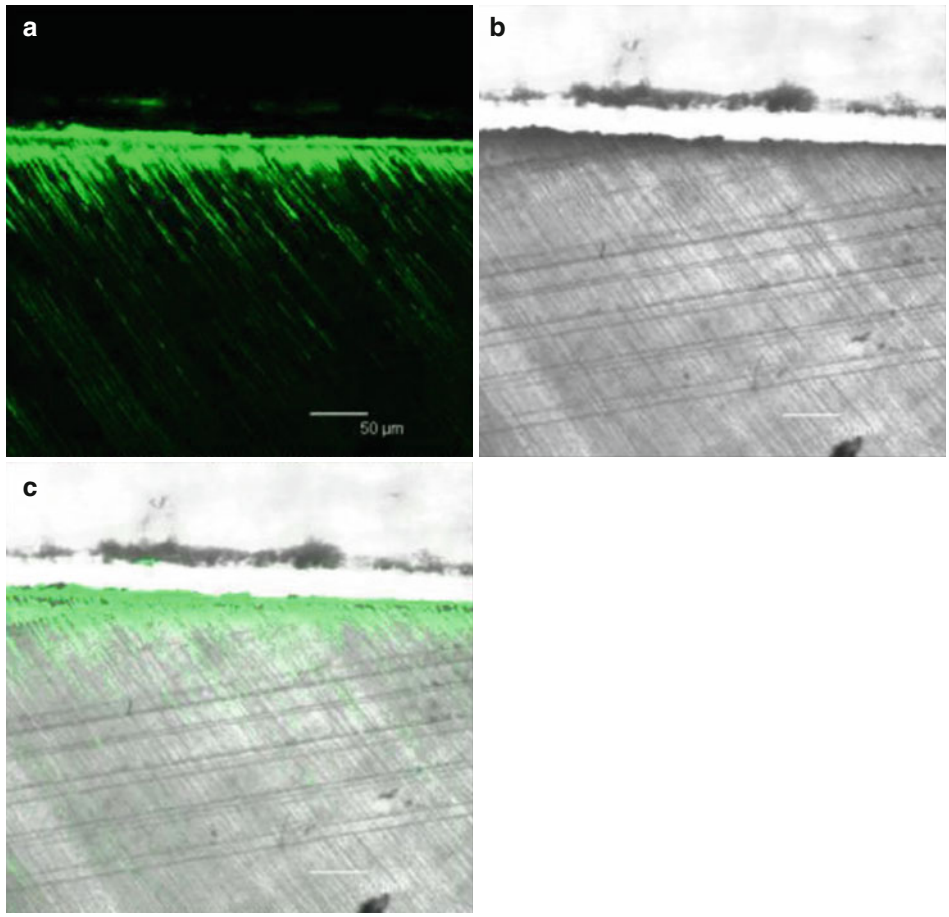
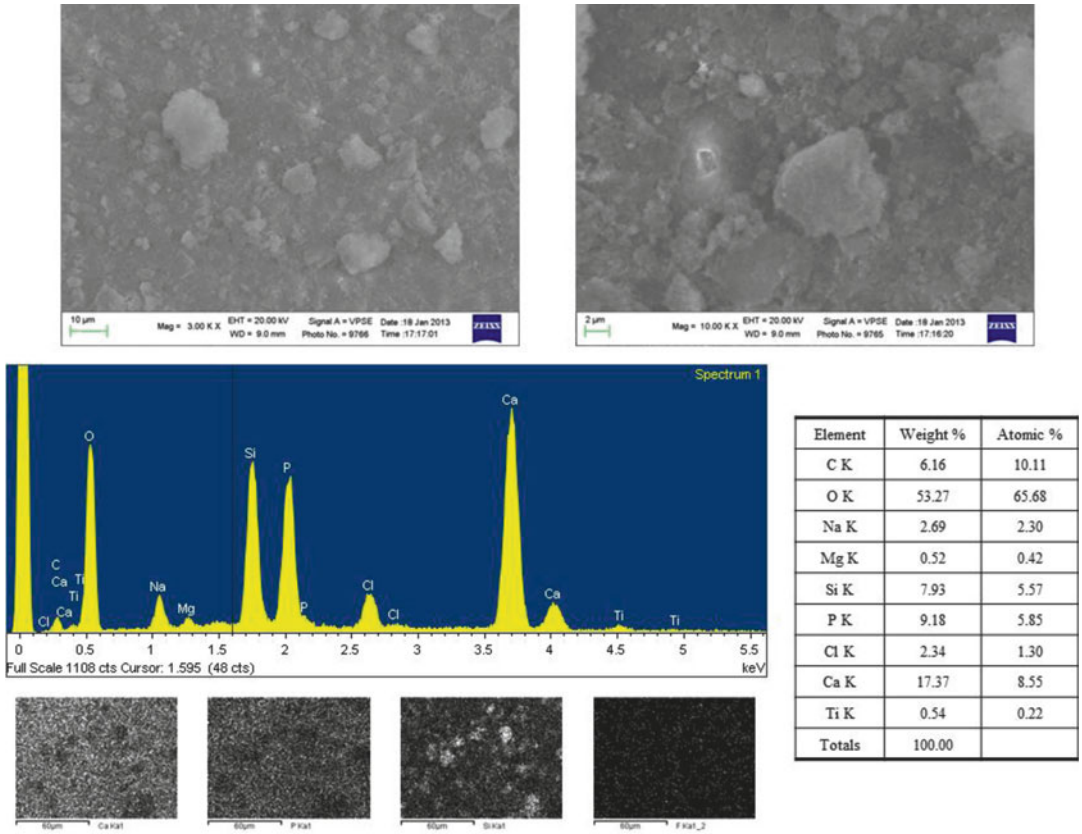


Fig. 6.9 Toothpaste mixed with a tracer (calcein solution 1%) was used to evaluate the penetration depth of the toothpaste into the dentine tubules by confocal scanning *optical* microscopy. A dentin disk was sectioned perpendicularly to the treated dentine surface. Transverse sections (200-micron thick, mark 50 m) were analyzed using an argon laser at 496 nm excitation and 515 nm emission wavelengths specific for calcein (**a**) or without laser source (**b**). Superimposing of the obtained images were also obtained (**c**). The penetration (highlighted by green staining due to calcein) showed a mean depth of 50 µm and reached a maximum depth of 60–100 µm



Element	Weight %	Atomic %
C K	6.16	10.11
O K	53.27	65.68
Na K	2.69	2.30
Mg K	0.52	0.42
Si K	7.93	5.57
P K	9.18	5.85
Cl K	2.34	1.30
Ca K	17.37	8.55
Ti K	0.54	0.22
Totals	100.00	

Fig. 6.10 The dentine surface treated with a commercial toothpaste and soaked 24 h in simulated body fluid (ESEM analysis 3,000 and 10,000×). At high magnification (10,000×), the surface appeared to be coated by deposits. EDX analysis provided both qualitative (X-ray spectrum) and semi-quantitative (table of the elements) measurements of the surface components. The main elements of dentine, e.g. calcium (*Ca*), phosphorous (*P*) and carbon (*C*), were detected together with the active elements of the toothpaste deposited on the surface with the components of the simulated body fluid. EDX provided a map/distribution of the elements on the surface

Raman and FTIR techniques may be considered to be valid methods to detect the modification of any of the reactive components that may be present on the dentine surface Vollenweider et al. (2007). For example, the application of a calcium oxalate mouthwash may induce the formation of crystal deposits that only Raman inspection may be able to confirm. A recent application of Raman has been proposed by Eliades et al. (2013).

These calcium oxalate crystals have also been detected by XRD analysis (Mongiorgi and Prati 1994) and by Raman and ATR-FTIR in a recent study (Eliades et al. 2013).

Focused ion beam scanning electron microscopy (FIB SEM) has also been recently proposed (Earl and Langford 2013) in order to detect more accurate sections of the specimens and to allow the observation of a dentine thin section by SEM and TEM (STEM) with EDS. This very sophisticated method allows for the study of small particle penetration (e.g. SiO_2 or TiO_2 particles) into the smear layer or into the dentine tubules (Earl and Langford 2013).

More recently solid-state nuclear magnetic resonance (NMR) spectroscopy has been used to investigate the ability of two bioactive glass-containing formulations and their ability to deliver Ca^{2+} ions in saliva and their effect on the crystal phases (Grootveld et al. 2009). Other investigators have also used ^{27}Al, ^{29}Si, ^{19}F and ^{31}P magic angle spinning nuclear magnetic reso-

nance (MAS-NMR) to characterise various restorative products, for example, fluoride and strontium containing bioactive glasses (Brauer et al. 2010; Brauer et al. 2013; Mneimne et al. 2011; Lynch et al. 2012; Fredholm et al. 2012) and a remineralising glass Carbomer® ionomer cement (Zainuddin et al. 2012). One of the interesting observations from these studies was the formation of fluorapatite (FAp) rather than fluorite (CaF_2), depending on the fluoride concentration, which may be of interest in dental applications (e.g. DH or remineralisation of enamel) as FAp is more chemically stable than hydroxyapatite or carbonated hydroxyapatite and able to withstand an acid challenge.

According to Grootveld et al. (2009), this technique has advantages over some of the other techniques mentioned in this chapter as it enables a rapid non-invasive and simultaneous study of a number of constituents present in saliva. Furthermore, according to these investigators, the technique enabled the investigation of chemical shift values, coupling patterns and coupling constants of resonances in the ^{1}H NMR spectra of the various components in the salivary biofilm following the interaction of the saliva with toothpaste products.

Conclusions and Future Research Trends

Following a review of a number of methods, it is evident that many of these techniques may (or must) be involved in the study of the dentine surface modifications and in the analysis of the effect of novel treatments on both the external and deeper dentine morphologies. The combination of some of these techniques offers the advantage to detect the effectiveness of a specific treatment (e.g. new toothpaste/mouth rinse products) and the chemical interaction between the material components and the dentine reactive surface. It should be acknowledged however as discussed in this chapter that these techniques have their advantages and disadvantages which is also true of the methodology utilised in both tubule occlusion and dentine permeability evaluation. The problems associated with the wide variability of the dentine specimens in both human and bovine teeth (and between erupted and unerupted teeth) appear to be unresolved, and perhaps a synthetic dentine substrate similar to the hydroxyapatite blocks used in enamel dissolution studies may be worth considering. Furthermore, it may be unreasonable to expect that all desensitising agents will be as effective in the in vitro and in vivo environments, for example, potassium salts and bioactive glasses. As mentioned care must be taken not to extrapolate the in vitro results into the clinical environment as it is impossible to fully mimic the dynamic nature of the interaction of saliva and the dentine surface in the laboratory.

Future studies must also be developed to detect the interaction of elements, for example, calcium and fluoride, with proteins of the intratubular dentine fluids and from saliva to have more information of their effective role in preventing (and reducing) DH (Suge et al. 2008; Gandolfi et al. 2012). The concept to occlude dentine tubules with a bioactive/biomimetic material able to modify its composition or able to induce the precipitation of insoluble fluorapatite (the basic composition of dentine) is one of the future options (Niu et al. 2013 see Chap. 11).

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7 Challenging the Traditional Approach for the Conduct of Dentine Hypersensitivity Studies: Person-Centric Studies Connecting the Patient with Their Practitioner to Optimise the Clinical Outcome

Frederick A. Curro and David G. Gillam

Introduction

Traditionally, dentine hypersensitivity (DH) has been assessed with both objective and subjective measures in clinical studies designed to evaluate the efficacy of desensitising products. The importance of conducting well-designed randomised controlled trials (RCTs) has been emphasised by both clinical investigators and regulatory bodies in Europe and the USA (e.g. ADA, FDA, ICP/GCP) (Gillam 1997; Holland et al. 1997; ICH 1996; ADA Council on Scientific Affairs 1998, 2009, 2012; Curro et al. 2000). One of the major problems however in assessing the level of pain associated with DH is the highly subjective nature of the condition which makes it extremely difficult for the clinician to evaluate the problem objectively in the clinical environment. Furthermore, the evaluation of the pain response from participants in clinical studies is particularly problematic, and this may be due to a number of issues, for example, the highly subjective nature of the problem and the influence of both Hawthorne and placebo/nocebo effects throughout the duration of the study. Other factors that may also impact on these studies include the lack of statistical power (small sample size) and lack of standardisation of the methodology used to determine treatment outcomes. More recently, however, the focus in assessing the subject's pain response whether in the research or practice-based environment has shifted from a biomedical model to a person-centred approach (Locker and Allen 2007; Curro et al. 2013; Robinson et al. 2014).

This chapter will therefore provide an overview on the traditional approaches to desensitising clinical studies designed to evaluate both in-office and over-the-counter (OTC) desensitising products as well as developing an argument for the inclusion of a person-centred approach when evaluating DH in both research and clinical practice.

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Traditional Approaches to Designing and Conducting Desensitising Clinical Trials

In both medicine and dentistry, clinical research has developed within the parameters and needs as described by the regulatory agencies and the process that is required to have an active ingredient

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approved for market distribution. The idea of designing a clinical study that was objective and without bias has however been difficult to achieve and most likely may not always in the best interests of the patient, prescriber and most importantly the clinical outcome. The required study to date for regulatory approval of desensitising products is the randomised controlled clinical trial (RCT), although this has been demonstrated as not being as representative of the actual drug use by the populace at large given the number of drug recalls (Kessler and Glasgow 2011; Silverman 2014). This has subsequently led to clinical studies that recognise the importance of the patient's input in the form of patient-reported outcomes and clinical studies that are patient centred. The complete assessment of the clinical findings should not however be one sided and based only on the interpretation of the investigator but should include the patient's response particularly in the case of the symptom pain where the objective results consist of a subjective component only expressed by the patient. Dental medicaments are primarily purchased by the consumer as over-the-counter (OTC) medications, and efficacy in the dose used is decreased to maintain the broadest safety profile possible. Patients generally receive a prescription from the clinician that is subsequently completed and dispensed at a pharmacy (chemist) where drug efficacy is evaluated over safety for use in a risk/benefit assessment.

According to the Acceptance Program Guidelines (ADA Council on Scientific Affairs 1998, 2009, 2012) for desensitising products, companies are required to provide efficacy data from at least two (independent) double-blind clinical studies, demonstrating a statistical significant effect of the active ingredient, on DH. Furthermore, all published studies demonstrating the effectiveness of the active ingredient must be fully referenced to include studies that do not show any effectiveness. Clinical data from all proprietary studies including those studies that do not show any effect must also be provided in the submission. Furthermore, there should be (according to these guidelines) a 20 % statistical significance between the control and experimental product groups for one sensitivity index in both studies submitted to the ADA although there appears to have limited or no published data to support this particular requirement. Setting a number for statistical significance can confound the results when applied to analgesic studies especially those agents designated OTC and is contrary to "personalized medicine". One may however challenge whether it is acceptable for investigators to simply express treatment success in terms of the degree of reduction produced in the clinical symptoms (DH) by setting arbitrary percentage changes rather than demonstrate the effect of any reduction on the individual's quality of life (person-based outcomes). Two recent reviews of products currently on the market against placebo (Brae et al. 2014; West and Davies 2014) and on professionally and self-administered dentine hypersensitivity agents show that there is sufficient evidence to support the use of a number of agents as well as showing that there is limited evidence to confirm the relative effectiveness of individual professionally applied agents.

Problems Associated with Clinical Studies

The treatment and management of DH especially for clinical research relies on how much information the person has to properly describe the stimuli applied for both reproducibility and accuracy. If one conducts sufficient studies, one realises that it may become very difficult to predict the outcome due to so many variables involved that can influence the results. For example, one confounder may be the abrasive base in the toothpaste which can function as a causative agent as well as a tubule occludent blocking the stimulus (e.g. from cold drinks). Other confounders may be the charge of the agent (e.g. toothpaste); since the tooth normally has a negative charge, agents with a similar negative charge take a much longer time to be effective (if successful), and during that time, the dentine surface environment may also change. The earlier the clinician can identify enamel wear, the less chance for the enamel thinning to reach the dentine especially the enamel/dentine junction, presumably the most sensitive area of the coronal part of a tooth. Current mechanisms include dentine surface occlusion of the

dentine tubules and nerve depolarisation by potassium nitrate (see Chap. 2). The complexity of the application of having an active agent reach its target site makes these clinical studies challenging in that a device (toothbrush) is used to apply the agent in a constantly diluted environment against a concentration gradient and completed with further rinsing and dilution of the area. This variability in how the active agent reaches its target site may therefore cause a degree of inconsistency in clinical trial outcomes. Clinical studies usually measure the (study) cumulative effect of a person using the active agent over a fixed period of time. Long-term DH studies are problematic in nature as the dentine surface is not necessarily the same as when the study first started as well as the pulpal tissue which can affect dentine tubular flow. Additionally, the process is self-limiting whereby secondary dentine is laid down to reduce the painful stimulus. DH studies are therefore measuring an outcome that is constantly in flux based on the tubular density, the effect of burnishing the dentine surface due to toothbrushing and the effect of the many active ingredients in the toothpaste which can cause an effect on the topography of the dentine surface. As a result of the topography of the exposed dentine surface changing, evaluating the tactile component of pain becomes a variable target which can also affect the air blast assessment. The questions therefore may be raised: (1) how does a clinical investigator measure DH? (2) what is the optimum time frame for a study? and (3) what is the optimal use of toothpaste for the condition?

DH should therefore be considered a discrete sensation experienced at a given time by the individual. The neuronal pathway of the teeth supports convergence so that what is experienced is a cumulative effect by the individual whereby an electronic pain diary would capture what the individual is experiencing over time. The temporal effect of the study should not exceed the physiological time it takes for the pulp to lay down secondary dentine. DH is a pain model inherent with many variables whereby long-term studies would not be reflective of the efficacy of an agent over time.

The only domain of the tooth that remains as a target for efficacy is the dentine tubule itself. Therefore, any intratubular medicaments require a system to deliver the active agents to the tubule and beyond and affect both the tubular fluid and eventually the cell body of the odontoblast. This mechanism which has the potential to minimise caries destruction facilitates remineralisation of the existing tissue and stimulates the cell body to generate further dentine to maintain the integrity of the dentine. One can imagine for the future a microparticle penetrating the dentine tubule coated with an active agent to direct the cell body of the odontoblast to maintain the integrity of the dentine (Chap. 2). This would potentially avoid the constant changing of the dentine surface due to the abrasives in the toothpaste. Highly abrasive toothpaste formulations may also affect the surface due to burnishing of the surface by the toothpaste and brush.

DH studies are further made more difficult with toothpaste formulations containing fluoride which may blunt the effect of any agent being tested. Additionally, the physiological placebo effect is as high as any analgesic study. Traditional over-the-counter medicaments have an efficacy range of between 10 and 20 %. This effect is above all the other hurdles just discussed which makes these study outcomes difficult to reproduce especially if the same pools of patients are used for more than one study which is often the case.

The application of toothpaste formulations for the treatment of DH has not been fully optimised in that it is a complex process. The individual applies a strip of toothpaste (usually one inch) on a device, a toothbrush, and brushes their teeth applying variable pressure within a time frame ranging from 30 s to 2 min, against a concentration gradient in the tooth, in an oral environment constantly being rinsed out with water. Can one imagine a more hostile environment for a clinical study? Applying a surface active agent without rinsing one's mouth during and at the end of brushing would in theory provide more contact time with the tooth and may subsequently initiate a shorter onset time.

Assessment of the Pain Response

According to Curro (1987), pain can be considered as a multidimensional experience consisting of motivational, cognitive, affective and discrimi-

Table 7.1 Relationship of DH to acute and chronic pain

	Acute pain	Chronic pain	DH
Conducting pathways	Rapid	Slow	Rapid
Tissue injury	Clearly causal	Minor or absent	Clearly causal
Autonomic response	Present	Absent	Present
Biological value	High	Low	High
Mood	Anxiety	Depression, anxiety	Anxiety
Social effects	Slight	Marked	Slight
Effective treatment	Analgesics	Variable, sometimes none	Variable, sometimes none
Dysfunction	Possible	Present	Possible
Learned behaviour	No	Yes	Yes
Somatisation	No	Can be present	Can be present
Hypochondriasis	No	Can be present	Can be present

Acknowledgement from Curro (1990)

native components. The motivational component concerns itself with the escape mechanism, for example, removing one's hand from a hot stove. The cognitive component is the past memory of the painful experience, for example, knowing that the stove was hot. The affective component is concerned with the anxiety and stress associated with the painful experience, and the discriminative component is concerned with the onset, duration, intensity and location of the pain. An understanding of clinical pain and the development of successful approaches to its management have been hampered by the relative importance of the affective component and subsequently render pain a private experience. Each of the components of pain has, however, been shown to be subserved by their own neuronal tract and specific neurotransmitter (Table 7.1).

According to Holland et al. (1997), DH should therefore be evaluated either in terms of the stimulus intensity required to evoke pain (stimulus-based assessment) or as the subjective evaluation of the pain produced by a stimulus (response-based assessment); however, as has been discussed in Chap. 9, these measures do not necessarily take into account the impact of DH on everyday life. Traditionally, the presenting stimuli can be grouped into five main categories: mechanical, chemical, electrical, evaporative and thermal (Gillam et al. 2000). Stimulus-based methods usually involve the measurement of a pain threshold; response-based methods involve the estimation of pain severity. It is important to recognise that the stimulus being used must be both reliable and reproducible and that the procedures involved should be scientifically valid. The subjective evaluation of changes in the individual's overall sensitivity to day-to-day experience may also be included in the assessment procedure at each visit; normally, this would be completed before the test stimuli are applied. This may be completed as a visual analogue scale (VAS) score, verbal score, labelled magnitude (LM) scales or part of a questionnaire at the end of a study although they may not necessarily take into account the impact of DH on the quality of life (QoL) of the participants (Gillam et al. 1997a, b, 2000; Heaton et al. 2013). Although subject diaries are often used in these studies, this may be primarily for compliance purposes rather than for QoL assessment per se. The number of time intervals where the participants' pain is assessed may to some extent depend on the length of the study as well as the type of product being evaluated (professionally applied [in-office] or OTC). For example, one or two midpoint evaluations may be acceptable for a 12-week study (baseline 4, 8, 12 weeks), or for a study where an immediate desensitising effect is being evaluated, a post-application assessment after 5 min would be required.

The plethora of devices used in both clinical research and practice-based studies however would suggest that no one device was universally accepted as the ideal method for assessing DH (Gillam and Newman 1993; Gillam et al.

Table 7.2 Factors that may influence efficacy in DH studies

Factors that may influence efficacy in clinical studies
The episodic behaviour of the condition
Highly subjective nature of the pain response
Innervation
Physiology of the pulp and its changing response to stimuli
Clinical efficacy of desensitising agents may be at the lower end of the therapeutic range
Profound placebo effect reported in clinical studies
Hawthorne effect
Random variation in patient symptoms over time (regression to the mean/mode)
Small sample size
Tooth site and number
Investigator technique
Investigator/subject relationship
Choice and lack of standardisation of objective assessment
Occurrence of false positives from Yeaple probe evaluation (tactile)
Study duration
Variation of individual intake in food and drink
Seasonal weather variations

Acknowledgement modified from Addy et al. (2007)

2000; Ide et al. 2001; Cuhna-Cruz et al. 2010). Furthermore, the stimuli used for testing the subjective response should represent real life and be hydrodynamic in nature. And if more than one stimulus is used in the assessment, the least severe stimulus should be used first, and the intervals between assessments should be sufficient to prevent any interaction. There is however limited published data on the recommended intervals between testing although a 10 min interval between tactile and thermal/evaporative stimuli has been accepted in clinical studies, the purpose of which to allow sufficient time for nerve recovery and for the patient to forget their last response (Gillam et al. 2000). Of the available devices used in the clinical studies, the cold air syringe (Gillam et al. 2000; Schiff et al. 2009, 2011) and a controlled tactile pressure probe (e.g. Yeaple probe, Xinix Research Inc, NH, Portsmouth, USA; Jay Sensitivity Sensor Probe, Global Health Research Group, New Delhi, India) (Gillam et al. 2000; Schiff et al. 2009, 2011; Hedge et al. 2013; Kakar and Kakar 2013; Kakar et al. 2013; Sowinski et al. 2013). Although these devices are often considered objective and reproducible when assessing DH, one cannot completely eliminate the occurrence of false positives that occur in particular with the Yeaple probe threshold measurements (Table 7.2). According to Curro et al. (2000), false positives are more likely to occur at the lower force levels (10–20 g. wt) and were almost twice as common at the qualifying visit than at subsequent visits. This may be the result of a possible learning effect on the part of both the subject and the assessor, and the number of these false positives may be reduced by having a pretreatment (allocation) training phase in the study design. The likely outcome of having a large number of false positives recorded for the tactile response is that proportionately this may increase the placebo response rather than the treatment response that in turn would reduce the size of the treatment effect (Curro et al. 2000). This observation may also be true for the thermal evaporative stimuli (e.g. cold air syringe). Other problems may also occur, for example, when assessing the subjective response using the various pain scales (see above), and one should not ignore the impact of the relationship between the assessor and subject or the learning curve experienced by the participant during the study that may in turn have an unintentional impact on the study results. Finally, one should consider the expectations of the individual participating in a clinical study and how they may interact over time. For example, participants with chronic conditions such as DH typically have episodic or fluctuating symptoms, and any potential change in these symptoms over time in clinical study may be one of improvement (the so-called expectancy effect) (Curro et al. 2000). Individuals participating in a clinical study may also anticipate that they will experience pain from a stimulus directed at a tooth, for example, when subjects are assessed (VAS) with the thermal/evaporative stimulus at the qualifying and subsequent visits. Initially, they may report a high pain score at the baseline, but when assessed again at a subsequent visit, they can reflect on the difference between their previous exposure to the stimulus and to the current discomfort and subsequently decide that

the pain was not as bad and then indicate a lower pain score. The use of a pretreatment session overview may however help reduce these anomalies.

As previously indicated, one of the problems, evaluating DH, is the highly subjective nature of the pain response despite the traditional approach to assess the pain response by the so-called objective methodology. The complete absence of pain from DH is probably the only true end-point measurement rather than attempting to quantify objective measures of tactile and thermal thresholds. However, this goal may be unrealistic for a number of reasons, and it is evident than when analysing the results from the various studies that while individuals within the test and control groups may report that they have a complete absence of pain, closer inspection of the means (and 95 % confidence intervals) clearly shows that there is still a level of unresolved pain. Therefore, a different approach in addressing the claims made on behalf of a Pharmaceutical or Consumer Health Care Company in relationship to the pain associated with DH, may therefore need to be investigated. Furthermore, both from the patient's and clinician's perspectives, it is important to manage the expectations of both parties as it may be unrealistic to expect the complete resolution of pain following OTC or in-office treatment. It may be more relevant and practical to consider the reduction of the impact of the treatment on the quality of life of the patient in that they are able to complete their day-to-day activities either by coping strategies or the associated pain is reduced.

Patient Selection, Study Design and Selection of Controls

Experienced investigators would probably agree that recruitment to DH clinical studies is fraught with difficulties, and this may be due in part to a number of reasons, for example, the limitation of sites that may exhibit DH is predominantly on the buccal or facial surfaces of the teeth which may be restricted due to attempts by clinicians to restore the non-carious cervical defects present in an individual's mouth. The authors estimate that newer restorative procedures have made recruitment of potential participants into DH studies more difficult ranging from 1 in 3 some 25 years ago to approximately 1 in 8 today which may considerably increase the costs (to institutions and companies) of conducting these types of studies. A further problem may be due to the nature of the condition itself both in terms of its history (may have periods of spontaneous resolution) and the subsequent pain response on screening. The impact of this particular problem may be underestimated; generally speaking, individuals are included into DH studies on the basis of having a previous history of DH which may lead to difficulties in recruitment particularly when assessing pain scores in studies with the current exacting and inclusion/exclusion criteria. It is important however when recruiting individuals for a clinical study that the entry criteria are reasonable and realistic; otherwise, the investigator will struggle to recruit adequate numbers within the allocated time frame for completion of the study. This is particularly true when dealing with a highly subjective clinical condition such as DH. Care must therefore be taken when screening prospective participants not to recruit individuals who either report minimal or extreme discomfort since the statistical probability of measuring the pain response can only stay the same, worsen or improve, respectively. This phenomenon is called regression towards the mean or mode (Yates et al. 1998; Addy et al. 2007) and according to Jeffcoat (1993) can either magnify a product's treatment effect if used on a severely affected population or minimise the effect when used in an under-affected population.

One of the inherent problems in conducting clinical studies is the interference of placebo and/or Hawthorne effects that may introduce bias into the study (Gillam 1997; Addy et al. 2007). This may be particularly true in pain studies such as relief of pain arising from DH, and one way to resolve this particular bias is the use of a double-blind placebo-controlled study (Jeffcoat 1993; Holland et al. 1997; ADA 1998, 2009, 2012). According to Schulz et al. (2010) the Randomized controlled trial (RCT), when appropriately designed, has been generally acknowledged as the gold standard for evaluating health care interventions. This viewpoint, however, has been recently challenged as a result of the number of 'black

box' warnings placed on drugs by the FDA and the number of drugs subsequently removed from the market place by the Regulatory Authorities due to safety concerns (Kessler and Glasgow 2011; Silverman 2014). RCTs are now viewed as too restrictive and not representative as point-of-use by providers. RCTs conducted by highly trained specialists recruiting a 'designer patient' using the drug in a restrictive environment hardly yields results that would be robust and mimic use for the population at large. RCTs should therefore be reserved for early phase clinical studies when the safety profile has not been determined, when the delivery is complicated, and when the drug is directed at a compromised patient. In this type of study, all participants are allocated (random assignment) to either the test or control group, and the difference in outcome across groups will determine any significant efficacy of the test group. The design is simple and requires minimal prior knowledge of the cause of the disease in each group. This type of design, however, may result in an unequal distribution of high-risk individuals with multiple active sites, although this feature may be more of a problem in studies of less than 30 subjects. The use of stratification techniques, however, can be used to give balance across the groups. It is usual to stratify potentially confounding factors such as numbers of teeth, baseline sensitivity levels, age, gender, etc. From a practical point of view, it is generally easier to assign a treatment to each of the participants. This type of design has been recommended for clinical studies evaluating both OTC and in-office products although other types of study design have been used in DH studies such as cross-over and split-mouth (Gillam 1997). The use of a pretreatment period study design which enabled the participant(s) to be randomised into test and control groups and as such allows the participant to act at his/her own control as well as to compare that subject to the randomised control and other groups may also be utilised in DH studies (Page et al. 1995). For example, there may be advantages in having a 2–4-week pre-study evaluation period for sensitivity studies in which the participant is introduced to the pain scoring methods (visual analogue scales (VAS)) and is placed on a placebo or fluoride toothpaste. It would be anticipated at the end of such a period that (a) the participants understand what is expected of them with regard to the various assessments used when measuring the pain response, e.g., VAS, Schiff Air Sensitivity scores, LMS and (b) participants actually have 'real sensitivity' before being entered into the main study. One observation may be relevant here with respect to the Schiff air test as the patient's reaction to the test is translated by the investigator thereby excluding the patient's response. Those individuals fulfilling the entry criteria following this pretreatment period can then enter the study. One disadvantage of this type of study design, however, is that it adds to both cost and time. Other study designs that have also been reported in the literature involve the use of an adjunctive therapy (e.g. the application of a potassium-containing mouth rinse following routine toothbrushing with a fluoride toothpaste) (Gillam et al. 1996a; Yates et al.1998). This type of study, while widely utilised in antimicrobial therapy studies, has not been used routinely in DH studies, but there would be advantages in incorporating such a study design in evaluating the additional effect above what would normally be expected from using a commercially available fluoride toothpaste. DH studies may also lend themselves to an adaptive design where the knowledge of the patient population actually enrolled in the study, the variance of the study end point, event rates, and possibly the treatment effect itself available at interim may be used to change the study design or key parameters in order to improve the chances of success. Such adaptation, if appropriately implemented, has the potential to save resources; however, this implementation requires that the statistical validity of the study's results be preserved (LaVange 2014). The US regulatory agency (FDA) has also recently issued draft guidance on adaptive designs, and the final version is in progress considering the public comments received (FDA guidance for Industry 2014).

According to Fleiss (1992), clinical studies may assess the efficacy, equivalence or superiority of a treatment and as such studies can be designed to test either products or ingredients of products. Products designed to reduce DH should therefore be tested in controlled clinical studies

in which the test product is tested against (a) a negative control to establish efficacy and (b) a positive control to determine relative potency. In the absence of any negative controls with no demonstrable desensitising effects and any internationally accepted benchmark positive control, the test product may be tested against a minus-active control.

One of the problems, however, in this respect is that there is no agreed positive or negative control (the so-called gold standard) in DH studies (Holland et al. 1997). For example, several published studies have used minus-active controls that may not be representative of the final commercially available product sold over the counter (in the case of OTC products) (Gillam 1997). Furthermore, the characteristics, bioequivalence, efficacy, etc., may be changed by addition/subtraction of different ingredients.

A further complication that continually appears to affect the interpretation of results from clinical studies of this nature is the reported placebo effect that can be as high as 40 % (Curro et al. 2000; West et al. 1997). Several investigators have also alluded to this obvious effect in their studies (Gillam 1997; Pearce et al. 1994; Chesters et al. 1992), but to what extent the placebo effect complicates the interpretation of the results of the study is difficult to predict. It should however be noted that according to Curro et al. (2000), the placebo effect observed in DH studies is not too dissimilar to those reported in other medical and dental therapeutic studies. For example, a review of 15 postoperative pain studies by Beecher (1955) quoted by Curro et al. (2000) concluded that on average symptoms were satisfactorily relieved by the placebo medication in 35 % of the patients (the placebo response range of 15–58 %). Compounding factors (Table 7.1) that may affect DH studies may also be complicated by the lack of acceptable positive and negative controls used in equivalence and superiority studies. Unlike gingivitis studies where the internationally accepted gold standard would be chlorhexidine, there does not appear to be an internationally accepted product which one could use as a positive control in such studies. Furthermore, the difficulty in using a negative control which may also exhibit a desensitising effect may also complicate the interpretation of the results and is also problematic (Gillam et al. 1996a, b; Gillam 1997; Pearce et al. 1994; Chesters et al. 1992). The use of a true placebo toothpaste, without any known desensitising ingredient, may however be problematic, and most studies would appear to use a fluoride-containing toothpaste as a negative control when evaluating a product. A final concern that may be expressed regarding these types of studies is whether the study population that are used for the studies are truly representative of those who suffer from the condition in real life, and perhaps more research should be initiated into the demographics of recruiting subjects for DH studies.

