ANNUAL REVIEW of Gerontology and Geriatrics

Volume 4, 1984

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Introduction

Our readers will note that this volume (Volume 4) of the *Annual Review of Gerontology and Geriatrics* reflects a change in the pattern of the series. At the outset, we solicited comments and criticism for the range and depth of the material covered in each issue. Helpful criticism was forthcoming not only from readers, but also from reviews in various journals. Predictably, some articles received the highest praise, while others appeared not to live up to the expectation of the reviewer. On a broader scale, however, we noted that such criticism also had relevance when applied to the structure of the volume. Physicians and medical journals reviewed the medical, biological, and clinical areas favorably, but those chapters outside the medical field secured less favorable treatment; behavioral science reviews predictably tended to be reversed.

It became clear that while in principle there was much enthusiasm at the prospect of an annual review covering the spectrum of activities in gerontology, readers themselves seemed more narrowly focused. Relatively few behavioral or social scientists or policy persons were deeply interested in the details of biological theory or of the diagnosis and treatment of specific conditions of the aged. By the same token, while physicians, biomedical, and behavioral scientists often shared an interest in areas outside their own expertise, the material they could appreciate was not of a focus and depth that would be valuable as a reference for those specializing in the topic. Simply put, the in-depth review of a relatively narrow area of gerontology was not of sufficient widespread reader interest, and more broadly written pieces were technically of limited value to those in the field under discussion.

The Board of Editors reviewed this situation on a number of occasions and decided that it would be appropriate to take two very important steps in response to the experience gathered from our first three volumes. The first step was to narrow the scope of each volume to either a biomedical and clinical medical focus or a behavioral and social sciences focus. Second, these volumes would appear in alternate years.

Our new policy reflects a decision to provide each volume with material relevant to specific fields, and, in some instances, it may be difficult to decide whether some material is more appropriately biomedical or psychosocial. We accept this as a problem. However, the editorial board does feel that the readership will be served better by a volume in which most of the articles are relevant to a narrower focus of interest and scholarly and professional activities, and to a narrower population of students in these fields.

Volume 4 was therefore delayed. It was determined that this volume would have a biomedical and clinical medical orientation. Volume 5, which will appear next year under the senior editorship of M. Powell Lawton and George L. Maddox, is organized to review areas of psychosocial and behavioral sciences and related issues of community services and social policy.

Besides two important articles relevant to the biology of aging, Volume 4 contains a major group of articles on significant clinical practices concerning the aged. Three clinically important areas that we feel do not get sufficient attention in professional journals relating to the care of the elderly are reviewed—oral and dental changes with aging, clinical gerodentistry, and podiatry relevant to the aged. We hope that these reviews will stimulate more interest in those significant clinical sub-specialties. The article by Professor Welford is of a subset of biobehavioral studies, that of the experimental psychology of psychomotor performance. Psychomotor activities do relate somatic and behavioral studies and therefore are included in this volume.

In response to a number of comments, we have also undertaken to lengthen the articles themselves and to limit the number of topics on which we focus. This volume clearly reflects the initial effort in undertaking that policy. Readers indicated that it would be more useful to have this stylistic change.

Once again we solicit the reader's response to this more highly focused approach. We remain optimistic in our belief that those in disciplines involved in the understanding of the aging process and care of the aged will make an effort to understand a wider range of disciplines relevant to the aging process in addition to their own area of expertise.

Our thanks to Evelyn McKissic for her most valued help in completing this volume.

Carl Eisdorfer, Ph.D., M.D.

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FORTHCOMING

THE ANNUAL REVIEW OF GERONTOLOGY AND GERIATRICS, Volume 5

Tentative Contents

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SECTION I

Biological Sciences

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CHAPTER 1

Aging and Neoplasia

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INTRODUCTION

No statement about the need to explore the link between cancer and aging speaks more strongly than the statistical relationship of these two phenomena. In the United States over one-half of all cancer occurs in the 11 percent of the population over age 65 (Butler and Gastel, 1979). This disproportionate degree of cancer in the elderly has been a continuing stimulus to research into the relationship between carcinogenesis and aging from the viewpoints of biochemistry, molecular genetics, immunology, nutrition, and hormonal influences, as applied to cell culture and animal models.

In the clinical arena, however, insufficient time has been devoted to the approach to cancer in the elderly (Yancik et al.,

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1983). At age 25 the probability of developing cancer within 5 years is 1 in 700 while at age 65 it is 1 in 14 (Aging and Cancer, 1976). However, policies concerning cancer screening and diagnosis in general have not specifically addressed an altered approach in the elderly (Eddy, 1980).

For a variety of reasons the clinical impact of, and therapy for, cancer has been most widely explored in the young. Most of the gains in the cure and/or control of cancer have been achieved through aggressive trials, often with extensive toxicity. Application of these therapeutic modalities to the elderly has been limited by a lack of knowledge and a general bias that the elderly are not able to tolerate such therapy because of age-related decrements in homeostatic reserve and other complicating chronic illnesses. This has led to a degree of "ageism" (Butler, 1975), often excluding the elderly from chemotherapy protocols or other interventions, and therefore, further limiting the acquisition of useful information. The application of such an age bias in the selection of therapy may still result in toxicity, although therapeutic benefit may be lost.

EPIDEMIOLOGY

The epidemiologic investigation of cancer in the aged has been plagued by a number of pitfalls (Oota, 1980). Lack of availability of, or failure to seek, health care and diagnostic studies, failure of the patient and the physician to recognize malignancy because of confounding disease, and the inaccuracy of death certificates may all lead to inaccurate reporting of cancer incidence and mortality in the elderly. One large autopsy study reported a cancer incidence of 32.5 percent in patients over age 65 (Suen et al., 1974). Studies from the general Swedish population where autopsy rates approach 70 percent support these numbers (Ponten, 1977). By age 80 the combined incidence of cancer confirmed during life or at autopsy is over 40 percent. If basal cell carcinoma and microscopic prostatic carcinoma are included, the incidence approaches 60 to 70 percent.

The most recent data concerning cancer incidence and mortality in the United States are now available from the Surveillance, Epidemiology, and End Results (SEER) Program of the

National Cancer Institute (Young et al., 1981). The project is an ongoing evaluation of 11 geographic areas differing with respect to demographic and social characteristics, representing 10% of the U.S. population. The study population is representative with respect to age, but tends to underestimate the black and rural populations. A major value of the data set is the quality control maintained by the participants, resulting in extremely accurate incidence rates (Newell et al., 1982).

Figure 1.1 is a compilation of the age-specific cancer incidence and mortality data from the SEER program (Crawford and Cohen, 1982b). The clinical impression that cancer is predominantly a disease of later middle life is supported by the curve of total cancer incidence versus age. However, as shown by the bar graph, age-specific cancer incidence continues to rise as a function of age. Thus the clinical impression that cancer is less of a problem for the elderly is a misconception based on lack of sufficient appreciation for changing population size. In reality the risk of developing cancer increases with age, and

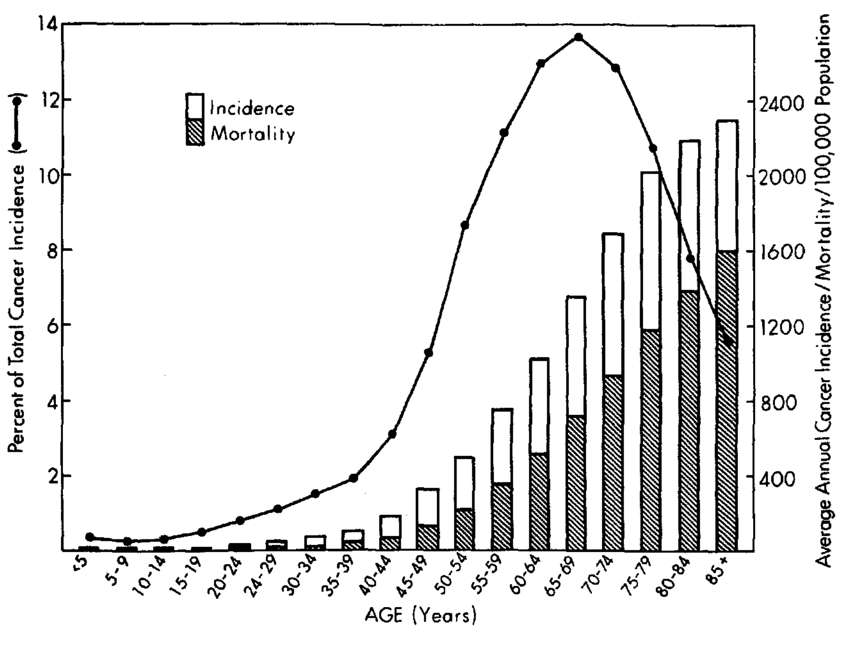

Figure 1.1. *Comparison of age of the percent cancer incidence for the population versus the age-specific cancer incidence/mortality.*

therefore neoplasia should be seriously considered in differential diagnosis.

Because of the coexistence of other diseases or the "compression of morbidity" in the elderly (Fries, 1980), and the less aggressive clinical course of some cancers in the elderly, another misleading clinical impression is that the elderly tend to die with cancer rather than of cancer. This has been supported by the data that deaths attributable to cancer decrease from 30 percent at age 50 to 10 percent or less at age 85 (King et al., 1982). This is largely due to the rapidly increasing denominator of deaths due to other causes with advancing age. Despite the marked increase in cardiovascular-related deaths with age, cancer remains the second leading cause of death in those over 65 (Libow and Sherman, 1981). Furthermore, as seen in Figure 1.1, the age-specific mortality of cancer rises with age at a rate that is actually greater than the increase in incidence, thus dispelling the notion that old people die with cancer rather than of cancer.

Figure 1.2 details the increases in specific cancers that occur with age. Only four cancers of adulthood are exceptions to this age–cancer relationship and have a median age of onset less than 50—Hodgkin's disease, acute lymphocytic leukemia, bone and joint cancer, and testicular cancer. Even these tumors have a second rise in incidence with advancing age. The magnitude of change in specific cancers with age has important implications in terms of screening, diagnosis, and management of cancer in the elderly and will be discussed subsequently.

Data extracted from one of the SEER participants, the Connecticut Tumor Registry, have combined all of the tumors with a median age incidence greater than 50 and have shown that there is a logarithmic rise in incidence of these cancers with age from the age of 30 to 80 (Dix and Cohen, 1980). This log relationship of neoplasia with aging suggests a very basic association.