The study duration may also vary according to the purpose of the study, the nature of the agent tested, the hypothesis of the mechanism of action, the outcome measurements and their sensitivity and error. According to Gore and Altman (1982), the duration of a clinical study is a critical factor in determining product effectiveness. The concentration of active ingredients presented in an over-the-counter (OTC) product will tend to be relatively low, and so the study must be of sufficient duration in order to allow the active agent(s) to demonstrate maximal clinical efficacy (Orchardson R, personal communication 1997). However, comparative studies including an inactive control (placebo) may also reveal a substantial 'placebo effect', which may follow a different time course to that of the active agent. The clinical study duration should therefore be sufficient in length as to minimise any 'placebo effects'. Although a number of published studies have demonstrated improvement ranging from 30 to 80 % reduction in sensitivity when comparing test pastes to other toothpastes and placebo (Clark and Troullos 1990), the results are conflicting and somewhat difficult to interpret, due in part to different methodologies and patient criteria. The majority of the published studies are between 6 and 12 weeks (some on 22 weeks) (Gillam 1997). It is worth acknowledging that most of these studies were of short duration looking at the immediate effect of the toothpaste on DH, and therefore, the majority of these studies do not appear to provide any meaningful data on the long-term efficacy of

OTC desensitising toothpastes. Furthermore, there have been relatively few studies (Gillam et al. 1992) that have monitored the effects of a dentifrice following a period of active product use. The results of these studies would also suggest that there is a carry-over effect of products following the cession of use. The implications of this would be that there should be a delay or wash in a period of 1–2 months prior to entry of subjects on desensitising products. Published in-office treatment studies would generally speaking have a range of duration from 4 weeks to 3 years depending on the period of follow-up. It is important however to acknowledge that the amount of time required for a particular desensitising agent to achieve clinical effectiveness is likely to be affected by several factors, including (a) variations in the motivation and compliance of individual participants and their ability to apply the product as intended and (b) the nature of the test agents and their likely mode of action. For example, most desensitising toothpaste formulations, namely potassium [chloride, citrate, nitrate] and strontium-containing salts [acetate, chloride] may take up to 4 weeks to be effective (Tarbet et al. 1979, 1980, 1982; West et al. 1997), whereas an applied in-office product such as a desensitising prophylaxis paste or sealant may provide instant relief for the patient (Gillam 1997; Milleman et al. 2012; Neuhaus et al. 2013; Schiff et al. 2009; Orchardson and Gillam 2006). In the dental practice environment however a patient who is suffering from extreme DH symptoms would expect some form of immediate treatment to relieve the pain rather than wait up to 4 weeks for relief of pain associated with DH. With regard to in-office products, there does not appear to be no internationally recognised gold standard; generally speaking, most reported studies follow the same study design as over-the-counter (OTC) products. One of the problems however that may still need to be resolved is the lack of homogeneity in the manner in which the traditional DH studies have been conducted, and consequently, there was no widespread agreement as to which of these treatment modalities was the ideal material or procedure to treat DH (Gillam 1992; Orchardson and Gillam 2006; Cunha-Cruz et al. 2010; Lin et al. 2013).

Table 7.3 Problems with the biomedical model

Subjective, unreliable and value laden
Exclusive
Questionable ethics and consumer participation
Normative needs are often high
The norms of dentists do not correspond to the functional norms or social needs of people
Based on the absence of disease rather than health
Ignores the functioning of the oral cavity or person
Ignores social and motivational factors
Excludes alternative treatments
Ignores health promotion and prevention

Acknowledgement derived from Sheiham et al. cited by Robinson et al. (2014)

The Argument to Shift from a Traditional Biomedical Model to a Person-Centric Approach

Defining the Traditional Biomedical Approach

The traditional biomedical model has been defined as a conceptual model of illness that excluded any psychological and social factors and included only biological factors in order to understand a person's medical illness or disorder (Definition of a biomedical model– medical definition 2014). Several investigators have however reported on the limitations of this model as it failed to take into account the individual health-related quality of life and any concerns the individual may have had regarding his/her health (Engel 1977; Locker and Allen 2007; Robinson et al. 2014). The need for the development of a new approach was addressed by Engel (1977) when he proposed a new biopsychosocial model in order to take into account the concerns of the patient within the social context in which he/she lives together with the healthcare systems developed by society to manage or treat the disruptive effects of the medical condition (illness). The criticisms and problems with the traditional biomedical approach to treating oral diseases have been expressed by Sheiham et al. (1982) cited by Robinson et al. (2014) (Table 7.3).

Definitions of Health-Related Quality of Life (HQoL)

According to Robinson et al. (2014), a number of definitions have been previously proposed to define HQoL, for example:

1. Physical, psychological and social domains of health seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions.
2. The impact of a perceived health state on the ability to live a fulfilling life.
3. The impact of disease and treatment on disability and daily functioning.
4. Optimal levels of mental, physical, role and social functioning, including relationships and perceptions of health, fitness, life satisfaction and well-being. It should also include some assessment of the patient's level of satisfaction and treatment, outcome and health status and future prospects.

The person-centric approach has been successfully introduced in the medical, nursing and dental environments as well as in clinical and research studies (McCormack and McCance 2006; Locker and Allen 2007; Curro et al. 2013; Gibson et al. 2014; de Silva 2014; Robinson et al. 2014). For example, according to Robinson et al. (2014), the measurement of an individuals' quality of life (OHQoL) in oral health-related research marked an important move from the biomedically dominated perspective to a patient-centred approach. According to Curro et al. (2013), the top-down deferential approach of the traditional biomedical model is no longer sustainable, and therefore, the dynamic shift to a person-centred approach may have distinct advantages in both the clinical environment and in the clinical research setting. For example, the biomedical model approach did not specifically address the concerns of the person and generally failed to include the person into the treatment decision-making process. Traditionally, those individuals participating in clinical research have been considered as 'subjects', and this to some extent provides emphasis on the protection of the individual and possible dissuade involvement of these individuals in the planning and execution of the clinical study. It may therefore be reasonable to suggest that involving the person into the decision-making process is consistent with a person-centred approach.

Defining Person-Centric Clinical Trials (PCCT)

The terms consumer and patient do not fully describe the scenarios covered by the term 'person'. A person is only a patient for the time they are in the dentist's chair, and a person is a patient for as long as they are ill. The term patient is subservient and non-inclusive of the person in health, treatment and management of a disease. It fosters the traditional information flow of the doctor to the patient. And even the term patient-centred has multiple meanings. PCCT uses the term "centric" to include the dynamic interchange between the patient and clinician, where the term "centered" is relatively static and does not connote the interchange. The more descriptive and inclusive term is described by 'person centricity', a more evolved term over patient centred (Curro et al. 2013; Robbins et al. 2013, 2014). The term allows for the person to be actively engaged in their own healthcare, treatment and management of condition. The term is now extended to conducting person-centric clinical studies whereby the person is now included in the assessment of treatment and/or evaluation of a drug person-centric clinical trials: an opportunity for the good clinical practice (GCP)-based research network (Curro et al. 2013).

Person-centric clinical trials defines the N=1 clinical study where that participant, subject or patient, is considered the primary outcome. The N of 1 PCCT is an example of a single-patient experiment with mutual agreement from both patient/subject and clinician to report the effects of treatment either positive or negative, as well as the signs and symptoms and other manifestations of the patient's overall response to the medication or active agent especially those designated as the outcome parameters. PCCT encompasses personalized medicine and responds to the question of "why does one person in one hundred have a reported adverse reaction". PCCT merges experimental clinical design with that of the practicalities of clinical practice by improving

the quality of the clinician patient encounter. PCCT studies primarily include patients of record from a clinician's office and as such have a known past medical/dental history which allows for a more discriminative interpretation of adverse reactions and side effects of drugs/devices being tested. PCCT makes the distinction between "N=1 patients" who are in a later stage effectiveness study from those who are termed subjects participating in a controlled clinical study evaluating efficacy in the earlier stages of drug development.

Dentistry is a very good example of person-centric care whereby the person visits a dentist twice a year for half an hour, and for the rest of the time the outcome of the treatment (or in the example of participating in a clinical trial) is in the hands of the person. One can therefore see how important the input of the person can be in both the normal clinical practice environment and in particular when participating in clinical studies). The recruitment of patients to a clinical study has been previously described (Robbins et al. 2014). The person's feedback is documented in the United States Food & Drug Administration guidance document on patient-reported outcomes (FDA Guidance for Industry Patient-Reported Outcome Measures 2009).

DH is a particular case in point of PCCT where the outcome is primarily dependent upon the person not the dentist. DH studies are classified as analgesic studies and have all the complexity associated with them including many confounding factors, the least of which is the high placebo response. DH studies are self-limiting where the pulp responds to such stimuli in a protective manner altering the sensation during the course of a study making the description more subjective than objective. Scheduled protocol patient visits can cause large data gaps in the interpretation of the clinical outcome. Discrete patient visits over an extended period of time do not necessarily capture the true effect of a drug as conditions are changing. PCCT allow for a continuous stream of data and fills in the voids between patient visits using mobile health devices, patient diaries, and remote data entry or by direct calling to the clinician's office for data entry in the source document. The methods of recoding are the means; it is the inclusion of the patient as an important part of the outcome that is the important concept to be recognized. The outcome is no longer dependent only on the investigator's interpretation of the patient's response. The variable of the patient's response being lost in translation is minimized or eliminated. PCCT requires that the investigator informs the patient/subject on their role in the clinical study so that their responses are valued equally by the investigator as they will provide more data points than that provided by discrete patient visits. Additionally, PCCT requires that both the practitioner (investigator) and the patient have a common goal to improve the clinical outcome either for efficacy or effectiveness, a distinct advantage when recruiting participants to a study from a practice. It should however be stressed that irrespective of the approach taken to test the outcome measures there will be factors e.g., the intra oral dilution of the toothpaste/mouthwash that would relatively unchanged during the study. For such studies, 'global person assessments' and 'person diaries' have become more prominent in clinical outcomes. In the past, they were considered secondary to the air blast and applied fixed force by a probe (as discussed above). Furthermore, the approach and principles outlined above for clinical studies may also be implemented in the practice environment by the clinician when managing DH as demonstrated by the PEARL Network studies (Curro et al. 2013).

RCT Versus Person-Centric Studies

Clinical studies on DH therefore may exemplify the concept of person-centric clinical studies whereby the 'person' themselves provide and contribute to the clinical outcome. The results relate to each individual as the ultimate N = 1 clinical study whereby the person's compliance is essential to the outcome. It is from this perspective that clinicians and regulatory agencies should view conducting future DH studies in order to improve the process of recognising and accepting desensitising products for the treatment of DH. PCCT are compatible with conducting an RCT either by randomizing the patient's at

the practitioner's site or by clustering the sites according to how the practitioner treats the condition under investigation using appropriate blinding techniques. PCCT lend themselves best to standard of care studies comparing effectiveness.

Discussion

The ideal goal for any dentine-desensitising agent/product is to, at least, minimise and hopefully abolish the symptoms of pain or discomfort associated with DH. However, a more realistic expectation might be for OTC/in-office treatments to reduce DH to levels that are acceptable to the subject or at least to reduce sensitivity to levels evident in symptom-free teeth and enable the subject to have an improved quality of life. The main objective therefore should be to produce a clinically significant reduction in clinical symptoms rather than a small but statistically significant reduction. Indeed, one could argue that despite the so-called objective methodology used to evaluate DH in terms of centimetres or grams, the final arbiter is the subject (absence/presence of pain/tolerance of pain). The final clinical outcome parameter itself is a variable affected by the temporal biological response of the pulp to a nociceptive response. Prolonged clinical studies are not of added value in the objective assessment of the product. Discrete measurements are not reflective of the response, and a more continuous measurement capturing the response in real time through, for example, mobile health devices, we believe, would be of added value to the understanding of the condition. DH studies truly describe the N=1 clinical study where no two patients are alike and where the patient has the greatest influence over the course of the study affecting the outcome. Their input is mandatory and most likely should be given considerable weight in the evaluation of the results. The person plus a continuous readout of the responses over time and against various stimulants would create a dynamic outcome instead of a static one. Treatment effects may, however, be expressed in terms of the degree of reduction produced in the clinical symptoms, but the wisdom of setting arbitrary percentage changes may be questionable. The degree of a product treatment effect that can be achieved will be influenced to some extent by the original baseline sensitivity levels, which should be neither too modest nor too severe in order to participate in a clinical study. The magnitude of the anticipated treatment effects should however be established at the outset of the study protocol design stage. The expected end point (e.g. the anticipated level of therapeutic effect) will influence the study design, and this may also be dependent on the mode of action of the test product and its intended clinical use. For example, whether the study is intended to establish efficacy/or equivalency/superiority of the test agent compared with a placebo or standard agent, and therefore, the intention of the study must be declared at the outset. Statistical methods of analysis should be in accordance with the ICH guidelines on statistical principles for clinical studies (1998) in concert with study design, preferably in consultation with a competent statistician, and these objectives should be clearly stated in the study protocols prior to the start of the study. Since DH studies are considered analgesic studies the issue of what is significant becomes very meaningful and is reflected in the N=1 concept of person-centric clinical studies. The effectiveness of an over-the-counter (OTC) or behind-the-counter medication has many views and encompasses the discussion of clinical significance versus statistical significance which in some cases excludes personalized or N=1 outcomes. The topic is only mentioned as the discussion is beyond the scope of this chapter. However, the use of a placebo in analgesic studies should be carefully considered especially in DH studies where a comparative agent may be better served. The high placebo response in analgesic studies as high as 50 % confounds the OTC efficacy of an agent. OTC drugs, devices and agents always sacrifice efficacy for safety and efficacy in OTC drugs has been stated to be in the range of 10–20 %. (The author FAC served on an OTC FDA panel; personal communication with FDA Director Michael Weintraub, MD). It should be acknowledged that the introduction of recom-

mended guidelines for conducting DH studies by Holland et al. (1997) has provided a stronger framework in order to evaluate the efficacy of desensitising treatment modalities and may have to some extent eliminated some of the confounding factors that were prevalent in the pre-1997 studies. However, it should be recognised that pain is a subjective experience which may depend on a number of factors, for example, the patient's previous pain experiences, the psychological profile of the subject and the levels of stress and individual pain threshold. Furthermore, it may also be extremely difficult to accurately assess the exact level of pain experienced among different individuals who come from different cultural backgrounds and who may have a difference in a previous pain experience. The question may therefore be asked which is the ideal technique to evaluate the patient's pain response in DH pain studies, since there are a number of both objective and subjective measures that are available to use, for example, air blast from a dental air syringe, force-controlled dental probes, visual analogue scales (VAS) and verbal rating scales (VRS), etc. (Gillam and Newman 1993; Gillam et al. 2000). More recently, person-centred outcome measures, for example, oral health-related quality of life (OHRQoL) measures have been used to evaluate the impact of DH in subjects with DH (Bekes et al. 2009; Bioko et al. 2010; Bekes and Hirsch 2013; de Oliveira et al. 2013). For example, the short (DHEQ-10/DHEQ-15) and long form of the Dentine Hypersensitivity Experience Questionnaire (DHEQ) has been utilised in recent DH studies (Baker et al. 2014; Machuca et al. 2014) (Chap. 9).

Future Trends

Although the authors of this chapter have considerable experience in conducting DH studies over many years using the traditional approach in order to assess DH, they have reconsidered whether this approach satisfactorily addresses the impact of DH on the person's quality of life or even addresses any of the person's concerns regarding their health. It is also apparent that the person-centred approach has been successfully introduced in both medical and dental environments and in clinical studies and may, therefore, be of benefit in determining outcomes both in conducting DH studies and in the management of DH in the clinical environment as demonstrated in the PEARL Network studies.

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8 Current and Novel Clinical Approaches for the Treatment of Dentin Hypersensitivity

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Brief Overview of the Chapter

According to Orchardson and Gillam (2006), the management of dentin hypersensitivity (DH) has been traditionally based on products or procedures (in-office [professionally-applied] and over-the-counter (OTC)/at-home) that may either block the dentin tubules on the exposed root surface or desensitise the nerves in the pulp (see Chap. 10). The clinician however is often faced with an array of products from the manufacturers all claiming to be effective in terms of both immediate and long-lasting relief from pain. Whether there is an ideal treatment or a so-called gold standard for DH, it is still a challenge. (Orchardson and Gillam 2006; Gillam et al. 2013). Furthermore several investigators have reported on the wide range of in-office and OTC products and procedures that have been used by clinicians in daily dental practice, and it was evident from these reports that there is considerable confusion for the clinician with regard to which of these products actually are effective in reducing DH (Gillam et al. 2002; Cunha-Cruz et al. 2010).

One of the problems that a clinician may face when examining a patient complaining of oral pain is the clinical diagnosis of the condition. This has been addressed in the earlier chapters of this book (see Chaps. 4 and 5), and it is evident that without a definite diagnosis of DH, the clinician cannot effectively manage the condition successfully. DH as previously defined is essentially a diagnosis of exclusion, and this will clearly take the clinician sometime in order to record the necessary information during the screening process and subsequent clinical examination (see Chap. 5). Once the clinician is confident that the correct diagnosis of DH has been made, then the management of the condition can be undertaken. However as indicated in Chap. 10, the provision or prescription of a particular in-office procedure or OTC product in itself without the removal of the essential components of the aethiological and predisposing factors that initiated the problem in the first place by the clinician, together with

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counselling and educating the patient (dietary changes/toothbrushing techniques, etc.) and subsequent monitoring the condition over time, will result in ineffective and unsuccessful treatment. The aim of this chapter therefore is to review the various products and procedures that have been recommended for the treatment of DH and any novel products that have been recently introduced, together with some recommendations for future development of desensitising strategies.

Classification of Desensitising Agents

The classification of the various treatments for DH can be a challenging process particularly if the precise mode of action is unknown. Grossman (1935) and Gillam (1997) reported that an ideal product for DH should have specific criteria in order to be both effective and acceptable to the patient and clinician. The ideal desensitising agent must be fast acting, be effective for long periods, be easy to apply, not dangerous to the pulp, not cause pain and not stain the teeth. There have been a number of previous classifications published in the literature, some relatively simply and others more complex in nature. For example, a simple classification of products into in-office and OTC/at-home products (Orchardson and Gillam 2006), or based on the mechanism of action (Gillam 2002; Miglani et al. 2010); or whether the desensitising products for in-office procedures (1) do not polymerise (varnishes/precipitants/primers containing HEMA), (2) undergo setting or polymerisation reactions (conventional glass ionomer cements, or resin-reinforced glass ionomers/compomers, adhesive resin primers, adhesive resin bonding systems); or whether these agents are used in conjunction with (3) the use of mouthguards, (4) iontophoresis combined with fluoride pastes or solutions or (5) lasers (Pashley 2000) (see also Table 8.1). One of the problems, however, when recommending or evaluating these approaches for the treatment of DH is that clinicians appear not only to be uncertain as to the most successful way in which to manage DH but also expressed a level of dissatisfaction with the various products and techniques available (Cunha-Cruz et al. 2010) (see Chap. 10).

Current Therapies for Dentin Hypersensitivity (DH)

Currently, many of the dentin desensitisers that have been used in treating DH have supported evidence from in vitro, in situ or in vivo studies (Orchardson and Gillam 2006). The mechanism of action for the majority of the desensitising agents in these studies was by tubule occlusion. There are however a number of problems with the application of both in-office and OTC/at-home products in that the tubular occlusion was not permanent in nature, particularly following the impact of an acid challenge to the surface deposit (see Chap. 6). Furthermore the resin or toothpaste precipitate in the dentin tubule may only provide a chemical-physical blockage rather than induce the initiation of new dentin (Calabria et al. 2012). Ideally a bioactive/biomimetic material able to modify its composition and/or induce the precipitation of insoluble fluorapatite would be a major advantage in the treatment of DH (see Chap. 6). According to Orchardson and Gillam (2006), the management of DH should be based on a stepwise approach based on the extent and severity of the condition. An inherent component of this approach was the importance of the removal of any aetiological or predisposing factors, counselling the patient with regard to dietary intake (e.g. excessive consumption of acidic drinks) and toothbrushing techniques and appropriate monitoring by the clinician (see Chap. 10). A more recent UK Guidelines publication on the management of DH by Gillam et al. (2013) also stressed the importance of not using a single treatment philosophy to treat DH but recommended management strategies based on the aetiology and predisposing factors of specific presenting conditions, namely, (1) patients with good oral hygiene associated with DH, (2) patients with toothwear and associated DH and (3) periodontally related DH together with an awareness of the potential impact of DH on the patient's quality of life (see Chaps. 9 and 10).

Table 8.1 Classification of dentin desensitisers and procedures according to the mechanism of action

Mechanism of action	Desensitising agents
Nerve desensitisation	Potassium nitrate, chloride, citrate, oxalate,
Protein precipitation	Glutaraldehyde, silver nitrate, zinc chloride, strontium chloride hexahydrate
Tubule occlusion	Stannous and sodium fluoride
	Strontium chloride
	Ferric oxalate
	Potassium oxalate
	Amorphous calcium phosphate
	Calcium phosphate
	Calcium carbonate
	Calcium hydroxide
	Calcium sodium phosphosilicate
	Tricalcium phosphate (TCP)
	Dental varnish (Clinpro™ 3M™ ESPE™) containing 5 % sodium fluoride with tricalcium phosphate (TCP)
	Prophylaxis polishing paste containing 1.23 % fluoride
	Prophylaxis polishing paste containing 1.1 % sodium fluoride +5 % NovaMin
	Sensodyne NUPRO (NovaMin® – Dentsply)
	1.1 % Sodium fluoride anticavity toothpaste (Clinpro™ 3M™ ESPE™ 5000)
	Vanish™ XT Extended Contact Varnish (light-cured resin-modified glass ionomer (RMGI) based on the patented methacrylate-modified polyalkenoic acid)
	Bioactive glasses (SiO_2–P_2O_5–CaO–Na_2O)
	Aluminium
	Gingival surgery – recovering the exposed dentin area
Neural action and tubules occlusion	Laser
	Neodymium-doped yttrium aluminium garnet (Nd:YAG), laser GaAlAs (gallium-aluminium-arsenide laser), erbium-YAG laser
Anti-inflammatory effect	Homeopathic medication – propolis
	Corticoid steroids
Covering the dentin surface	Tooth restoration
	Periodontal surgery

Adapted from Miglani et al. (2010)

In-Office (Professionally Applied) Treatment

Following a successful diagnosis of DH, the clinician will base the treatment on the extent and severity of the condition. For example, where the problem is mild to moderate in nature (see Chap. 5), then an OTC/at-home approach may be initiated with the caveat that if the pain does not resolve before the next appointment (or if this approach was ineffective), then the patient may return for a more invasive in-office (professionally applied) procedure. If the pain is localised to one or two teeth and is severe in nature, the clinician may opt for an in-office procedure using one of the restorative materials as suggested by Pashley (2000). There is a tendency however to apply an in-office treatment following several attempts to resolve the patient's pain following the unsuccessful use of an OTC/at-home product. There are however a vast array of desensitising products currently available which may make the choice of the most appropriate product both confusing and difficult for the clinician (Cunha-Cruz et al. 2010).

Fluoride Application

According to Cummins (2010), fluoride in the form of gels, varnishes and resins has been recommended for an in-office treatment for DH

(Gaffar 1999; Orchardson and Gillam 2006; Ritter et al. 2006; Merika et al. 2006; Hoang-Dao et al. 2008; Yilmaz et al. 2011; Trushkowsky and Oquendo 2011; Petersson 2013). High-level fluoride-based desensitisers (solutions, gels and varnishes) have also been reported to provide an instant and relative long-term relief of DH (Al-Sabbagh et al. 2009; Gaffar 1999; Ozen et al. 2009; Petersson 2013; Pradeep et al. 2012; Ritter et al. 2006; Schmidlin and Sahrmann 2013). For example, a single topical application was reported to relieve DH for 3–6 months (Al-Sabbagh et al. 2009; Glockner 2013; Ritter et al. 2006). The combined use of fluoride with iontophoresis has also been reported in the literature (Gangarosa and Park 1978; Brough et al. 1985; Gangarosa 1994; Singal et al. 2005; Gupta et al. 2010; Aparna et al. 2010; da Rosa et al. 2013; Patel and Langalia 2014); however, the clinical effectiveness of this technique (with or without fluoride) has been questioned (Gillam and Newman 1990; Pashley 2000). The mode of action of topically applied fluorides is by tubule occlusion in the form of calcium fluoride (Table 8.1) although the resultant layer is generally not resistant to the frequent acid challenges in the oral environment, resulting in reapplication in order to maintain any efficacy (Cummins 2010; Calabria et al. 2012). Fluoride compounds however have been reported to demonstrate low permeability values in vitro in laboratory studies, which may suggest that the transient effect in reducing DH observed in clinical trials may be as a result of the other properties of the varnish rather than the physical precipitation of crystals inside the dentin tubules. A combination approach using a fluoride mouthrinse has also been recommended by several investigators (Glockner 2013; Marinho et al. 2004). Although currently there does not appear to be a systematic review exclusively addressing the role of professionally applied fluoride varnishes in DH in randomised clinical trials (Ozen et al. 2009; Sharif et al. 2013; Thrash et al. 1994), there was some evidence reported in the published literature that indicated that professionally applied fluoride varnishes were effected in relieving pain associated with DH (Orchardson and Gillam 2006; Sharif et al. 2013).

Potassium Salts

Potassium salts have also been used for the treatment of DH (Hodosh 1974; Pereira et al. 2005; Sauro et al. 2006; Cummins 2010) and have been reported to react with the exposed dentin section with a precipitation of calcium compound crystals onto the dentin surface and sub-superficially into the dentin tubules to effectively occlude the dentin tubules (Pereira et al. 2005; Calabria et al. 2012; Cummins 2010; Markowitz and Pashley 2008) (see Chap. 2). Potassium has also been combined with an oxalate formulation (Cunha-Cruz et al. 2011). Three types of oxalate formulations (6 % ferric, 30 % dipotassium and 3 % monohydrogen monopotassium) have also been classically indicated to occlude the dentin tubules and reduce DH (Al-Sabbagh et al. 2009; Pashley et al. 1987, 2001; Schmidlin and Sahrmann 2013). For example, 3 % Potassium oxalate solutions have been used to treat DH, and the resultant oxalate crystals have been reported to be more resistant to an acid challenge compared to the precipitated fluoride crystals (Pereira et al. 2005; Calabria et al. 2012). The in vitro testing of desensitising agents has been traditionally through the observation of the surface and subsurface of the dentin tubules using a number of techniques, for example, SEM scanning electron microscopy and CLSM confocal laser scanning microscopy, and comparing images before and after conditioning and treatment application (Fig. 8.1a, b) (see Chap. 6). By comparing the images of potassium oxalate-treated dentin before and after an acid challenge (Figs. 8.2b and 8.3a), one can observe the greater precipitation of crystals inside the dentin tubules following an acid challenge. This observation may also be seen with other formulations based on crystal precipitation, except for fluorophosphates.

Several investigators have reported that any relief from DH may be transient in nature as the precipitated crystals may be dissolved or removed over time (Al-Sabbagh et al. 2009; Cooley and Sandoval 1989; Kerns et al. 1991; Knight et al. 1993). According to Al-Sabbagh et al. (2009), oxalate-containing phytocomplexes however may be an alternative to the traditional oxalate preparations. For example, Sauro et al. (2006)

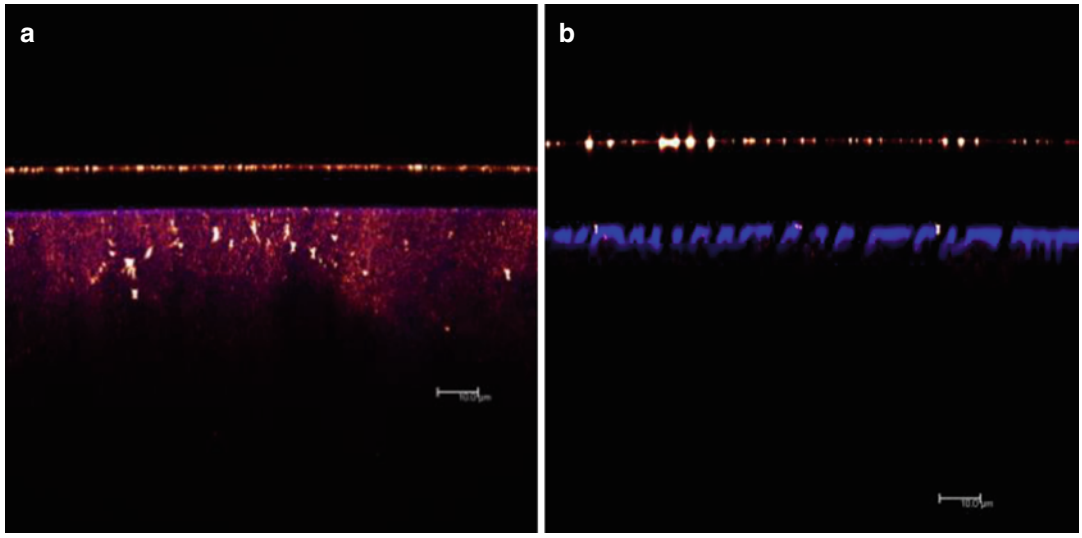

Fig. 8.1 Confocal laser scanning microscopy (CLSM, *XZ* axis) of mineralised sound dentin. (**a**) and after dentin conditioning with phosphoric acid (**b**)

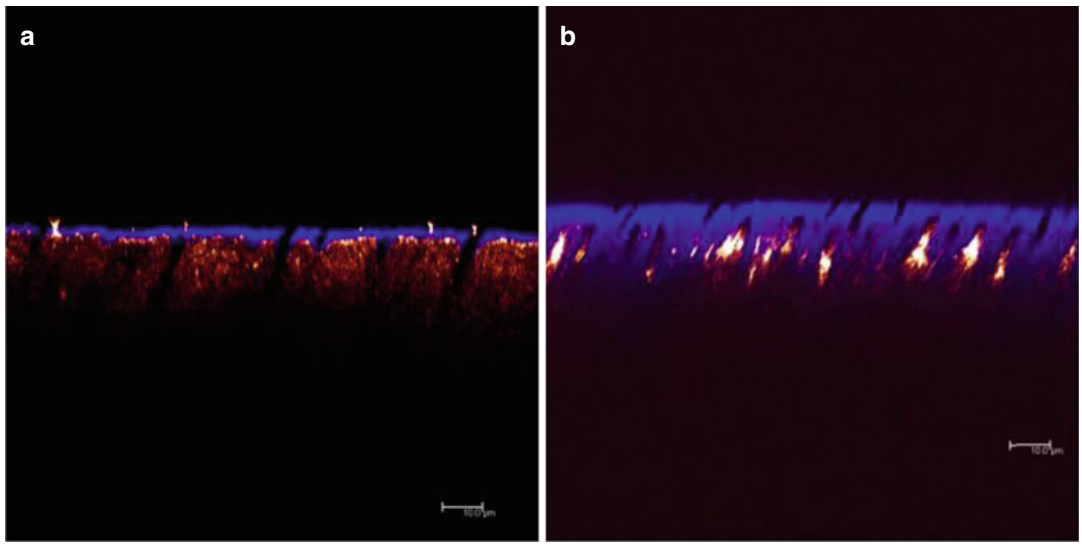

Fig. 8.2 Confocal laser scanning microscopy (CLSM, *XZ* axis) of demineralised dentin (**a**) treated with 1.23 % acidulated fluorophosphate (APF) (**b**) and 3 % potassium oxalate (KOx). Reflexive deposits can be seen inside dentin tubules of the specimen treated with KOx; in the APF specimen reflexive particles appear infiltrated in the body of intertubular dentin, similar to untreated dentin in Fig. 8.1a

reported that these complexes reduced dentin permeability following a single application in an in vitro study. These investigators also postulated that these complexes may protect the smear layer formed by scaling procedures on the root dentin from an acid challenge (Sauro et al. 2007).

A number of reviews recognised that, with the possible exception of the 3 % monohydrate monopotassium, oxalate preparations were not considered to be effective desensitising products based on evidence-based clinical criteria (Al-Sabbagh et al. 2009; Cunha-Cruz et al. 2011;

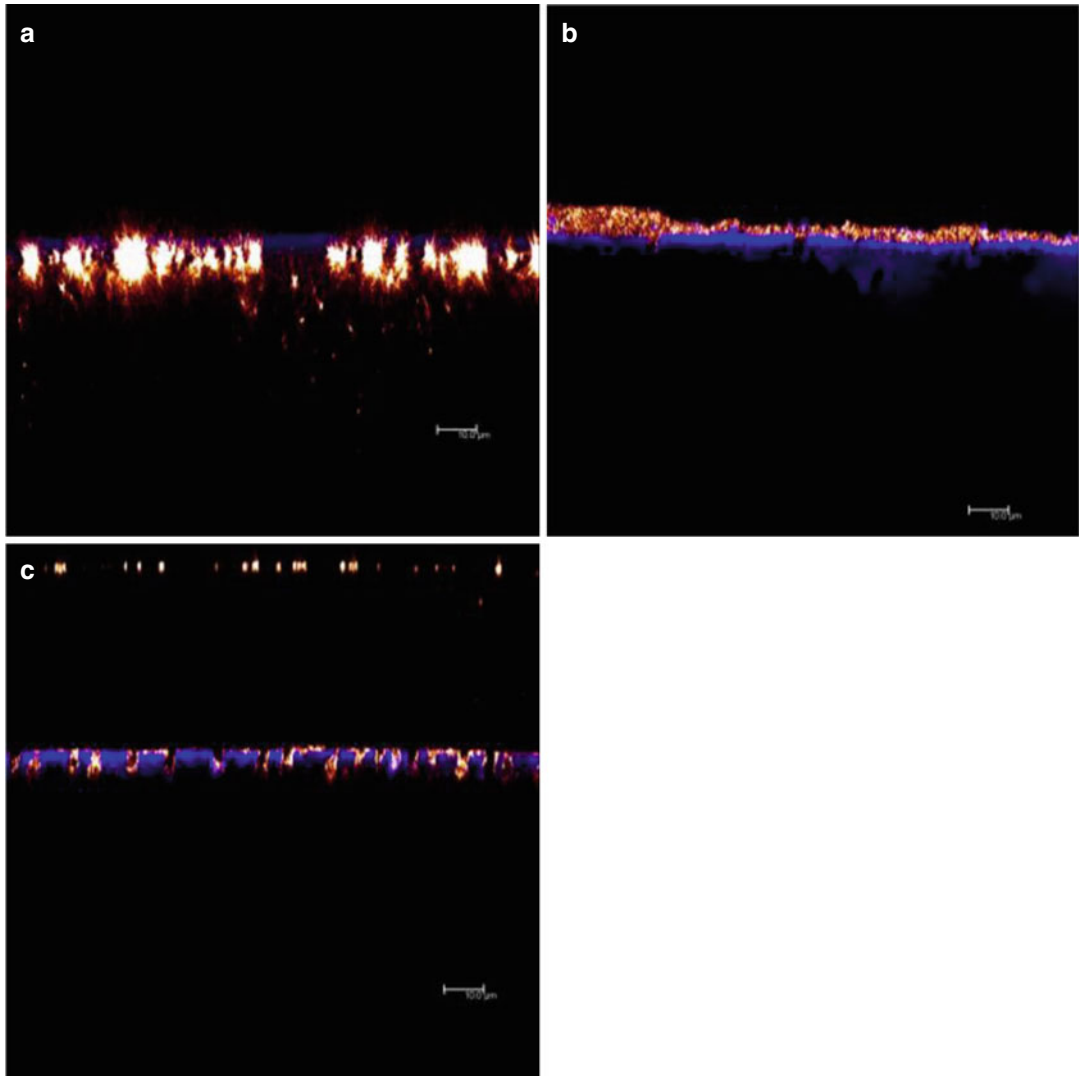

Fig. 8.3 CLSM *XZ* axis images of specimens before and after acid challenge. (**a**) Compared with Fig. 8.2b, the specimens treated with KOx challenged with citric acid show greater concentration of crystals inside the dentin tubules. (**b**) Specimen treated with Desensibilize NanoP® with clusters of crystals on dentin surface. (**c**) Specimen also treated with Desensibilize NanoP® shows crystals displaced into the dentin tubules after an acid challenge

Gillam et al. 1997; Orchardson and Gillam 2000; Schmidlin and Sahrmann 2013; Sharif et al. 2013).

Calcium Phosphate Compounds

Currently there appears to be limited data on the clinical effectiveness of calcium compounds in reducing DH although calcium hydroxide has been reported to immediately reduce DH in over 90 % of treated teeth in clinical studies (Al-Sabbagh et al. 2009; Levin et al. 1973). Calcium phosphate has also been reported in in vitro studies to be more effective than potassium oxalate in occluding the dentin tubules (Al-Sabbagh et al. 2009; Suge et al. 2005).

Recently, nano-hydroxyapatite-based agents (e.g. Desensibilize NanoP® and Clinpro white varnish [Clinpro]) with bioactive and biocompatibility potential have been reported to

be effective both as a remineralising and desensitising agent (Calabria et al. 2012; Hanning and Hanning 2010; Tschoppe et al. 2011). These agents contain nano-sized particles, which act in a similar manner to dental apatite in regard to their morphology, structure and crystallinity arrangement (Vandiver et al. 2005). These novel approaches were based on technology that explored the bioactivation with natural compounds with a view to improve the stability of the surface precipitate on the tooth surface following an acid challenge (Fig. 8.3). These images are consistent with the results of dentin permeability following dentin treatment with both potassium oxalate and Desensibilize NanoP®-FGM (Calabria et al. 2012).

One of the problems, however, with most of the products utilising an occlusive strategy was that the precipitate was unable to withstand the continual impact of the acid challenge in the oral environment. This issue has subsequently led investigators to develop innovative bioactive formulations to enhance the remineralising or tubule-occluding properties of the marketed products (Cummins 2010; Markowitz and Pashley 2008; Reynolds 1997; Reynolds et al. 2008; Rusin et al. 2010; Calabria et al. 2012; Nongonierma and Fitzgerald 2012; Pei et al. 2013) (see Chap. 6).

Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), a milk derivative, has also been reported to be effective in remineralising enamel and dentin (Reynolds 1997; Kumar et al. 2008; Reynolds et al. 2008; Agnihotri et al. 2012; Nongonierma and Fitzgerald 2012). CPP is a bioactive peptide released from caseins, which has been shown to enhance bivalent mineral solubility and also optimise binding ability to minerals, as calcium. Amorphous calcium phosphate (ACP) is the precursor of hydroxyapatite and in an oral environment in the presence of saliva was converted to hydroxyapatite. At the tooth surface interface, both calcium and phosphate are able to precipitate as stable hydroxyapatite (Nongonierma and Fitzgerald 2012). According to investigators, however, the effectiveness of ACP was only comparable to that of a placebo after approximately 3 months (Al-Sabbagh et al. 2009; Yates et al. 1998). According to Reynolds et al. (2008), CPP-ACP may also be successfully incorporated into commercial toothpaste products for the treatment of DH to enhance the occlusion of the dentin tubules through 'remineralised dentin' technology.

A number of recent products containing tricalcium phosphate (TCP) has been recently developed for the dental market (3M™ ESPE™ St Pauls Minneapolis, USA), namely, (1) a dental varnish (Clinpro™ 3M™ ESPE™) containing 5 % sodium fluoride with tricalcium phosphate (TCP), (2) a prophylaxis polishing paste containing 1.23 % fluoride, (3) prescription toothpaste 1.1 % sodium fluoride anticavity toothpaste (Clinpro™ 5000) and (4) Vanish™ XT Extended Contact Varnish, which is a light-cured resin-modified glass ionomer (RMGI) based on the patented methacrylate-modified polyalkenoic acid. The indications for use are based on remineralising of the enamel and blocking the open dentin tubules (tubule occlusion) (Vanichvatana and Auychai 2013; Asaizumi et al. 2013).

Several investigators have, however, reported conflicting results when comparing either an ACP (Schemehorn et al. 2011) or an MI Varnish with RECALDENT™ containing CPP-ACP (Cochrane et al. 2014) with 5 % ACP with TCP or CPP-ACP with a functionalised tricalcium phosphate (fTCP). According to these investigators, varnish ACP and MI Varnish had the highest release of calcium and fluoride ions compared to the TCP varnish.

Other calcium-containing desensitisers designed for in-office use are formulations containing arginine and calcium carbonate. These formulations have been reported to effectively occlude the dentin tubules and to provide immediate and lasting relief for DH (Pei et al. 2013; Hamlin et al. 2009; Schiff et al. 2009). According to the manufacturers, arginine is an amino acid naturally available in saliva, which presents a positive charge. Since dentin is negatively charged, arginine may play an important role, in association with calcium, favouring its deposition on the dentin surface. This mechanism is attributed to the deposition of an arginine, calcium carbonate and phosphate complex that physically occlude the dentin tubules and was resistant to normal

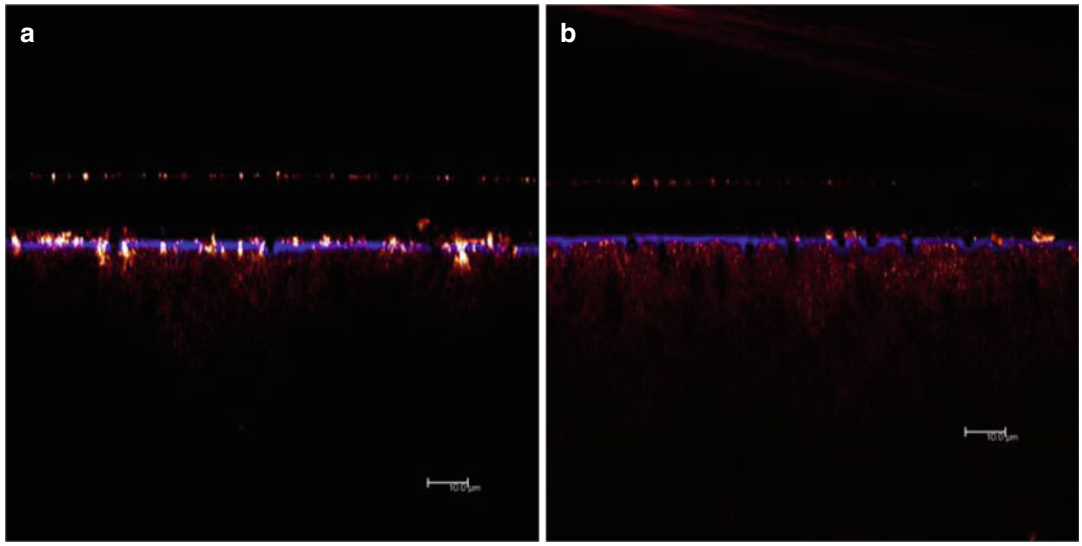

Fig. 8.4 CLSM *XZ* axis of dentin specimens treated with Pro-Argin™ before (**a**) and following an acid challenge (**b**)

pulpal pressures and to an acid challenge (Cummins 2010; Hamlin et al. 2009; Schiff et al. 2009; Pei et al. 2013). Pro-Argin™ technology is currently available as an in-office and as an OTC/at-home toothpaste that can be used in association with in-office treatment, for example, scaling and polishing procedures (Hamlin et al. 2009). According to Calabria et al. (2012), there is evidence from CLSM techniques that polishing with a Pro-Argin™ prophylaxis paste was effective in depositing these crystals in covering the dentin surface and occluding the subsurface of the dentin (Fig. 8.4a). Arginine-based products have also been reported to promote relief of DH compared to a negative control in clinical studies (Kapferer et al. 2013). However, there is some concern that these formulations are not able to resist to an acid challenge, as shown in Fig. 8.4b.

Calcium Sodium Phosphosilicate (Bioactive Glass)

Calcium sodium phosphosilicate, for example, NovaMin®, based on the original 45S5 Bioglass® formulation by Larry Hench (2006) was previously used for as a synthetic bone grafting material (PerioGlas®) (US Biomaterials Corp., Jacksonville, FL, USA; now NovaBone®). According to the manufacturer, a bioactive glass material (e.g. NovaBone) has the ability to release Si, Ca and phosphate ions and initiate the upregulation and activation of a family of genes in osteoprogenitor cells, a process defined as osteostimulation (Price et al. 1997; Xynos et al. 2000; Loty et al. 2001; Sollazzo et al. 2010). Both PerioGlas and NovaBone products have been reported to be effective as a synthetic bone graft material in a number of dental indications, for example, in periodontal intrabony defects (Zamet et al. 1997; Park et al. 2001; Sculean et al. 2002), bone regenerative procedures (Yukna et al. 2001), bone augmentation prior to implant placement (Norton and Wilson 2001), furcation defects (Anderegg et al. 1999; Giusto 2005) and extraction sockets (Kates et al. 1998). The original 45S5 Bioglass® formulation was later adapted for use in toothpaste formulations and prophylaxis polishing pastes for the treatment of DH (NovaMin Technology Inc., Alachua, FL, USA; now GSK). According to Lynch et al. (2012), the proposed mode of action for both the toothpaste and the polishing paste was considered to be through the precipitating of hydroxycarbonate apatite (HCA) onto the dentin surface and subsequently occluding the dentin tubules.

In-office prophylaxis pastes containing both arginine/calcium carbonate and bioactive glasses

(e.g. calcium sodium phosphosilicate) have subsequently been reported to provide effective clinical pain relief from DH following application (Cummins 2010; Gendreau et al. 2011; Hughes et al. 2010; Pradeep et al. 2012; Pradeep and Sharma 2010). According to Sharif et al. (2013), however, there is currently insufficient evidence on its clinical efficacy in reducing DH following in-office procedures.

Dentin Bonding Agents/Adhesives and Adhesive Restorations

The application of dentin adhesive materials for relieving DH has been also reported by several investigators (Bruton et al. 2000; Mehta et al. 2014). Previous adhesive systems were based on the application of phosphoric acid to promote the interlocking of the resin material to the dentin surface. However, the need of an acidic dentin conditioning before the application of an adhesive may theoretically increase pulpal sensitivity. Although there were concerns that these organic matrix-enriched materials may fail to resist the repeated impact of an acid challenge in the oral environment, a number of glutaraldehyde-based agents (e.g. Gluma Desensitizer™) have been historically indicated for DH treatment (Schmidlin and Sahrmann 2013; Vora et al. 2012). Although the concern about its biocompatibility still persists, there is evidence of its effectiveness in treating DH (Orchardson and Gillam 2006; Schmidlin and Sahrmann 2013; Vora et al. 2012). The introduction of self-etching agents, however, has reactivated interest in applying these adhesive systems as dentin desensitisers. According to Pei et al. (2013), these products are relatively easy to apply and appear to be less aggressive to the dentin-pulp complex than the other etch-and-rinse systems. These agents also have been reported to promote a micro-mechanical interlocking through a hybridisation process, but due to the presence of functional monomers in mild self-etch adhesives, they have the potential to interact chemically with the calcium ions from the residual hydroxyapatite that remains available within the submicron hybrid layer (Pei et al. 2013; Inoue et al. 2005). The functional monomers may also interact with the calcium ions from the smear layer, potentially resulting in additional chemical bonding.

The long-lasting effectiveness of any kind of adhesive system as a dentin desensitiser, for example, the self-etching adhesives, alone or in association with restorative materials, however, remains unclear. For example, it is recognised that dentin in a non-carious lesion is hypermineralised, and theoretically this may be an obstacle to dentin hybridisation. However any superficial layer of any type of material on the exposed dentin may not be able to resist to any outward fluid movement. According to Francisconi et al. (2009), the tooth may be subjected to significant stress concentration at the cervical region during either mastication or during toothbrushing which may present a challenge to the ability of an adhesive material to resist these forces. Although a strong interaction with the dentin substrate and the occlusion of the dentin tubules are mandatory for a long-lasting protective effect of the exposed dentin by a desensitising agent, this does not appear to occur on the exposed dentin of a cervical non-carious lesion. As illustrated in Fig. 8.5b, the hybrid layer is barely seen, and the resin tags only superficially penetrate the tubule openings in a dentin specimen from a non-carious cervical lesion. In Fig. 8.5a, however, in a sound cervical young dentin specimen, there was the presence of long resin tags and a well-defined hybrid layer (Calabria et al. 2010).

Adhesives may also be indicated for severe cases of DH that failed to respond to the other treatment modalities (Al-Sabbagh et al. 2009; Glockner 2013; Schmidlin and Sahrmann 2013; Swift et al. 2001). It is evident from the published literature that there is a vast array of products claiming to be effective in reducing DH. For example, dentin bonding agents (e.g. Scotchbond, Gluma Desensitizer, etc.) have been reported to be effective in reducing DH for up to 18 months post application (Al-Sabbagh et al. 2009; Brahmbhatt et al. 2012; Copeland 1985; Dondidall'Orologio et al. 1999; Ianzano et al. 1993; Kakaboura et al. 2005; Sharif et al. 2013; Schüpbach et al. 1997; Sethna et al. 2011; Yu

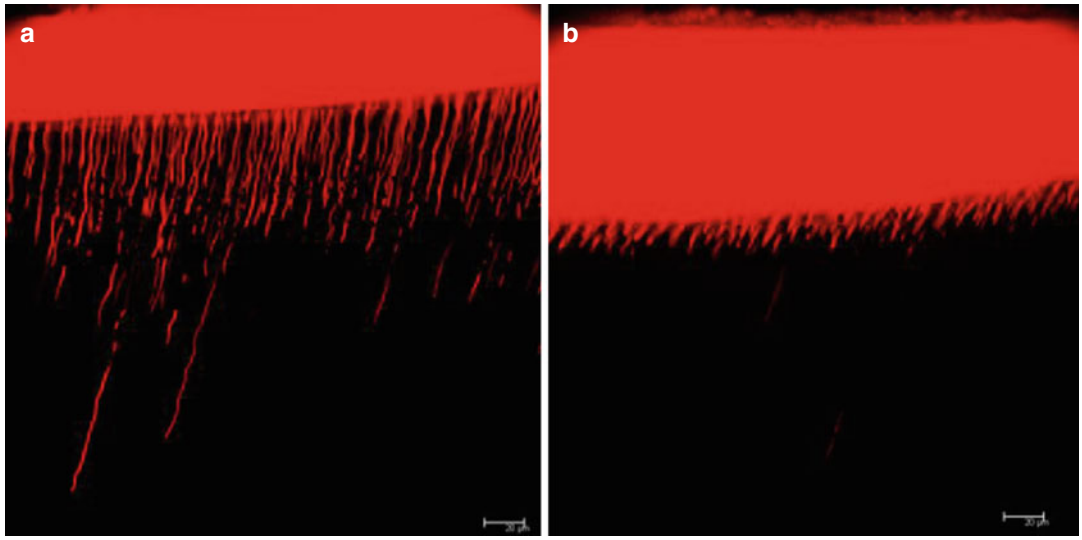

Fig. 8.5 CLSM images from sound cervical young dentin (**a**) and from a non-carious cervical lesion (**b**)

et al. 2010). According to several investigators, however, the available in vitro and well-conducted clinical studies have provided only limited data on the effectiveness of these products (Al-Sabbagh et al. 2009; Sharif et al. 2013; Tay et al. 1994). A further problem with some of these products is the lack of a filler material which may possibly favour wear from the surface of the material (Schmidlin and Sahrmann 2013).

Glutaraldehyde-based products have also been reported to reduce DH by protein precipitation, and these products have been reported to be effective in treating DH in the clinical environment (Duran et al. 2005; Glockner 2013; Kakaboura et al. 2005; Schmidlin and Sahrmann 2013; Schüpbach et al. 1997). Although several investigators have reported immediate pain relief to DH following application (Aranha et al. 2009; Lopes and Aranha 2013), reapplications are subsequently required in order to maintain the reduction of DH (Lopes et al. 2013). According to several investigators, however, there are biocompatibility hazards associated with these products that cannot be ignored (Arenholt-Bindslev et al. 1987; Schmidlin and Sahrmann 2013; Schweikl and Schmalz 1997). With respect to the glutaraldehyde-containing adhesives, several investigators have reported immediate and long-term relief of pain associated with DH (Dondidall'Orologio et al. 2002; Lopes and Aranha 2013; Qin et al. 2006; Schüpbach et al. 1997).

Although a minimal invasive approach is preferred when treating DH with restorative materials (Orchardson and Gillam 2006), the clinician may be confronted with significant loss of the tooth structure associated with DH which would require restoration of the tooth shape in order to maintain its aesthetic and function. In this situation, restorative intervention may be recommended using glass ionomer cement (GICs) and resin-based materials which are generally indicated when a more resilient material is desirable. For example, where a class V restoration is necessary, an adhesive restoration is a valid option (Schmidlin and Sahrmann 2013). Large and deep cervical non-carious lesions, regardless of the degree of pain, must be restored in order to recover dental anatomy and preserve health of gingival tissue. GICs or composite restorations have been used for these purposes, but evidences supporting their success is weak (Al-Sabbagh et al. 2009; Polderman and Frencken 2007). Several investigators have also used GICs in association with periodontal procedures, including root coverage procedures, where it has been reported that the placement of a GIC may favour the attachment of the periodontal fibres and release fluoride

(Tantbirojn et al. 2006; Polderman and Frencken 2007; van Dijken and Pallesen 2008; Francisconi et al. 2009; Santos 2014)

Laser Technology

According to a number of investigators (Al-Sabbagh et al. 2009; Kimura et al. 2000; Moritz et al. 1998; Schmidlin and Sahrman 2013; Bader et al. 2014), the clinical effectiveness of laser technology (e.g. Er:YAG, Er, Cr:YSGG, CO_2, GaALAS and low-level diode) in treating DH ranged from 5.2 to 100 %, depending on the laser type and parameters used in the clinical studies. For example, an Nd:YAG laser has been reported to minimise discomfort immediately following application (Al-Sabbagh et al. 2009; Kara and Orbak 2009; Lan and Liu 1996; Liu et al. 1997; Lopes and Aranha 2013). Furthermore, according to Lin et al. (2013), a Nd:YAG laser may also have a supplementary analgesic effect when compared with the other high-power lasers. The clinical efficacy of GaAlAs laser has been reported to be based on tubule occlusion and possibly by interrupting neural transmission (Tengrungsun and Sangkla 2008), but this reported success may be less evident than that reported by the application of a dentin bonding agent. The long-term effectiveness of lasers compared to the other types of treatment approaches has also been favourably reported (Aranha et al. 2005; Birang et al. 2007; Gholami et al. 2011; Kara and Orbak 2009; Lopes and Aranha 2013). However, the reported clinical effectiveness of lasers in the treatment of DH has also been challenged by Schmidlin and Sahrmann (2013) and Sgolastra et al. (2011). According to several investigators, there were no significant reductions in DH in comparison to the other types of laser and placebo therapies (Al-Sabbagh et al. 2009; Lier et al. 2002; Martens 2013). Furthermore, lasers in general are less effective in cases of severe DH (Al-Sabbagh et al. 2009; Kimura et al. 2000). There do not however appear to be any major adverse effects when using lasers if they are used in accordance with the manufacturers' instructions (Lopes and Aranha 2013).

The mechanisms involved in the laser treatment of DH are relatively unknown (Kimura et al. 2000). The mechanism of the high potency laser devices appears to promote the closure of the exposed dentin tubules, primarily, by producing a melting effect of the dentin. According to Bader (2014), there appears to be a degree of uncertainty as to whether there is also a synergic effect if lasers are combined with other occlusive pretreatments, which, in turn, may help to promote a more stable layer to obliterate the dentin tubules. The low-potency laser has been reported to diminish the neural response to hypersensitive stimuli (Bader et al. 2014), although there does not appear to be any strong evidence to support the use of laser therapy for this purpose due, in part, to the lack of consensus of the type of laser and the parameters that should be incorporated into standardised and efficient protocols.

Combined Treatment of Lasers with Other Treatment Approaches

The combination of techniques (e.g. laser technology with a fluoride varnish) may also be a strategy in the treatment of DH. The rationale for this approach is the association of the combined effects, which may result in significant better outcomes (Duran and Sengun 2004; Erdemir et al. 2010; Ipci et al. 2009; Lin et al. 2013; Lopes and Aranha 2013). Dentin desensitisers with an occluding potential may be used in association with low-level lasers in order to simultaneously block the dentin tubules and decrease the level of neural stimulation which may in turn initiate the formation of tertiary dentin (Farmakis et al. 2012; Lopes and Aranha 2013; Lopes et al. 2013). A similar indication of this combined use has been in the recommendation of an OTC product (e.g. toothpaste) following an in-office treatment (Rösing et al. 2009).

Although the evidence from both randomised controlled trials and systematic reviews supports the clinical use of lasers in treating DH (Deng et al. 2011; He et al. 2011; Sharif et al. 2013), further well-conducted studies with appropriate clinical protocols comparing the use of both low

or high frequencies and any association with the other alternatives discussed for treating DH should be implemented (Al-Sabbagh et al. 2009; Ipci et al. 2009; Petersson 2013; Schmidlin and Sahrmann 2013).

Other Restorative-Based Procedures

Periodontal Plastic Surgery (Root Coverage Procedures)

Periodontal disease may lead to changes in the periodontal tissues, and the consequent recession of the marginal tissues (gingival recession) has been reported to be associated with DH as a result of the exposure of the root surface to the oral environment. Both nonsurgical and surgical periodontal procedures together with the effects of periodontal disease on the teeth and their supporting structures may also impact on the patient's aesthetics and quality of life due to the pain associated with DH (see Chap. 3). The clinician should be aware of the various etiological and precipitating factors associated with gingival recession (e.g. anatomical, plaque, restorative procedures, patient habits, smoking, etc.) (see also Chap. 4). Furthermore the clinician should also consider how to manage both the patient's and his/her own expectation when proposing a treatment plan for resolving the problem of the aesthetics associated with gingival recession (e.g. posttreatment, presence of the so-called black triangles, etc.) (Fig. 8.6).

This may present a problem if both the perception and expectations expressed by the patient are either ignored or not met (by the clinician) to their satisfaction. Root coverage procedures associated with root scaling and the covering of the exposed root through periodontal surgical procedures have been reported to reduce or completely abolish DH over time (Orchardson and Gillam 2006; Lin and Gillam 2012). According to Douglas de Oliveira et al. (2013a), root coverage procedures (both partial and complete coverage) have been reported to decrease pain and improve a patient's quality of life although currently there appears to be insufficient scientific evidence to associate root coverage procedures with the complete suppression of DH (Douglas de Oliveira et al. 2013b).

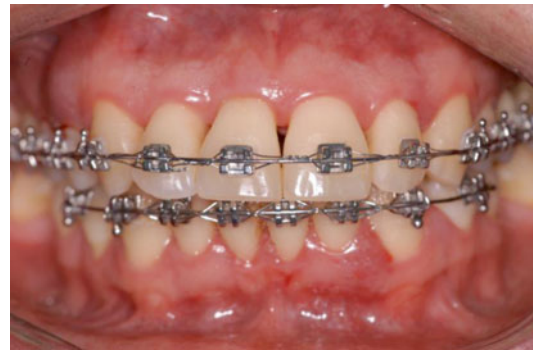

Fig. 8.6 Clinical photograph of patient with so-called black triangles which may cause aesthetic concerns

As indicated above, gingival recession may also occur in the healthy tissues and has been related to a combination of anatomical and physiological aspects of each individual tooth. For example, gingival recession was more often observed on the buccal surfaces compared with other surfaces of the teeth as a result of anatomical factors. According to Kassab and Cohen (2003), more than 50 % of the population in their study had at least one or more sites with gingival recession of 1 mm or more (see Chap. 3).

Gingival recession may be also associated with the periodontal biotype, and the analysis of this factor is essential for the planning of surgical procedures for root coverage. Three different periodontal biotypes have been described in the published literature, namely, the thin scalloped, the thick flat and the thick scalloped (Seibert and Lindhe 1989; Zweers et al. 2014). The teeth in the thin scalloped category have the characteristics of a thin gingival tissue with a more pronounced contour of the gingival margin, with a greater height of the interproximal papilla and with an underlying thin buccal bone that can present with fenestrations. The thick biotype category is characterised by thicker bone tissue surrounding the teeth and covered by a thick and smooth contour gingival tissue, which results in a small height of the papilla. The thick scalloped category displays the characteristics of the two other patterns (Fig. 8.7a–c).

It is important for the clinician to have sufficient knowledge of the relevant characteristics of each of

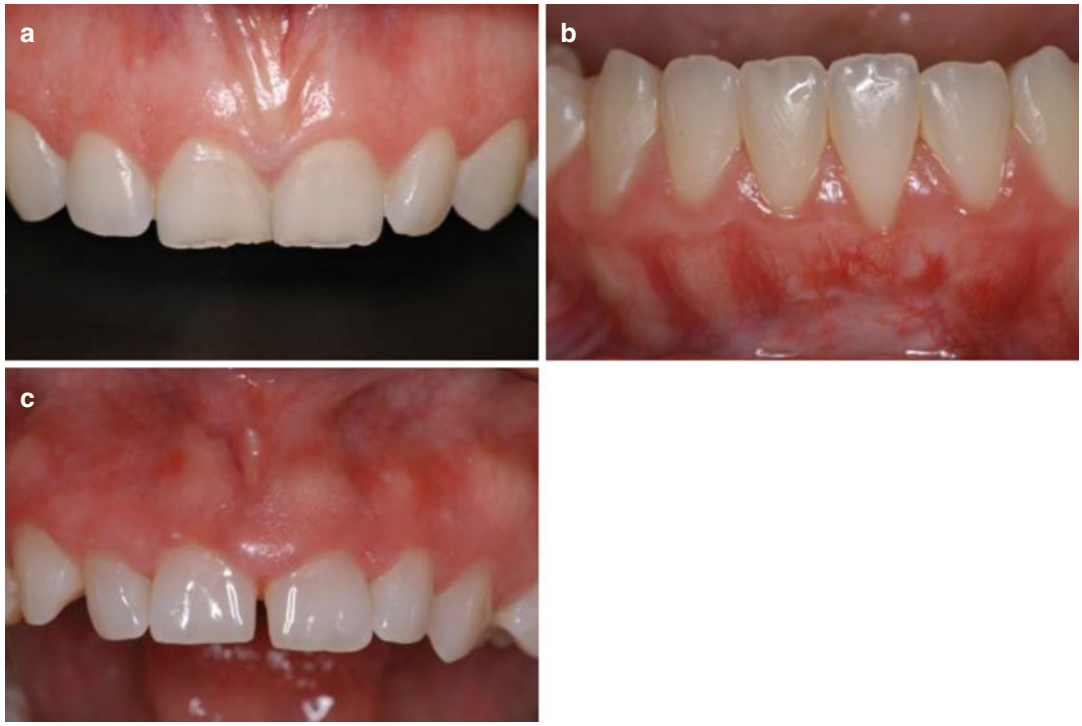

Fig. 8.7 Clinical pictures of (**a**) normal, (**b**) thin and (**c**) thick gingival biotypes

the biotypes, both in health and disease, particularly when planning root coverage procedures, as the different biotypes may respond differently both during the surgery and, subsequently, in the wound healing process. For example, thin biotypes may tear easily during probing and surgical intervention and root coverage may not be optimum, whereas in a thick biotype, the thickness of the flap may be related to a higher mean gain of complete root coverage (Seibert and Lindhe 1989; Müller et al. 2000; Hwang and Wang 2006). Due to the higher incidence of gingival recession in the thin biotype, the aim of the planned surgical procedures should not only consider the root coverage aspect but also the resultant aesthetics together with the treatment of DH (Ahmedbeyli et al. 2014; Cairo et al. 2014; Polack and Mahn 2013; West et al. 2013).

According to Gillam (2014), several classifications for treating gingival recession have been recommended in order for the clinician to facilitate both a diagnosis and a template for the correction of gingival recession defects. One of the classifications that has been favoured over the last three decades is the Miller classification system ([I–IV] (Miller 1985) (Table 8.2, Fig. 8.8a, b) which enabled the clinician to predict successful outcomes of the surgical procedure based on type of

Table 8.2 Miller's classification of gingival recession (GR)

Classification	Criteria
Class I	Marginal tissue recession that does not extend to the mucogingival junction (MGJ) with no interproximal tissue
Class II	Marginal tissue recession that extends to or beyond the MGJ, with no periodontal attachment loss (bone or soft tissue) in the interdental area
Class III	Marginal tissue recession that extends to or beyond the MGJ with periodontal attachment loss in the interdental area or malpositioning of teeth
Class IV	Marginal tissue recession that extends to or beyond the MGJ with severe bone or soft tissue loss in the interdental area, to a level apically to the buccal/labial soft tissue margin and/or severe malpositioned teeth

Acknowledgement modified from Kassab and Cohen (2003)

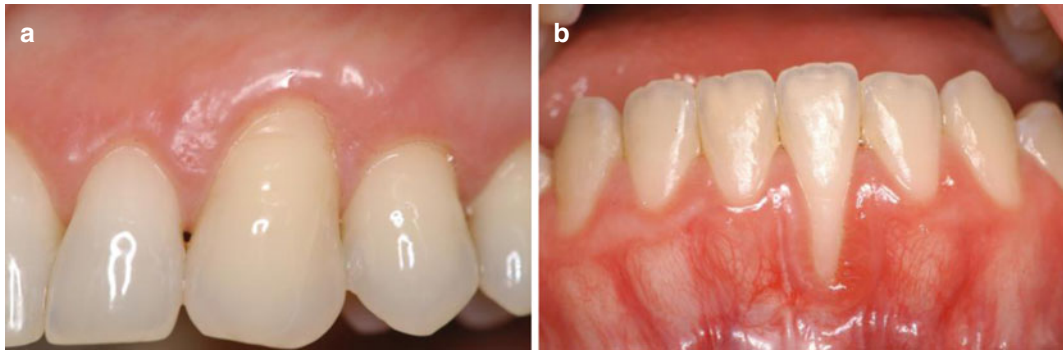

Fig. 8.8 (**a**, **b**) Examples of a Miller' Class I (**a**) and Class II marginal defect (**b**)

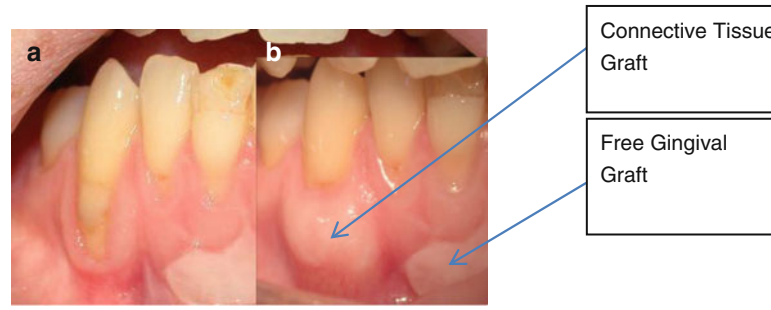

Fig. 8.9 (**a**, **b**) Example of a root coverage procedure using free gingival and connective tissue grafts (**a**) pretreatment and (**b**) posttreatment connective tissue graft: Acknowledgement for [Courtesy of D. Chatzapoulou]

defect, taking into account the anatomical features. A number of materials and techniques have been reported in the published literature, and these include guided tissue regeneration (GTR), coronally advanced flap and Emdogain (CAF + EMD), connective tissue graft (CTG) and free gingival graft (acellular dermal matrix allograft/Mucograft ADM) (Gillam 2014) (Fig. 8.9).

Irrespective of the surgical procedures, associated techniques, flap design or materials, the desired outcome for treating gingival recession defects is that the resulting gingival tissue covering the root surface must have the characteristics of a thick keratinised mucosa that will enable optimum plaque control without any change in the graft's position (e.g. apical direction). When the root coverage along with an increase in thickness is desired, a systematic review of studies indicates an association of repositioned flap with subepithelial connective tissue graft as the best option, and this association can be considered as the gold standard surgery for root coverage (Chambrone et al. 2008).

Several investigators however have reported that in some patients, the clinician may not be able to treat the gingival recession defect by the conventional surgical root coverage procedures described above, and therefore, the remaining exposed root dentin may require a restorative approach, for example, the provision of a partial laminate porcelain veneer, composite material or glass ionomer or contouring of the defect with a finishing bur (Zalkind and Hochman 1997; Tugnait and Clerehugh 2001; Drisko 2002; Özgünaltay and Önen 2002; Santamaria et al. 2007). In patients where there has been extensive periodontal destruction resulting in open gingival embrasures (so-called black triangles), which may be aesthetically unacceptable for the patient (Sharma and Park 2010), a relatively simpler option to the techniques described above may be utilised, for example, a prosthetic gingival veneer (Greene 1998).

Gingival Augmentation

The various methods of soft tissue augmentation for root coverage procedures may also be an option depending on the condition of the hard and soft

tissues (Al-Sabbagh et al. 2009; Chambrone et al. 2012; Schmidlin and Sahrmann 2013). According to Al-Sabbagh et al. (2009), however, there are limited clinical data to support this technique as part of a treatment approach in treating DH.

Over-the-Counter (OTC) Products

Individuals with mild to moderate local or generalised DH may decide to resolve any pain associated with DH without going to see a clinician by purchasing desensitising products that have been advertised in the media or through recommendation by a close friend or family member. According to Mantzourani and Sharma (2013), there are three main reasons that contribute to this behaviour: the need of a fast and urgent relief, the easy availability of these products in the market and their low cost, as this does not include the expenses of professional appointments and subsequent remedies. Desensitising products that are available through pharmacies or commercial outlets are called OTC or at-home care products in the form of toothpaste, gel or mouthrinse formulations. These OTC products are available without a medical prescription, but their indications for use are limited in that if the individual continues to have pain for longer than 2–4 weeks, they are advised to see a clinician. These OTC/at-home products may also be recommend by the clinician in association with in-office treatments (see Chap. 10), when the pain is associated with generalised DH, which is mild to moderate in severity.

OTC consumer products are generally based on formulations with the same active ingredients as for in-office products although the concentration permitted in OTC products may be considerably lower than those used by the clinician, for example, fluoride concentrations used in the office compared to fluoride concentrations used in OTC toothpastes. The constituents of these OTC products are usually formulated using a variety of salts (with different concentrations depending on whether the formulation is in a toothpaste, gel or mouthrinse) with the objective of reducing pain by dentin tubule occlusion or nerve desensitisation. Most of the OTC products available to the consumer are toothpaste products, although there is a number of mouthrinses currently available in the market. Although these rinses may deliver the therapeutic agent to all tooth surfaces in the oral cavity, one disadvantage would appear to be the necessity to deliver lower concentrations of a therapeutic agent in the mouthrinse compared to a toothpaste formulation (Markowitz 2013). The mechanism of action of the mouthrinses however is similar to a toothpaste formulation depending on the formulation used to deliver the therapeutic agent. Examples of these salts are potassium nitrate, potassium chloride, potassium citrate, sodium fluoride, strontium chloride, strontium acetate, dibasic sodium citrate, formaldehyde, sodium monofluorophosphate, stannous fluoride, amine fluoride, arginine, hydroxyapatite, calcium carbonate, calcium sodium phosphosilicate (bioactive glass) and amorphous calcium phosphate (Miglani et al. 2010; Orchardson and Gillam 2006; Karim and Gillam 2013; Talioti et al. 2014) (Table 8.3).