THE RELATIONSHIP BETWEEN CANCER AND AGING

According to the epidemiologic data in Figures 1.1 and 1.2, the rate of increase in age-specific cancer incidence tends to slow and in some cases specific cancers may actually decline in inci-

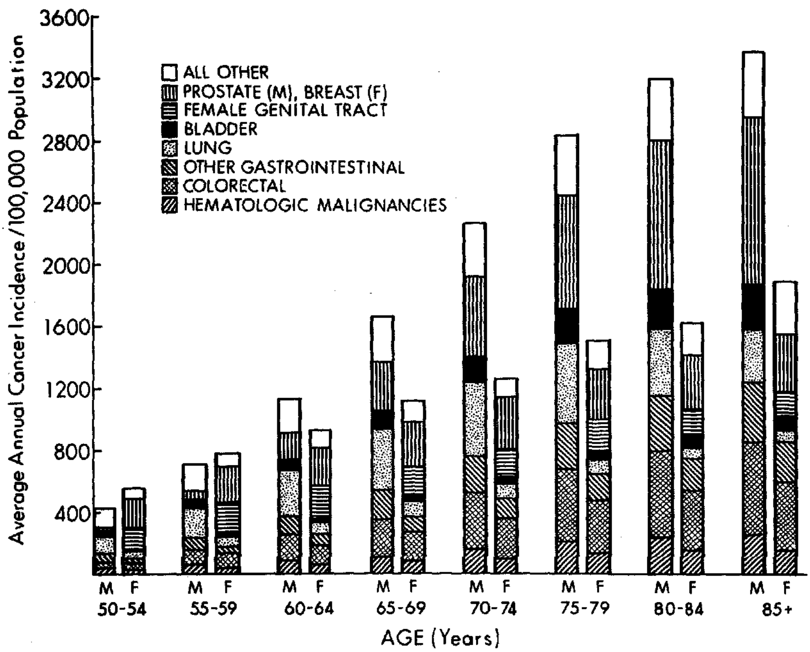

Figure 1.2. Age-specific incidence for the major types of cancer. Data tabulated from the Surveillance Epidemiology End Results Incidence and Mortality data, all areas except Puerto Rico, 1973–1977.

dence over the age of 80. Autopsy data support this (Ishii et al., 1979). While clinical reporting and even autopsy data in this country may underestimate the incidence of cancer in the extreme elderly, there is other support for slowing of the rate of increase of cancer with age over 80. Autopsy series from Sweden show that while the incidence of prostate cancer rises through age 80 to a peak incidence of 50 percent, further advances in age are not associated with a further rise in cancer incidence (Lundberg and Berge, 1970). Thus cancer is not a universal accompaniment of aging, as are some degenerative processes such as atherosclerosis. Rather cancer represents a group of diseases which are dramatically increased in expression with advancing age. The corollary is that "the most prominent factor determining susceptibility to cancer is age" (Miller, 1980).

Experimental data also link the processes of aging and neoplasia (Pitot, 1978). Altered enzyme responses and rates of

DNA repair along with a decreased capacity for drug metabolism occur in both aging and neoplastic cells. The aging process may be explained by the progressive accumulation of deleterious free radical reactions from oxygen metabolism at the cellular level (Harman, 1981). That antioxidants decrease both aging and carcinogenesis in animal models has led to the postulate of a common mechanism for both through cumulative damage from oxygen free radicals (Oberley et al., 1980). Similarly, dietary manipulations seem to have similar influences on each process, with unsaturated fats accelerating both processes, while fasting slows aging and decreases tumor incidence in animals. However, there are also major differences in that aging cells have a finite life span *in vitro* and a relatively stable karyotype, whereas neoplastic cells are immortal and have unstable karyotypes. Thus experimental data suggest that carcinogenesis and aging are related but distinct processes.

Attempts to explain this relationship between neoplasia and aging result in two basic concepts. First, the passage of time may simply be permissive in the clinical expression of cancer allowing more time for expression of previous carcinogenic stimuli. Alternatively specific changes of the aging process may enhance the development of cancer. Data exist to support both hypotheses (Magee, 1977).

To understand the clinical interactions of aging and neoplasia it is essential to understand the basic processes (Thomas, 1980). No central mechanism of carcinogenesis has been accepted in the past, due to the apparently widely divergent influences of genetics (Knudson, 1980) and the environment (Higginson, 1980). However, recent insights from tumor virology and genetic engineering have provided support for a common basis. Although viruses probably play a minor role in human carcinogenesis, studies of viral genes that induce cancers in mammals have resulted in an "oncogene" model applicable to most cancers (Bishop, 1982). Best studied is the Rous sarcoma virus, which induces a sarcoma in chickens through production of a protein kinase that causes malignant transformation of a normal chicken fibroblast. This viral oncogene has a normal counterpart, a mammalian cellular gene that produces a similar or identical protein kinase, although in much lower amounts, that appears important to the physiologic regulation of the cell. Furthermore, this normal gene can be manipulated to produce excessive amounts of the protein kinase with resultant malignant transformation of the cell. This same "oncogene" and others are part of the normal human genome. Thus the cancer-gene concept suggests that there are a group of cellular genes required for normal growth and development but capable of causing malignant transformation of a normal cell if the genetic information is altered or inappropriately expressed, such as through mutagenic or carcinogenic stimuli (Lebowitz, 1983). Thus acute leukemia occurring in a patient with Down's syndrome or lung cancer occurring in a cigarette smoker could share the common pathway of increased expression of a cellular oncogene secondary to altered regulation of DNA. This theory also fits well with the concept that many cancers result from an autonomous clonal proliferation of a once normal cell that is no longer able to terminally differentiate, or "partially blocked ontogeny" (Potter, 1978). Other theories of carcinogenesis exist (Upton, 1982), but this model serves as a useful framework to discuss the interaction of aging with neoplasia.

Certainly the oncogene model would be compatible with an age-related accumulation and expression of genetic damage (Cairns, 1983). Somatic mutations are estimated to occur at a rate of 1 in 10^6 cell divisions, with 10^{16} cell divisions occurring in the lifetime of man (Cairns, 1975). The rate of DNA synthesis is increased and messenger RNA template stability is altered. Thus the opportunity for aberrant DNA regulation is present in aging cells (Hayflick, 1977).

A series of observations have been made with regard to sister chromatid exchanges (SCEs) in normal and aged human cells and in tumor cells (Schneider et al., 1981). SCEs may reflect one type of reparative response to DNA damage and are used in screening for mutagenic and carcinogenic agents (Schneider and Lewis, 1981). In response to the mutagen, Mitomycin-C, *in vitro,* human cells from old donors compared to young donors have fewer SCEs and greater chromosomal aberrations (Schneider and Kram, 1978). This is consistent with the *in vivo* findings of increased karyotypic abnormalities in normal aged human cells (Pitot, 1977) and more frequently abnormal karyotypes in older patients with acute myelogenous leukemia (Rowley, 1981).

Apart from age-related genetic changes, carcinogenesis could be influenced by altered processing of carcinogens themselves in the elderly. Current concepts suggest that a chronic multistep process is necessary for the phenotypic expression of cancer (Pitot, 1983). This involves activation and metabolism of pro-carcinogens which then serve as initiators that, through alterations in DNA and perhaps other substrates, lead to a biochemical lesion in the initial cell population (Farber, 1981). Subsequently a promoting agent is necessary to transform an initiated lesion into a neoplastic growth. Finally progression occurs with the development of metastases (Pitot, 1982). While many chemical agents serve as initiators or promoters or both, the distinction is important. Initiation is an irreversible process involving DNA damage to a cell. On the other hand, promotion can occur immediately or at a point in time remote from the initiating lesion, but is reversible. Promotors include a wide variety of chemical and dietary agents in the human environment such as dietary fat, asbestos, and alcoholic beverages (Pitot, 1982).

Experimental data on potentiation of carcinogens in aged animals are conflicting. In one series, the incidence of skin tumors in mice treated with benzpyrene was independent of age, but directly dependent on dose (Peto et al., 1975). In another model, when dimethylbenzanthracene was applied to skin grafts from young and old mice, an increased incidence of cancer was seen in the old skin grafts (Ebbeson, 1973). Induction of cancer in animal models is always difficult to extrapolate to the human system. However, human cell culture experiments have begun to explore the metabolic activation and inactivation of a variety of carcinogens and have shown a striking individual variation, by as much as 50- to 100-fold in their metabolism (Harris et al., 1980). While a decline in drug metabolism has been described in elderly cancer patients (Higuchi et al., 1980), it is not yet clear what modifying effects age has on the ratio of activation to inactivation for carcinogens (Anisimov and Turusov, 1981).

Conceptually it seems logical that the steps of promotion and progression in neoplasia might be altered in the setting of an age-related decline in physiologic functions. Certainly the risk of neoplasia can be altered experimentally by hormonal manipulation (Riley, 1981) and by nutritional influences (Fernandes et al., 1979). Widely implicated also has been the association of an age-related decline in immune function, or immune senescence (Weksler, 1982). Of interest in this regard is the prevention of spontaneous tumors in aged mice by immunopharmacologic manipulation (Bruley-Rosset et al., 1981). The interrelationship of these and other systems in the genesis and promotion of cancer is a complex topic which has been reviewed in more detail elsewhere (DeVita et al., 1982; Holland and Frei, 1982).

The argument against a modulating effect of aging on the course of neoplasia is based on epidemiologic data, the only means for the study of human carcinogenesis and aging *in vivo*. In lung cancer where the carcinogenic stimulus is clear, age per se is not a risk factor, independent of prolonged exposure time (Doll, 1978). However, it may be that epidemiology is not a sufficiently sensitive approach. In animal models, a shorter latency period for the development of cancer in aged versus young mice has been shown after prolonged ingestion of a carcinogenic diet (Clapp et al., 1981) and also after implantation of tumor cells into old versus young mice (Rockwell, 1981). Neoplasia in these aged mice would appear to represent more than the passive acquisition of genetic insults. Thus from rapidly growing areas of research, there is evidence that implicates age-related genetic, biochemical, and physiologic changes that may alter or enhance the steps of initiation, promotion, and progression of neoplasia in the elderly.