Fluoride-Containing Toothpaste, Gel or Mouthrinse Formulations

According to Cury and Tenuta (2014), fluoride is the most important therapeutic substance used in toothpaste products and may provide a reduction in dental caries and together with the other beneficial therapeutic substances incorporated into toothpastes (e.g. triclosan/copolymer or zinc) may also have additional benefits in reducing the dental biofilm, gingivitis, periodontitis, calculus formation and halitosis (malodour). Although conventional fluoride-containing toothpaste formulations have been suggested for the treatment of DH, there are limited data to support this claim (Orchardson and Gillam 2006; West 2008). Toothpaste and mouthrinse formulations containing sodium, stannous or amine fluoride (NaF, MFP, AmF and SnF_2) have been used as OTC/at-home remedies to alleviate DH (Morris et al. 1999; Plagmann et al. 1997; Pradeep et al. 2012; Rösing et al. 2009). Nevertheless, inconsistent data are available on its clinical effectiveness (Pradeep et al. 2012). Earlier investigators

Table 8.3 Examples of selected toothpaste formulations for the treatment of DH available either on prescription or OTC

Mechanism of action	Commercial toothpaste (and mouthrinses)	Compounds
Dentin tubule occlusion	Colgate Sensitive Pro-Relief (Pro-Argin technology)	Calcium carbonate and arginine – an amino acid naturally found in saliva – 0.8 % arginine, PVM/MA copolymer, pyrophosphates and 0.05 % sodium fluoride in an alcohol-free base mouthwash
	Sensodyne Repair and Protect (NovaMin® technology)	Fluoride, calcium and phosphate ions
	Sensodyne Pronamel	Fluoride and potassium nitrate
	Sensodyne Rapid Relief	8 % Strontium acetate in a silica base, 1,040 ppm sodium fluoride
	SootheRx (NovaMin® technology)	Calcium sodium phosphosilicate (new hydroxyapatite)
	AMFLOR (Pharmaceuticals)	3.85 % Amine fluoride
Clinician-prescribed fluoride toothpaste formulations	Fluoridex (Philips Oral Healthcare)	5,000 ppm Fluoride
	Colgate Gel Kam Sensitive	Stannous fluoride 0.4 % w/w, 1,000 ppm F
	Colgate Duraphat	2,800 ppm Fluoride
Neural desensitisation	Potassium-containing products	Potassium chloride, citrate, nitrate and oxalate and fluoride compounds
Dentin tubule occlusion and neural desensitisation (other products)	Sensitive toothpaste (Himalaya herbals)	Spinach – natural oxalate compound

acknowledged that fluoride containing toothpaste formulations may have a beneficial desensitising effect (Kanouse and Ash 1969; Orchardson and Gillam 2000) and in some studies provided similar results to those reported for the specific desensitising toothpaste formulations containing nerve desensitising or dentin tubule-occluding agents (Gillam et al. 1997; Orchardson and Gillam 2000; West et al. 1997). Several investigators have used fluoride-containing formulations in clinical trials as a placebo control rather a desensitising product per se, when evaluating desensitising products (Gillam et al. 1996b; West et al. 1997; Yates et al. 2004; Pradeep et al. 2012; Rösing et al. 2009).

The mode of action of fluoride in anticariogenic, remineralising and DH strategies was based on its ability to react with hydroxyapatite and form fluorapatite, which was to be considered less susceptible to acid dissolution than hydroxyapatite due to its lower critical pH (Featherstone 2000). Calcium fluoride may also be deposited on the dentin surface when fluoride is incorporated in a toothpaste, mouthrinse or varnish, subsequently blocking the dentin tubules in vitro. With respect to these fluoride compounds, the fluoride ions apparently do not contribute effectively to dentin tubule occlusion (Petersson 2013), probably due to the small size of calcium content precipitated crystals (Calabria et al. 2012). Figure 8.2 shows the pattern of calcium fluoride crystal precipitation (a) in comparison with calcium oxalate crystals (b) from both fluoride-containing formulations and potassium oxalate formulations (in-office products). As demonstrated by these pictures, fluoride precipitates predominantly in the body of the intertubular dentin. Relatively small number of particles can be observed inside the tubules, whereas in the potassium oxalate sample, a large number of dentin tubules are occluded below the surface of the dentin. These CLSM images can also be compared with mineralised and acid conditioned dentin (a and b – in Fig. 8.1). This apparently ineffective action observed in in vitro studies does not however correspond to the clinical studies using fluoride formulations, and this may be

due to the difficulties in completely mimicking the oral environment in the laboratory (see Chap. 6). A number of these studies have demonstrated that DH may be reasonably well controlled by using a fluoride-containing toothpaste (1,450 ppm) during the duration of the study, especially in the combination with the various tubule-occluding agents discussed in this chapter.

The incorporation of metal ions (e.g. zinc, tin, strontium and potassium) and abrasive components in a toothpaste or mouthrinse formulation (e.g. alumina, silica, calcium carbonate, zinc, etc.) may also have a synergistic effect with the active ingredient on the dentin surface and block the dentin tubules (Gillam 1992; Petersson 2013). For example, a F-toothpaste with 0.454 % stannous fluoride (SnF_2) has been reported to be more effective in reducing DH following 4 weeks of daily use when compared to a toothpaste with 0.76 % MFP (Schiff et al. 2000). He et al. (2011) also reported a significant improvement in both significantly immediate and ongoing relief from a 0.45 % SnF_2 toothpaste compared to a 0.76 % sodium monofluorophosphate (MFP) toothpaste utilised as a negative-control group. Other desensitising agents in combination with fluoride and associated metal ions (e.g. strontium, 8 % arginine and calcium carbonate) have also been reported to be effective in clinical studies (Orcahrdson and Gillam 2006). Amine fluorides (AMFLOR™, Pharmaceuticals) have also been used in toothpaste and mouthrinse formulations to alleviate pain associated with DH, although currently there are limited data on its effectiveness as a desensitising agent. A recent study by Pradeep et al. (2012) however reported that a amine fluoride toothpaste formulation had a similar effect on DH, compared to a calcium sodium phosphosilicate and potassium nitrate containing toothpaste.

The adjunctive use of a fluoridated mouthrinse therapy in controlling DH in conjunction with the regular use of a desensitising toothpaste may also be recommended (e.g. potassium and amine fluoride) (Yates et al. 2004; Petersson and Kambara 2004; Glockner 2013; Petersson 2013; Pradeep et al. 2012), although currently there are limited data on their effectiveness (Petersson 2013). Other fluoridated mouth rinse formulations incorporating the various desensitising agents mentioned in this chapter may also enhance the effectiveness of fluoride toothpaste formulations (Petersson and Kambara 2004) and perhaps favour the remineralisation of dentin (Glockner 2013).

Irrespective of the actual active agent, the effectiveness of OTC products is dependent of the individual (patient or consumer) maintaining regular and effective oral hygiene practices by applying the toothpaste and/or mouthrinse on a twice daily basis (Petersson 2013). However, depending on the nature of these OTC products, its active component may take up to 2–4 weeks to achieve relief of DH (Talioti et al. 2014) (see also Chap. 10). One of the problems in evaluating the claims of these desensitising products in clinical studies is the lack of heterogeneity of the published studies which makes the results difficult to understand (Karim and Gillam 2013; Talioti et al. 2014). Furthermore, as discussed in Chap. 7, placebo and non-placebo effects may also impact on the results from these studies, although Lin et al. (2013) in a systematic review reported that despite these observed effects, both in-office and OTC products, techniques and treatment approaches may have a real effect on DH.

With regard to the effectiveness of the regular use of a fluoride-containing toothpaste in reducing DH, it was observed that the prevalence was higher in regions where individuals regularly used fluoride toothpaste and lived in fluoridated water area. This may, to some extent, question the apparent effectiveness of fluoride in minimising DH (Rösing et al. 2009; West 2008). According to Rösing et al. (2009), there are, however, limited data supporting the sole use of OTC fluoride products for treating DH, but fluoride in combination with tubule-occluding toothpaste and mouthrinse formulations may be a valuable option in terms of preventing and controlling other oral conditions, namely, plaque, caries, gingivitis, malodour, etc. (Cummins 2010; Pradeep et al. 2012; Glockner 2013; Petersson 2013). There is no evidence supporting the efficacy of these anticaries claims for specific desensitising toothpaste and mouthrinse formulations per se, but only appended claims of fluoride efficacy from the anticaries studies (so-called piggyback claims) (see Chap. 1). Whether high concentration of fluoride in

in a toothpaste, for example, 2,800/5,000 ppm (Duraphat) (see Table 8.2), may be effective as desensitisers has not been fully explored, although they have a recognised anticaries effect and may be effective in preventing and controlling root caries (Bizhang et al. 2009; Nordström and Birkhed 2010; Walsh et al. 2010; Srinivasan et al. 2014).

Strontium-Containing Products

Although strontium (historically in the form of strontium chloride and more recently as strontium acetate) in toothpaste formulations have been extensively evaluated in clinical studies over the last 50–60 years and reported to be effective in treating DH compared to placebo controls (Kobler et al. 2008; Liu and Hu 2012; Sharif et al. 2013; Markowitz 2009; Mason et al. 2010), nevertheless there was controversy over whether these formulations were effective in treating DH (Schiff et al. 1994; Rösing et al. 2009; Cummins 2010; Karim and Gillam 2013). Furthermore, Jackson (2000) in a review on the studies on strontium containing toothpaste formulations reported that none of these studies demonstrated a consistent, significant improvement in the participants' symptoms from DH when compared with the negative-control toothpaste. There was also, according to Jackson (2000), no supportive evidence from the published literature that the strontium salts enhanced the deposition of the toothpaste ingredients or increased the durability of this deposit on the tooth surface. The main mode of action of strontium formulations (acetate/chloride) was considered to be one of tubular occlusion based on in vitro studies (Ling and Gillam 1996; West 2008) although the actual effect attributed to strontium in clinical studies has yet to be defined (Rösing et al. 2009). Recently, the original strontium acetate-based toothpaste was reformulated as Sensodyne(®) Rapid Relief containing 8 % strontium acetate in silica base and 1,040 ppm sodium fluoride. There have been a number of in vitro, in situ and in vivo studies that have demonstrated that the mode of action is by tubule occlusion and that the surface deposit is more resistant to an acid challenge compared to the arginine-based products (Hughes et al. 2010; Mason et al. 2010; Parkinson and Willson 2011; Olley et al. 2012; Seong et al. 2013). The two in vivo studies by Hughes et al. and Mason et al. (2010) reported that the newly formulated strontium acetate toothpaste was effective in reducing DH compared to a fluoride control toothpaste (Mason et al. 2010) and to a marketed control toothpaste containing 8 % arginine, calcium carbonate, and 1,450 ppm sodium monofluorophosphate (Hughes et al. 2010). However Schiff et al. (2009) in a 16-week crossover design study comparing Colgate Sensitive Pro-Relief (also marketed as Elmex Sensitive Professional) and Sensodyne Rapid Relief reported that following 8 weeks of brushing with Colgate Sensitive Pro-Relief provided significant reduction of mean DH values compared to the Sensodyne Rapid Relief toothpaste. A further observation from this study was that the Colgate Sensitive Pro-Relief subjects achieved significantly improved reductions in DH following the crossover from the initial use of brushing with the Sensodyne Rapid Relief toothpaste. However those subjects who initially brushed with the Colgate Sensitive Pro-Relief toothpaste did not benefit from the crossover to the Sensodyne Rapid Relief.

Potassium-Containing Products

Potassium-containing products (nitrate, chlorine and citrate) including both toothpaste and mouthrinse formulations have been reported to be effective in reducing DH compared to placebo controls (Orchardson and Gillam 2000; Frechoso et al. 2003; Markowitz 2009). Of these formulations, 5 % potassium nitrate toothpaste formulations have been the most extensively evaluated desensitising toothpaste (Rösing et al. 2009). Overall, the majority of the published studies have reported better results with the use of potassium-containing toothpaste formulations, in comparison to controls (Chesters et al. 1992; Collins et al. 1984; Nagata et al. 1994; Orchardson and Gillam 2000; Pradeep et al. 2012; Schiff et al. 1994, 1998; Silverman 1985; Silverman et al. 1996; Tarbet et al. 1980, 1982) or compared to other desensitising toothpaste

formulations (10 % strontium chloride (Orchardson and Gillam 2000; Silverman et al. 1996; Tarbet et al. 1982), 2 % sodium citrate and or 1.4 % formaldehyde (Orchardson and Gillam 2000; Tarbet et al. 1982). However there was an ongoing debate as to whether the actual clinical effect was due to the potassium ion per se (Orchardson and Gillam 2006; Poulsen et al. 2001, 2006; Rösing et al. 2009; Karim and Gillam 2013; Lin et al. 2013; Schmidlin and Sahrmann 2013). For example, there has been a degree of controversy as a result of its proposed mode of action (nerve desensitisation) based on an animal model (Markowitz et al. 1991; Markowitz and Kim 1992) which postulated that potassium ions are able to diffuse along the dentin tubules and decrease the excitability of the intradental nerve fibres (A fibres) by blocking the axonic action, and subsequently reduce DH (Schmidlin and Sahrmann 2013; Boneta et al. 2013). Several investigators have however challenged this mode of action as indicated above and have suggested that these formulations may instead be through tubule occlusion and attributed to other constituents in the formulation (e.g. abrasives) than the potassium ion per se (Addy and Mostafa 1989; Ling et al. 1997; Gillam et al. 1996a, b; Pashley et al. 1984; West et al. 1997; Orchardson and Gillam 2000). According to Jackson (2000) and Panagakos et al. (2009), a potassium-containing toothpaste formulation was, no more effective than regular fluoride containing toothpaste.

As described above, the focus in the majority of the earlier desensitising studies was on toothpaste formulations, and relatively few studies have been conducted examining the effectiveness of desensitising agents containing potassium mouthrinse formulations. Several investigators have reported that these mouthrinse formulations containing potassium nitrate and sodium fluoride (Gillam et al. 1996a; Pereira and Chavas 2001), potassium citrate or sodium fluoride (Yates et al. 1998) or a mixture of fluorides (Yates et al. 2004) may reduce DH. Gillam et al. (1996a) have demonstrated that a 3 % potassium nitrate and sodium fluoride mouthrinse significantly reduced DH compared to a sodium fluoride mouthwash, after 2 and 6 weeks of use. Pereira and Chavas (2001) also demonstrated that after 2 weeks, there were no statistically significant differences between the two groups using tactile and thermal stimuli. At 6 weeks, however, the 3 % potassium nitrate and 0.2 % sodium fluoride mouthwash demonstrated a significant difference in DH when stimulated by cold air, as compared to the control 0.2 % sodium fluoride mouthwash.

More recently, a potassium oxalate mouthrinse containing 1.4 % potassium oxalate (Listerine Advanced Defence Sensitive (LADS)) has been developed by Johnson & Johnson Consumer and Personal Products Worldwide, Skillman and Morris Plains, NJ, USA. There are however limited data on its long-term effectiveness on DH with only two randomised clinical studies (RCTs) of 5 days and 4 weeks, respectively (Sharma et al. 2013a, b). The investigators reported that in both studies, the potassium oxalate mouthrinse significantly reduced DH to the negative-control groups (Sharma et al. 2013a, b). Further RCTs however would be required before making any further comment on the efficacy of this product in reducing DH. Although it may be postulated that with the combination of potassium and oxalate there would be dual mode of action in reducing DH (namely, nerve desensitisation [potassium] and tubule occlusion [oxalate]), the two published in vitro studies used a tubule-occluding model to demonstrate the mode of action by the oxalate deposit. Two studies demonstrated that the LADS mouthrinse was significantly more effective in tubule occlusion (intratubular penetration was more evident) (Eliades et al. 2013; Sharma et al. 2013c) and in reducing dentin permeability than the other test products. Furthermore according to these investigators, the tubule occlusion associated with LADS was substantially more stable in resisting an acid challenge compared to the other test products.

Calcium-Containing Compounds

Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP)

Casein phosphopeptide (CPP) (Recaldent™ technology, GC Tooth Mousse) was primarily developed for both anticaries and remineralisation

strategies rather than for the treatment of DH per se. Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) was previously marketed as GC Tooth Mousse (Recaldent™), which was a water-based, sugar-free dental topical crème. According to Reynolds et al. (1998), the CPP component (casein derived from the milk protein) was proposed by Reynolds (1997) to provide bioavailable calcium and phosphate ions at the tooth surface (e.g. enamel). The stabilisation of ACP component by the CPP ensured the delivery of both Ca and PO_4 ions onto the enamel surface for remineralisation to CPP, and formulated as CPP-ACP, this subsequently prevented the dissolution of both calcium and phosphate ions that supersaturate saliva (Reynolds 1997). A number of studies have reported that CPP-ACP can effectively remineralise the enamel subsurface lesions (Lata et al. 2010; Cai et al. 2003). The manufacturers suggested that CPP-ACP would be ideal to treat DH on the basis of its remineralising potential, and a number of in vitro and in vivo studies were conducted which demonstrated that calcium phosphate preparations deposit a mineral precipitate onto the dentin. surface, block dentin tubules and reduce dentin permeability in the dentin disk model and reduce DH in patients (Ebisu 2002; Suge et al. 2002; Cherng et al. 2004; Geiger et al. 2003; Azarpazhooh and Limeback 2008; Gandolfi et al. 2010; Walsh 2010). According to Wegehaupt et al. (2011), however, it is questionable that the casein CPP-ACP formulation would demonstrate any long-lasting effect on DH. A recent systematic review by Talioti et al. (2014) reported that although the CPP-ACP containing products may provide some benefit in reducing DH, there was insufficient data from the published studies to support any claims of efficacy in reducing DH.

Functionalised Tricalcium Phosphate (f TCP)

According to Vanichvatana and Auychai (2013), fTCP is produced by the solid-state ball milling of beta-tricalcium phosphate and sodium lauryl sulphate and has been demonstrated by several investigators to prevent calcium ions from prematurely interacting with ionic fluoride and forming calcium fluoride, thus delivering more fluoride and calcium ions to the enamel surface (Karlinsey et al. 2010, 2012). fTCP has also been reported to have remineralising effects in both in vitro and in situ studies (Karlinsey et al. 2009a, b; Mensinkai et al. 2012; Vanichvatana and Auychai 2013). fTCP has recently been commercially developed and is now available as a 950 ppm fluoride toothpaste (Clinpro Tooth Creme; 3 M ESPE, Saint Paul, MN, USA). Asaizumi et al. (2013) also assessed the effect on 0.21 or 1.1 % NaF toothpaste containing functionalised tricalcium phosphate (fTCP) on the density of white spots in vitro, and Mensinkai et al. (2012) in an in situ remineralisation study of white-spot enamel lesions compared a nonfluoride toothpaste with 500 and 1,100 ppm F-containing fTCP toothpaste. Although there appears to be data on file (technical reports) on the effects (tubule occlusion and dentin permeability) of TCP products on DH (e.g. Vanish™ XT Extended Contact Varnish), there does not appear to be any data currently available in the published dental literature.

Pro-Argin-Based Toothpaste and Mouthrinse formulations

Pro-Argin, a calcium carbonate and arginine complex based on Kleinberg's original formulation Sensistat (Kleinberg 2002), has been introduced into the consumer market as a desensitising toothpaste (Colgate® Sensitive Relief with Pro-Argin™ technology) and more recently as a desensitising mouthrinse (Colgate-Palmolive Co, New York, NY) (Mello et al. 2013a, b; Hu et al. 2013; Boneta et al. 2013) for the treatment of DH. Arginine is an amino acid found naturally in saliva. The combination of arginine and calcium carbonate mimics the saliva's ability to occlude the open dentin tubules, subsequently reducing the fluid flow and making the tooth surface more resistant to an acid challenge and thermal stimulus (Petrou et al. 2009) (see also section on strontium-based toothpaste). Pro-Argin™ toothpaste have also been reported to reduce DH in randomised clinical studies when compared to either placebo or comparator products (Petrou et al. 2009; Ayad et al. 2009; Docimo et al. 2009a, b;

Que et al. 2010; Fu et al. 2010; Boneta et al. 2013). Several clinical studies have also reported that a Pro-Argin™ mouthrinse containing 0.8 % arginine, PVM/MA copolymer, pyrophosphates and 0.05 % sodium fluoride in an alcohol-free base mouthrinse was effective compared to control mouthrinses in reducing DH (Hu et al. 2013; Boneta et al. 2013). Several investigators have suggested a role for a arginine-based toothpaste in managing DH (Fu et al. 2010; Que et al. 2010; Sharif et al. 2013) although Sharif et al. (2013) has suggested that more robust and well-designed randomised clinical studies should be conducted to determine their clinical efficacy in reducing DH. Furthermore according to Sharif et al. (2013), larger sample sizes are required in the clinical studies with a longer study duration included in the study design.

Calcium Sodium Phosphosilicate (Bioactive Glass)

As previously described, bioactive glasses (calcium sodium phosphosilicate), for example, NovaMin® developed by NovaMin Technology Inc. (Alachua, FL, USA) based on the original 45S5 Bioglass® formulation by Larry Hench (US Biomaterials Corp., Jacksonville, FL, USA; now GSK) (Hench 2006) has been incorporated into toothpaste products for the treatment of DH. The proposed mode of action is by the precipitating of hydroxycarbonate apatite (HCA) onto the dentin surface and subsequently occluding the dentin tubules (Litkowski et al. 1998; Gillam et al. 2002; Forsback et al. 2004; Tai et al. 2006; Vollenweider et al. 2007; Burwell 2006; Burwell et al. 2009; Wang et al. 2010; Pradeep and Sharma 2010).

One advantage of the precipitated HCA layer was that it was chemically and structurally similar to both natural enamel and dentin (Burwell 2006; Gendreau et al. 2011). There have however been concerns over the long-term durability of HCA in the oral environment, and it has been postulated that the formation of fluorapatite (FAp) rather than HCA was preferable as this layer may be more resistant to acid attack and would less likely to dissolve when the teeth are exposed to an acid challenge. Brauer et al. (2010) recently demonstrated that fluoride-containing bioactive glasses form FAp rather than HCA in physiological solutions.

As described previously, the original 45S5 Bioglass® formulation was marketed as a desensitising toothpaste for the treatment of DH, namely, NovaMin™ (NovaMin Technology Inc., Alachua, FL, USA; now GSK Consumer HealthCare, UK). The new NovaMin™ toothpaste is based on an anhydrous toothpaste formulation with silica and amorphous calcium sodium phosphosilicate with fluoride (not currently with fluoride in the USA). The toothpaste has been demonstrated to be effective in occluding the dentin tubules in vitro and reported to be resistant to an acid challenge as well as demonstrating clinical efficacy compared to other desensitising products (Andersson and Kangasniemi 1991; Forsback et al. 2004; Du Min et al. 2008; Pradeep and Sharma 2010; Litkowski and Greenspan 2010; Narongdej et al. 2010; Dong et al. 2011; Wang et al. 2011a, b; Gendreau et al. 2011; Rajesh et al. 2012; Pradeep et al. 2012; Sharif et al. 2013; Petersson 2013). However one of the problems in evaluating the results from the clinical studies is the lack of homogeneity in the methodology and designs of the studies which makes the analysis of these results difficult (Talioti et al. 2014) (see Chap. 1).

Innovative Developments in the Treatment of Non-carious Cervical Lesions as a Strategy for the Management of DH

Protease Inhibitors

According to Kleter et al. (1993), once dentin is exposed to oral environment, the collagen layer is also exposed to the variations in pH which may subsequently result in a mineral depleted layer which may hamper the ionic diffusion of minerals from the saliva into the demineralised area (the degree of collagen loss is based on the demineralisation rate). In order to preserve the demineralised organic matrix, it would therefore be reasonable to use products that would be expected to reduce the progression of dentin loss

(Kato et al. 2012). The exposed organic matrix is relatively resistant to mechanical forces but was reported to be susceptible to biochemical degradation by proteases, for example, metalloproteinases (MMPs) from the saliva and from the dentin matrix itself (Tjäderhane et al. 1998).

In order to potentially preserve the organic dentin (collagen) matrix, several investigators have examined the role of known protease inhibitors, for example, polyphenol epigallocatechin-3-gallate (Demeule et al. 2000), chlorhexidine (Gendron et al. 1999; Carrilho et al. 2009; Scaffa et al. 2012) and ferrous sulphate (Kato et al. 2010). Initially the results are promising as the amount of dentin loss was reduced by 39–100 % with a number of these protease inhibitors in association with different vehicles (Kato et al. 2009, 2010; Magalhães et al. 2009). According to Kato et al. (2012), the data from these studies would suggest that the mechanism of action of these substances in preventing dentin erosion was due to their ability to inhibit the proteases, thus preserving demineralisation of the dentin matrix. These investigators also studied the protective effect of 400 μM polyphenol epigallocatechin-3-gallate, 0.012 % chlorhexidine, 1 mM ferrous sulphate solution and 1.23 % NaF solution, before submitting the dentin specimens to collagen degradation with *Clostridium histolyticum*, confirmed by the assaying of hydroxyproline in artificial saliva. The results demonstrated that the concentrations of hydroxyproline were significantly lower for the groups treated with polyphenol epigallocatechin-3-gallate, chlorhexidine and ferrous sulphate, respectively, when compared to the groups of sodium fluoride, placebo or with the untreated group. These results strongly suggested that the preventive effect of the protease inhibitors tested against dentin erosion was due to their ability to reduce the degradation of demineralised organic matrix (Kato et al. 2012).

Recently, Calabria et al. (2014) investigated the effect of a titanium fluoride (TiF4) solution on the hydraulic conductance of dentin, in comparison with a potassium oxalate gel, a sodium fluoride varnish and solution. The investigators reported that the TiF4 solution reduced dentin permeability by approximately 35 % (a similar percentage to that of a sodium fluoride solution). The permeability of the dentin specimens treated with potassium oxalate and a sodium fluoride varnish was reduced 85 and 65 %, respectively, in the same experiment. However, the association of these salts with TiF4 or with any other protease inhibitors has not been currently investigated in a clinical study.

Although there appears to be limited data available on these protease inhibitors, it may be speculated that if these inhibitors were able to reduce the subsurface demineralisation of organic dentin matrix either as a product or in association with the traditional desensitisers, then they may be relevant for the prevention of dental erosion and the treatment of DH.

Clinical Evidence of the Efficacy of OTC and In-Office Products

After almost 100 years of research, the clinical management of DH continues to be largely empirical in nature and very challenging to the clinician (Glockner 2013; Orchardson and Collins 1987; Pradeep et al. 2012). In view of the wide range of agents and procedures used to treat DH (Ling and Gillam 1996; Orchardson and Gangarosa 1994; Orchardson and Gillam 2000; Cunha-Cruz et al. 2010), it would be unreasonable for the clinician to expect that one particular product would resolve every aspect of the problem or that these particular treatment strategies would be appropriate for every individual (Lin et al. 2013; Gillam et al. 2013; Schmidlin and Sahrmann 2013) (see Chap. 10).

In general, in-office treatments are successful in treating DH in patients with a localised severe problem in one or more teeth, depending on the desensitiser used to treat the problem. OTC products which are recommended for mild to moderate generalised DH usually demonstrate a reduction in DH over time (Brauer et al. 2010; Wang et al. 2010). The advantage of using products available for home use is that they are immediately available for treatment when compared with those products applied by the professional. One disadvantage however is that more time is required for the remission of symptoms

(2–4 weeks), while those applied in-office promote immediate relief (Lynch et al. 2012; Pradeep et al. 2012) (see Chap. 10).

Conclusions

The continual introduction of new desensitising materials and treatment approaches would appear to suggest that there is no ideal desensitising product or clinical approach that can fully satisfy the original postulates of Grossman or fully address the impact of DH on the quality of life of patients (Grossman 1935; Gillam 1997) (see Chap. 9). It may however be unreasonable to expect that any one desensitising product or treatment approach would successfully resolve all the clinical factors associated with DH, and therefore the search for the ideal desensitising agent must be implemented (Gillam et al. 2013; Schmidlin and Sahrmann 2013). Furthermore there does appear an existing problem in both terms of the confidence of the clinician in successfully treating DH and in identifying an ideal desensitising product and treatment approach (Cunha-Cruz et al. 2010; Schmidlin and Sahrmann 2013; van Loveren 2013). There is, therefore, a need for the establishment of evidence-based clinical guidelines that may be used in daily practice (Al-Sabbagh et al. 2009). The recent publication by Gillam et al. (2013) attempted to address this particular problem, but there is clearly a need for such guidelines to be simple and pragmatic in order for the clinician to implement them successfully in clinical practice. The importance of a simple stepwise approach that may be supplemented with both diagnosis and preventive (counselling) measures, as well as long-term monitoring, is also imperative for any successful management strategy (Orchardson and Gillam 2006; Gillam et al. 2013; Lussi and Hellwig 2013) (see Chap. 10).

Future Trends

Clinicians in their daily practice must therefore consider two different aspects regarding the patient's experience of DH. One is related to the patient's discomfort and their need for an immediate pain resolution. The other is in regard to the entire spectra of events that may lead to a non-pathological exposure of dentin tissue in the oral environment. Both of these aspects demand that the clinician has not only a wide range of knowledge and clinical experience in order to offer the best treatment and the corrective strategies to their patients. Furthermore it is essential that well-controlled randomised clinical studies are undertaken in order to investigate new materials and their properties under rigorous clinical conditions. Currently there does not appear to be an ideal desensitising product (which successfully mimics the natural tissue) that can be effectively utilised in both in-office and in OTC/at-home environments. It is therefore imperative that researchers responsible for the development of new materials direct their attention into areas of research with targeted formulations that can mimic and restore the natural structures of the tooth.

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9 The Impact of Dentine Hypersensitivity on Oral Health-Related Quality of Life

Katrin Bekes and Christian Hirsch

Quality of Life in Dentistry

Quality of Life and Health-Related Quality of Life

"Quality of life" (QoL) as a term was first introduced in 1920 by the British economist Arthur Cecil Pigou (1920), in a book about economics and welfare discussing governmental support for the lower class and its impact on their lives, as well as on national finances. Later on, the expression "QoL" was defined in many ways and was used differently by various investigators, owing to its elusive nature. It became apparent that although one may intuitively know what it means, its abstract nature makes a clear definition difficult.

In medicine and dentistry, a paradigm shift has occurred in recent years, as patient (person)-centered outcomes including QoL research have been receiving increasingly more attention (see Chap. 7). Once regarded as a secondary outcome, occasionally useful to complement biologic and clinical markers of disease, it has been stated that "QoL issues are now at the forefront of public health policy" (Slade 2002). According to the World Health Organization, QoL can be defined as an individual's perception of his/her position in life, in the context of the culture and value systems in which he/she lives, and in relation to his/her expectations, goals, and concerns (World Health Organization 1993).

Health contributes to QoL, and the real impact of health and disease on QoL is known as health-related quality of life (HRQoL) (Naito et al. 2006). As with QoL, the concept of HRQoL is multifaceted and complex; therefore, defining it is a challenge (Cimprich and Paterson 2002). There is consensus that it captures people's perceptions relating to factors that are important in their everyday lives (Slade 2002). The definition of health by the World Health Organization as "a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity" (World Health Organization 1948) implies that health is no longer seen as merely the absence of a disease but as a concept that focuses on the whole person (Absi et al. 1987). It is this idea of wholeness that led to the development of the concept of HRQoL.

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Oral Health-Related Quality of Life

What Is Oral Health-Related Quality of Life?

Oral health-related quality of life (OHRQoL) is a subset of HRQoL that focuses on oral health and orofacial concerns. OHRQoL is "a multidimensional construct that reflects (among other things) people's comfort when eating, sleeping, and engaging in social interaction; their self-esteem; and their satisfaction with respect to their oral health" (DHHS 2000). OHRQoL attempts to capture the subjective side of oral health. Thus, the concept of OHRQoL brings a new perspective to clinical dental care and research. It describes the way in which oral health affects a person's ability to function, psychological status, social factors, and pain or discomfort (Inglehart and Bagramian 2002). As Inglehart noted, "it shifts the focus of clinicians and researchers from the oral cavity alone to the patient as a whole" (Inglehart and Bagramian 2002).

Concepts of Oral Health

Following the traditional approach, oral health measures are based on clinical standards. Usually, oral health is described by using clinical oral disease indicators (indices), as they provide a quantitative method for measuring, scoring, and analyzing dental conditions in individuals and groups. An index describes the status of individuals or groups with respect to the condition to be measured. For example, the severity of periodontal disease is documented by clinicians using parameters, for example, bleeding on probing, probing pocket depth, and clinical attachment level (Ng and Leung 2006). However, important as these objective measures are, they may only reflect the end point of the disease processes. They give no indication of the impact of the oral disease processes or oral disorders on function or psychosocial well-being and provide little insight into the impact on daily living and quality of life (Allen 2003). To continue with this example, this means that other symptoms of periodontal disease, including those resulting from chronic inflammation and the destruction of tooth-supporting tissues (such as redness, bleeding on brushing, loosening of affected teeth, and persistent bad breath), are not normally documented by clinicians. However, such symptoms are highly relevant from the patient's point of view and often have a considerable adverse impact on their daily QoL (Locker 1988; Ng and Leung 2006).

On these grounds, Locker developed a conceptual framework for measuring oral health status (Locker 1988). It was based on the World Health Organization classification of impairment, disability, and handicap and attempted to capture all possible functional and psychosocial outcomes of oral disorders. Locker stated that disease can lead to impairment, which may then lead to a functional limitation or pain/discomfort, either physical or psychological. Any of these outcomes may lead to physical, psychological, or social disability, which was defined by Locker "as any limitation in or lack of ability to perform activities of daily living." As a final consequence, handicap can occur. It is characterized by social disadvantage (e.g., social isolation). Functional limitation may also lead directly to handicap.

How Can Oral Health-Related Quality of Life Be Measured?

As noted previously, OHRQoL is a multidimensional construct that cannot be observed directly. It needs to be visualized by means of suitable indicators. This could be done using a questionnaire approach. Several measurements to assess OHRQoL have been developed over time as a result of increased concern about the impact of oral conditions on a person's quality of life. Fundamentally, there are three categories of OHRQoL measure as indicated by Slade (2002): social indicators, global self-ratings of OHRQoL, and multiple-item questionnaires of OHRQoL. Multiple-item questionnaires are among the most widely used methods to assess OHRQoL (Al Shamrany 2006).

Given that the definitions of OHRQoL are vague, it is not surprising that there is a significant heterogeneity in focus, length, and format of the multiple-item questionnaires developed to evaluate OHRQoL. Nevertheless, all of them have to fulfill a set of attributes and criteria for the assessment of health status and QoL measurement that were defined by the Scientific Advisory Committee of the Medical Outcomes Trust (Aaronson et al. 2002).

In addition, OHRQoL measures can be classified as either generic instruments that measure oral health overall or condition-specific instruments. In some instances, generic measures are too broad for accurate assessment of the links between specific oral conditions and OHRQoL, so that it is desirable to develop specialized instruments. For example, for dentine hypersensitivity (DH), a condition-specific patient-reported measure was developed recently (Boiko et al. 2010).

The Oral Health Impact Profile

A technically sophisticated and internationally widely used OHRQoL instrument is the Oral Health Impact Profile (OHIP), which was developed by Slade and Spencer (Fig. 9.1) (1994). It differs from other OHRQoL measures in that it is based on both Locker's conceptual framework (Locker 1988) and input from dental patients with a variety of oral conditions (Slade and Spencer 1994). The questionnaire attempts to

Question	Domain	Item
1	FL	Have you had difficulty chewing any foods because of problems with your teeth, mouth or dentures?
2	FL	Have you had trouble pronouncing any words because of problems with your teeth, mouth or dentures?
3	FL	Have you noticed a tooth which doesn't look right?
4	FL	Have you felt that your appearance has been affected because of problems with your teeth, mouth or dentures?
5	FL	Have you felt that your breath has been stale because of problems with your teeth, mouth or dentures
6	P1	Have you felt that your sense of taste has worsened because of problems with your teeth, mouth or dentures?
7	P1	Have you had food catching in your teeth or dentures?
8	P1	Have you felt that your digestion has worsened because of problems with your teeth, mouth or dentures?
9	P1	Have you had painful aching in your mouth?
10	P1	Have you had a sore jaw?
11	P1	Have you had headaches because of problems with your teeth, mouth or dentures?
12	P1	Have you had sensitive teeth, for example, due to hot or cold foods or drinks?
13	P1	Have you had toothache?
14	P1	Have you had painful gums?
15	P1	Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?
16	P1	Have you had sore spots in your mouth?
17	FL	Have you felt that your dentures have not been fitting properly?
18	P1	Have you had uncomfortable dentures?
19	P2	Have you been worried by dental problems?
20	P2	Have you been self conscious because of your teeth, mouth or dentures?
21	P2	Have dental problems made you miserable?
22	P2	Have you felt uncomfortable about the appearance of your teeth, mouth or dentures?
23	P2	Have you felt tense because of problems with your teeth, mouth or dentures?
24	D1	Has your speech been unclear because of problems with your teeth, mouth or dentures?
25	D1	Have people misunderstood some of your words because of problems with your teeth, mouth or dentures?
26	D1	Have you felt that there has been less flavor in your food because of problems with your teeth, mouth or dentures?
27	D1	Have you been unable to brush your teeth properly because of problems with your teeth, mouth or dentures?
28	D1	Have you had to avoid eating some foods because of problems with your teeth, mouth or dentures?
29	D1	Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures?
30	D1	Have you been unable to eat with your dentures because of problems with them?
31	D1	Have you avoided smiling because of problems with your teeth, mouth or dentures?
32	D1	Have you had to interrupt meals because of problems with your teeth, mouth or dentures?
33	D2	Has your sleep been interrupted because of problems with your teeth, mouth or dentures?
34	D2	Have you been upset because of problems with your teeth, mouth or dentures?

Fig. 9.1 Oral Health Impact Profile (OHIP) (Acknowledgement to Slade and Spencer 1994). *FL* functional limitation, *P1* physical pain, *P2* psychological discomfort, *D1* physical disability, *D2* psychological disability, *D3* social disability, *H* handicap

35	D2	Have you found it difficult to relax because of problems with your teeth, mouth or dentures?
36	D2	Have you felt depressed because of problems with your teeth, mouth or dentures?
37	D2	Has your concentration been affected because of problems with your teeth, mouth or dentures?
38	D2	Have you been a bit embarrassed because of problems with your teeth, mouth or dentures?
39	D3	Have you avoided going out because of problems with your teeth, mouth or dentures?
40	D3	Have you been less tolerant of your partner or family because of problems with your teeth, mouth or dentures?
41	D3	Have you had trouble getting along with other people because of problems with your teeth, mouth or dentures?
42	D3	Have you been a bit irritable with other people because of problems with your teeth, mouth or dentures?
43	D3	Have you had difficulty doing your usual jobs because of problems with your teeth, mouth or dentures?
44	H	Have you felt that your general health has worsened because of problems with your teeth, mouth or dentures?
45	H	Have you suffered any financial loss because of problems with your teeth, mouth or dentures?
46	H	Have you been unable to enjoy other people's company as much because of problems with your teeth, mouth or dentures?
47	H	Have you felt that life in general was less satisfying because of problems with your teeth, mouth or dentures?
48	H	Have you been totally unable to function because of problems with your teeth, mouth or dentures?
49	H	Have you been unable to work to your full capacity because of problems with your teeth, mouth or dentures?

FL=Functional limitation, P1=Physical pain, P2=Psychological discomfort, D1=Physical disability, D2=Pscyhological disability, D3=Social disability, H=Handicap

Fig. 9.1 (continued)

measure the effects of both the frequency and the severity of oral problems on functional and psychosocial well-being. It is a scaled index; it consists of 49 statements that have been rephrased as questions and grouped into seven domains (functional limitation, pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap). For each OHIP item, the patient is asked how frequently he/she experienced the impact of that item during the last month. Responses concerning item impact are given using an ordinal rating scale (0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often). The summary score (sum of item responses resulting in a range of 0–4×49 = 0–196) represents a "problem index" that characterizes the OHRQoL. A "0" summary score indicates the absence of any problems, higher OHIP scores represent more impaired OHRQoL, and a summary score of "196" indicates that all problems were experienced very often in the last month. The patient's score can be evaluated by comparison to a table of standard values representative of different populations (John et al. 2003, 2004).

The 49-item version of the OHIP gives detailed information and is a sophisticated instrument when OHRQoL is the primary outcome in a clinical setting. However, it is rather time consuming and requires a substantial effort for the respondents. Consequently, short forms (21 items, 14 items, 5 items) have been developed (Locker and Allen 2002; Slade 1997) and proposed for use in settings where the time burden of a long OHRQoL questionnaire needs to be minimized. A version with 14 items is most frequently used (Baba et al. 2008).

A Condition-Specific Patient-Reported Measure

The Dentine Hypersensitivity Experience Questionnaire (DHEQ)

In some instances, generic measures are insufficient in assessing the links between oral conditions

Question	Domain	Item
1	Restrictions	pleasure out of eating
2	Restrictions	cannot finish meal
3	Restrictions	longer to finish meal
4	Restrictions	problems eating ice-cream
5	Approach coping	modification in eating
6	Approach coping	careful when breathing
7	Approach coping	warming food/drinks
8	Approach coping	cooling food/drink
9	Approach coping	cutting fruit
10	Approach coping	putting a scarf over mouth
11	Approach coping	cold drinks/foods
12	Approach coping	hot drinks/foods
13	Approach coping	contact with certain teeth
14	Approach coping	change toothbrushing
15	Approach coping	biting in small pieces
16	Approach coping	other food
17	Social	longer than others to finish
18	Social	choose food with others
19	Social	hide the way of eating
20	Social	unable to take part in conversations
21	Social	painful at the dentist
22	Emotions	frustrated not finding a cure
23	Emotions	anxious of eating contributes
24	Emotions	irritating sensations
25	Emotions	annoyed I contributed
26	Emotions	guilty for contributing
27	Emotions	annoying sensations
28	Emotions	embarrassing sensations
29	Emotions	anxious because of sensation
30	Identity	difficult to accept
31	Identity	different from others
32	Identity	makes me feel old
33	Identity	makes me feel damaged
34	Identity	makes me feel unhealthy

Fig. 9.2 Impact scale of the Dentine Hypersensitivity Experience Questionnaire (DHEQ) (Acknowledgement to Boiko et al. 2010 and Baker et al. 2014)

and OHRQoL. For this reason, an OHRQoL measure specific for the impact of DH was recently developed, based on interviews with people with DH (Boiko et al. 2010; Gibson et al. 2010): The Dentine Hypersensitivity Experience Questionnaire (DHEQ) (Fig. 9.2). This instrument aims to measure the day to day impact of specific events associated with DH on QHRQoL. The questionnaire was developed using a multistaged impact approach and an explicit theoretical model. As a result, the DHEQ questionnaire has 48 items containing a description of the pain (six items), a measurement of pain via visual analogue scale (3), a scale to capture the subjective impact of DH (34), a global oral health rating (1), and a scale to record effects on overall life (4).

The impact scale comprises 34 items and has five subscales based on the initial domains of the Wilson and Cleary model (1995): functional restrictions (four items), coping (12), social impact (5), emotional impact (8), and identity (5). The items have coded responses on 7-point Likert scales (labeled strongly disagree, disagree, disagree a little, neither agree nor disagree, agree a little, agree, and strongly agree, coded 1–7, respectively). The summary measure ("total score") of the impact scale is calculated as the sum of the item scores per participant (possible range 34–238).

The higher the total score of the DHEQ is, the more impaired the patient's OHRQoL is.

The DHEQ has been reported to demonstrate good psychometric properties (Boiko et al. 2010). It is longitudinally reliable, valid, and responsive and can discriminate between treatments of different efficacy (Baker et al. 2014). Moreover, a 10- and 15-item short form of the DHEQ has recently been derived (Machuca et al. 2014).

Dentine Hypersensitivity and Its Impact on Oral Health-Related Quality of Life

Dentine Hypersensitivity (DH)

As shown in the other chapters of this book, DH is a significant global clinical oral health problem in the adult population (Mantzourani and Sharma 2013) (Chap. 3) that is characterized by short or transient sharp pain arising from exposed dentine in response to an array of stimuli (such as thermal, mechanical, osmotic, or chemical elements) that cannot be ascribed to any other forms of dental defect or disease (Canadian Advisory Board on Dentin Hypersensitivity 2003) (Chaps. 4 and 5). The cold stimulus has been reported to cause the greatest problem to people affected by DH, as it increases the outward flow of fluid in the dentinal tubules, whereas a thermal hot stimulus produces contraction of the fluid in the tubules (Matthews and Vongsavan 1994).

Nevertheless, pain has extremely variable characteristics, ranging from discrete discomfort to extreme severity (McGrath 1986, 1994; Porto et al. 2009). In addition, not all people experiencing tooth sensitivity seek treatment to desensitize their teeth, because some do not perceive DH to be a severe oral health problem (Gillam et al. 1999). However, the influence of pain experienced can be considerable and can affect daily activities depending on the source of discomfort (e.g., pain associated with consuming hot or cold foods and beverages [coffee, ice cream], during tooth brushing, or sometimes even while breathing) (Schuurs et al. 1995; Gillam et al. 2002). In these instances, these symptoms are highly relevant from the person's point of view and often have a considerable adverse impact on daily quality of life (Locker 1988).

Oral Health-Related Quality of Life in Patients with DH

To date, there has been limited research conducted that has explored DH from a patient perspective (Bekes et al. 2008, 2009; Boiko et al. 2010; Baker et al. 2014; He et al. 2012). For example, existing clinical reviews have focused only in a limited manner on this topic (Bekes and Hirsch 2013; Sixou 2013). In the clinical environment, the patients' experiences of pain have been only been recorded in response to a stimulus (Gillam and Newman 1993; Rees and Addy 2002; Gillam et al. 2000), with little consideration given to the impact of DH on everyday life. Therefore, knowledge about the influence of DH on OHRQoL is still incomplete, and very few studies have been devoted to this aspect of DH.

The first data that were published using an instrument that examined patients' self-perception of health and well-being to explore the impact of DH on OHRQoL came from a study that was conducted in Germany (Bekes et al. 2009). OHRQoL impairment was evaluated in 656 patients seeking care for their hypersensitive teeth in German dental practices. The study participants were asked to complete the adapted German version of the OHIP (OHIP-G) (John et al. 2002) prior to treatment. When their OHIP summary scores were analyzed and compared with those in a sample of the German general population ($n = 1{,}541$) (John et al. 2003), the distribution of OHIP-G summary scores in patients with DH and in the general population was found to be different. The general-population participants had an OHIP-G median score of 5, compared to a median score of 30 in the patient group (Fig. 9.3). The 10 % of the subjects with the highest OHIP-G summary scores presented scores of 36 or higher (general population) and 66 or higher (patients). The mean OHIP-G summary score value of the study participants from the general population was 12.2

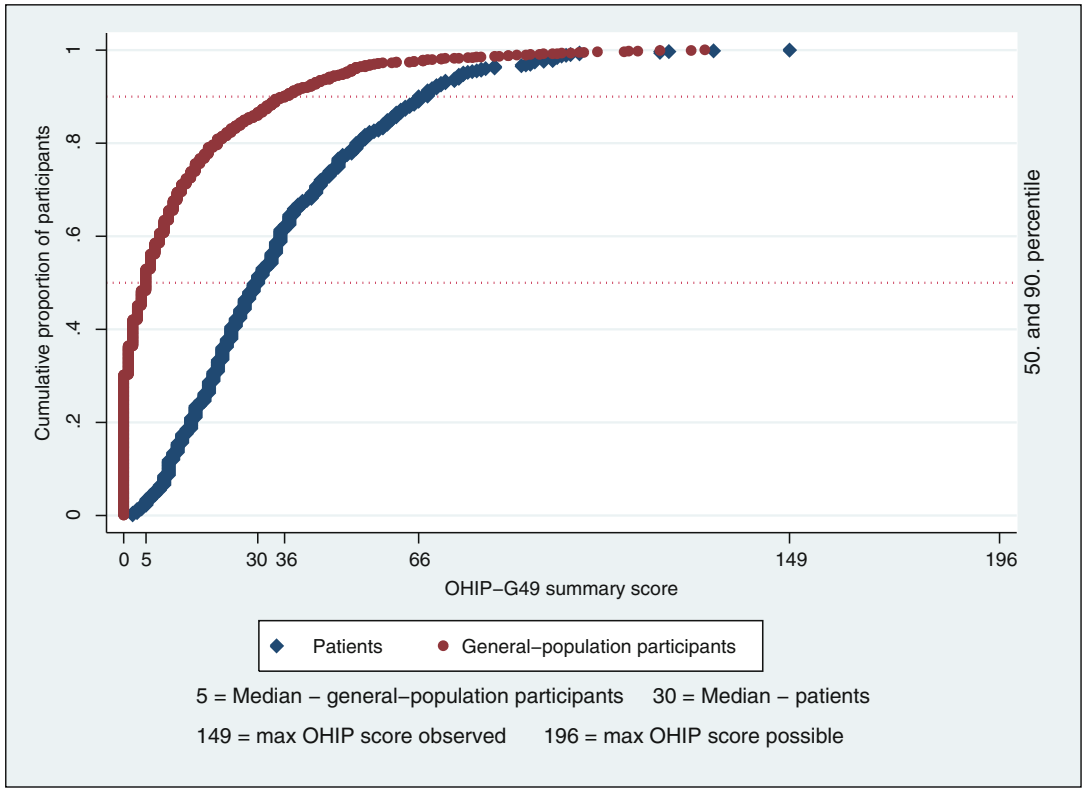

Fig. 9.3 Empirical cumulative distribution functions of Oral Health Impact Profile-G summary scores for general-population participants and patients with DH (reproduced from Bekes et al. 2009) Bekes et al. 2009)

(±18.4), while the patients' mean OHIP-G summary score was 34.5 (±22.6). The difference in the mean values of 22.3 was clinically meaningful and statistically significant ($P < 0.001$). These results demonstrated that the patients with DH had impaired OHRQoL. The results also indicated that the influence of gender on OHRQoL depended on the population. In the general-population sample, female subjects had lower OHIP scores than male subjects ($P = 0.003$), whereas in the patient group, female patients had higher OHIP scores than male patients, but the difference was not statistically significant ($P = 0.27$). Lastly, age showed a curvilinear association with OHRQoL, with lower OHIP scores associated with younger and older adults and higher OHIP scores (reporting more problems and indicating impaired OHRQoL) associated with middle-aged adults in both populations. The difference between younger (15–39 years) and older adults (40+ years) was statistically significant in the general population ($P < 0.001$). In the patient group, the difference was similar in magnitude to that and close to statistical significance ($P = 0.08$).

The results reflect findings for patients seeking care for their condition and certainly cannot be generalized to individuals experiencing DH but not seeking care. Moreover, the results relate to patients seen by general dentists and may not be generalized to those that could be obtained by health professionals who are more trained or calibrated in the assessment of DH. However, the setting is representative for typical patients who initially present in dental practice and where the general dentist is confronted with providing diagnosis and treatment for the challenging clinical problem of DH (Bekes et al. 2009).

The same investigators evaluated OHRQoL in 713 patients with DH before and after treatment intervention (Bekes et al. 2008). The treatment regimen was a 21-day home use of desensitizing dentifrice (elmex SENSITIVE toothpaste) in combination with a dental rinse (elmex SENSITIVE dental rinse) and a special toothbrush (elmex interX SENSITIVE toothbrush) twice a day for oral hygiene. The patients completed the OHIP-G before and after treatment intervention. Following the intervention, OHRQoL improved considerably, with a mean decrease of 13.5 OHIP-G units ($P<0.001$). In particular, 50 % of the patients showed a decrease of 11 or more OHIP-G units. No statistical significances however were observed for gender or age. The study had some limitations, as it was not randomized and did not include a control or placebo group. However, it was the first study undertaken to evaluate the effect of a DH treatment on OHRQoL and not solely from that of the clinician's perspective. Moreover, the study demonstrated that it is possible to measure the success of a treatment for DH with an OHRQoL instrument, the OHIP.

The disease-specific DHEQ that was introduced recently (Boiko et al. 2010) provided an alternative to the "generic" OHIP for assessing OHRQoL in patients with DH. It directly addressed the problems associated with sensitive teeth. Initial work with this newly developed measure examined whether it met the gold-standard guidelines for QoL instruments (Aaronson et al. 2002). For this initial analysis, the DHEQ was first applied in a general-population sample and in a sample of patients clinically diagnosed with DH (Boiko et al. 2010). The DHEQ instrument demonstrated good psychometric properties and was internally consistent (Cronbach's $a=0.86$) and reliable (ICC = 0.92) and demonstrated high validity scores. The DHEQ indicated that patients with DH had higher scores on the DHEQ (147.6 ± 5.98) than the general population (130.96 ± 35.06), indicating that these patients had an impaired OHRQoL. In particular, the DHEQ detected functional limitations (e.g., problems with eating ice cream), coping behaviors (e.g., careful when breathing, warming food/drinks, avoiding contact with certain teeth), emotional (e.g., annoying sensations), and social impacts (e.g., difficulties conversing) caused by DH.

These results were underlined and confirmed by a subsequent longitudinal study including three clinical studies with 311 participants (Baker et al. 2014). Each study compared the efficacy of a test and control toothpaste in providing relief from DH. Participants brushed at home twice daily for 8 or 12 weeks respectively. The DHEQ was administered before and after treatment. The results demonstrated significant decreases in total DHEQ scores ($P<0.001$), as well as all domain scores (except for identity and restriction once each), across all the trials. The coping domain showed the largest effect size, followed by the emotional domain; the identity domain showed the smallest decrease. In this analysis, the DHEQ was found to be highly useful for assessing changes in functional and personal experiences of DH, improvements in QoL status, and responsiveness to anti-sensitivity treatments.

Future studies will need to examine the DHEQ translated into other languages in order that the results can be compared cross-culturally as a first step to the DHEQ being accepted for use internationally. Until now, only a second (Chinese) version has been reported (He et al. 2012). However, this condition-specific measure for measuring impacts of DH on OHRQoL may detect changes in functional and personal experiences of DH. DHEQ data may therefore be used to evaluate negative emotions specifically related to DH and aid in the development of effective interventions and health policies to address DH. However, the OHIP has relevance to determining the impact of DH as well. Although the extent to which OHIP is appropriate to measure the specific impacts of DH is unclear (Bekes and Hirsch 2013), its utility is not limited to this special patient group. For this reason, it has the advantage that it can be used in patients with other oral diseases and across conditions, therefore allowing DH to be compared with other oral conditions and enabling to the broader influence of hypersensitive teeth on patient's perceived health to be characterized.

Future Trends

Patient-reported outcomes and in particular the concept of OHRQoL have gained popularity in recent years (see Chap. 7). This new perspective on health suggests that the ultimate goal of dental care, which is good oral health, should no longer be seen as the absence of caries or periodontal disease and that a patient's mental and social well-being also has to be considered (Inglehart and Bagramian 2002). Evaluation of OHRQoL allows for this shift from traditional medical and dental criteria, as it captures the aim of this new perspective and focuses on subjective patient social and emotional experiences, as well as physical functioning, in defining appropriate treatment goals and outcomes (Sischo and Broder 2011).

In the future, it is desirable to evaluate OHRQoL in the clinical environment, as its measurement may identify issues on an individual level previously not recognized that could potentially be addressed through appropriate interventions; repeating the measurement subsequent to therapy would allow assessment of the efficacy of the intervention (Barnes and Jenney 2002). It could also guide choices and perhaps encourage new development. In regard to conditions such as DH, it may prove to be a valuable asset for clinicians when assessing their patients' quality of life before, during, and after treatment of various clinical conditions (Sixou 2013).

Conclusion

The concept of OHRQoL brings a new perspective to clinical dental care and research, as it allows insight into how a patient's oral health affects his/her well-being and quality of life at a given point in time. In patients with DH, limited data about OHRQoL are available, knowledge is still incomplete, and further research is desired. Nevertheless, preliminary data have shown that patients with DH report substantial OHRQoL impairment and that the impact of this experienced oral pain on patients' perceived health is considerable. Thus, OHRQoL measurement provides additional information about the magnitude of the condition of DH and should be considered as a useful addition to clinical tests to assess the severity and impact of the reported problem.

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10 Advances in the Management of the Patient with Dentine Hypersensitivity: Motivation and Prevention

David G. Gillam and Christoph A. Ramseier

Introduction

The aim of the first part of the chapter is to reflect on how the management of dentine hypersensitivity (DH) has been traditionally recommended in clinical practice and the steps taken to provide simple and practical guidelines for the busy clinician. The second part of the chapter will develop the recommendations on how to manage DH by concentrating on techniques (e.g. motivational interviewing) used in both medicine and dentistry to effect behavioural changes when providing instructions to patients enabling them to not only recognise the need for change but also to take ownership of their problem whether it is through an improvement in oral hygiene practice or taking steps to limit the effects of acidic food or drink on initiating DH.

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Management of Dentine Hypersensitivity (DH)

The management of dentine hypersensitivity (DH) has been traditionally based on products that may either block the dentine tubules on the exposed root surface or desensitise the nerves in the pulp (Orchardson and Gillam 2006). The clinician when faced with a patient with DH would generally treat the condition on the basis of the extent and severity of the problem. For example, if the patient complained of severe pain which was localised to one or two teeth, then the clinician would treat the problem in the clinical setting (Dental office or surgery) with a restorative product (Table 10.1). Alternatively if the pain was generalised and of a mild to moderate nature, then the clinician may consider recommending an over-the-counter (OTC) product (Table 10.1). Patients may also complain of pain following restorative procedures, for example, nonsurgical and surgical periodontal procedures, and the clinician may, depending on the extent and severity of the problem, recommend a treatment regime that would resolve the problem (Orchardson and Gillam 2006). It is important however to acknowledge that the diagnosis of DH is somewhat problematic in nature, and therefore it is essential that the clinician excludes all other clinical conditions that have a similar pain history to that of DH (see Chap. 5). In a busy practice this may be a challenge, but in order to successfully manage DH, it is essential

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Table 10.1 Overall management strategy options for treating dentine hypersensitivity (Gillam et al. 2013 modified)

Gingival recession	Tooth wear	Periodontal treatment
Clinical evaluation Clinical measurement of the gingival recession defect Take study casts and clinical photographs to monitor condition over time Check and monitor periodontal health Identification and correction of predisposing or precipitating factors Use of pain scores to assess and monitor DH (e.g. visual analogue scores)	**Clinical evaluation** Identify cause of tooth wear (enamel loss) Record severity of lesions, if possible, using a recognised index (Smith and Knight 1984; Bartlett et al. 2008) Take study casts and clinical photographs to monitor condition over time Check and monitor periodontal health Use of pain scores to assess and monitor DH (e.g. visual analogue scores)	**Clinical evaluation** Periodontal disease or periodontal treatment as the primary cause of exposure of dentine and associated DH Check and monitor periodontal health (6-point pocket charting) Use of pain scores to assess and monitor DH (e.g. visual analogue scores)
Patient education (including preventive advice) Show patient the affected site(s) Explain probable cause for recession Explain factors triggering sensitive teeth episodes Encourage patients to modify their oral hygiene regimen in order to reduce damage to gingivae (e.g. reducing brushing force, correction of toothbrushing technique) Reduce excessive consumption of acid foods and drinks	**Patient education (including preventive advice)** Show patient the site(s) and explain probable cause of the tooth wear lesion(s) Recommend an oral hygiene regimen to minimise risk of further tooth wear Where appropriate recommend reducing frequency of consumption of acidic food and drink	**Patient education (including preventive advice)** Reinforce the need for good oral hygiene Show patient the site(s) affected by periodontal disease and explain probable cause of the exposed dentine Guide the patient to improve “at-home” oral hygiene regimen Instruction on measures of reducing periodontal risk factors, for example, diabetes, smoking and obesity

Corrective clinical outcomes Reduce excessive consumption of acid foods and drinks Manufacture of silicone gingival veneers Orthodontic treatment Restorative correction of recession defect and subgingival margins of fillings and crowns Polymers: sealants/varnishes/resins/dentine-bonding agents Laser obturation of dentine tubules Use of desensitising polishing pastes Pulpal extirpation (root canal treatment)	**Corrective clinical outcomes** Provide high fluoride remineralising treatment (pre-emptive phase) Provide professional desensitising treatment to relieve DH Encourage patient to seek advice from a medical practitioner, if tooth wear was caused by conditions with the work environment or reflux/excessive vomiting (psychiatric evaluation may also be appropriate) Restorative correction in the form of composite build-up, crowns may also be appropriate	**Corrective clinical outcomes** *Initial phase* Nonsurgical periodontal procedure(s). DH treatment (including desensitising polishing pastes/fluoride varnishes) *Re-evaluation* Follow-up assessment on periodontal status and DH *Corrective phase* Surgical periodontal procedure(s), e.g. guided tissue regeneration, coronally advanced flap + enamel matrix derivatives, connective tissue graft (flap), free gingival graft (acellular dermal matrix allograft) DH treatment (including desensitising polishing pastes/fluoride varnishes) **Follow-up management** *Maintenance phase* Supportive periodontal therapy Ongoing monitoring of periodontal health DH treatment (including desensitising polishing pastes/fluoride varnishes) Oral hygiene advice
Recommendations for home use (including toothpaste/mouth rinse formulations) Oral hygiene implementation as per recommendation Strontium chloride/strontium acetate Potassium nitrate/chloride/citrate/oxalate Calcium compounds Calcium carbonate and arginine and casein phosphopeptide + amorphous calcium phosphate Bioactive glass Nano-/hydroxyapatite Fluoride in higher concentration (2,800/5,000 ppm F [prescription]) Amine/stannous fluoride	**Recommendations for home use (including toothpaste/mouth rinse formulations)** Oral hygiene implementation as per recommendation Toothpaste and mouth rinse formulations (see recommendations for gingival recession)	**Recommendations for home use (including toothpaste/mouth rinse formulations)** Oral hygiene implementation as per recommendation Regular brushing with an antibacterial toothpaste to aid plaque control Short period, the use of a 0.2 % chlorhexidine solution for plaque control Use of a desensitising mouthrinse twice daily for DH control (when appropriate) Long term monitoring (see recommendations for gingival recession)

for the clinician to take time and determine the correct diagnosis before providing treatment. There is often a tendency for the busy clinician to simply prescribe or recommend a treatment without determining the aetiological and predisposing factors that may have been instrumental in initiating the problem (see Chap. 4) and if not correctly managed or monitored will continue to impact on a patient's quality of life (oral health-related quality of life, OHRQoL) (Bekes et al. 2008; Bioko et al. 2010; Bekes and Hirsch 2013) (see Chap. 9). This approach would therefore involve not only educating the patient but also the clinician, and it is important to recognise that the clinicians will need to adopt management strategies and goals that will effectively encourage behavioural changes in the lifestyle of their patients. In order to accomplish these goals, the clinician will need to motivate and engage the patient in order to effect the recommended changes in behaviour. The question however arises whether the clinician can effectively diagnose, manage and monitor DH within the constraints of clinical practice (Gillam 2013). There have been a number of treatment paradigms that have been previously reported in the published literature, and there is however a recognition that they may be impractical to implement in the clinical environment (Addy and Urquhart 1992; Canadian Advisory Board on Dentin Hypersensitivity 2003; Orchardson and Gillam 2006). Recently, guidelines have been published from a UK Expert Forum on DH (Gillam et al. 2013) which recognised that there was a need to promote simple guidelines that can be readily applied in general practice, although the Forum acknowledged that a simple one-strategy approach to the problem may not necessarily satisfy all patients. One of the key components from the guidelines document was that the authors linked recommended management strategies to three specific groups of patients rather than recommend a blanket management for all patients with DH. These patient groups included (1) patients with gingival recession caused by mechanical trauma, (2) patients with tooth wear lesions and (3) patients with periodontal disease and those receiving periodontal treatment (Table 10.1). It is also evident from the majority of clinical studies for the treatment of DH that patient compliance with both oral hygiene and dietary regimens was paramount in order to achieve satisfactory treatment outcomes and predictable long-term success. In this context it may be appropriate to recognize that individuals who experience DH as a result of meticulous oral hygiene practices may be easier to adopt relatively small changes in their healthcare behaviour ; compared to individuals who have addictive behaviour and/or chronic health problems including periodontal disease. The second part of the chapter will discuss how a clinician may attempt to engage their patients to follow an individualised oral care regimen which can be incorporated into the management strategy for treating DH. This will enable the patient to modify any risk factors associated with the development and progression of DH and subsequently prevent or reduce these effects. For example, apart from the standard of care for oral hygiene practices, these regimens include dietary counselling as well as instructions to avoid brushing the teeth following the intake of acid-containing drinks.

The Challenge of Changing Health Behaviour in the Management of Medical and Dental Conditions

It is generally recognised that one of the problems in clinical practice (medical or dental) was the lack of compliance or adherence to the instructions provided by the clinician during therapy. Compliance may be defined as the process of complying with a regimen of treatment, for example, taking medication (Definition of Compliance 2013), although the term adherence may be the preferred term to use. Adherence may therefore be defined as the extent to which the patient continues the agreed-upon mode of treatment under limited supervision when faced with conflicting demands, as distinguished from compliance or maintenance (The American Heritage® Medical Dictionary 2010; Definition of Adherence 2010). This term may therefore be considered a more general term representing "the extent to which a patient follows medical instructions" (Definition of Adherence 2001). The lack of compliance or adherence to instructions provided by a healthcare professional is not however unique to dentistry. According to Wertheimer and

Santella (2003), noncompliance occurred in approximately 50–75 % of patients taking prescribe medication with the rate of noncompliance higher in patients with a chronic illness. A further problem that may arise is that (as previously indicated) a patient with a diabetic condition who has a sedentary lifestyle who simply complies with the medical instructions relating to their prescribed medication alone without any changes in behaviour and lifestyle activity will not necessarily improve their medical condition.

It may however be unrealistic to expect every patient to understand and comply with professionally driven instructions particularly when treating chronic diseases and health conditions, for example, diabetes, obesity, smoking, alcoholism and periodontal disease. For example, the patient's attention and comprehension levels may be optimal during the first 15 min of a visit, but their ability to absorb and retain any further information may subsequently decline thereafter. It is therefore important to provide patients with simple clear instructions which they can understand and routinely implement as part of their day-to-day activities. This process may however take a number of visits and requires the clinician to build up a rapport with the patient, show empathy and have a close working partnership with the patient in order to effect the changes in behaviour that would reduce or eliminate the underlying problems associated with DH (e.g. drinking erosive drinks). Before illustrating how a clinician may work with a patient in order to effect a change in their daily intake of food and drink associated with DH, it may be beneficial to observe how clinicians in medicine and dentistry have attempted to effect changes in behaviour. For example, according to Ramseier (2005) there was emerging evidence that the patient's individual behaviour may be influential or even critical for the success of periodontal therapy as evidenced by the limited success of periodontal therapy in patients lacking the appropriate behaviour to maintain their periodontal condition. It is also important that the maintenance of periodontal health should be supported by appropriate behavioural changes, for example, regularly self-performed plaque control, avoidance of tobacco and glycaemic control with diabetes mellitus type 2, since patients with inadequate oral hygiene measures, tobacco usage and uncontrolled glucose levels have been reported to have an unsatisfactory periodontal status. According to Ramseier (2005), both plaque control and smoking cessation are important measures in the management of chronic periodontitis. Therefore, it would appear to be appropriate to (1) include assessments of patient behaviour and if necessary (2) apply effective behaviour change counselling methods in the maintenance of the patients' periodontal condition.

Reasons for the Lack of Compliance or Adherence Instructions Provided by the Medical and Dental Profession

As previously indicated it was evident from the published literature that noncompliance of both medical and dental patients is a major problem when delivering healthcare guidance and instruction as part of the treatment process. This appeared to be a problem in patients with long-term or chronic conditions, for example, diabetes, hypertension, cardiovascular disease (Khan et al. 2012) and in the dental environment chronic periodontal disease which may also be associated with these systemic conditions (Loesche and Grossman 2001; Kim and Amar 2006). According to Khan et al. (2012), noncompliance can be due to a number of factors, for example, those that are (1) patient centred, (2) therapy related or (3) healthcare system related.

The reasons for noncompliance are therefore complex in nature and may also vary not only between patients but also depend on the particular situation the patient may be experiencing at the time. For example, the reasons for noncompliance in the Khan et al. (2012) diabetes study included the unavailability of transport, forgetting the appointment, not attending the clinic since the visit was considered unnecessary as the patients were taking medicine from other sources and failure to follow instructions on exercising regularly. According to Tan (2009), the fear of receiving dental treatment, economic factors and indifferent behaviour on the dentist's part, higher incidences of stressful life events or insecurity in personal relationships may be reasons for patient noncompliance.

Mendoza et al. (1991) reviewed records of patients undergoing periodontal maintenance over a 3-year period and reported that the most common reason given by patients for noncompliance was that a general dental practitioner providing their periodontal treatment. Some patients also considered the treatment too expensive, whereas a significant number of patients considered that they no longer need the recommended treatment.

Fardal (2006) also reported that patients gave a variety of reasons (e.g. health reasons, lack of motivation, fear, financial reasons, own dentist providing the periodontal care, dissatisfied with the treatment, did not see the need for future treatment and a faulty recall procedure) when he interviewed noncompliant patients who returned to his practice for periodontal maintenance. The study by George et al. (2007) however, reported that the 'lack of time to attend' and not the' fear of the Dentist' was the major reason for non attendance in their study. This observation was in contrast to that cited by Fardal (2006) and Tan (2009).

Patient Education and Changing Behaviour in the Medical and Dental Environment

It is therefore evident that in order to successfully treat a patient's medical or dental condition, the clinician has to establish a good rapport and close working partnership with the patient. One of the problems historically was the often one-sided relationship between the clinician and the patient where the clinician simply gave instructions to the patient of what was expected in order for them to comply (the so-called clinician-centred approach) (see Chap. 7). For example, demonstrating a brushing technique or a flossing technique on a demonstration model will often fail to determine whether the patient could actually master a particular brushing technique or whether they have the dexterity to be able to floss their teeth. According to Freeman (1999), this failure to actively involve the patient in the treatment process essentially renders the patient as a passive listener of information which they were unable to assimilate into their day-to-day experience. This prescriptive approach failed to give the patient any opportunity to gain autonomy, motivation, competency and a readiness for change (Williams and Bray 2011). One of the problems with this traditional clinician-centred approach was that the message was often considered judgemental in nature and this subsequently meant that the patient became resistant to any prescribed recommendations for changing their lifestyle behaviour and may actually set up the patient for subsequent failure at the next appointment (Freeman 1999; Williams and Bray 2011). According to Freeman (1999), a readiness to change can provide a bridge between the clinician and the patient with respect to understanding a patient's perceived lack of motivation in order to change their lifestyle behaviour. The clinician should therefore be aware when attempting to provide information designed to change a patient's oral hygiene practices or a major lifestyle behaviour, that the patient should be involved in the process and not be an impassive observer of information that discourages him/her to assess the advantages or disadvantages of accepting or not accepting the rationale for changing the behaviour (ambivalence).

According to Partovi (2006), the patient must be motivated before the education process can take place, although motivation without compliance or adherence to a recommended procedure (e.g. changing oral hygiene practices: flossing) may lead to failure unless some form of preplanning of behavioural interventions has been discussed with the patient (Schuz et al. 2006).

Introduction to Motivational Interviewing in the Management of Dentine Hypersensitivity: A Different Approach

Definition of Motivation

Motivation has been defined as (1) the act or an instance of motivating or providing with a reason to act in a certain way, (2) the state or condition of being motivated and (3) something that motivates (inducement, incentive) (Definition of Motivation Dictionary.com 2013). One of the problems when discussing the concepts of compliance and

motivating and educating the patient is that we forget that the clinician also has to embrace these qualities. It may be possible that the characteristics that may mark out the patient, for example, lack of motivation, denial, failure to see the need (or relevancy) to change and resistance to change, may also affect the clinician. The consequence of this type of apathy will ultimately lead to disillusionment for both parties, and the opportunity to initiate the changes that would benefit the patient will be lost.