CLINICAL PRESENTATION OF CANCER IN THE ELDERLY

While advances are being made in the understanding of the interaction of neoplasia and aging on the experimental and epidemiological levels, progress in the clinical aspects of these processes has been slower. Because of the marked heterogeneity of the elderly as a population due to both variations in physiologic aging and co-morbid diseases, the clinical dictum has been for individualization of therapy. While this is an important concept in many elderly patients, it has been often inappropriately applied so that older patients have been excluded from systematic treatment protocol studies, the standard source from which oncologists gain information on response to and toxicity of therapy (Begg et al., 1980).

Despite the fact that over one-half of all cancers occur in the elderly, the existing data base in regard to management is quite limited. The clinician formulates a plan often based on his biases from past clinical experiences with elderly patients. Such clinical judgment may be excellent, but often it is too narrow-sighted an approach. Future improvement will require a decision process stratifying the elderly by groups in terms of risk/benefit ratios for each type of cancer and its appropriate intervention. However, until clinical research provides the necessary data base, the physician must depend upon his clinical judgment, but hopefully using a consistent framework that can be modified as data accumulate in this area.

THE DIAGNOSIS OF CANCER IN THE ELDERLY

Cancer, like other diseases in the elderly, often escapes early detection by the patient, partially because of the pervasive attitude that "feeling bad" is a normal part of aging and does not necessarily warrant a physician's attention. Thus the warning signals of cancer are often ignored until late, as evidenced by the relationship of age to advanced stage for some, but not all, cancers in the elderly (Holmes and Hearne, 1981).

Similar pitfalls in the recognition of neoplasia in the elderly exist for the physician caring for an elderly patient with multiple disease processes (Hodkinson, 1978). Changes in bowel habits may be attributed to decreased motility, rather than the possibility of colon cancer. Anemia is more common in the elderly and may not alert the physician to other processes. General symptoms of anorexia, weight loss, or decreasing performance status may be secondary to failing social competence, depression, or early dementia, but may also be the first clue of a malignancy. The age–cancer relationship depicted in Figures 1.1 and 1.2 emphasizes the need to maintain a high index of suspicion for neoplasia in elderly patients despite complicating medical problems.

Furthermore, the frequency of multiple primary cancers increases with age (Howell, 1980). This index of suspicion must be balanced against the physician's judgment concerning the value of a cancer workup in an individual patient. As a group, the elderly receive more medical care, frequently resulting in abnormal lab tests that may lead to fruitless but expensive and often hazardous investigations. A study of the diagnosis of bronchogenic carcinoma at a major university hospital emphasizes this dilemma for the physician (Cechner et al., 1980). In this autopsy study, men over 70 were the most likely group to have had clinically undetected lung cancer and also the most likely group to have had a mistaken clinical diagnosis of lung cancer.

NATURAL HISTORY

Observation of the natural history of cancer has led to a variety of opinions, with some believing cancer may be more indolent in the elderly, whereas others believe that it is more aggressive (Peterson and Kennedy, 1979). The time-honored marker of success, the five-year survival rate, may not be an accurate means of comparing young and old patients, particularly at the extremes of age or in the presence of co-morbid diseases. Unfortunately more accurate measurements of clinical doubling time (Shackney et al., 1978) or *in vitro* kinetic studies of tumors (Hansen et al., 1981) have not been systematically evaluated with respect to patient age. Clinical observations are often biased by marked variations in lead time; i.e., the shortened survival of the patient who presents in a late stage due to lack of medical sophistication versus the apparent longer survival of patients whose cancer is detected fortuitously because of medical attention for other problems.

Despite these problems, some variations in biological aggressiveness with age have been suggested for several cancers. Malignant melanoma has a relatively constant five-year survival for women until age 60, after which a sharp decline occurs (Shaw et al., 1978). Furthermore, increasing age has been correlated with increasing depth of skin penetration by the melanoma (Levine et al., 1981). Age greater than 60 is a risk factor for death from thyroid cancer that is independent of histologic type, extent of tumor, or type of treatment (Cady et al., 1979). Additionally, differences in histologic subtype exist. Anaplastic carcinoma of the thyroid, a virulent counterpart of the better differentiated forms, occurs predominantly in the elderly. Thus, changes in biology of cancer with age may in some situations relate to changes in grade or subtype of cancer rather than to an effect of age per se. Another example of this change in subtype occurs in breast cancer where the clinical impression exists that this disease has a more benign course in the elderly. In fact this may be secondary to the increased frequency of estrogen receptor positive breast cancer in postmenopausal women (Lemon, 1982). The presence of the estrogen receptor protein is associated with a better prognosis, with a longer disease-free survival and more slowly growing tumor. There is some evidence to suggest that elderly patients with bronchogenic carcinoma are less likely to have metastatic disease at the time of diagnosis and also at the time of death, suggesting less aggressive tumor growth and spread in the aged (Ershler, Socinski, and Greene, 1983). Thus each type of cancer and its confounding variables must be studied in detail before drawing conclusions about the influence of age per se on neoplasia.

The influence of neoplasia on age is better defined. For most cancers survival rates decrease with progressive age of the patient, even after correction for age-related expected survival (Ries, Pollack, and Young, 1983). The progressive decline in physiologic function with age accompanied by co-morbid diseases and a loss of social and financial support systems often makes cancer even more ominous in the elderly than in the young. The diagnostic studies and therapy of cancer often overwhelm the adaptive ability of the elderly patient, particularly in the absence of support from the family and/or community.

CLINICAL DECISION MAKING

Estimates of the benefit versus risk of diagnostic and therapeutic interventions are less well defined in the elderly than in younger patients. To accurately predict the benefit/risk ratio for an intervention, the physician needs to know the functional reserve of the patient. While known disease processes can be considered in some semi-objective fashion, chronologic age alone cannot. Unfortunately there is no simple practical way to measure physiologic age at a tissue level that would tell us the "margin of safety" that exists in aging cardiovascular, pulmonary, or renal systems (Kark and Wardle, 1980). In some situations, invasive means may be warranted to make an accurate assessment (Del Guercio and Cohen, 1980). More often the physician applies his clinical judgment to assess whether or not an aggressive approach is in the best interest of the patient.

The first consideration must be whether making a diagnosis will in some way alter the patient's quality or quantity of life. In some situations the combination of advanced age and co-morbid disease may make any evaluation difficult and the rewards for a diagnosis nil, if the patient were unable to withstand appropriate therapy. Too often, however, chronologic age alone has been used to exclude patients from standard diagnostic and therapeutic approaches without understanding the normal survival of the elderly. In fact, the average life expectancy for a 70-year-old man is 11 years and for a 70-year-old woman it is 15 years (Kovar, 1977). For these men and women the majority of their remaining years will be spent in an independent life style (Katz et al., 1983). Even at age 85 men have a life expectancy of 5.3 years and women have one of approximately 7 years. To put this in oncologic terminology, the median 5-year survival for a 70-year-old is 93 percent and for an 80-year-old is 63 percent. Without intervention any cancer that is not indolent should be expected to alter survival.

More difficult to assess than quantity of life, but often more important to the aged patient, is quality of life. In addition to the impact of diagnostic and therapeutic interventions on health status and functional level, the physician must consider the impact on the financial and social status of the patient.

THERAPY

The goal of therapy in any patient must be clearly understood, i.e., is it a curative attempt, or one aimed at improving the quantity and/or quality of life? Extreme age and co-morbid disease may limit the physician's attempts at curative therapy. Palliative therapy, a mainstay of cancer treatment at most ages, achieves increased significance in the elderly where maintenance of function may be more difficult. Thus, the second question must be, What are the patient's expectations of therapy and what support systems exist for achieving such expectations? Is there a spouse in good health? What is the proximity and willingness to help of family and friends? The team concept has been well developed in cancer therapy and it is essential in the management of the elderly cancer patient (Dugan and Scallion, 1984). Care of such patients often requires the skills of the physician, nurse oncologist, social worker, psychologist, and chaplain with assistance from the dietitian, dentist, and physical therapist working together in conjunction with the patient, family, and friends. Such a support group should be the basis for cancer management in the elderly. From such a group, individual problems more common in the elderly can be addressed such as differences in pain perception or response to analgesics (Harkins and Warner, 1980; Kaiko, 1980), need for nutritional support (Ching, 1979), counseling (Linn and Linn, 1981), and nursing assessment (Dugan and Scallion, 1984). From this base one can then consider specific therapeutic interventions.

SURGERY

The topic of surgery in the elderly has been well reviewed recently (Johnson, 1983). Numerous studies exist to document that chronological age per se is not a contraindication to surgical intervention, although large surgical series do show an overall increase in mortality by as much as 50 percent in patients over 70 (Schein, 1979; Turnbull, 1978). Operative mortality often increases more dramatically in patients over 80 (Santos and Gelperin, 1975). Deaths are most commonly due to cardiac events, pulmonary emboli, pneumonia, and other infections. While age greater than 70 has been shown to be an independent risk factor, this may relate to an inability to adequately assess cardiopulmonary reserve (Goldman et al., 1977). By invasive preoperative monitoring of the elderly, 23 percent of the group of patients who had been "cleared" for surgery were found to have unacceptable risks for major surgery under general anesthesia (Del Guercio and Cohn, 1980). Thus careful preoperative assessment is critical in the elderly patient (Feigal and Blaisdell, 1979) and in some situations may warrant invasive monitoring.

Risk for complications varies with this procedure. Surgery for gynecologic malignancy in patients over age 75 resulted in a higher incidence of wound complications but otherwise resulted in no differences in complications than for younger patients (Pierson et al., 1975). Operative mortality was 6 percent and 4 percent in two series of patients over age 65 undergoing craniotomy for brain tumors (Stewart et al., 1975; Tomita and Raimondi, 1981). In another study a thorough evaluation of operative risk factors for colon resection in the elderly revealed a mortality rate of 5 percent for the age-group 70 to 80 and 17 percent for those patients over 80 with a relatively constant morbidity rate of between 30 to 35 percent for all patients over age 50 (Boyd et al, 1980). The mortality rate correlated best with the number of preexisting medical conditions, which were more frequent with age. For example, patients over 70 with two or more complicating medical conditions had an operative mortality of 16 percent, whereas no patient withour preexisting conditions died regardless of age.