Motivational Interviewing (MI)

As indicated above, the traditional health education approaches provided by clinicians were often considered to be ineffective in changing patient behaviour. For example, in periodontal care, conventional oral hygiene instructions frequently lacked any long-term effect and therefore require continual reinforcement (Wilson et al. 1984; Demetriou et al. 1995; Schuz et al. 2006). This would infer that there may be a false assumption inherent in the health education approach itself which would tend to suggest that behaviour change was simply a function of the patient having a requisite knowledge or understanding and that all the clinician had to do was provide the relevant information.

Motivational interviewing (MI), in contrast, is based on a different assumption of human behaviour change which concluded that knowledge in itself was insufficient to bring about any behaviour change and that motivation to change was elicited "from within the patient" rather than externally imposed upon the patient by a clinician. MI has also been defined as "a client (patient)-centred, directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence" (Rollnick and Miller 1995). According to Rollnick et al. (2008), MI was initially developed as a brief intervention for problem drinking in which patient motivation was an obstacle to a change in behaviour (e.g. refrain from drinking). It soon became evident that this model would be beneficial in dealing with other health problems and subsequently MI was reported to have positive results in the management of various chronic diseases.

Motivational interviewing has also been defined as a collaborative, goal-oriented method of communication with particular attention to the language of change. It is intended to strengthen personal motivation for, and commitment to, a specific goal by eliciting and exploring an individual's own reasons for change within an atmosphere of acceptance and compassion (Andrews 2012 citing Miller and Rollnick 2009). An easier definition that may benefit someone outside the medical or dental profession would be "Motivational interviewing is a collaborative conversation to strengthen a person's own motivation for and commitment to change" (Andrews 2012). In other words the MI approach for effecting change may provide an alternative strategy for promoting lifestyle changes that are essential for improving patient outcomes (Freudenthal 2013). MI has also been described as a skilful clinical style for eliciting from patients their own good motivations for making behaviour changes in the interests of their own health (Miller and Rollnick 2002; Rollnick et al. 2008). According to these investigators, the so-called spirit of MI has been described as collaborative, evocative and honouring of patient autonomy. The use of MI in clinical practice was based on four general principles: (1) to listen with empathy in order to understand and explore the patient's own motivations; (2) to develop discrepancy between the patient's current behaviour and how they would ideally like to behave; (3) to roll with resistance, e.g. by resisting the righting reflex and (4) to empower the patient's self-efficacy, encouraging hope and optimism. A helpful acronym RULE (resist, understand, listen and empower) has been suggested by Rollnick et al. (2008) in order to remember these principles. According to Miller and Rollnick (2009), it is important for clinicians to recognise that MI is not (i) the trans-theoretical model of change (pre-contemplation, contemplation, preparation, action) (Prochaska and DiClemente 1983), (ii) a way of tricking people into doing what you want them to do, (iii) a specific technique, (iv) a decisional balance, (v) an assessment feedback, (vi) a cognitive behaviour therapy, (vii) a client-centred therapy, (viii) easy to learn, (ix) practice as usual and (x) a panacea.

Evidence for the Effectiveness of MI in Changing Behaviour in Medical and Dental Health Conditions

MI originated in the field of addictive behaviour therapy but has increasingly been applied to a wide variety of other behaviour change issues for example, tobacco use, diet and exercise (Miller 1983; Burke et al. 2004; Hettema et al. 2005). The evidence from these studies appears to be robust and generally 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 behaviour (drugs, alcohol, smoking and gambling); health behaviour such as diet and exercise; risk behaviour; and treatment engagement, retention and adherence (Burke et al. 2003, 2004; Bacon et al. 2004; Hettema et al. 2005; Rubak et al. 2005; Lundahl et al. 2010). For example, Rubak et al. (2005) reported that in brief encounters of 15 min, 64 % of studies showed an effect. Furthermore when the intervention was delivered by physicians, an effect was observed in approximately 80 % of studies suggesting that it was reasonable for clinicians who are not counselling experts to effectively deliver MI in brief encounters. Data analysed in meta-analysis studies has also demonstrated positive impacts when using MI in tobacco use cessation programmes (Butler et al. 1999; Lai et al. 2010; Lundahl et al. 2010; Wakefield et al. 2004; Borrelli et al. 2005) as well as in changing dietary behaviour (dietary intake, fat intake, carbohydrate consumption, cholesterol intake, body mass index (BMI) weight, salt intake, consumption of fruit and vegetables, alcohol reduction and exercise (Woollard et al. 1995; Mhurchu et al. 1998; Resnicow et al. 2001; Bowen et al. 2002; Richards et al. 2006).

Researchers have also investigated the impact of MI in the dental environment 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 behaviours for caries prevention (Weinstein et al. 2004, 2006). The results from this study would appear to be consistent with results from meta-analyses studies that reported MI to be efficacious for dietary change (Burke et al. 2003; Hettema et al. 2005; Lundahl et al. 2010). Other short- and long-term studies have also demonstrated a positive impact on (1) oral hygiene as measured by plaque indices, (2) gingival inflammation as assessed by gingival indices and (3) association of greater patient satisfaction with improvement in oral hygiene (Almomani et al. 2009; Jönsson et al. 2009a, b, 2010; Godard et al. 2011). A number of reviews have also indicated the potential of MI in improving dental care (Nalini and Punithavathy 2010; Gao et al. 2013) although the impact on improving periodontal health remains unclear (Brand et al. 2013; Gao et al. 2013). To date there does not appear to be any published studies on the role of MI in the management of DH although such an approach may be beneficial in changing behaviours that may lead to the initiation of the condition (Chap. 4) as well as having an impact during the management and monitoring phases of treatment (Table 10.1).

The Implementation of Motivational Interviewing over Single and Multiple Appointments in Order to Effect Changes in Behaviour in Patients with DH

The implementation of MI in the management of DH may therefore be a promising approach to help change behaviour that have been implicated in the initiation and progression of the condition. It is also important to acknowledge that when treating the condition the clinician should not lose sight of the behavioural causes of DH or the need to counsel patients on the effectiveness of treatment. This type of intervention may therefore be suitable for implementation into the management guidelines for specific patient groups with DH as proposed by Gillam et al. (2013). The question as to whether a single or multiple appointment strategy approach should be used may depend on a number of factors, for example, the extent and severity of problem, the availability of the patient, the frequency of monitoring during the maintenance phase, the readiness or willingness of the patient to engage in the consultation process and consider the advantages and disadvantages of

accepting or rejecting the recommended changes in behaviour and the motivation and subsequent adherence (compliance) to the clinician's recommendations to change behaviour. One of the problems in implementing any changes in patient behaviour in the management of DH is the busy schedule of the clinician within the clinical environment, and therefore a pragmatic approach may need to be adopted in order to not only manage the patient's discomfort but also to change behaviour to reduce or prevent future effects of DH. It is also important for the clinician to set an agreed agenda (Rollnick et al. 1999) with the patient as there may be more than one health behaviour issue that may impact on their DH. For example, incorrect toothbrushing techniques, excessive acidic food and drink in the diet or smoking may also damage both hard and soft tissues (see Chap. 4). The clinician therefore should be prepared to manage both his/her expectation as well as the patient when considering changes in behaviour. According to Bandura (1995), achieving small changes may make a patient feel more able and confident to make other changes, and as such it is important to start where the patient feels most comfortable and encourage them to suggest what area they would like to talk about, rather than simply selecting what the clinician considers as a right course of action. This may be achieved by using an agenda setting chart containing a number of circles with picture representations of the various different issues in DH and some blank circles for other factors to be inserted by the patient. The patient then selects the issue that they would like to talk about first.

According to Miller and Rollnick (2002), in order to be an effective MI practitioner, the clinician needs to embody the underlying philosophy of MI over multiple appointments rather than simply applying a collection of counselling techniques. Recently, Suvan et al. (2010) presented a specific patient activation fabric model implementing the spirit of MI into a single appointment in order to capture the interdependent elements of the dental visit using the concept of interwoven threads. This model attempts to blend communication, information exchange and the use of behavioural change tools with the clinical assessment and treatment (Fig. 10.1).

Communication with the Patient with DH

There are a number of different styles that are used in conversation with other people in everyday life. However in a clinical situation, when dealing with a patient with DH, it would be more appropriate from time to time to specifically adapt to their individual behavioural needs and to allow them to communicate their chief complaints in their own way. A three-style model for healthcare clinicians to communicate with their patients in daily practice has been recommended by Rollnick et al. (2007) which uses the following styles, e.g. directing, guiding or following style. According to Rollnick et al. (2007), some patients may require 'direction' – particularly those who have stated that they want further advice or support when considering changing healthcare behaviour. Other individuals, however may have more pressing concerns and therefore need to be 'followed' although these individuals appear to know what they need to do but have not necessarily managed to accomplish any changes to their health behaviour. These individuals should be more receptive to a 'guiding' style when considering changing their healthcare behaviour. Furthermore, four main communication skills may be used by the clinician, and these can be summarised by the acronym OARS which stands for (1) *open* (-ended) questions, (2) *affirmations*, (3) *reflective* listening and (4) *summarising* (Catley et al. 2010). It is important however for the clinician to be aware or sensitive to any changes in the patient's reaction to a particular style of communication, and it may be necessary if there is a breakdown within the communication process that the clinician uses a different style in order to maintain the rapport between both patient and clinician (Catley et al. 2010; Koerber 2010).

Giving Advice to Patients in the Clinical Environment

One of the problems that may be encountered in the clinical environment is that the clinician may attempt to provide the information regarding a

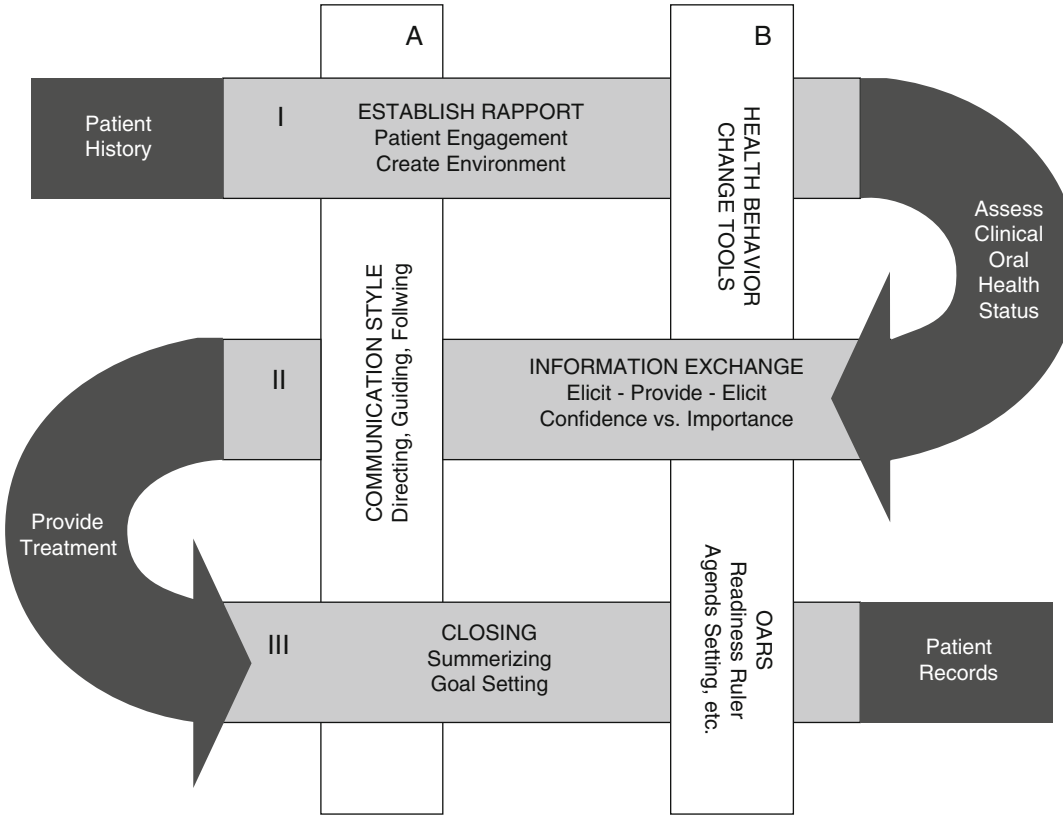

Fig. 10.1 The patient's history and patient's records positioned at the start and end depict the critical elements of documentation that serve to weave one dental visit into the next. The *horizontal bands* depict the three core strands of conversations constituting the visit. These bands labelled as "Establish Rapport", "Information Exchange" and "Closing" transition directly into the curves, representing the clinical assessment or treatment that takes place between the conversations as part of the flow of the appointment. The bands are woven together through the vertical ribbons that signify the specific elements of the communication and interaction characterising the approach. These vertical ribbons represent communication style and health behaviour change tools and are consistent, yet flexible, recurring throughout the appointment ready to provide stability. Acknowledgement: patient activation fabric for the dental visit (implementation model) (From Suvan et al. 2010)

clinical condition (e.g. dietary advice to reduce the effects of acidic drinks in association with the timing of toothbrushing) far too early in the consultation process. This may convey to the patient that the clinician has a particular agenda to pursue, and therefore the patient may feel pressurised to accept the recommendation even though they may not have been ready to accept this information at such an early stage in the consultation. It is also important to recognise in this context the difference between advice-oriented health education and MI as it may be appropriate to simply provide information to address the patient's questions, misapprehensions or lack of knowledge. It is therefore essential for the clinician (in the MI process) to provide information when the patient is willing and interested in receiving the information (the so-called advice with permission) (Moyers et al. 2003). A three-step process that may be used as a framework for providing advice in an MI-consistent style has been outlined by Rollnick et al. (1999a) as follows: (1) e*licit* the patient's readiness and interest in hearing the information, (2) p*rovide* the information in as neutral a fashion as possible and (3) e*licit* the patient's reaction to the information presented. In practice when addressing the patient's perspective of a particular clinical problem, the clinician

may actually reveal gaps in the patient's knowledge, questions and concerns and misapprehensions which in turn may lead to the patient being more willing to accept the relevant information.

As indicated above it may take a number of visits for the patient to make any significant changes in health behaviour, and the clinician must be careful not to force the pace of change; otherwise, both parties may become frustrated by the lack of change particularly with highly ambivalent patients.

It is critical for the clinician to acknowledge the problems in assessing a patient's readiness to change their behaviour as this will involve learning about both the patient's motivation and self-efficacy to change (Rollnick et al. 1999b). Several scales that assess both motivation and self-efficacy (where the clinician seeks to discover the patient's specific motivators and values) have been described which link these motivators and values to the desired behaviour change (Rollnick et al. 1999b).

Clinical Scenario Incorporating MI Principles in a Patient with DH Who Drinks Excessive Orange Juice

The following clinical scenario demonstrates the way MI may be used in conjunctive with a management strategy designed to reduce and prevent the impact of DH on a patient's day to day lifestyle by changing behaviour that may influence the aetiological causes and predisposing factors implicated in DH (Table 10.1) (see Chap. 4). As previously indicated the clinician may decide on a specific communication style depending on the individual patient and implement the various behaviour changes by judging the response of the patient during the consultation visit (Table 10.2). It may therefore be possible for the clinician to implement MI during the initial stages of the management strategy as previously outlined (see Table 10.1).

Table 10.2 Example of an individual management strategy using MI principles for a patient with DH who drinks excessive orange juice

Clinician	Patient	Strategy
Initial visit		
May I share with you some information about dentine hypersensitivity?	Yes	Ask permission/elicit
Aetiology of DH		Providing information
Treatment options		
Options to limit erosive drinks in the diet		
What do you think about all of this?	I was not aware of the effect of erosive drinks on my teeth	Elicit
From the dental examination today, it appears that you consume acid food on a regular basis	Yes, I drink orange juice a lot	
May I speak to you about your diet?	Yes	Ask permission
Do you understand that drinking juices may damage your teeth and cause you pain?	I do not care. I enjoy drinking orange juice; it is good for me	Agenda setting chart
May I ask you whether you could cease drinking orange juices?	Honestly, no. I don't want to quit even if you wanted me to	
I hear that you don't want to quit. How do you feel about talking a little bit about your habit?	No, I don't want to speak about it right now	Rolling with resistance
I hear that you don't want to speak about it right now. May I ask you again at a next visit?	That's ok	
Follow-up visit		
May I ask you to speak about your habit of drinking juices?	Well, I know that it is harmful for my teeth. But I am kind of used to it, you know. So I probably won't change	Ask permission

(continued)

Table 10.2 (continued)

Clinician	Patient	Strategy
So you kind of want to change but you can't change right now?	Well, yes, kind of	Reflection
What may be your personal advantages if you would change?	Well, I may have less sensitive teeth	Ambivalence
		Pros (and cons)
		Advantages to change?
		Disadvantages to change?
		Advantages not to change?
		Disadvantages not to change?
On a scale of 0–10 when 10 will be the highest motivation, how motivated would you be to change?	Maybe a 4	Use of a readiness scale
		Asking about motivation
On a scale of 0–10 when 10 will be the highest confidence, and how confident would you be to succeed?	I think that I am at a 3	*Asking about self-efficacy*
Well, according to the previous achievements you already made, I feel that you will succeed to change your diet after all	Thanks, it feels good to hear that	Increasing self-efficacy
Well, how could you help yourself reducing dental erosions?	Well, I might want to wait a bit before brushing my teeth again	Reflecting and summarising
	Or	
	I might take a straw when drinking my orange juice	

Conclusions

One of the problems that the busy clinician may face when managing DH is to simply prescribe or recommend a treatment without determining the aetiological and predisposing factors that may have been instrumental in initiating the problem which if not managed or corrected may continue to impact on a patient's quality of life. Traditionally clinicians expect their patients to change their health behaviour because it is good for their overall health, and any information exchanged between the clinician and patient was based on a clinician-directed philosophy which not only failed to empower the patient but was also ineffective in motivating the patient to change behaviour. It is therefore important for the clinician to adopt management strategies and goals that will effectively encourage behavioural changes in the lifestyle of their patients (Catley et al. 2010; Koerber 2010). The introduction of patient-centred approaches, for example, motivational interviewing that actively encourages the involvement of the patient in taking ownership of their oral condition, is therefore essential in current dental practice. It is acknowledged that for many clinicians in a busy practice, this approach may be difficult to implement due to a number of different constraints in the practice environment. This approach may also be very challenging for some patients, and the clinician will need to show patience and empathy with the patient during the duration of the treatment. The introduction of motivational interviewing may however be of great benefit in motivating patients with DH particularly in the early stages of management of the condition.

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11 Future Strategies for the Development of Desensitising Products

Robert Hill and David G. Gillam

Introduction and Brief Overview of the Chapter

Dentine hypersensitivity (DH) is a clinical problem that may impact on the quality of life of individuals who experience discomfort when eating and drinking hot and cold food and drink during their day to day activities. Currently there is no ideal desensitising product (over the counter [toothpaste, gel or mouthwash] or dentist applied) that provides both fast-acting and long-lasting protection against the pain associated with DH. Currently toothpaste, gels and mouthwash formulations are designed to reduce or relieve pain arising from DH based on either their (1) tubular-occluding components (e.g. silica, calcium carbonate, various apatites, oxalates or bioactive glass) or (2) nerve desensitisation properties (e.g. potassium ions) based on the hydrodynamic theory (see Chap. 2). A number of novel products have either been reformulated from existing products or developed as biomimetic materials as an alternative to the traditional desensitising products for treating DH, inhibiting caries and promoting remineralisation. The present chapter will focus attention on the physical and chemical properties of both traditional and novel products recommended for the treatment of DH as well as introducing more recent advances into the development of biomimetic products for the treatment of DH.

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The Rationale for Treatment

Although the Brännström hydrodynamic hypothesis (Brännström 1963; Brännström and Åström 1972) does not necessarily explain all aspects of the mechanism of pain associated with DH (see Chap. 2), nevertheless it does underpin the development of new product formulations and therefore forms the rationale for measuring dentine fluid flow or hydraulic conductance and tubule occlusion in the in vitro environment prior to clinical evaluation (see Chap. 6).

As previously mentioned in Chap. 2, the hypothesis is based on the concept that the parallel dentine tubules act as a capillary bore which enables fluid flow to move bidirectionally in relation to stimuli. Implicit in the mechanism of hydrodynamic fluid flow through the open dentine tubules are a number of important features contained in the Hagen–Poiseuille equation, namely, variations in pressure, the radius of the tubule, the viscosity of the fluid and the length of the tubule.

Dentine however is composed of numerous dentine tubules approximately 5,000–20,000/mm^2

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in number, and their radius and length will vary depending on the region of the dentine (mid-coronal/root dentine). Dentine tubules may therefore vary from approximately 1 to 5 μm in diameter. In the mid-coronal region of dentine which is often used for fluid flow studies, there are about 15,000 tubules/mm^2. The tubules near the dentine–enamel junction (DEJ) are generally smaller in size, approximately 2 μm, whereas the tubules nearest to the pulp may be as large as 5 μm. The tubules in root dentine close to the cervical margins of the crown-root area of the tooth where clinically DH has been reported to be more prevalent (see Chaps. 4 and 5) are generally smaller in diameter (approximately 1 μm). Ideally dentine from this area of the tooth should be utilised for in vitro studies to determine the potential of desensitising products and their ability to block the open dentine tubules. However there are a number of reasons that have traditionally precluded investigators using sections from this area of dentine, namely, the anatomy, size, number of the dentine tubules and the perceived difficulty in cutting sections from cervical dentine compared to mid-coronal sections.

As previously discussed in Chap. 2, the importance and significance of determining the effects of a desensitising product or an acid challenge based on the Hagen–Poiseuille equation may be demonstrated by the observation that an increase by a factor of two in the radius of the tubule will result in a 2^4 or 16-fold increase in the fluid flow. Conversely a reduction in fluid flow through partially occluding the dentine tubules will result in a dramatic reduction in fluid flow and dentine permeability, and it may therefore not always be necessary to have complete tubule occlusion following the application of a desensitising product. Although the dentine disc has been utilised in in vitro studies for both tubular-occluding properties and dentine permeability studies, nevertheless due to the regional variation in numbers of tubules and variations in fluid flow depending on the proximity of the tubules to the pulp, this may account for the large experimental scatter observed in the various published in vitro studies. A further observation may also be appropriate in that saliva is often absent in these in vitro studies, and therefore certain desensitising products that rely on the interaction of the saliva, for example, bioactive glass toothpaste formulations, should ideally include an immersion period in artificial saliva prior to testing in order to mimic the clinical environment. In addition it would also be of benefit to include an acid challenge post tooth brushing in order to simulate either a caries challenge or the consumption of an acidic beverage and then assess the durability of the tubule occlusion of the desensitising product. A further observation when interpreting the results from these studies is that the apparent surface coverage of the dentine following an application of a desensitising product may not actually reduce the fluid flow, whereas an apparently scarce surface coverage may actually have profound effects on fluid flow values. This observation may initially be confusing but can be explained by the example of potassium oxalate application where the tubule occlusion is not necessary on the dentine surface but rather subsurface (see Chap. 2). Similarly toothpaste formulations that occlude the dentine tubules not just at the surface but also occlude the tubules deep beneath the surface may be postulated to provide a more durable longer-lasting treatment. From a practical viewpoint, toothpaste formulations that simply cover the dentine surface without any penetration into the dentine tubules are more likely to be removed more readily either by acid dissolution or abrasive wear.

Current Approaches

The current treatment approaches in the management of DH have been addressed in Chaps. 8 and 10, and therefore the focus of the following section will be on the physical and chemical characteristics of the selected components and the significance of their inclusion into desensitising products in the management of DH.

Pro-Arginine-Based Products

Arginine is a natural amino acid and it is found in saliva. Arginine has been postulated to form a calcium–arginine complex with calcium carbonate on the tooth surface and within the dentine tubules (Kleinberg 2002; Cummins 2010). Typical commercial toothpaste formulations contain 8 % w/w arginine (Docimo et al. 2009). The chemistry of this process is poorly understood and has not been characterised in any detail. Despite this, arginine

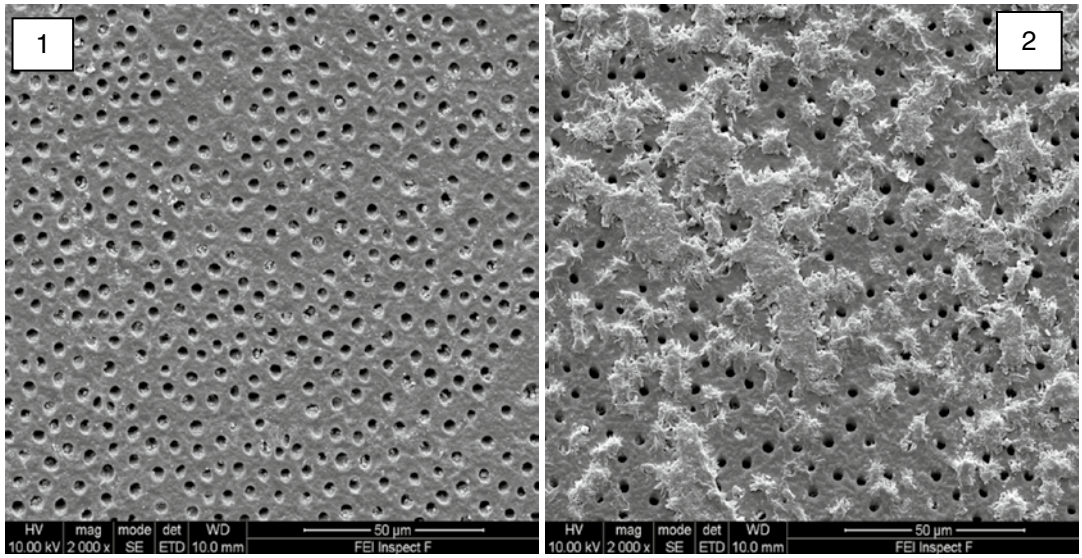


Fig. 11.1 SEM of mid-coronal dentine section before (*1*) brushing and (*2*) after brushing with Colgate ProRelief toothpaste

toothpaste formulations containing calcium carbonate particles are very effective at tubule occlusion (see Fig. 11.1). In many cases the "arginine–calcium complex" appears to form preferentially on the surface of the enamel. Arginine bicarbonate which is the most frequent form used in this toothpaste formulation is an amino acid found naturally in saliva and has adhesive properties that are attractive for occluding the dentine tubules. Arginine bicarbonate is prepared from arginine (a basic amino acid) by titrating the arginine with gaseous carbon dioxide until a pH of approximately 7 is reached. At this pH the arginine is completely converted to arginine bicarbonate; the pH is then adjusted to between 8 and 9, which facilitates complex formation and binding of the arginine to the tooth surface. The presence of a slightly soluble calcium salt, which is generally calcium carbonate, facilitates the tubule occlusion; however a variety of calcium phosphate salts can also be used (Kleinberg et al. 2003).

Strontium Salts

Strontium salts have been used in desensitising toothpaste formulations for over 50 years (Markowitz 2009) (see also Chap. 8). Originally strontium chloride was used but more recently strontium acetate at a loading of 8 % w/w has been used. The acetate form has been used to reduce the risk of strontium precipitating as strontium fluoride when a fluoride source is included in the toothpaste formulation. The main mode of action of strontium formulations (acetate/chloride) as discussed in Chap. 8 has been suggested to be by tubular occlusion (Fig. 11.2), although the actual effect attributed to strontium in clinical studies has yet to defined (Rösing et al. 2009). When applied to tooth surfaces, it is believed that an adsorption of strontium ions occurs on the odontoblastic processes or in the dentine tubules, thus blocking the transmission or neural impulses from the dentine surface to the dental pulp. The strontium ion is a normal constituent of tooth structure at trace element concentrations and has a low systemic toxicity. In fact in recent years, strontium salts have been approved for the treatment of osteoporosis where 1–2 g/day is administered. It is thought that this mechanism of strontium binding provides a mechanism to control and manage DH. It is also thought that detergents or surface-wetting agents in the toothpaste enhance the effectiveness of soluble strontium ions by facilitating the penetration of strontium ions into the tooth structure.

Another possibility is that soluble strontium ions may aid apatite formation. The strontium ion is only

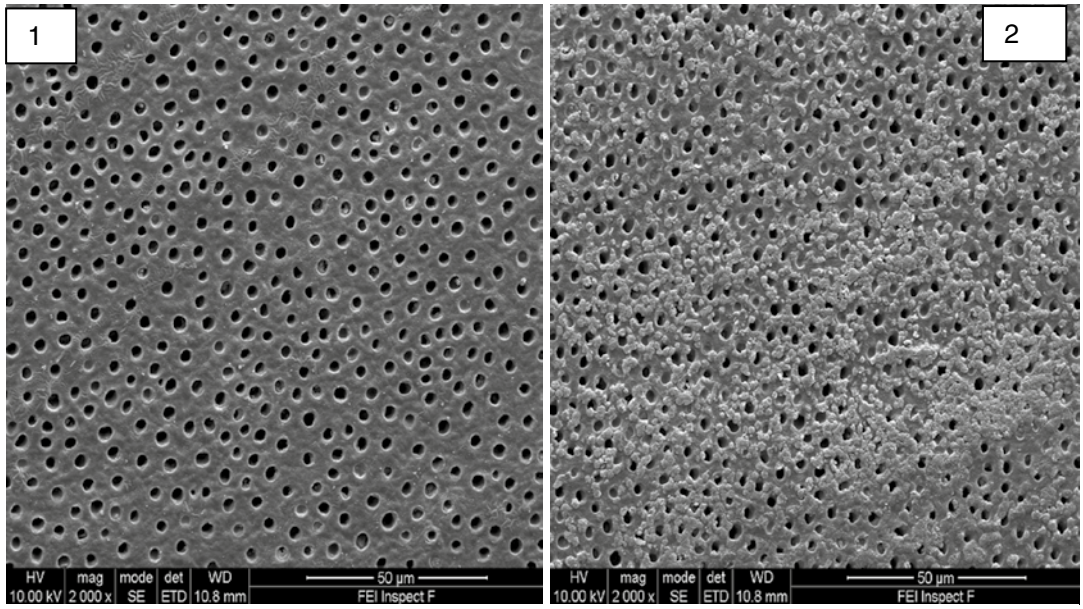


Fig. 11.2 SEM of mid-coronal dentine section (*1*) before brushing and (*2*) after brushing with Sensodyne rapid relief toothpaste

slightly larger than the calcium ion and strontium can completely replace calcium in the apatite crystal structure. It is thought that the solubility product of a mixed calcium strontium apatite may be lower than that of calcium hydroxyapatite or strontium hydroxyapatite (Pan et al. 2009; Ni et al. 2012).

Consequently soluble forms of strontium in toothpaste may cause apatite to precipitate from saliva. This may be aided by the presence of fluoride. The original strontium chloride toothpaste formulation did not contain fluoride since the fluoride was thought to initiate the precipitation of strontium fluoride (SrF_2); however this problem can be reduced by using strontium acetate as the source of strontium. However much of the initial tubule occlusion and reduction in dentine fluid flow may be due not to the strontium ion per se but rather to the presence of small silica particles added as an abrasive that are capable of entering the dentine tubules.

Hydroxyapatite

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ is the basis of the mineral phase of enamel and dentine. Enamel contains approximately 98 % by weight apatite whilst dentine contains approximately 60 % by weight. Hydroxyapatite (Ha) has been used as a remineralising additive in toothpaste formulations for many years, particularly in Asia, but only recently been used for the treatment of DH (Park et al. 2005; Kang et al. 2009; Kim et al. 2009; Yuan et al. 2012). Most Ha toothpaste formulations, however, do not contain fluoride, since Ha is promoted as an alternative remineralising addi-

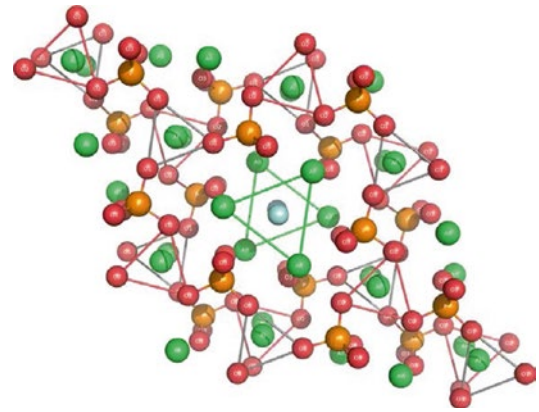


Fig. 11.3 The crystal structure of apatite. The *green spheres* represent calcium, the *orange* phosphorus and the *red* oxygen, whilst the *light blue* are hydroxyl (Acknowledgement: Figure from Powerpoint presentation by Wolfram Hoeland, Ivoclar Lichtenstein)

Table 11.1 Commercially available hydroxyapatite containing toothpaste formulations

Toothpaste I	Company	Principal active ingredients
UltraDEX recalcifying and whitening	Periproducts	Hydroxyapatite
		Sodium monofluorophosphate
BioRepair plus	BioRepair/ACDOCO	Zinc-substituted hydroxyapatite
Pepsodent ultra complete sensitive	Unilever	Hydroxyapatite
MentaDent P	Unilever	Hydroxyapatite
Megasonex	Goldspire	Hydroxyapatite
Apagard	Sangi Co	Hydroxyapatite

tive to fluoride. The apatite crystal structure is shown in Fig. 11.3.

The open nature of the crystal lattice makes it relatively easy to substitute other ions in the crystal lattice. Manufacturers in recent years have taken advantage of this feature to produce substituted hydroxyapatites. These include strontium-substituted hydroxyapatite, $Ca_{(10-X)}Sr_x(PO_4)_6(OH)_2$; zinc-substituted hydroxyapatite, $Ca_{(10-X)}Zn_x(PO_4)_6(OH)_2$; and hydroxycarbonated apatite (HCA) where carbonate ions are substituted for orthophosphate ions.

Some of these toothpaste formulations presented in Table 11.1 are currently promoted as nanohydroxyapatites (nanoHA). In these products the crystallite size is typically 20–100 nm. However the hydroxyapatite particle size is always much larger and consists of many hundreds of aggregated nanocrystals. This is shown schematically in Fig. 11.4 and in the broader diffraction lines (XRD patterns) for Enamel and a Ultradex hydroxyapatite toothpaste (Fig. 11.5). These toothpaste formulations generally contain polymers with carboxylic acid functional groups that are capable of chelating calcium ions in the apatite particles and the apatite in enamel and serve to stick the particles to the tooth surface and prevent them from being washed away by salivary flow. The fine nanoHA crystals dissolve preferentially at the expense of the enamel apatite when the pH is reduced and thus have a protective function. In order to be effective for occluding the dentine tubules, particles <5 μm are required (in the formulation) that are capable of entering the dentine tubules.

Figure 11.6 shows the particle size distribution of a nanoHA toothpaste suitable for treating DH. The shaded area indicates the particles smaller than the dentine tubule size.

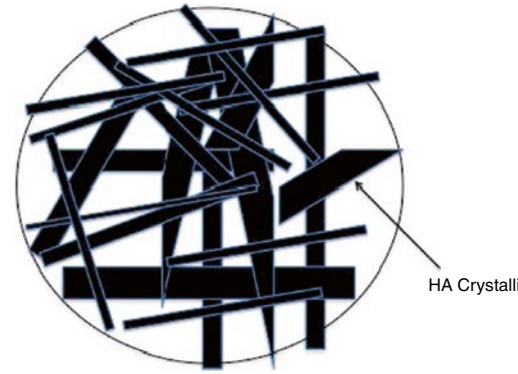


Fig. 11.4 Schematic of aggregated nanocrystals of hydroxyapatite forming a large particle

The crystallite size for nanoHA can be obtained from Scherrer's line-broadening analysis of the X-ray diffraction pattern. Crystallites larger than about 200 nm result in broadening of the diffraction lines. Figure 11.5 shows the X-ray diffraction patterns for (a) enamel, (b) a microcrystalline HA and (c) a nanoHA. The broadening of the diffraction lines is clearly seen on comparing the microcrystalline and nanocrystalline HAs. It is worth noting the similarity of the nanoHA diffraction pattern with that of enamel.

$$D = 0.9\lambda / (\beta_{002} \cos\theta)$$

where D is the crystallite size in nm, λ is the wavelength of the incident X-rays (0.154 nm), β_{002} is the width at half height of the 002 reflection and cos θ is the cosine of the X-ray incident angle.

Most nanoHA containing toothpaste formulations do not contain a source of fluoride. However incorporation of fluoride is considered to be beneficial. For example following the acid dissolution

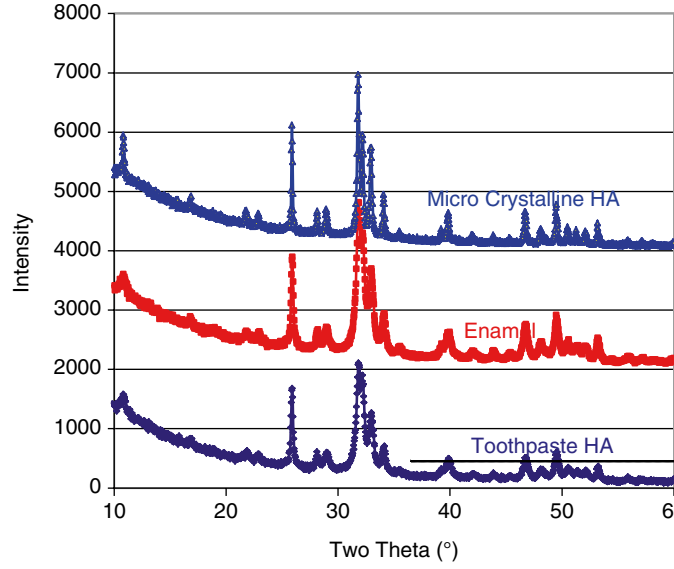


Fig. 11.5 XRD patterns for a microcrystalline hydroxyapatite, Enamel and Ultradex. Note the broader diffraction lines for Enamel and the Ultradex hydroxyapatite indicating nanocrystals. Note the almost identical diffraction patterns for Ultradex and Enamel

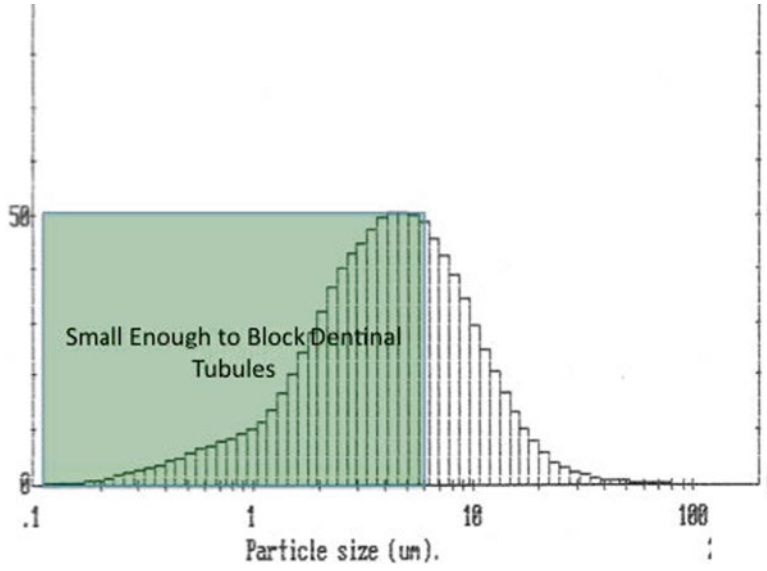


Fig. 11.6 Ultradex hydroxyapatite particle size distribution

of the nanoHA particles in the presence of fluoride these particles are reprecipitated as a fluoridated apatite. This reprecipitation process probably aids both remineralisation and tubule occlusion.

Figure 11.7 shows the 19F MAS-NMR spectra of a tooth demineralised at the surface and subsequently treated with a nanoHA toothpaste (with 1,000 ppm fluoride) under acidic conditions. (0.1 M acetic acid pH=4.5). There is no significant fluoride in the tooth before treating and after demineralisation. However after treating with the Ha toothpaste with fluoride, the ^{19}F spectrum shows a peak at −103 ppm, corresponding to the formation of fluorapatite (FAP).

In addition to Ha containing toothpaste formulations, there is also one oral rinse that contains both nanoHA and fluoride. Figure 11.8 shows

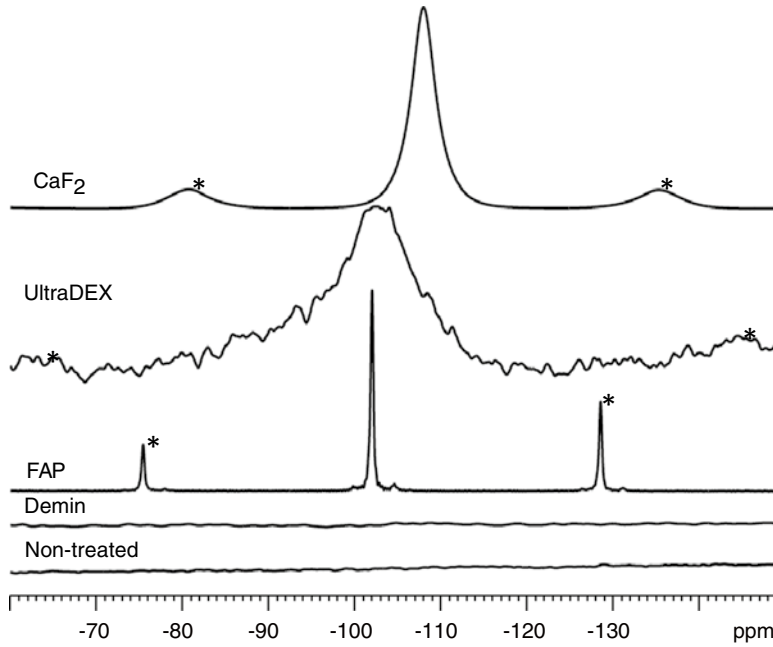


Fig. 11.7 ^{19}F MAS-NMR spectra for the enamel samples (non-treated, demineralised and nHA oral rinse treated)

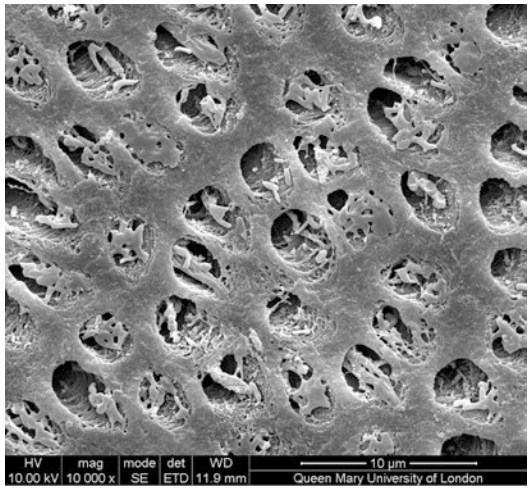


Fig. 11.8 Occlusion of dentine tubules following exposure to a nanoHA oral rinse

the tubule occlusion that occurred following a series of demineralisation-remineralisation and oral rinse cycles with a nanoHA mouthrinse. The tubules which were initially open in this etched mid-coronal section are partially occluded by needle-like crystals of fluoridated apatite.

Table 11.2 45S5 glass composition in mole percent

SiO_2	P_2O_5	CaO	Na_2O	NC
46.10	2.50	26.90	24.4	2.10

Calcium Phospho-silicate (NovaMin®)

NovaMin®, which is based on the 45S5 bioactive glass composition (Table 11.2), has been used successfully in toothpaste formulations as a remineralising additive and for treating DH (see Chap. 8). The 45S5 glass particles dissolve in the mouth releasing Ca^{2+} and PO_4^{3-} ions and are thought to form hydroxycarbonated apatite (HCA) on the tooth surface.

It is worth pointing out that the 45S5 composition (see Table 11.2) was designed as a bone substitute and was never designed or intended for use originally as an additive for the treatment of DH in a toothpaste formulation.

In a NovaMin® toothpaste, some of the bioactive glass particles are small enough (<5 µm) to enter the dentine tubules and occlude them (Fig. 11.9). In the presence of saliva, which is a supersaturated calcium phosphate solution, the bioactive glass particles dissolve releasing Ca^{2+}

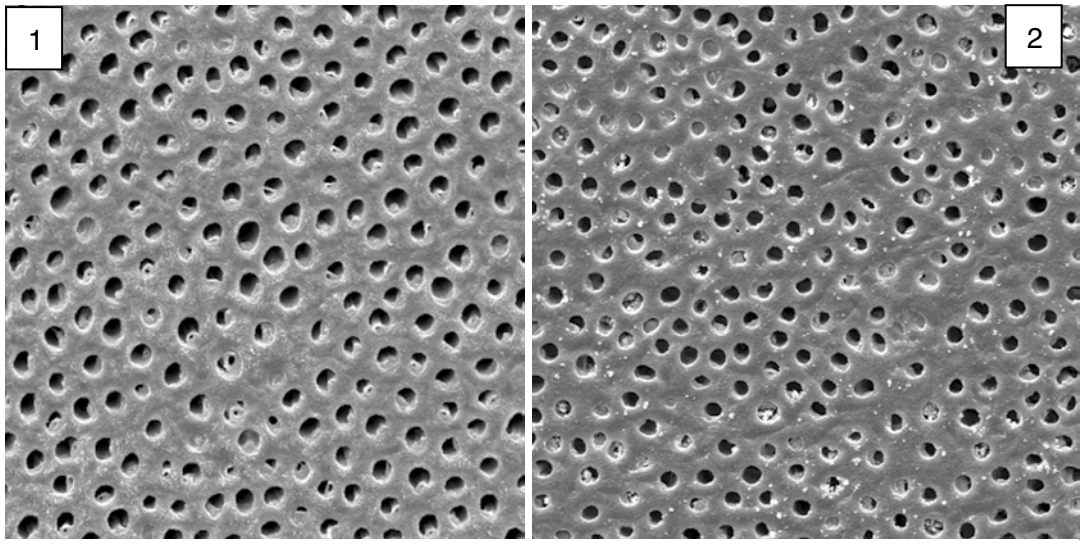
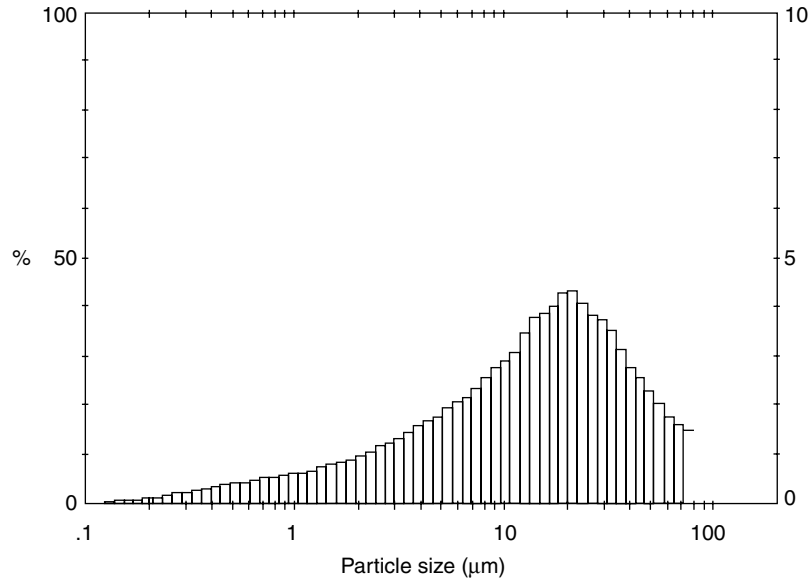


Fig. 11.9 SEM of the open dentine tubules from a mid-coronal section (*1*) before and (*2*) after brushing with a bioactive glass toothpaste

Fig. 11.10 Particle size distribution of NovaMin



and PO_4^{3-} ions, which is believed to result in the formation of HCA (Jones 2013). The NovaMin® particle size distribution is broad and shown in Fig. 11.10. Particles smaller than about 5 µm can occlude the dentine tubules, whilst the larger particles in the distribution take much longer to dissolve and provide longer-term release of Ca^{2+} and PO_4^{3-} ions.

NovaMin® toothpaste formulations are similar to the HA toothpaste formulations and contain a carboxyl functional polymer to provide the required viscosity to the toothpaste. However the polymer also plays an important role in chelating calcium ions in apatite and calcium ions in the NovaMin® glass and acts to promote the adhesion of the glass particles to the tooth and prevents the

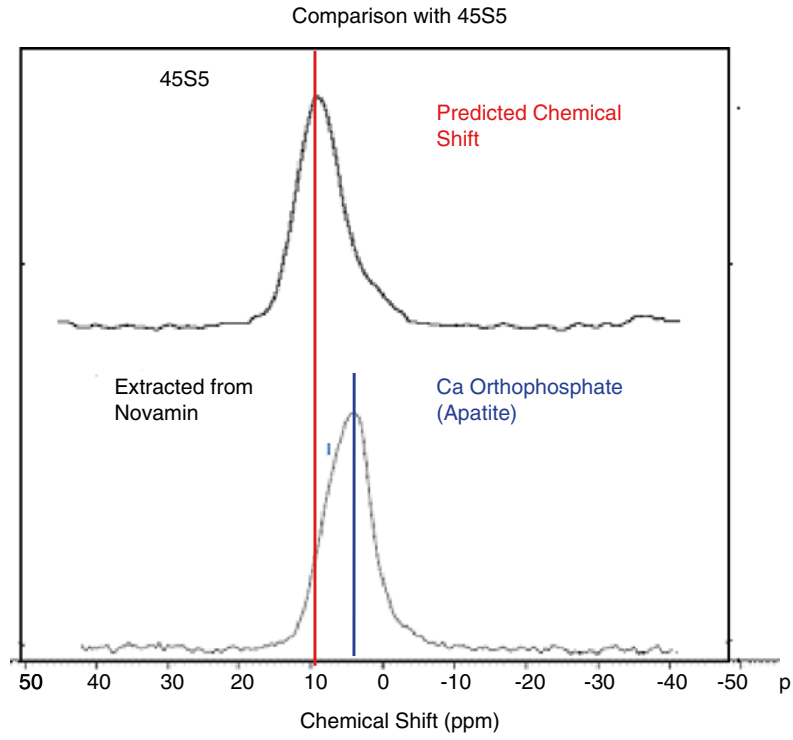


Fig. 11.11 ^{31}P ssNMR spectra of 45S% glass and glass extracted from NovaMin® toothpaste

particles from being washed away by salivary flow. In most cases the polymer used is poly(acrylic acid) which is the same polymer used in glass ionomer cements and which enables them to bond to the apatite phase of enamel and dentine.

The NovaMin® toothpaste formulations are glycerol rather than water based, and this is to prevent the glass reacting with water during storage in the toothpaste tube before use. In the early NovaMin® toothpaste formulations, the 45S5 glass reacted with small amounts of water in the glycerol during storage. Approximately 50 % of the phosphate content of the glass can convert to HCA in the toothpaste during storage. ^{31}P solid-state nuclear magnetic resonance spectra for the glass extracted from the toothpaste and the 45S5 glass synthesised in the laboratory are shown in Fig. 11.11.

The latest test versions of NovaMin® toothpaste formulations contain a fine particulate silica gel to preferentially absorb any water in the toothpaste, thereby preventing it from reacting with the bioactive glass.

There is increasing evidence that bioactive glasses preferentially form an apatite-like material both on the tooth surface and within the dentine tubules. The apatite-like material grows preferentially on the highly mineralised peritubular dentine on the inside of the dentine tubule. It is postulated that the HCA in the peritubular dentine preferentially nucleates apatite crystals. Bioactive glasses have also been shown to remineralise demineralised dentine (Mneimne et al. 2014; Mneimne 2014) (Figs. 11.12, 11.13 and 11.14).

There is also increasing evidence that bioactive glasses dissolve more rapidly and also form apatite more rapidly at acidic pHs associated with caries rather than at pH = 7 or higher. This feature is particularly attractive as bioactive glasses will act to mitigate the pH fall during a caries or acid erosion challenge and will simultaneously release Ca^{2+} and PO_4^{3-} ions. In this sense bioactive glasses are considered to be smart materials that respond to their environment.

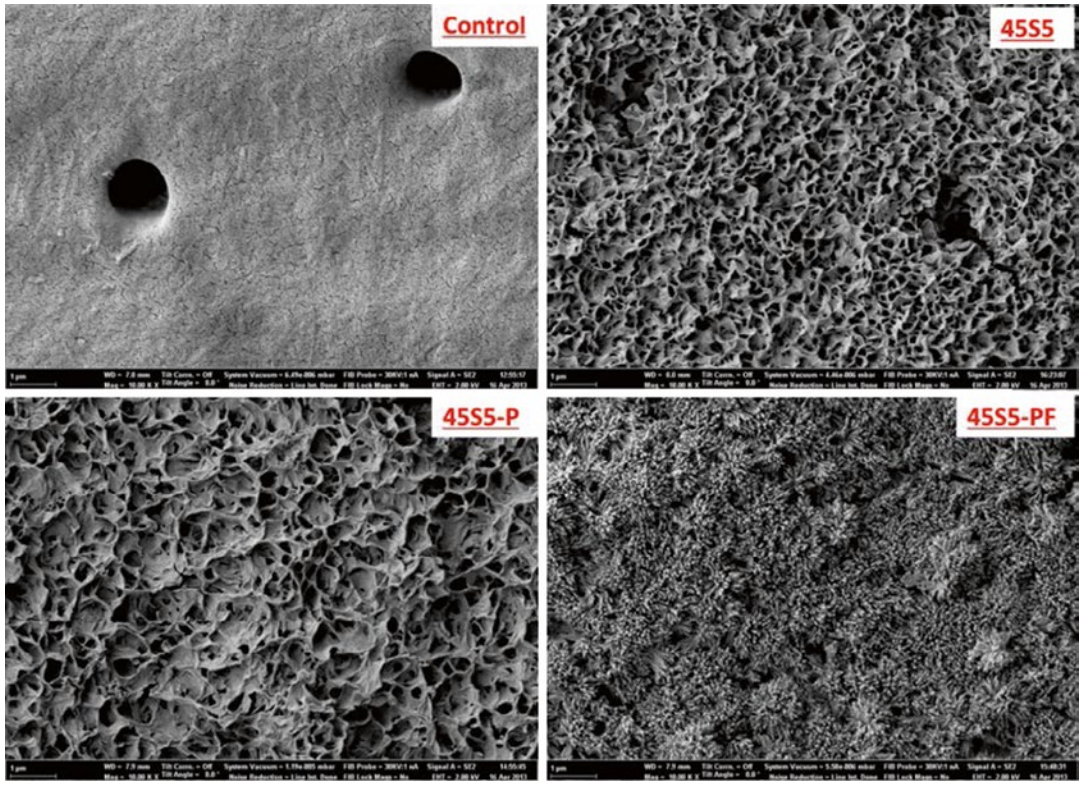


Fig. 11.12 Dentine surfaces treated with different bioactive glass toothpaste formulations. (**a**) Control, (**b**) 45S5, (**c**) 45S5-P, (**d**) 45S5-PF

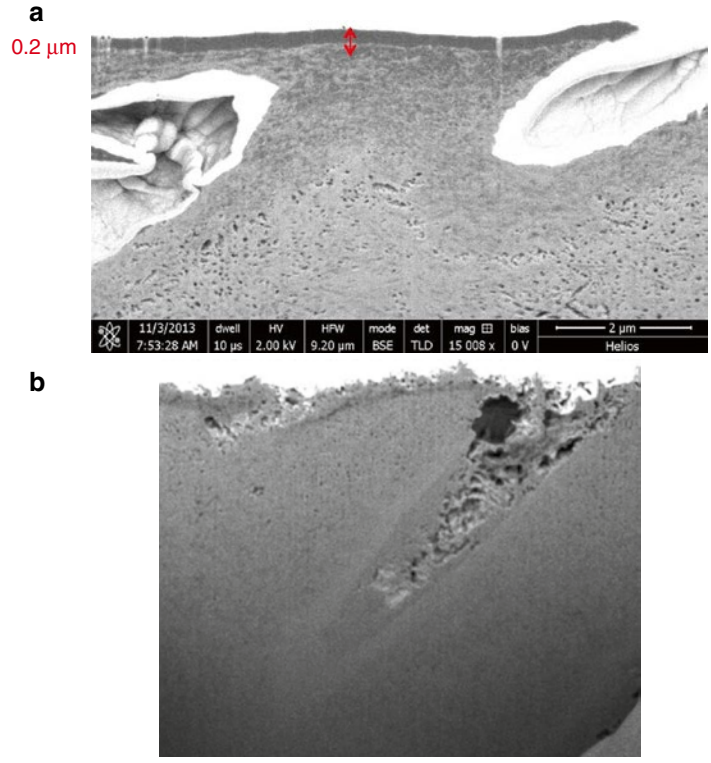


Fig. 11.13 FIB-SEM images of a dentine cross section showing the remineralisation of etched dentine surfaces following application of a bioactive glass and immersion in artificial saliva. (**a**) Control section, the arrows depict the demineralised layer. (**b**) Bioactive glass treated section

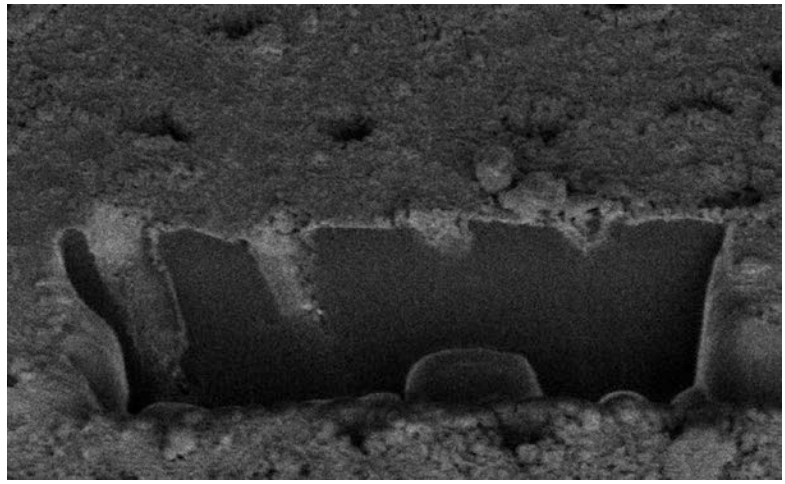


Fig. 11.14 Focused ion beam scanning electron micrograph (FIB-SEM) showing tubule occlusion following the application of a bioactive glass toothpaste

Self-Assembly Peptides

The self-assembly of biological macromolecules is widespread in nature. Examples include the spontaneous folding of proteins and the formation of a double helix from two strands of DNA. Molecular self-assembly enables production on the nanometre scale and is a form of nanotechnology and therefore may have potential for a number of applications in dentistry. Biological mineralisation and especially odontogenesis involves biological self-assembly of proteins prior to mineralisation.

Enamel formation, for example, occurs via the 3D self-assembly of amelogenin which then acts as a nucleating template for apatite crystal formation. There is therefore enormous scope for self-assembling proteins that promote mineralisation.

A self-assembling peptide system was recently introduced as a non-invasive treatment for early-stage dental caries (Kirkham et al. 2007; Brunton et al. 2013). The self-assembling peptides diffuse into the subsurface micropores and form a 3D scaffold, mimicking the proteins' function during tooth development to support apatite crystallisation and reverse early tooth decay (Fig. 11.15).

The peptide P11-4 (Ace-Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Gln-Gln-NH2) can self-assemble into a matrix, triggering a biomimetic mineralisation and repair mechanism. The glutamic acid residues on the surface act as nucleation sites for apatite formation and result in remineralisation of the lesion. The process of self-assembly is however quite sensitive to pH and ionic strength. Within the carious lesion, the pH and ionic strength favour the self-assembly process.

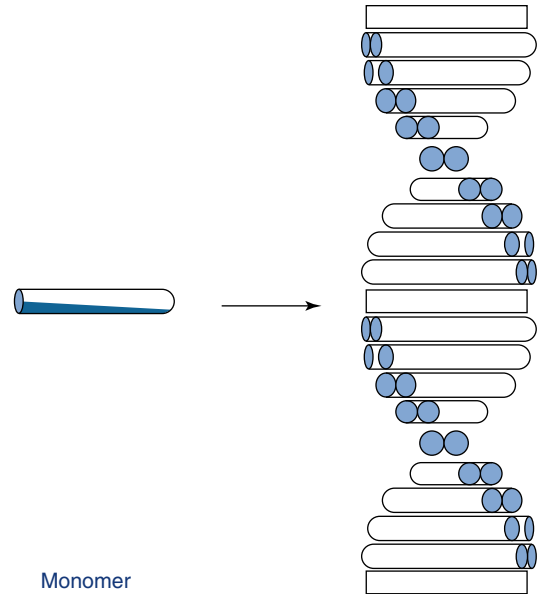


Fig. 11.15 Schematic of the self-assembling process

Recently the first self-assembled peptide product for DH has been launched, called Curodont DeSenz®. This product is thought to use the same peptide as used in the remineralisation and repair of carious lesion, but because the conditions for self-assembly of the peptide at

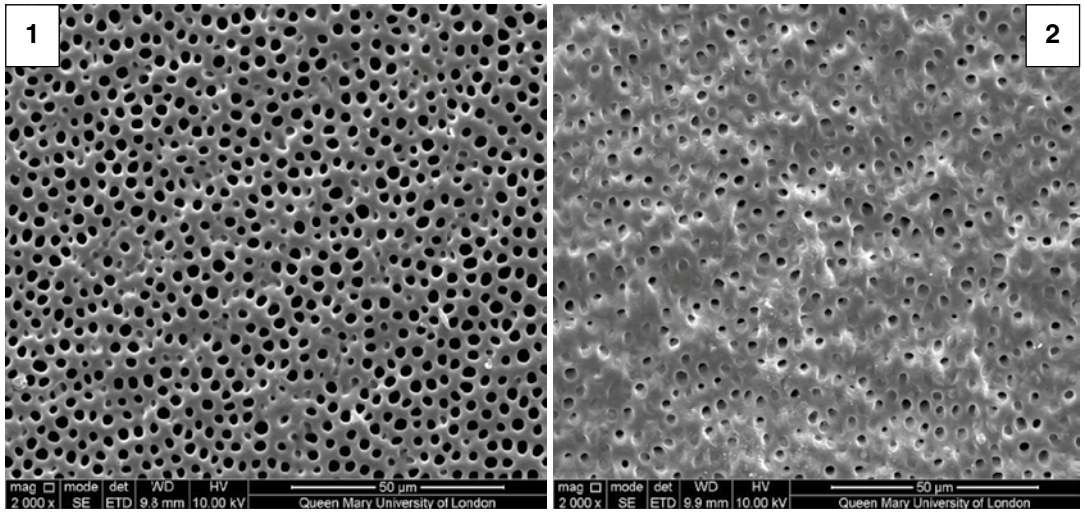


Fig. 11.16 SEM of etched mid-coronal dentine (*1*) before and (*2*) after treatment with Curodont DeSenz®

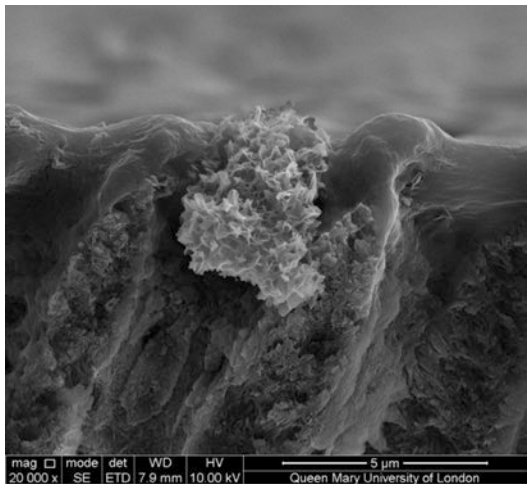


Fig. 11.17 SEM showing a remineralised Curodont DeSenz® particle occluding a dentine tubule following immersion in artificial saliva

the tooth surface and within the dentine tubules may not be ideal, the current product uses pre-self-assembled particles.

However it may be possible that following treatment with the self-assembled peptide, the majority of tubules are occluded as there was a corresponding 64 % reduction in hydraulic conductance following the application of Curodont DeSenz® on to the dentine section (Fig. 11.16) (Chen et al. 2014).

Figure 11.17 shows a SEM cross section as opposed to a top-down view of a self-assembled peptide particle occluding a dentine tubule following immersion in artificial saliva. The particle contains numerous plate-like crystals with a Ca:P ratio close to the apatite stoichiometry which indicates the self-assembled peptide particle is providing a surface for the preferential nucleation of apatite.

Future Innovations

There are relative few options for improving on the existing desensitising products, for example, arginine, strontium and Ha toothpaste formulations, as these are fairly well-established technologies. However there is considerable potential for improving on the existing calcium phosphosilicate or bioactive glass toothpaste formulations. This is largely a result of the bioactive glass that is currently used having been developed and optimised as a bone substitute.

Consideration of the Ideal Design Criteria for a Desensitising Product Including Toothpaste Formulations

Both Grossman (1935) and Gillam (1997) previously attempted to provide recommendations for

Table 11.3 Recommendations for an ideal desensitising product based on a calcium phospho-silicate or bioactive glass toothpaste

Rapid apatite formation (<6 h) in the mouth
Rapid apatite formation (<6 h) in the mouth
Formation of FAp rather than HCA
Particle size distribution that includes small <3 μm particles for entering the dentine tubules that give rise to tubule occlusion and larger particles for more sustained release
Strontium for its caries inhibition and remineralising potential as well as for its possibility of binding to the odontoblast surface
Fluoride releasing
Potassium releasing to reduce nerve sensation
pH rise <8.0
No harder than enamel at 3.5 GPa
Inexpensive to produce (note that strontium compounds are expensive)

an ideal desensitising product from a clinical perspective; however it is clear from the literature that there does not appear to be an ideal desensitising product that is suitable for every clinical actuality (Gillam et al. 2013). However it may be possible to consider this from a physical/chemical viewpoint and the following example is based on the design criteria for a calcium phospho-silicate or bioactive glass toothpaste for treating DH (Table 11.3).

The Development of Improved Calcium Phospho-silicate Toothpaste Formulations

Although the 45S5 or NovaMin® performs remarkably well as an additive for toothpaste formulations and has been reported to be clinically effective, it was however never designed for this purpose. There is therefore enormous scope for designing improved glass compositions for the treatment of DH. For example, the current NovaMin® toothpaste has several major drawbacks:

(i) The apatite formed is generally thought to be a HCA. HCA is however more soluble than HA; consequently the HCA formed will not be particularly resistant to acids in the mouth. A fluorapatite (FAP) formation would therefore be more durable.

(ii) The 45S5 glass has a hardness of about 4.7 GPa compared to enamel at about 3.5 GPa. In terms of abrasive wear during tooth brushing, it would be desirable to have a glass that is similar to the hardness values of natural enamel in order to minimise the loss of enamel.

The 45S5 glass is however too hard for a DH toothpaste where a softer dentine surface may be (1) exposed and (2) where the enamel is thinner (as in the cervical region), and therefore it is desirable to have a very low-abrasivity toothpaste. The move in development in recent years has been towards toothpaste formulations with lower abrasivity although NovaMin®-based toothpaste formulations are almost certainly abrasive to some degree, and therefore it would be desirable to produce a glass that was softer and ideally no harder than enamel (3.7 GPa).

(iii) The NovaMin® glass generates a high pH upon dissolution. This was considered to be a major concern, but it is now considered that saliva effectively buffers the pH rise. However, whereas a high pH is desirable for hydroxyapatite formation and was considered necessary by some researchers for glass degradation, via the alkaline hydrolysis of Si-O-Si bonds of the glass network, pHs >8.0 are still considered excessive. Furthermore even where there is an insignificant global pH rise, localised pH rises could theoretically still occur.

(iv) It would be desirable that a remineralising glass for treating DH to have an additional bactericidal feature. Although this was claimed for NovaMin® toothpaste, one view is that this was largely a result of the pH rise. Therefore there is probably no inherent bactericidal action of NovaMin® other than through a pH rise. If the pH rises sufficiently in order to kill or inactivate the bacteria, it may also have an adverse effect on the oral soft tissues. Assuming NovaMin® is effectively buffered by oral fluids, then there would be no significant bactericidal action.

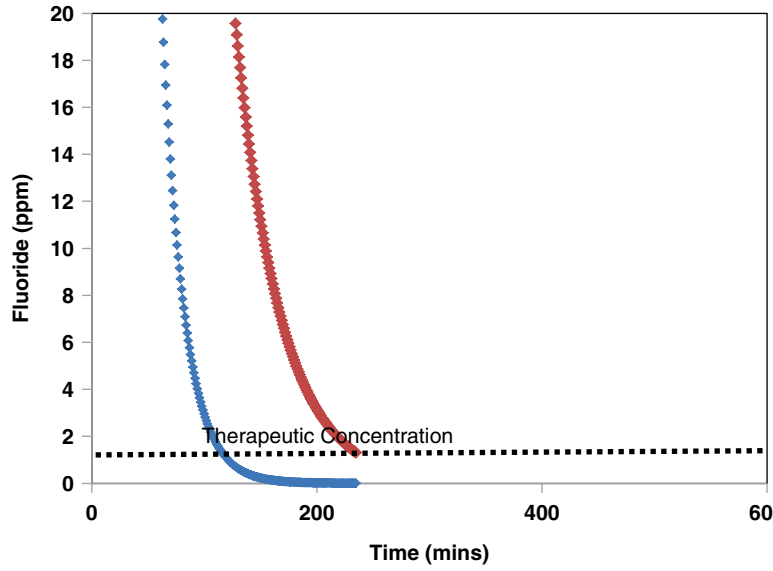


Fig. 11.18 Calculated salivary fluoride concentrations in saliva following brushing with a 1,450 ppm fluoride toothpaste (*blue*) and a 5,000 ppm prescription toothpaste (*red*)

(v) It is desirable that a toothpaste has some anti-caries activity, for example, by delivering fluoride ions or strontium ions as NovaMin® by itself appears to lack this feature.

(vi) It would be desirable if the glass acted to reduce nerve transmission in order to deal with the scenario where there was ineffective blocking of the dentine tubules.

(vii) Apatite formation and blocking of the dentine tubules may however take several weeks (in the in vivo environment) with NovaMin®. Patients are looking for an immediate relief of DH and pain. A toothpaste that acts more quickly to block the dentine tubules is likely therefore to provide more noticeable benefits to the individual, and this may equate to a greater uptake in toothpaste formulations for DH.

All these deficiencies of NovaMin® can be overcome by designing new bioactive glass compositions specifically tailored for dental applications.