In series of thoracotomies in elderly patients, the surgery is further complicated by direct compromise of the cardiopulmonary system, which undergoes a significant age-related decline apart from any specific disease process (Libow and Sherman, 1981). Thus, functional reserve has even greater importance here. In a series of 150 patients with lung cancer who had "lung sparing" procedures, the hospital mortality was 4 percent compared to a 17 percent mortality in other reported series (Breyer et al., 1981). Moreover, the 5-year survival for this group was 27 percent, which is comparable to other series which involve more aggressive surgical resection.

Thus chronological age does not preclude surgery, but it does increase the probability of coexistent decline in functional reserve and complicating diseases which must be carefully evaluated. Moreover, one must consider not only immediate postoperative problems, but more long-term problems of recuperation, difficulty in returning to preoperative functional status, and the potential for further complications during that prolonged recuperative phase (Schein, 1979). Clinically, this is a well-recognized problem for the elderly, but limited data exist to objectively assess this parameter. Clinical experience and common sense would suggest that the narrower the functional reserve of the patient preoperatively, the more difficult it will be for rehabilitation. Finally, despite the uncertainties involved in intra- and postoperative recovery, the marginally compensated elderly patient may well be able to tolerate the acute stress of surgery better than the chronic stress of radiation treatment or chemotherapy.

RADIATION THERAPY

No clinical evidence exists that a given cancer varies in its radiosensitivity as a function of patient age. However, one study found a decreased radiation dose-response curve for tumors in aged mice compared to the same tumors in young mice (Rockwell, 1981). Radiation effect on normal tissue is said to be enhanced by 10 to 15 percent in the elderly (Gunn, 1980). Those organs with most marked physiologic decline such as the lungs would be in most jeopardy. Also, side effects may be more hazardous, as in radiation therapy delivered to the oropharynx or oral cavity, because of the resultant loss of taste, dryness of the mucous membranes, and involution of the salivary glands. Combined with the precarious nutritional intake in the elderly, this can be lethal unless careful attention is given to nutritional support (Nixon and Lawson, 1983). Additionally, the usual treatment schedules often must be altered for the elderly due to their inability to tolerate daily treatment secondary to nausea, weakness, etc. Otherwise treatment may be compromised by decreased daily dose rates, unscheduled absences from treatment, or decreases in planned total dose. Anticipation of these problems may be handled by an altered schedule, such as a split-dose schedule. With these adjustments, potentially curative radiation therapy can even be given. In other situations palliative radiation for means of pain control or to treat local obstructive symptoms can be used very effectively in elderly patients.

CHEMOTHERAPY

Although knowledge is beginning to accumulate in regard to drug metabolism in the elderly (Greenblatt et al., 1982; Ouslander, 1981), limited data exist in regard to altered handling of specific chemotherapeutic agents in the elderly. Because of the variability in the biology of tumors in the elderly, no conclusions can be reached about chemotherapeutic responsiveness in specific tumors as a function of age per se. However, more information is available concerning the toxicity of these agents in aged patients. The major limiting factor for most drugs is bone marrow toxicity. In patients with the "anemia of aging," a decrease exists in granulocyte reserve as measured by CFU-C or bone marrow precursor cells (Lipschitz and Thompson, 1980). Furthermore, long-term cultures of mouse bone marrow cells indicate a limited proliferative capacity of normal stem cells with age (Reincke, 1982). Most other data are less objective, involving anecdotal reports of life-threatening myelotoxicity. Drugs with the most prolonged myelosuppression such as the nitrosureas may be particularly difficult to use in the elderly. However, one recent study using bischloroethylnitrosourea (BCNU) in combination with cyclophosphamide and prednisone in patients with myeloma showed no increased toxicity in elderly patients (Cohen et al., 1983). Clearly, further studies are warranted to determine proper drug dosage in elderly patients and risk factors predisposing to bone marrow toxicity.

In terms of other drug toxicity, patients over age 70 may be at increased risk for pulmonary toxicity from Bleomycin (Ginsberg and Comis, 1982). This may relate partially to a decrease in Bleomycin hydrolase in aged lungs (Muggia, 1981). The cardiotoxicity of Adriamycin in the elderly is more controversial. In one series age was a risk factor (Bristow et al., 1978), but in a larger series, preexistent cardiac disease rather than age was the major predisposing factor (Praga et al., 1979). In other situations it is not clear that age per se is a predisposing risk factor, but because of age-related increases in the frequency of coexistent diseases, toxicity may be more common and the result of toxicity more dramatic. A case in point is the peripheral neuropathy associated with Vincristine. Peripheral neuropathies are much more frequent in the elderly and may be subclinical until a neurotoxic agent is administered. Furthermore, a younger patient may be able to compensate for paresthesias or even some degree of motor weakness, whereas these complications may be disastrous in an elderly patient who already has a compromised strength and balance. For other general toxicities of chemotherapy, the reader is referred to an excellent review (Perry, 1982).

It is not surprising, given this range of known and unknown toxicities, that chemotherapy in the elderly has not been thoroughly evaluated. However, recent studies suggest that the elderly who have been included in protocol studies may indeed tolerate therapy as well as younger patients (Begg et al., 1980). In reviewing 19 studies from the Eastern Cooperative Oncology Group (ECOG), toxicity from chemotherapy was not different for patients under age 70 versus those over age 70, except for hematologic toxicity (Begg and Carbone, 1983). This difference could be accounted for by two drugs, methotrexate and methyl 1-(2-chloroethyl) 3-4 -methylcyclohexyl -1-nitrosourea (methyl CCNU). The toxicity of methotrexate may well have been secondary to the renal clearance for this drug and failure to adequately reduce the dose in the setting of diminished renal function in the elderly. In these studies, response rates and survivals were not different in the elderly versus the young. In another review of older myeloma patients, not only was the toxicity equivalent but response to treatment was equal to, or better than, that for younger patients (Cohen et al., 1983).

These studies are retrospective and may inherently be biased in terms of the elderly patient selection. However, they should lessen the reluctance to withhold chemotherapy based on chronologic age alone. Hopefully, prospective studies will further evaluate specific benefits and toxicities for chemotherapy in the elderly, as has been done for younger patients.

APPROACH TO SPECIFIC NEOPLASMS

The general management of specific cancers has been thoroughly reviewed (Devita et al., 1982; Holland and Frei, 1982).

However, some specific points with respect to management in the elderly need to be emphasized for selected cancers.

Hematologic Neoplasms

Hematologic neoplasms represent only a small fraction of cancer incidence and mortality in the elderly. However, these neoplasms represent a major area of advancement in therapy for younger patients and therefore have been the subject of many reports in the elderly. In some diseases such as chronic lymphocytic leukemia and nodular lymphoma, the course is often relatively indolent and these patients can be well managed with low doses of oral chemotherapy and/or palliative radiation therapy while maintaining a good functional level. The monoclonal gammopathies also arise predominantly in the elderly and treatment strategies have in general taken into account the homeostatic reserve of such patients (Crawford and Cohen, 1982a). Hodgkin's disease in the elderly often presents in advanced stages, and although this is a largely curable disorder in younger adults, curative therapy in the elderly may be more difficult (Nissen and Pajak, 1982). Likewise, the possible cure of some patients with diffuse histiocytic lymphoma has occurred largely in younger patient populations (Jones et al., 1979).

Perhaps the most dramatic neoplasm is acute leukemia in the elderly. This is a rapidly fatal disorder without treatment. However, treatment itself may result in fatalities in many patients. In major leukemia centers, identical remission rates can be achieved for patients under and over age 60 (Foon et al., 1981). However, in most cases, the elderly have an increased susceptibility to fatal infectious and bleeding complications during the period of bone marrow aplasia. Furthermore, elderly patients are more likely to have an antecedent hematologic disorder, or "preleukemia," which is an adverse prognostic factor (Keating et al., 1981). Sorting out whether a patient is evolving from a preleukemic state and may be best supported with blood products or requires aggressive chemotherapy for any hope of more than short-term survival requires the expertise of a skilled hematologist. Designing therapy to meet the goals of an informed patient and family is crucial.

Lung Cancer

As emphasized earlier, the approach to the elderly patient with operative lung cancer should depend on the patient's pulmonary function and chances for a functional postoperative recovery. For inoperative non-small cell lung cancer, management is palliative with control of pain and maintenance of function the major goals. For small cell carcinoma of the lung, aggressive chemotherapy has prolonged survival (Greco, Oldham, & Bunn, 1981). While a retrospective series suggests that patients greater than age 70 had toxicity and response rates equivalent to younger patients (Beggs et al., 1980), a prospective series with current aggressive chemotherapy has not been reported in the elderly.

Colon Cancer

Gastrointestinal malignancies have been a frustrating area of management for all age-groups. Apart from screening programs, early diagnosis is difficult and so chances for curative surgical intervention may be diminished. Chemotherapy has had limited benefits in advanced stages. The progressive rise in colon cancer with age warrants a continued index of suspicion for this disorder with the possibility that early detection will result in successful surgical intervention (Cohen et al., 1978). Reports that the healthy aged can undergo surgery without undue risk are encouraging (Boyd et al., 1980). In other areas, such as esophageal cancer, newer palliative procedures such as insertion of a Celestin tube may improve nutrition and be very beneficial in the elderly (Mee, 1981).

Prostate Carcinoma

This disorder of elderly males has been largely the domain of urologists and radiation therapists, and treatment strategies for local control and possible cure have been well reviewed (Murphy, 1983). For advanced disease, palliation of symptoms is the major objective. Orchiectomy provides an advantage over diethylstilbesterol of lower cardiovascular side effects with equivalent response (Garnick et al., 1982). Recent trials of chemotherapy for hormonal failures have also been encouraging (Torti and Carter, 1980).

Breast Carcinoma

Undertreatment has been a common problem for the elderly woman with breast cancer. Recent studies showing similar survival rates for women over and under age 70 who have undergone surgery suggests that denying standard surgical procedures such as mastectomy and axillary lymph node dissection on the basis of age alone is inappropriate (Herbsman et al., 1981). Breast cancer is in general a systemic disease. The importance of axillary lymph node dissection may not be as part of a curative procedure, but rather staging, since positive nodes signal a likelihood for subsequent relapse. Adjuvant chemotherapy has dramatically reduced early relapse in premenopausal women and may result in a real increase in curability (Fisher et al., 1981). Of interest is a retrospective series which showed that the increased benefit of adjuvant chemotherapy in premenopausal but not postmenopausal women could be explained by the total dose of chemotherapy employed (Bonnadonna and Valagussa, 1981). Those postmenopausal women who received full-dose chemotherapy had a response equivalent to the premenopausal woman. A prospective series is needed to document the implications of this study in terms of both response and toxicity to maximum therapy in the elderly patient.

In the setting of metastatic disease, estrogen receptor status of the cancer is critical. The multiple modalities of endocrine manipulation available can often be used in a sequential fashion to provide years of quality life (Fisher and Carbone, 1982). In hormonal failures, chemotherapy can often be used to achieve similar palliative effects. In this palliative setting, reduced doses may be adequate to achieve benefit while limiting toxicity (Creech et al., 1980).

Thus while ignorance still remains in terms of precise benefit/risk ratios for therapeutic intervention in elderly patients with cancer, the age barrier to intervention has been broken in almost all areas of cancer therapy. The clinician must explore the range of curative and palliative therapies available within the limits of tolerance of the patient as defined by functional status and potential rather than age.

SCREENING

Guidelines for cancer screening have looked carefully at the earliest stage at which screening would begin as shown by Table 1.1, which lists the American Cancer Society recommendations. Despite the prevalence of cancer in the older population, little adjustment in the specific recommendations is made for increasing age. Criticism of these guidelines has recently been addressed (Eddy, 1981) and the factors involved in recommending a specific screening test are complex (Love and Camilli, 1981). Moreover, the entire concept of the periodic health examination has come under closer scrutiny (Scherr, 1981). Different studies vary markedly in their assessment of the value of various procedures as screening tools. The American College of Physicians has recommended that each physician individualize his plans for patient examination. Thus, although the elderly are often under medical attention for coexistent diseases, screening for cancer is often not performed. The lack of a more directed approach to cancer screening is a striking example of the passivity of our health care system in addressing the health needs of the elderly (Besdine, 1980).

A case in point would be the pelvic examination in the elderly patient. The ACS guidelines recommendation for a continuation of the annual pelvic examination, but discontinuation of pap smears at the age of 65, was made on the basis of the low incidence among the elderly population who *had been previously screened.* The SEER data show that the age-specific incidence in mortality of cervical cancer rises progressively with age to age 85 (Young et al., 1981), presumably because of patients who have escaped screening at a younger age. Thus pap smears may still be of value in this subgroup. Endometrial cancer and ovarian cancer

Table 1.1
Summary of ACS Recommendations for the Early Detection of Cancer in Asymptomatic Persons

Test or Procedure	*Sex*	*Age*	*Frequency*
Sigmoidoscopy	M & F	Over 50	Every 3–5 years; after 2 negative exams 1 year apart
Stool guaiac slide test	M & F	Over 50	Every year
Digital rectal examination	M & F	Over 40	Every year
Pap test	F	20–65; under 20, if sexually active	At least every 3 years after 2 negative exams 1 year apart
Pelvic examination	F	20–40 Over 40	Every 3 years Every year
Endometrial tissue sample	F	At menopause women at high risk[a]	At menopause
Breast self-examination	F	Over 20	Every month
Breast physical examination	F	20–40 Over 40	Every 3 years Every year
Mammography	F	Between 35–40 Between 40–49 Over 50	Baseline Every 1 or 2 years Every year
Chest x-ray			Not recommended
Sputum cytology			Not recommended
Health counseling and cancer checkup[b]	M & F M & F	Over 20 Over 40	Every 3 years Every year

[a]History of infertility, obesity, failure of ovulation, abnormal uterine bleeding, or estrogen therapy.
[b]To include examination for cancers of the thyroid, testicles, prostate, ovaries, lymph nodes, oral region, and skin.
Adapted from Eddy, D.: Guidelines for the cancer-related checkup. *CA 30*:194, 1980; with update per American Cancer Society Recommendations, *CA 33*:255, 1983.

and mortality are highest in patients over 70. Additionally, vulvar carcinoma is uniquely a cancer of extreme age. Thus, multiple reasons exist to continue the annual pelvic examination in the elderly. Although such screening procedures may not be applicable to some debilitated patients, physician bias, lack of patient education, and some increase in technical difficulties have led to the underutilization of this examination in the elderly in general.

Physicians caring for the elderly should consider the potential value of cancer screening in this high-risk group unless they feel that the patient's coexistent medical problems would preclude further diagnostic and therapeutic intervention even if a screening test were positive. Certainly an annual exam including a breast examination, pelvic examination, rectal examination, and stool guaiac slide test are reasonable. Sigmoidoscopy, mammography, and other laboratory testing for cancer and other diseases may be tailored to the individual. Hopefully, future health policy strategies will specifically address the questions of benefit versus risk for all these screening procedures in the elderly.

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CHAPTER 2

Genomic Plasticity in Aging Human Cells

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After maturity physiologic decline occurs in virtually all systems (1). Many factors have been implicated as causative mechanisms ranging from defective macromolecules within cells to altered neurohumoral feedback loops between organs. The original source of these alterations is still unknown, but concepts have emerged at two different levels of functional organization. First, aging as a property of multicellular organisms may arise from interactions of constituent cells, perhaps from a single "pace-maker" focus which triggers senescence. Second, aging may be an intrinsic property of all cells, and even though modifiable by external cues, each cell may age autonomously. Whichever alternative turns out to be primary, it must still be explicable in molecular terms as a loss of genetic information.

Aging may be defined as a loss of adaptation to the environment. While this clearly distinguishes aging from development, these two processes are often similar and likely to operate along the same continuum from conception through maturity to old age. Most would accept as genuine aging such diverse processes as graying of hair, wrinkling of skin, and arteriosclerosis, but they would reserve embryogenesis, somatic growth, and pubescence for development. Both kinds of phenomena are clearly time dependent but the interface between them is often blurred (2). Thus involution and new development are frequently juxtaposed even at early and middle stages of the life span (3). Cogent examples are the placenta versus the fetus during gestation and the supplanting of deciduous teeth by permanent teeth during infancy. Atrophy of the thymus occurs during childhood when virtually all other organs continue to grow and mature. The menopausal ovary involutes relatively abruptly in comparison to other organs in middle-aged females. The loss of various proteins during fetal life including gamma globin, carcinoembryonic antigen, and alpha fetal protein exemplify specific forms of molecular involution that are developmental rather than senescent (4). In short, attempts to delineate when development is succeeded by aging may be futile. Perhaps the major distinction is that during aging, in contrast to development, no proteins or organs arise with essentially new structures or functions. Rather it appears that many genes previously repressed during development tend to be reexpressed in isolated albeit increasing numbers of cells (see below).

In this review we will discuss previous studies in our laboratory on cellular aging, predominantly using the model of cultured human fibroblasts to illustrate how physiologic decline and certain age-dependent disorders such as cancer may originate at the cellular level. In particular, we provide evidence for genomic plasticity which may participate in the extinction of cellular replicative capacity during cellular aging and also predispose to the rising number of pathologic foci in various tissues. We will also attempt to explain the individual variation that occurs progressively between aging individuals in the rate of decline of organ-by-organ physiologic capacity and in the ascendancy of age-dependent diseases.

CELLULAR PROLIFERATION DURING LIFE IS GENETICALLY PROGRAMMED

The best example of a genetic program is the complex sequence triggered by fertilization of the ovum. In precision of timing and efficiency of organogenesis, the nine months of human gestation represent the highest order of program schedules. *In utero*, tissue expansion is accomplished by proliferation of diverse cells with similar growth trajectories, but these peak just before birth (Figure 2.1). Late in fetal life and during infancy, growth of virtually all organs continues at a decreasing rate, while during adolescence, organ growth virtually ceases as the somatic proportions of adulthood are attained. Thereafter, tissue homeostasis is maintained with only a fraction of the mitotic activity seen during intrauterine life except following cell injury. It is significant that the "resting," unstressed mass of each organ is maintained essentially constant in normal adults. But in response to heightened physiologic demand, adult tissues expand with a blend of proliferation (hyperplasia) or increased cell size (hypertrophy) depending on highly characteristic mitotic properties determined by differentiation. Three main types of cells can thus be distinguishable, whether parenchymal or stromal, based on their replicative capacity in adulthood.

Continuous Replicators

Cells capable of dividing throughout life are those of the gastrointestinal, hematopoietic, epidermal, and spermatogenic systems. Frank insufficiencies in these systems are rare in the elderly although stem cell compartments undergo gradual atrophy while residual cells generally decrease their replicative vigor.

Intermittent Replicators

Such cells normally turn over slowly but appropriate stimuli will evoke a proliferative response. Damage to the liver, for example, stimulates a regenerative burst in surviving hepatocytes. The connective tissue fibroblast will under normal steady-state conditions divide infrequently to replace losses by wear and tear. But following injury, they are capable of responding with cell proliferation to the extent that wound healing is complete. The tissue culture fibroblast is similar to its *in vivo* counterpart in that it divides following the "injury" of subculture until density-dependent inhibition occurs in confluent monolayers.