For example, these compositions may include the following:

(i) Fluoride-containing bioactive glasses that form fluorapatite, as well as releasing fluoride over the time between tooth brushing. Fluoride is thought to knock out octacalcium phosphate (OCP) formation and favours direct formation of apatite even at concentrations as low as 0.05 ppm. The solubility product of FAP is lower than that of HAP so its formation occurs more readily and at a lower pH. The ability to release fluoride in addition to Ca^{2+} and PO_4^{3-} ions is particularly attractive. Conventional fluoride-containing toothpaste formulations use soluble sources of fluoride, which are eluted away fairly rapidly by the salivary flow in the mouth. Figure 11.18 shows the calculated concentrations of fluoride in saliva following brushing with selected toothpaste formulations containing different concentrations of a water-soluble fluoride. The calculations have been performed assuming a salivary flow of 2.5 ml. min^{-1} and a salivary volume of 2.5 ml, and at time zero (immediately after brushing), the actual fluoride concentration was one tenth of the original concentration in the toothpaste. These calculated figures are in agreement with the figures quoted in the published studies with the limited published studies. The fluoride concentration falls exponentially with time (for a 1,450 ppm fluoride toothpaste) below the level required to inhibit caries (approximately 1 ppm) in under 2 h. In contrast a fluoride-containing bioactive glass dissolves slowly, releasing a

controlled level of fluoride above the minimum effective dose, and can maintain this concentration for longer than the time between tooth brushing (12 h).

(ii) Compositions that release bactericidal elements, for example, zinc, and also release zinc preferentially when subjected to an acidic or cariogenic challenge.

(iii) High-phosphate-content bioactive glasses that result in a reduced pH rise and more rapid apatite formation.

(iv) Nerve-desensitising compositions where sodium is fully or partially replaced by potassium in the glass composition.

(v) Glass compositions that contain chloride that dissolve faster and are softer and less abrasive towards tooth enamel.

Improvements in the Science and Technology of the Development of Toothpaste Formulations and How Drawbacks in Current Toothpaste Formulations May Be Overcome

If we use the example of a NovaMin® toothpaste, then we can consider the above-mentioned criteria in turn remembering that many of these points are interrelated. For example, if we recognise that HCA is more resistant to acid dissolution than OCP (that is also proposed to form with calcium phospho-silicate) and FAp is even more acid resistant, how can we favour the formation of FAp at the expense of HCA or OCP?

Strontium exhibits complete solid substitution in all apatites but cannot however substitute fully into OCP. Octastrontium phosphate does not exist. It is likely that some strontium can substitute for calcium and possibly up to 25 % of the calcium. It may be that more strontium than this destabilises OCP and favours HCA. A mixed calcium/strontium hydroxyapatite with about 9:1 ratio has a lower solubility product than CaHA or SrHA. Replacing strontium for calcium in the glass will therefore both favour HCA formation and destabilise OCP formation. Furthermore strontium surprisingly expands the glass network and results in faster glass dissolution, which also speeds up HCA formation. The downside to strontium incorporation into the glass is that the faster glass dissolution also results in a more rapid and undesirable pH rise. Strontium also has the disadvantage that the more expanded, more weakly bonded glass structure is more prone to crystallisation.

Given that FAp is more acid resistant than hydroxyapatite and HCA, it would be desirable to form FAp.

There are two routes to achieving this:

(i) Soluble fluoride salts can be incorporated into the formulation along with the glass.

(ii) Fluorine can be incorporated into the glass structure.

Option (i) fluoride could be added as sodium fluoride or sodium monofluorophosphate. Of these two species, the latter is the more attractive option, since simply adding a source of fluoride ions alone is more likely to result in fluorite formation. Body fluids and saliva at rest have a Ca:P ratio of approximately 2.6 compared to the apatite stoichiometry of 1.67. Once the phosphate in saliva has been consumed, excess fluoride will form calcium fluoride, whose formation is undesirable. High fluoride concentrations in the saliva may also lead to direct fluorite formation. Using sodium monofluorophosphate in the formulation will add to the phosphate concentration and will therefore help mitigate against these problems.

Option (ii) however is a much better strategy. For example, incorporating a soluble fluoride into the formulation results in an initially very high fluoride concentration in saliva which is needed because we require a reasonable high fluoride concentration many hours after tooth brushing and as a result of salivary exchange (probably about every 1–5 min. during the day), but salivary flow and salivary volumes are very variable depending on the individual. However, there will be a virtually exponential decay in the fluoride concentration. The high concentration initially is undesirable and may lead to fluorite formation. What is required is a constant but relatively low fluoride concentration in the mouth, which can be achieved by using a fluoride-containing glass in particulate form that sticks to the teeth and gingivae slowly releasing fluoride along with calcium and phosphate in ratios that favour FAp formation and preferably with a slight excess

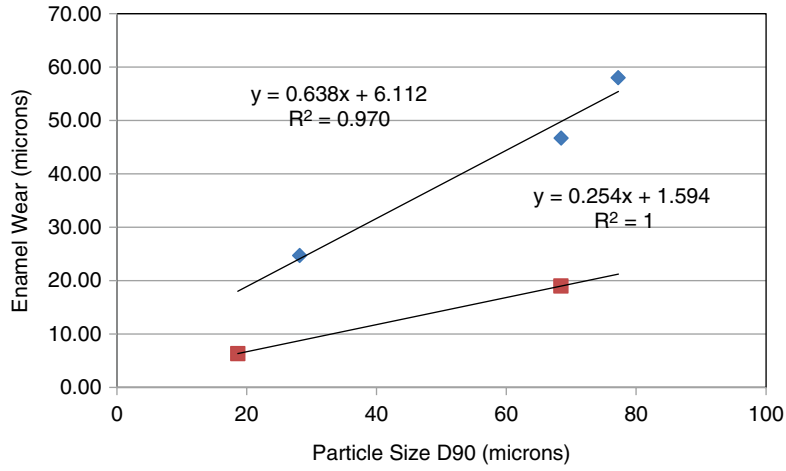


Fig. 11.19 Enamel wear of 45S5 bioactive glass containing toothpaste formulations as a function of D90 particle size. The red squares are round ball-milled samples and the blue points are percussion-milled samples that give rise to more angular particles (Mahmood et al. 2014)

of fluoride since calcium and phosphate will also be supplied from the saliva. Recognising that body fluids/saliva has a Ca:P ratio of about 2.6 compared to 1.67 for apatite, it is probably more important that the glass delivers phosphate than Ca. The existing NovaMin® has a Ca:P ratio of close to 5 and thus releases more Ca than phosphorus.

Increasing the phosphate content of bioactive glasses (providing this is completed in the correct manner, e.g. keeping the network connectivity (NC) of the glass close to two which is not necessarily obvious) results in (1) faster apatite formation and (2) an increase in apatite formation.

Reducing the Abrasivity of the Toothpaste

The finer the particle size and the less angular the particle, the less abrasive the glass will be. The analogy here is of glass/sandpaper. The harder the glass is, the more abrasive it will be.

Reducing the particle size reduces the abrasive wear, but this would knock out the long-term release of ions from the glass that would be probably undesirable. Though it would be possible to blend two or more glasses, for example, a small particle size less soluble glass with a particle size <45 μm, with a more soluble glass with a particle size <45 μm to give the same release kinetics as a single glass with a particle size <90 μm (the size range of NovaMin®). Having a particle size <50 μm would also remove the "gritty texture" of the existing NovaMin® toothpaste and would therefore result in a better tactile sensation to the toothpaste, e.g. a smoother feel rather than a gritty feel as with existing NovaMin® toothpaste formulations (Fig. 11.19).

The grinding route will also influence particle shape and vibratory milling gives sharp angular particles, whilst ball milling gives rounded particles. Rounded particles should give less abrasive wear. Particle shape can be altered by post-grinding treatments; for example, dropping the particles through a high-temperature furnace at a temperature above glass transition temperature (Tg) or through a plasma torch will result in the glass particles minimising their surface energy by forming perfect spheres. However these treatments would add to the cost of production. It is also important to note that such treatments post grinding will reduce the surface area and will relax strains in the glass particle surface that have a significant influence on glass reactivity. Strained bonds put the glass into a more reactive state.

A simpler option and a less expensive option would be to reduce the hardness of the glass so that it is closer to the hardness of enamel. The hardness of glasses is related to the strength of bonding in the glass structure. There are very few published hardness values in the published literature for low NC bioactive-type glasses. However there is a strong linear correlation between the glass

transition temperature and hardness (Farooq et al. 2013). The more disrupted the glass, the lower the Tg and the lower the hardness. Tg reduces with:

(i) Increasing alkali metal content.
(ii) Moving down a group in the periodic table. Potassium-containing glasses are softer than the equivalent sodium-containing glasses. Replacing strontium for calcium results in slightly lower Tgs and hardness values.
(iii) Mixing alkali metals.
(iv) Reducing SiO_2 content.
(v) Increasing P_2O_5 content.
(vi) Increasing fluorine content.

Of these (i) and (vi) give large reductions in Tg. Alkali metal content however cannot be increased very much without risking the glass crystallising. Replacing sodium for potassium does not change the glass dissolution kinetics significantly and having a little sodium, for example, a mixed glass, gives a further slight reduction. Incorporation of potassium is also valuable for giving potassium ion release for eliminating the pain associated with DH and therefore may be worth pursuing.

Incorporation of fluoride drops the Tg dramatically, as well as resulting in faster and quicker apatite formation, formation of apatite at a lower pH and formation of FAP and fluoride release.

The correlation between Tg and hardness for bioactive glasses must be regarded as a guide because it is (i) an extrapolation into an area outside the normal compositional range, i.e. lower SiO_2 content, and (ii) bioactive glasses may have two glass transition temperatures; the first is thought to correspond to the silicate glass phase and the second to the orthophosphate phase. In the case of very rapidly quenched glasses, the phase separation process may be suppressed and the scale of phase separation may be exceedingly small, and the first glass transition may be a combined glass transition temperature. As the glass is heated past the first Tg, it may well phase separate, further resulting in a second Tg. In the case of the 45S5 composition, the second Tg is not apparent because it is masked by crystallisation. Since the first Tg probably corresponds to the silicate matrix glass phase, it would be expected to dominate the hardness.

Reducing the pH Rise in the Oral Environment

The pH rise can be reduced by reducing the alkali metal content, but this will result in a harder, more abrasive glass. Increasing the phosphate content reduces the pH rise significantly as does increasing the fluorite content. Phosphate content has the most significant effect. The phosphate in bioactive glasses is probably present as a separate nano-sized phase and as an amorphous orthophosphate. The phosphate phase is dispersed in the silicate phase. Phosphate glasses when they dissolve give an acidic pH and silicate glasses a basic pH. By adjusting the volume fraction of the phosphate phase relative to the silicate phase, the pH rise can be manipulated. Again care has to be taken to put in additional phosphate without altering the degradable silicate matrix glass composition.

Providing a Real Bactericidal Action in a Toothpaste Formulation

Strontium has a mild bactericidal action against many of the bacteria involved in caries (Guida et al. 2003) Fluoride has also a bactericidal action at acidic pHs (Malts and Emilson 1982).

Caries Inhibitory Properties

Fluoride has well-documented caries inhibitory properties. Strontium also has been associated with a caries inhibitory role and together their action is supposedly synergistic. Caution has however to be exercised with fluoride – more is not always better. Excess is more likely to result in CaF_2 formation or even SrF_2 or mixed Ca/SrF_2 where strontium is present. It is also important to note that whereas FAp is more stable than hydroxyapatite to acid dissolution, there can be no hydrogen bonding along the c-axis channel in pure FAp, and it has been argued that a mixed 50/50 fluoro/hydroxyapatite will be more stable because of hydrogen bonding between fluorine and the hydrogen of the hydroxyl group (Elliott

1994). There may therefore be an optimum fluoride content in the apatite corresponding to a fluoride content less than the stoichiometric amount.

Not only can bioactive glasses prevent caries, but they may also prevent acid erosion. Bioactive glasses can also promote remineralisation in carious lesions or acid erosion lesions, and the evidence indicates that high phosphate- and fluoride-containing glasses can do this more effectively than the conventional low-phosphate glass (Mneimne 2014).

A very useful feature of bioactive glasses is their ability to dissolve more rapidly under acidic conditions. Since the first step in glass degradation of bioactive glasses is the ion exchange of Na^+ and Ca^{2+} ions for H^+ ions, a lower pH accelerates glass dissolution and the release of Ca^{2+} and PO_4^{3-} ions for remineralisation. In a practical sense, bioactive glasses are "smart materials" and respond to their chemical environment. The pH sensitivity of bioactive glasses can be enhanced further by incorporating zinc oxide into the glass. Zinc is incorporated into the glass structure as an intermediate oxide forming ZnO_4 tetrahedra and forming Zn-O-Si bonds. These bonds can be acid hydrolysed in a similar fashion to the Al-O-Si bonds in glass (ionomer) polyalkenoate cements where Al_2O_3 also acts as an intermediate oxide.

Blocking Nerve Transmission

Replacing Na_2O by K_2O will result in K^+ ion release and may serve to aid in blocking nerve transmission without changing the key properties of the glass and as already mentioned previously will reduce glass hardness slightly. Glass particles that are small enough to enter the dentine tubules are likely to deliver potassium ions more effectively than larger particles.

Increased Speed and Amount of Apatite Formation

Increasing the phosphate content and fluorine content dramatically increases the speed of apatite formation, as well as the amount of apatite formation in the case phosphate. If the glass is more efficient in producing apatite, the glass fraction in the formulation may be reduced, giving a considerable cost saving. The dissolution of bioactive glasses is generally very rapid and the slow step is the nucleation of apatite. Glasses that have crystallised to small quantities of apatite form further apatite faster, and pre-existing apatite crystals formed during glass formation or as a result of reaction with water from the atmosphere at the glass surface can act as seed crystals or nuclei. Similarly glass powders/toothpaste formulations may be seeded with small, typically less than 3 μm, FAP or HA crystals to nucleate apatite within the dentine tubules more effectively. HA is readily available and considerably cheaper than bioactive glasses (6 Euros/Kg compared to 50–100 Euros/kg). HA as discussed earlier is already used in the treatment of DH as a tubular occluding agent.

Water-Based Toothpaste Formulations

It is not feasible to produce a water-based version of a calcium phospho-silicate toothpaste. The problems of water absorption during manufacture and subsequent apatite formation can probably be avoided by incorporating silica gel to preferentially absorb water and prevent it reacting with the glass. Water absorption by the glycerol once opened by the consumer is a significant concern. For example, if the toothpaste cap is left open, how long would it take for the glycerol to absorb water and apatite formation to commence? A further concern would be with regard to whether this influences the effectiveness of the toothpaste. More sophisticated packaging, for example, a self-closing tube, or simply selling in smaller tubes might also be useful.

Anti-gingivitis Properties

It has been previously reported that NovaMin® has an anti-plaque and anti-gingivitis action, (Allen et al. 2001; Tai et al. 2006), but there is no obvious mechanism of action. Zinc oxide can be incorporated into bioactive glass formulations, and zinc salts, notably zinc citrate and zinc chloride, have also been widely

used in toothpaste formulations for their bactericidal and anti-gingivitis action (Lynch 2011). Zinc oxide has been widely used in skin creams, wound dressings as well as dental cements where it has a well-documented bactericidal and wound-healing role (Lansdown et al. 2007).

Octacalcium Phosphate (OCP)

Octacalcium phosphate, $Ca_8(PO_4)_6H_2 \cdot 5H_2O$ (OCP), is thought to be a precursor to HCA formation when the pH is <9. It is considered to be a precursor phase in biological apatite formation. OCP is thermodynamically less stable than hydroxyapatite (Ha) or HCA, but its formation is kinetically favoured probably as a result of having a lower activation energy for nucleation. OCP is structurally and crystallographically similar to hydroxyapatite and can co-crystallise with Ha. OCP is considered to be calcium deficient compared to Ha and contains two acidic phosphate groups and a water layer. The X-ray diffraction patterns for OCP and HA are almost identical, but OCP contains an additional diffraction line at 4.6° two theta corresponding to a water layer. OCP converts with time in an aqueous environment to a calcium-deficient apatite and where carbonate is present to a calcium-deficient carbonated apatite. Fluoride ions are known to aid the conversion of OCP to apatite. OCP is therefore attractive as a potential remineralising additive in toothpaste formulations. However, to the knowledge of the authors, OCP has never been incorporated into toothpaste.

OCP tends to form as thin plate-like crystals with similar aspect ratios to flake glass which make it attractive for treating DH. The conversion process is a solid-state transformation so the plate-like morphology is retained after conversion to the apatite. OCP is much more soluble than HCA, and it is likely therefore that any toothpastes containing OCP will incorporate a source of fluoride for catalysing the transformation of OCP to apatite and for the formation of a more acid-durable fluoridated apatite.

Whereas as mentioned above there are no known OCP-based toothpaste formulations, OCP may, however, be formed as a transitory precursor phase with some existing compositions (including bioactive glass-based toothpaste formulations) and in natural tooth remineralisation processes with saliva.

Systems Involving Formation of Apatite-Like Phases from Calcium Phosphate Salts

One attractive solution to treating DH is to form the tooth mineral within the dentine tubule and on the tooth surface. Calcium phosphate cements have been developed at the Paffenberger Dental Institute, which have largely been used as a bone cement and grafting material in orthopaedics and have recently been used for treating DH (Komath and Varma 2003; Ambard and Mueninghoff 2006).

A much higher water content and a finer particle size for the powder is used than would be the case for a classic calcium phosphate cement in order for the cement paste to have a low viscosity and be able to enter the dentine tubules.

The product Teethmate Desensitiser® consists of a mixture of tetracalcium phosphate ($Ca_4P_2O_9$) and dicalcium phosphate anhydrous ($CaHPO_4$) to which water is added. The two salts dissolve and are claimed to reprecipitate as Ha, the mineral phase of tooth (see Fig. 11.20). However, the phase formed initially is actually OCP, $Ca_8H_2(PO_4)_6 \cdot 5H_2O$, which has a very similar X-ray diffraction pattern to Ha but has an additional diffraction line due to the water layer in its structure at 4.68° two theta. The phase formed within the tubules has a plate-like appearance which is typical of OCP.

Teethmate Desensitiser® provides good tubule occlusion, and it has been reported that it provides a tensile bond strength to dentine close to 10 MPa (Thanatvarakorn et al. 2013a, b); however, calcium phosphate cements particularly with high water contents have compressive strengths lower than this figure, and the tensile strength would be expected to be a fraction of their compressive strength. OCP is much more acid soluble than Ha, and the long-term durability of this product when faced with an acid challenge remains to be evaluated. Despite these criticisms, there is potential in this type of product for treating DH, and it does

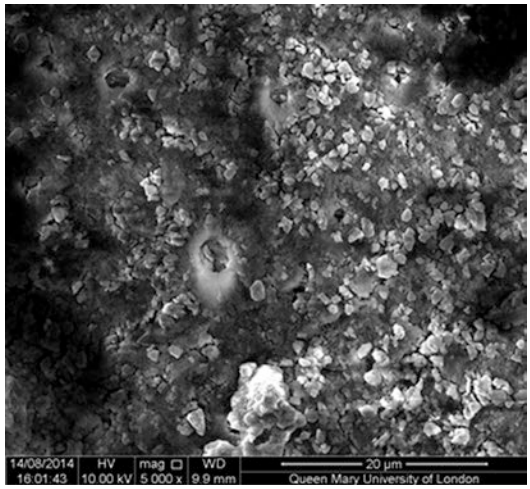


Fig. 11.20 SEM of a dentine disc section following the application of Teethmate Desensitiser®

avoid issues of toxicity associated with resin-based systems (Choudhary et al. 2012; Mehta et al. 2014).

Recently researchers at QMUL have developed calcium phosphate cements based on fluoride-containing bioactive glasses as an alternative to using calcium phosphate salts, and the phase formed is a fluoridated apatite which would be expected to be much more durable than the OCP in the Teethmate Desensitiser® product.

Systems Designed to Stimulate Odontoblast and Tertiary Dentine Formation

One aspect that has been rarely considered in DH is the natural response of the tooth to damage and open tubules. Tertiary dentine is produced by odontoblasts in the pulp chamber in response to the open dentine tubules. This tertiary dentine lacks the organised orientated dentine tubule structure of primary dentine. The formation of tertiary dentine acts to seal the sensitive pulp from external stimuli and bacterial infection. Because tertiary dentine has no organised dentine tubule structure, it effectively acts to occlude the dentine tubules from within. Odontoblasts are similar to osteoblasts in bone and produce collagen and form apatite. Osteoblasts are upregulated by various factors including strontium, zinc and fluoride ions as well as by bioactive glasses. Silicon release in the form of soluble silicates has been shown to activate many of the genes involved in bone formation. It is possible that odontoblasts too may be stimulated to produce tertiary dentine by components from DH toothpaste formulations that are capable of diffusing down the dentine tubules. It is important to note that the process of tertiary dentine formation is likely to be slower than surface tubule occlusion. However treatments that result in tertiary dentine formation are likely to have long-term efficacy compared to treatments that give only surface occlusion of the dentine tubules. It is surprising given the well-known influence of strontium ions on upregulation of osteoblasts and the prevalence of strontium in many dental restorative materials including toothpaste formulations that the influence of strontium on odontoblasts has not been investigated.

Hybrid Materials

Flake Glass Varnish

A flake glass varnish would not be sold as an over-the-counter product, for example, a toothpaste, but would be used as an in-office treatment as an alternative to existing varnish treatments. Flake glasses are thin plates of glass that can be from 0.1 to 10 µm thick and vary in width from 10 to 500 µm. A scanning electron micrograph of flake glass particles is shown in Fig. 11.21.

Flake glass epoxy composites are currently used as corrosion and wear-resistant coatings on the inside of crude oil pipelines. The flake particles align parallel to the surface of the pipe. This is shown schematically in Fig. 11.22. The flake particles act as a barrier to water ingress. The flake glass particles also dramatically improve the abrasive wear behaviour and, since they are much harder than the resin, protect the composite coating from abrasive wear by small sand particles in the crude oil.

Figures 11.23a, b show the microstructure of an aligned flake glass varnish developed for dental use. Such a varnish is likely to be much more durable in

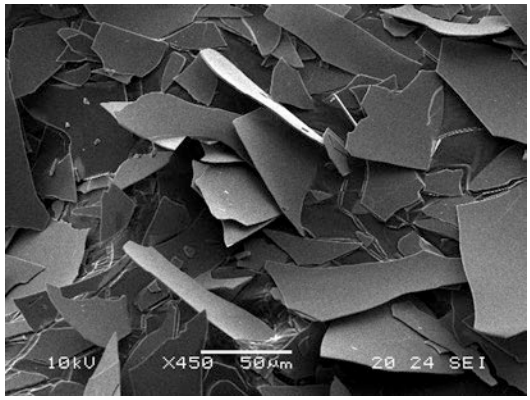


Fig. 11.21 Scanning electron micrograph of flake glass particles

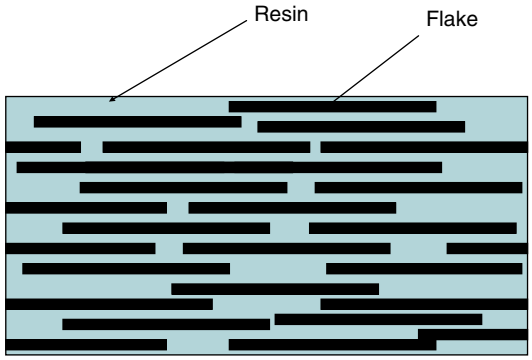


Fig. 11.22 Schematic of an aligned flake glass composite

the mouth than conventional unfilled varnishes. Another advantage of these varnishes is that the flake particles act as barriers to oxygen diffusion into the coating, and this dramatically reduces the formation of the oxygen-inhibited layer, resulting in a very high degree of polymerisation. Such flake glass varnishes are particularly attractive for a long-term in-office treatment for DH.

Conclusion

There are as discussed a diverse range of treatments for DH; some of these treatments are relatively mature technologies that offer relatively few options for further optimisation. The newer treatments, based on the formation of apatite-like phases, may however offer a greater scope for improved treatments. Amorphous calcium phospho-silicate-based technologies appear to offer the greatest potential for future development of products due in part to their ability to (1) incorporate a wide range of additional therapeutic ions into an amorphous glass and (2) control their release over time.

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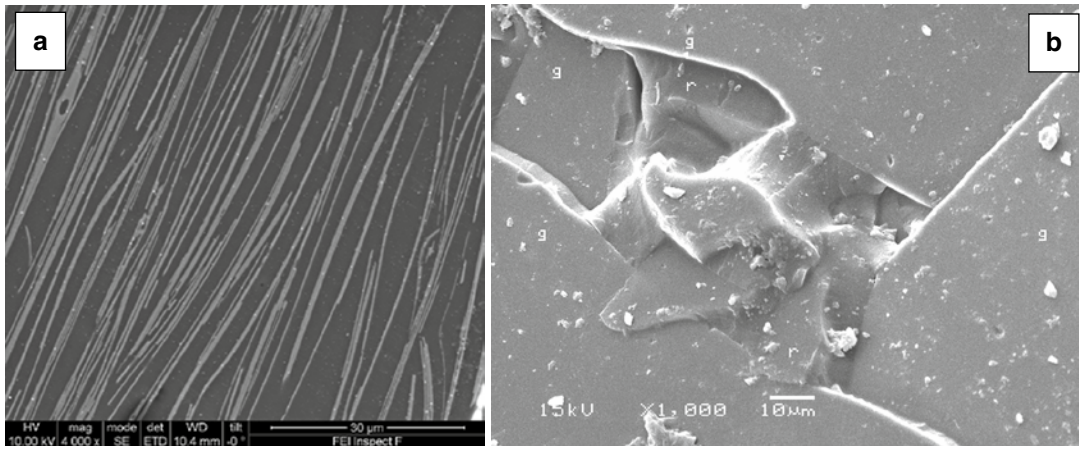

Fig. 11.23 (**a**) (*Left*) SEM cross-section of aligned flakes in a flake glass coating and (**b**) SEM of top-down view

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Closing Remarks Quo Vadis?

12

David G. Gillam

There's no end to the publishing of books, and constant study wears you out so you're no good for anything else. (Ecclesiastes 12:12)[1]

The main purpose of the book was to provide an overview on DH in order to both educate and update readers on the latest research results regarding the development of new products and any advances in clinical management strategies and perhaps more importantly for clinicians the implications for everyday clinical practice. There is no doubt, however, that for both the hard-pressed researcher and the busy clinician, dentine hypersensitivity (DH) is somewhat enigmatic in nature and the condition has consistently challenged both the clinician and the researcher to develop new strategies and new products in order to treat the condition. As Gottfried Schmalz indicated in the foreword of the book, the topic of DH has attracted considerable interest in recent years as demonstrated by the number of publications listed in the published literature. This observation concurs with the earlier concerns of Emling (1982) who indicted that:

> There may well be no single phenomenon in all of science which has occupied so much attention over so much time and yielded so few results as dentin hypersensitivity. Its causes have remained obscured throughout the existence of mankind. (Emling 1982)

The question may, however, arise: why write another book on DH? Perhaps the reader will have some sympathy with the exhortation expressed by Solomon in the book of Ecclesiastes regarding the need of researchers to constantly study and publish the outcomes of their labours. There is no doubt, however, that previously, as indicated in Chap. 1, there were concerns expressed by both researchers and clinicians with regard to the apparent lack of knowledge and understanding of the condition and in particular the terminology used to define DH (Emling 1982; Johnson et al. 1982; Dababneh et al. 1997). Nevertheless as Martin Addy indicated, there have been considerable advances in both the knowledge and understanding regarding DH in recent years and yet, as expressed by the various contributors in this book, there are still areas of research and clinical practice that need to be addressed. For example, the question of the role of pulpal inflammation in DH is still relatively unclear and somewhat controversial (Dababneh et al. 1997), and there are questions relating to whether the hydrodynamic theory can explain all aspects of stimulus transfer to the pulp (see Chap. 2). The role of the odontoblast in DH is also enigmatic; generally speaking, most published texts have consigned its role to the past and yet as Markowitz and Pashley (2008) have indicated that, following more recent evidence, this requires a reappraisal of its role (see Chap. 2). Furthermore

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[1] The Message The Bible in Contemporary Language Copyright Peterson EH (2002)

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according to Markowitz and Pashley (2008), although there was evidence to suggest that by increasing dentine permeability teeth become more sensitive, what is uncertain however is the degree to which dentine permeability needs to be reduced in order to effectively desensitise teeth.

The question as to whether the true prevalence of DH is reported in the published literature has also been addressed (see Chap. 3), and there appears to be some confusion with what is exactly being reported. For example, there are a wide range of values from the questionnaire and clinically based studies and where the studies were conducted (e.g. general or private practice, university/hospital, patients with or without periodontal disease, consumer based, etc.). Furthermore the methodology used when conducting these studies also varies and therefore there appears a need for more consistent and reproducible methodology when reporting the prevalence of DH. One of the problems that has also caused controversy has been the redefining of DH and root sensitivity (RS) (Sanz and Addy 2002), although to date there does not appear to be any published studies that have separated the precise prevalence values based on the treatment history of these individuals in order to distinguish the two clinical aspects of tooth sensitivity.

Undoubtedly there are a number of diagnostic challenges facing the busy clinician when examining patients complaining of dental pain in general and more specifically with DH (Gillam 2013). For example, (1) are clinicians under- or overestimating the problem, (2) is the condition being adequately diagnosed and successfully managed by clinicians in daily practice, (3) are clinicians aware of the impact (real or imagined) on the quality of life (QoL) in patients complaining with DH and (4) is the condition adequately monitored by clinicians in daily practice? It would appear that according to Gillam (2013) clinicians do not routinely screen/examine their patients for DH unless the patient prompts them, and this practice therefore needs to be reconsidered.

These questions have however been addressed by Ryan Olley and David Bartlett (see Chap. 4) and Nicola West and Joon Soon (see Chap. 5), although it should be acknowledged that a thorough clinical examination with a detailed medical and dental history may not only take time but may also challenge the clinician to provide an accurate differential diagnosis of DH within the constraints of a busy dental practice. It may therefore be suggested that consideration should be made to incorporate the various relevant aetiological factors and predisposing features implicated in the initiation and development of DH by recording dietary histories, clinical evidence of tooth wear (e.g. BEWE scores), clinical models (from impressions) and photographs, pain and QoL scores, etc. in the patient's clinical record (see Chaps. 4 and 10).

From the published literature, there are a plethora of recommended products and treatments that have been claimed to be successful for treating DH; nevertheless there have been inconsistencies in the design and methodology of in vitro, in situ and in vivo models used by researchers. For example, it is very difficult to mimic the oral environment in the laboratory environment, and care should therefore be taken not to extrapolate the results from the in vitro studies into the clinical environment.

Nevertheless as Carlo Prati and colleagues have indicated in Chap. 6, the in vitro investigation of an experimental desensitising product may provide evidence of the potential effectiveness in successfully blocking the dentine tubules when the product is applied onto the dentine surface. The question however arises as to whether these in vitro models (including laboratory methodology, e.g. scanning electron microscopy) are suitable for evaluating all potential desensitising agents; for example, potassium-containing toothpastes may not provide evidence of the mechanism of action of potassium in a dentine disc section (see Chap. 2). Furthermore, most, if not all, of the OTC toothpaste formulations require the interaction of saliva to enable the ingredients to be precipitated onto the tooth surface, and if saliva is not incorporated into the experimental design, would the precipitated deposit be similar to that deposited in the oral environment? It should be noted, however, that the development of a desensitising product from concept through to the introduction of the product into the professional or consumer market is a lengthy and well-regulated process (Markowitz and Pashley 2008) and, depending on the specific claims made for the

product (e.g. medicinal claims), may also involve exacting regulatory oversight (e.g. US Food and Drug Administration [FDA] and the Medicines and Healthcare Products Regulatory Agency [MHRA], UK) prior to its acceptance as a desensitising product. The development and evaluation of current, novel and future products designed to treat DH either from an in-office or over-the-counter perspective has been addressed (professionally applied) in Chaps. 8 and 11, and there is no doubt that there is currently more emphasis in developing new biomimetic materials for the remineralising of both enamel and dentine. For example, the development of bioactive glass (calcium phospho-silicate or bioactive glass toothpaste formulations), self-assembling peptides, protease inhibitors, functionalised tricalcium phosphate (f TCP), polymer-induced liquid precursors (PILP), etc. for possible dental applications including remineralisation, anti-caries and tubule occlusion (Niu et al. 2014, see Chaps. 8 and 11). However for the clinician, the availability of the number of these products that are available for treating DH is somewhat overwhelming and to some extent has caused a degree of confusion as to which product was the most appropriate to use. It is also evident that rather than enabling the clinician to be more aware of the appropriate use of these products, the converse may be true in that clinicians have reported a lack of confidence when using these products when treating DH (Cuhna-Cruz et al. 2010). The question that may therefore be considered is whether or not the clinician's awareness of desensitising products was (1) based on a commercial or marketing perspective that was driven by the industry literature, (2) based on personal exposure or awareness from colleagues in the practice environment or (3) derived from personal reading of the evidence-based clinical studies published in the literature. In fairness to the busy clinician, it may be unreasonable to expect them to spend hours reading papers or attending lectures without the hands-on experience of using these materials under supervision. The onus therefore may be for both industry and academia to provide more appropriate and practical guidelines for treating DH in clinical practice (see Chap. 10).

There are, however, a number of problems that may, however, be encountered by the clinician when evaluating the efficacy of a desensitising product in the clinical environment, and these have been addressed by Rick Curro and David Gillam in Chap. 7. From a historical prospective (pre-1997), these studies have been criticised for the lack of homogeneity in the methodology used to evaluate DH and in the study design per se (Cummins 2010). Following the recommendations of Holland et al. (1997), it was evident that there were improvements in terms of the controls used as well as in the objective methodology employed in the studies. However, as discussed by Rick Curro and David Gillam in Chap. 7, the clinical outcomes from these studies were not person centred in nature and therefore failed to address the impact of the clinical outcomes from the subject's perspective. More recently there has been a greater emphasis of the impact of DH on the quality of life (QoL) of those individuals who experience pain associated with DH, and no doubt these measures will increasingly be included in the study design of clinical trials (Robinson 2014, see also Chap. 9).

The shift of a top-down practitioner-centred model to a person-centred model as discussed in Chaps. 7 and 10 may therefore have implications not only for research but also for the clinical management of the condition. The emphasis in the future evaluation and management of DH should there involve the individual in the development of (1) the clinical trial process and (2) the management and treatment strategies. This undoubtedly will mean a change in the mindset of both the clinician and the individual in the clinical trial and practice environment; for example, the clinician should take steps to include the individual in the research and treatment process, and the individual needs in return to be fully motivated and compliant (see Chap. 10). Furthermore as indicated by Gillam et al. (2013), the management of DH should not be simply providing an in-office prescription/procedure or an OTC product without first removing any aetiological factor associated with DH and providing the necessary advice to minimise any future detrimental effects on the hard and soft tissues (see Chaps. 4 and 10). In other words, one of the most importance aspects in the management of DH is the education of both the clinician and the individual patient under treatment. It is also important to emphasise to the

clinician that there is no one treatment therapy for all the problems associated with DH and that the condition should be monitored depending on the extent and severity of the problem (Orchardson and Gillam 2006; Gillam et al. 2013).

Summary

There is always the temptation when reviewing the literature to be very selective in one's interpretation of what has been previously described, and it is evident that the topic of DH has been thoroughly discussed in numerous publications and journals. The authors of this book have, however, not ignored the valuable contributions of those researchers and clinicians who have made a major impact on our understanding of the condition. There have undoubtedly been major improvements in our understanding of both the development of new products and improvements in the clinical management of DH although it is important to recognise that as we consider and implement these changes, there are still challenges to be overcome in the future.

> Obtundants have been tried by hundreds of dentists and then faded out of the memory of men. Such has been the fate of every obtundant for sensitive dentine, except for a few now on trial, that have come forward during 70 or more years of clinical practice. But the relief of suffering is an ever-present duty and the search for this very desirable thing should continue. (Black 1908)

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