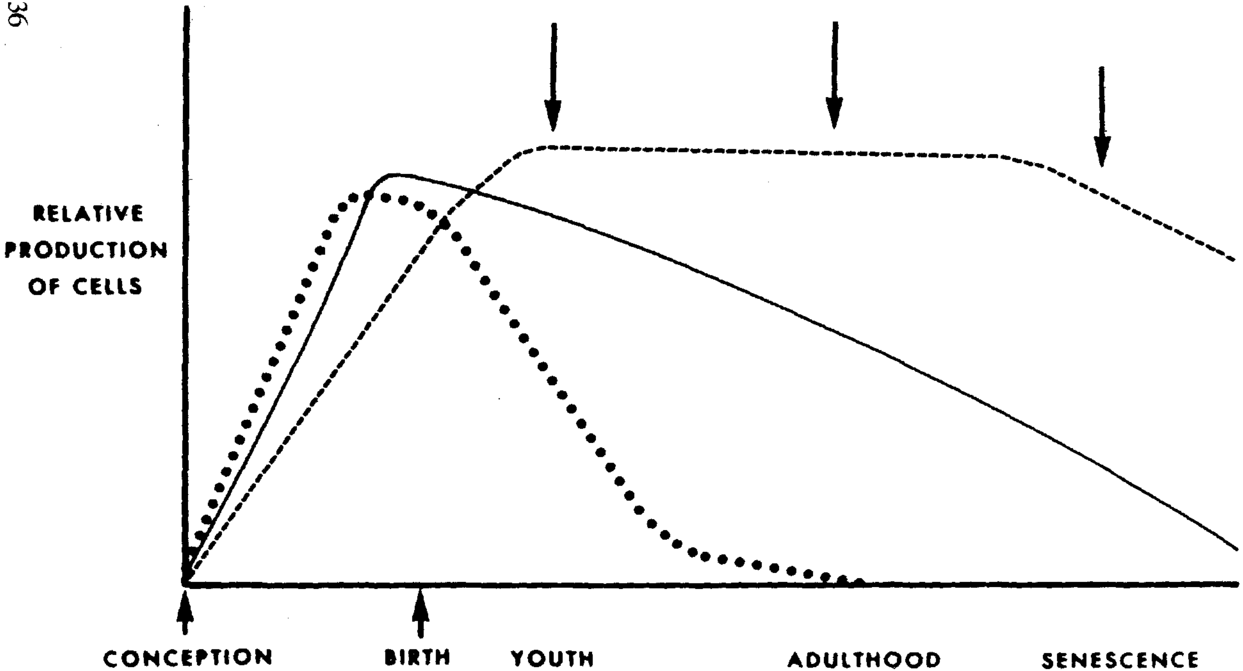

Figure 2.1 Replicative capacity of cells during various stages of the life span. Cells are classified according to their replicative capacity, after somatic growth ceases; -----, continuous replicators; ——, intermittent replicators; ......, nonreplicators; ↑, discrete events on a time scale that is otherwise a gradual and continuous sequence; ↓, stimuli for cell division. (Reprinted by permission of the *New England Journal of Medicine* from Goldstein, S., The Biology of Aging, *285*:1120–1129, 1971.)

Nonreplicators

Neurons and cardiac and skeletal muscle cells lose essentially all replicative capacity before adolescence. Hence, any injury or other stimulus for repair is followed by hypertrophy of surviving cells and/or infiltration by nonspecific connective tissue cells such as the fibroblast.

Clearly the trend *in vivo* is toward decreased replicative capacity with shrinkage of stem cell compartments in all cell types. Paradoxically there is an increase in multifocal hyperplasias leading progressively to benign and malignant neoplasms (5). The juxtaposition of these two opposites, replicative senescence and reemergence, is of great interest in contemplating mechanisms and will be discussed below.

A MODEL FOR CELLULAR AGING: THE CULTURED HUMAN FIBROBLAST

Over the past two decades several studies have marshaled evidence to support the validity of this system as a model for aging. Hayflick and Moorehead (6) were the first to document the limited replicative life span of cultured human fibroblasts. Hayflick (7) subsequently showed that increased donor age was a negative determinant of replicative capacity, and many studies have then gone on to demonstrate formally that an inverse correlation exists between the donor age and the cumulative limit of mean population doublings (MPD), a measure of the replicative life span (8–11). Moreover, fibroblasts cultured from patients with the genetically determined disorders of premature aging, progeria, and the Werner's syndrome, have curtailed culture life spans or generally poor growth capacity or both (9, 11–13). Similar growth deficits have also been demonstrated in skin fibroblasts established from individuals with Down's syndrome and other trisomies as well as the chromosomal breakage syndromes inherited as autosomal recessive traits (see ref. 12). However, in some of these cases the specific environmental eliciting factor must be applied to cells before replicative capacity is compromised, e.g., sunlight or UV radiation in xeroderma pigmentosum (2). The diabetic genotype also seems to be detrimental to cell growth although its effect is subtle (13). In total, it is clear that the physiologic age, the sum total of genetic and environmental influences accumulated over the life span, rather than chronologic age is of paramount importance in determining the replicative capacity of cultured fibroblasts.

We emphasize that fibroblasts represent only one of myriad cell types within the organism. Nonetheless, it appears that cultured fibroblasts from specific anatomic sites and parenchymal cells of diverse types grown *in vitro* also have a finite life span that is inversely proportional to donor age (9, 14–16). Therefore, the study of cultured cells derived from subjects of various ages and with specific disorders of premature aging can provide major insights into basic mechanisms of biologic aging.

REPLICATING CELLS HAVE A BIOLOGICAL CLOCK

There are two crucial issues in the limited replicative life span of the fibroblast: does the replicative limit depend on factors independent of cell division, i.e., does "metabolic time" lead to exhaustion of replicative potential? Or does the replicative limit depend on events related to cell divison, i.e., DNA replication and mitosis, such that cells have a clear maximum number of generations? Two early studies adduced evidence for the second possibility. In the first case Dell'Orco et al. (17) reduced the serum content of growth media from the normal 10 percent to 0.5 percent which leads to virtually total arrest of DNA synthesis and mitosis with preservation of cellular viability. They held some cultures in stationary phase for up to six months (equal to about one life span of continuously replicating cells) followed by restoration of serum concentration to the usual 10 percent. Such cultures then resumed normal proliferation and went on to achieve the same number of maximum MPDs as cultures whose growth was uninterrupted by serum deprivation.

In the other study (18) cells were maintained in normal growth medium (containing 15 percent fetal calf serum in this case) but in the confluent density-inhibited state for up to three months with complete replacement of medium weekly. After this time, cells which were freed from the stationary phase and subjected to continuous subculture went on to achieve virtually the same maximum number of MPD before phaseout as uninterrupted cells. In both cases (17,18) the additional calendar time accruing was highly significant. These studies clearly indicate that cells "count" or record each round of division rather than other kinds of time-dependent metabolic events.

More recent experiments in our laboratory have confirmed and extended the concept of the replicative counter (19). In brief, 40,000 cells were inoculated in a small drop into the center of a Petri dish. On incubation, cells first adhere, then proliferate in a circular expansion such that radial growth is linear with time. Autoradiographic studies with H-thymidine incorporation as an index of DNA synthesis showed that virtually all DNA replication occurs within a small rim of cells at the circumferential edge. After some three or four weeks, cells in this outer rim decrease their growth rate and ultimately cease dividing due to senescence.

We then asked whether the centrally located cells which were density inhibited and hence did not divide had a greater replicative capacity remaining than peripheral cells. Additionally, we asked whether cells at intermediate radial positions showed a continuous distribution of replicative capacities. Several areas of the circular outgrowth were harvested at different radial positions (19) and subcultured as individual isolates until senescence. The additional number of MPD until senescence was then determined for each isolate and the results plotted in Figure 2.2. Regression analysis indicated that the proliferative capacity remaining decreased linearly with distance from the center of the outgrowth at a rate of 1.33 ± 0.14 MPD per mm. The theoretical generation distribution for such a circular outgrowth of cells was also determined and revealed a linear distribution spanning 31 generations (Figure 2.3). Knowing the initial MPD level of fibroblasts used to initiate the outgrowth (MPD 18) and the maximum MPD attainable in replicate cells subcultured in parallel (MPD 55), we could predict the number of additional MPD accruing before senescence (Figure 2.3). This was 37 MPD for the most central cells (r' less than 5 mm from the center) and 6 MPD for the most periph-

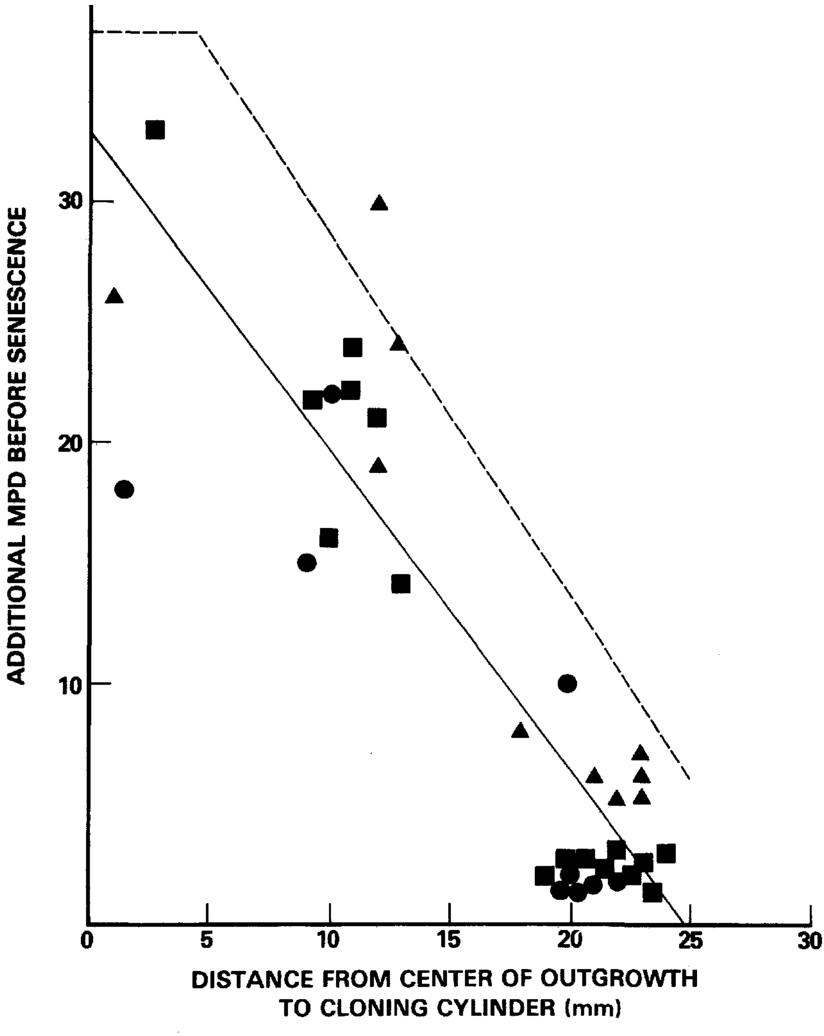

Figure 2.2 Additional MPD before senescence plotted against radial position of cells at various points within the outgrowth. Additional MPDs before senescence were determined for cells from three individual circular outgrowths (●, ▲, ■). The least squares line, $r = -0.87$ (———) and the theoretical line (------) are shown. (Reprinted by permission of Alan R. Liss, Inc., from Harley, C.B., and Goldstein, S. Cultured Human Fibroblasts: Distribution of Cell Generations and a Critical Limit, *Journal of Cellular Physiology* 97:509–519, 1978.)

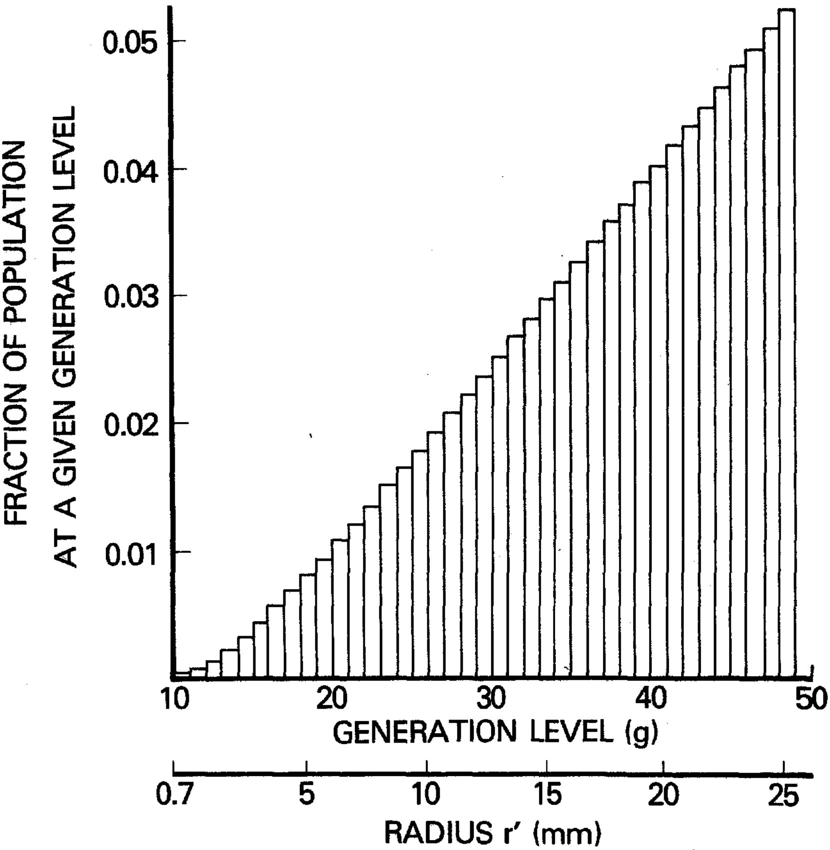

Figure 2.3: Continuous distribution of cell generations created by clonal outgrowth. The number of cells occupying each generation level (g) at a radius r' was determined by an iterative procedure. Since all cells undergo 10 divisions before r' is greater than 0.7 mm the abscissa begins at g = 10, r =0.7. (Reprinted by permission of Alan R. Liss, Inc., from Harley, C.B., and Goldstein, S. Cultured Human Fibroblasts: Distribution of Cell Generations and a Critical Limit, *Journal of Cellular Physiology* 97:509–519, 1978.)

eral cells (at r' equals 25 mm). The predicted value (Figure 2.2) for the replicative capacity remaining in cells at a given radius showed a decline of 1.55 MPD per mm, remarkably close to the experimental value of 1.33 per mm above. That experimental points lie 6 MPD below the theoretical line likely reflects a minor loss of proliferative capacity due to a slight residue of cell division in the density-inhibited central region.

Our data confirm that fibroblasts "count" the number of replicative events to a uniform maximum limit. Also important is that cells in the circular outgrowth exist along a heterogeneous but ordered scale of MPD (Figure 2.3). Thus a progressively more vigorous "stem cell pool" resides within shorter radial positions of the circle and is available for proliferative bursts. Yet these "young" cells are increasingly depleted with repeated cell division. Cells at successively higher generation levels are more abundant, but they proceed continuously toward senescence not only in their proliferative capacity but also in functional reserve (20, 21). In the case of solid organs *in vivo,* young stem cells would have the capacity to generate large populations via asynchronous cell division thus producing a tissue composed of a heterogeneous mixture of cells with respect to replicative and functional age. In the case of marrow cells, which release their mature progeny into the circulation, cells would become widely disseminated but they would still be heterogeneous in terms of replicative and functional age. Moreover, the inexorable tendency is toward progressive cell senescence. In either case, however, the model obviates the need to postulate immortality of stem cells. Rather it indicates how proliferative capacity of cells in specific tissues could easily exceed the replicative needs over a "normal" life span, and yet in some cases exhaustion could occur, focally if not generally.

GENETIC INFORMATION IS LOST DURING AGING

Aging and the strict barrier of mortality in all metazoan species must somehow relate to impaired flow of information within the sequence from nuclear DNA to the final gene product. Information could be lost in two ways:

1. Via random deterioration related to a gradual accumulation of errors or other damage that reaches a threshold beyond which viability is impossible;
2. Via a genetic process emanating from differentiation and development.

The best-known example of a stochastic model is Orgel's hypothesis that errors in crucial informational macromolecules, particularly those responsible for protein synthesis, lead autocatalytically to an error "catastrophe." This theory has been widely tested but virtually no experimental evidence has been found to support it in a variety of studies (22, 23). To our knowledge, the single exception has been the observation of increased infidelity of DNA polymerase in MRC-5, a human strain of fetal lung fibroblasts, as they traverse their limited replicative life span (24, 25). However, an error-prone DNA polymerase should generate genetic mutations at an increasing rate, at several widespread loci, but this has not been borne out in direct testing (26).

While random elements are clearly involved (27; see ref. 28), a largely deterministic "programmed" mechanism, perhaps akin to differentiation, appears increasingly likely as the underlying basis of cellular aging (29–31). In contemplating that cells may age by a mechanism related to differentiation, we were led to consider whether alteration occurred in the structure of nuclear DNA, particularly the 20 to 30 percent of the genome composed of repetitious DNA sequences (32). We now review recent studies in our laboratory which have examined this subject in several strains of human diploid fibroblasts at intervals of their limited replicative life span ("aging *in vitro*") with additional data on circulating lymphocytes from donors of different ages ("aging *in vivo*").

A SPECIFIC FAMILY OF REPETITIOUS DNA SEQUENCES IS DEPLETED DURING AGING OF HUMAN FIBROBLASTS IN VITRO

Human fibroblast DNA was labeled *in vitro* with C-thymidine over three population doublings, then purified, cleaved with Eco RI restriction endonuclease, and electrophoresed on agarose gel followed by densitometric scanning of autoradiographs. The two prominent DNA bands at 340 and 680 base pairs, representing the "hRI" family of tandem repeats, were found to be progres-

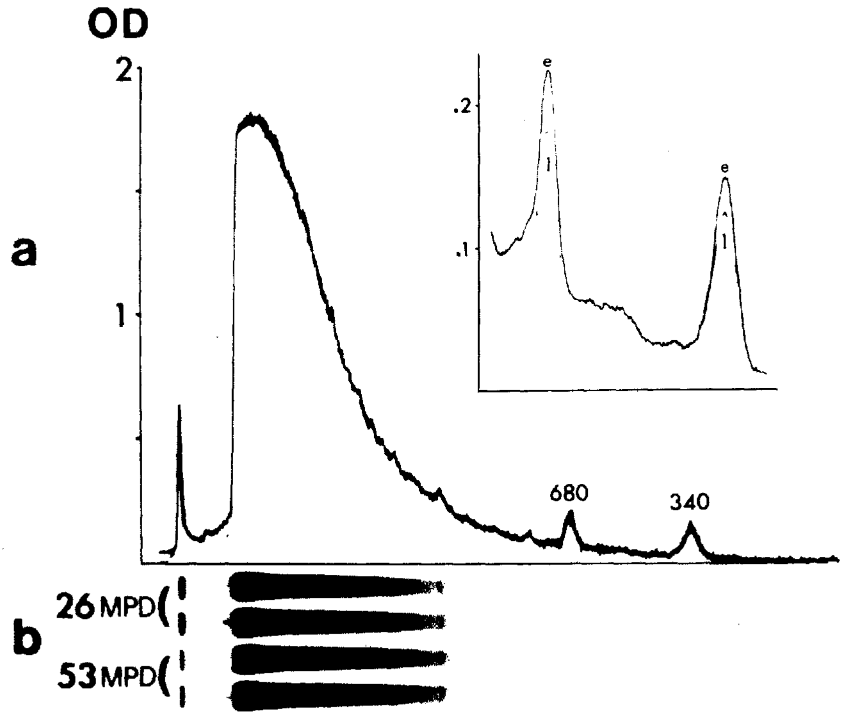

Figure 2.4. Autoradiographs and densitometric scans after agarose gel electrophoresis of C-DNA digested with EcoRI. Normal fibroblast strain A2 was labeled over 3 MPD with C-thymidine at early passage (e) and at late passage (l) followed by a purification of DNA and EcoRI digestion. DNA was electrophoresed from left to right (b) followed by drying of gels and autoradiography with X-ray film. Densitometric tracing (a) shows superimposition of early and late-passage patterns. Insets are peak tracings at 340 and 680 bp on an enlarged scale and show about 15 percent reduction in each size class of hRI fragments at late passage. (Reprinted by permission from Shmookler Reis, R.J., and Goldstein, S. Loss of Reiterated DNA Sequences during Serial Passage of Human Diploid Fibroblasts in vitro. *Cell 21*:739–749, 1980. Copyright © by M.I.T.)

sively depleted over the cellular life span (Figure 2.4). In three cell strains derived from young normal donors, the range of decrease in the hRI bands was 7.5 to 23 percent over 17 to 27 mean population doublings (MPD) and averaged 0.62 percent loss per MPD (33). Similar results were obtained in these cell strains by the nonautoradiographic method of ethidium bromide staining. A third independent method, that of saturation hybridization, revealed an even more pronounced difference between early and late-passage DNA (Figure 2.4). Plateau levels, determined by double reciprocal transformation of the data in (Figure 2.5) and linear extrapolation to the ordinates (33), revealed a 50 percent loss in this cell strain from early to late passage.

OTHER REPETITIOUS SEQUENCES ARE LOST DURING CELLULAR AGING

If the diminution in number of hRI sequences were accompanied by a general loss of reiterated sequences, this might be apparent from reassociation kinetics. Using a kinetic analysis of early and late-passage fibroblast DNA, those DNA sequences

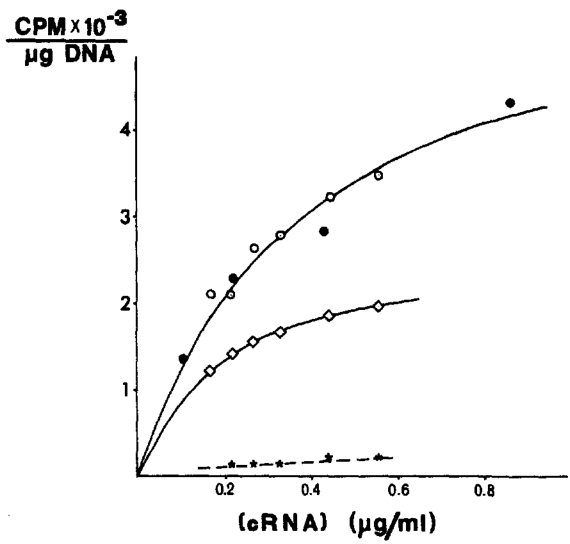

Figure 2.5. Saturation hybridization of ^{3}H-cRNA transcribed from a purified hRI sequence to filter-bound DNA from A2 fibroblasts at early passage in duplicate experiments (●, ○) and at late passage (△). Control hybridization to melon cDNA (*) is also shown. (Reprinted by permission from Shmookler Reis, R.J., and Goldstein, S. Loss of Reiterated DNA Sequences during Serial Passage of Human Diploid Fibroblasts in vitro. *Cell 21*:739–749, 1980. Copyright © by M.I.T.)

reassociating most rapidly at Cot values of 0.05 or less (implying at least 10^5 copies) were found to be depleted in late-passage cells by about 24 percent compared to those of early passage (Figure 2.6). At Cot values higher than 1, primarily representing unique sequences, Cot ≡ to 5,000, reassociation curves converged and could no longer be distinguished. It is difficult to ascertain the repetition frequency of the depleted

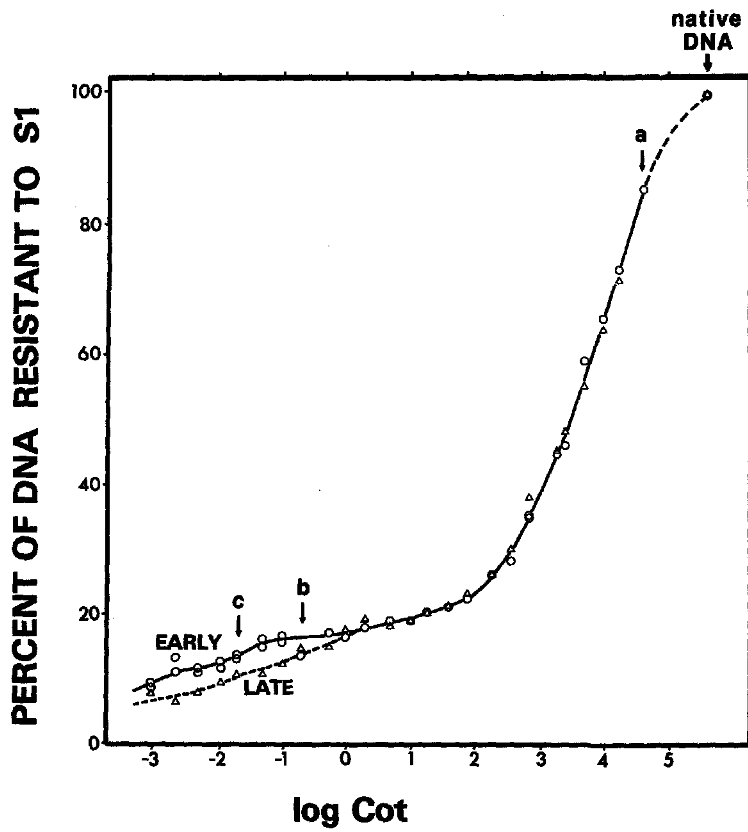

Figure 2.6. Reassociation kinetics of ^{14}C-DNA from A2 fibroblasts at early (○) or late (△) passage. Following reassociation double-stranded DNA duplexes were assayed by their resistance to S1 nuclease. Arrows at a, b, c indicate Cot of 40,000, 0.2, and 0.02, respectively. Native DNA indicates S1 nuclease resistance of sonicated native DNA without denaturation and reassociation. (Reprinted by permission from Shmookler Reis, R.J., and Goldstein, S. Loss of Reiterated DNA Sequences during Serial Passage of Human diploid Fibroblasts in vitro. *Cell 21*:739–749, 1980. Copyright © by M.I.T.)

sequences but it was clear at low Cot values that significant differences between early and late-passage DNA were reproducible. Other studies (34) reveal that three other discrete highly repetitive sequences characterized as bands of 45, 110, and 175 base pairs generated by the restriction endonuclease Msp I were also found to diminish in the same three normal strains of fibroblasts at late passage.

Alternative explanations for the apparent loss of highly reiterated DNA sequences during aging *in vitro* were carefully considered. Certain of the later could have been produced by DNA divergence, base modification, cell cycle changes, or specific chromosomal loss, rather than by DNA sequence deletion. The first two possibilities could be ruled out by examining the Tm's of reassociated DNA:DNA or DNA:RNA duplexes and by direct analysis of cytosine methylation, respectively. The third possibility, arrest in the S phase of the cell cycle, would lead to failure to replicate the specific repetitive DNA sequences if they were indeed late replicating. This mechanism was ruled out following analysis of published data by Macieira-Coelho et al. (35, 36) and Yanishevsky et al. (37). The last possibility, that chromosomes were lost intact or as segments containing the specific reiterated sequences, was excluded by direct karyotypic analysis using chromosome banding techniques (33). We have concluded, therefore, that late-passage cells have deleted a portion of their repeated sequences either by unequal recombination or by excision. In fact, a mathematical treatment revealed plausible parameters to support the notion that hRI sequences could be lost by unequal recombination followed by selection for those cells containing reduced amounts of repetitious DNA (38). However, the alternative that the sequences are excised from the genome cannot be ruled out (see below).

AMPLIFICATION OF EXTRACHROMOSOMAL CIRCULAR DNA ELEMENTS DURING CELLULAR AGING

DNA rearrangements which could account for loss of highly repetitious sequences would clearly be most common among such sequences but would be difficult to identify as individual events because of their very repetitiousness: the hRI repeat family, for example, comprises more than 300,000 copies/haploid genome (39). In order to characterize the instability of highly repetitious DNAs, we required a unique or low-repetition sequence which is interspersed among them. Calabretta et al. (40) probed a human DNA library and isolated just such a sequence from a cloned fragment of human DNA 15 kilobase pairs (kbp) in length. This fragment contained at least 10 copies of the highly reiterated Alu repeat unit, of which there are over 500,000 copies dispersed throughout each haploid genome (41). They excised and subcloned a 0.8-kbp region situated between clusters of 4 and 3 Alu repeats, and on hybridizing this "Inter-Alu" probe against DNA from human tissues, found a low repetition number of no more than 50 copies/cell. Polymorphism was observed between tissues of a single donor and between lymphocytes of different leukemic and normal donors in both the Inter-Alu banding pattern and copy number. This was visualized as polymorphism in the length of restriction fragments and variable intensities of autoradiographic bands, respectively, due in great part to extrachromosomal molecules (putatively circular) containing this sequence. A 4.8-kbp band which constituted the principal size class of circles hybridizing to the Inter-Alu probe in many tissues also contained Alu repeats but differed from genomic copies of Inter-Alu with respect to mapping of adjoining restriction sites (40). These observations represent an important milestone in studies of human DNA and are consistent with the idea that the Inter-Alu/Alu repeat cluster is transposable. In the studies that follow, we have utilized this DNA probe to explore genomic plasticity in human fibroblasts during aging *in vitro* and in lymphocytes undergoing aging *in vivo* (42).

Cellular Aging *in Vitro*

Six human fibroblast strains were examined at early and late passage. DNA samples, either undigested or following cleavage with Bam HI restriction endonuclease, were examined on Southern blots after hybridization to Inter-Alu probe labeled with ^{32}P (Figure 2.7). In each case after Bam HI digestion, the genomic

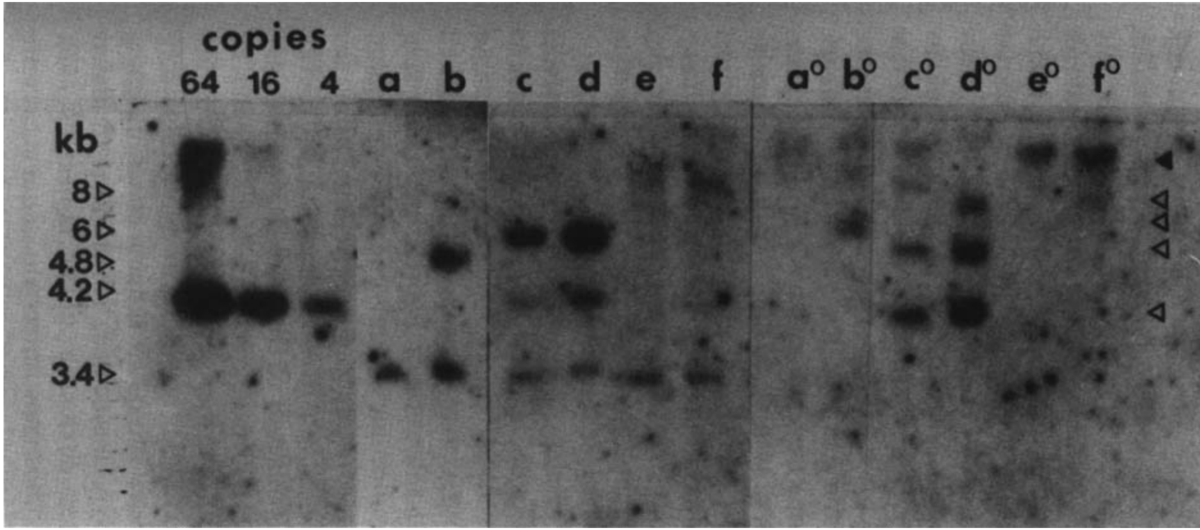

Figure 2.7. Integrated and extrachromosomal Inter-Alu copies in DNA of three fibroblast strains at early and late passage. DNA samples from strain A2 at early (a) and late (b) passage, strain DS at early (c) and late (d) passage, and strain TM at early (e) and late passage (f). Lanes a–f contain DNA samples cleaved with BamHI while lanes a°–f° contain undigested DNA samples which were electrophoresed, transferred to nitrocellulose, and hybridized to the Inter-Alu ^{32}P-DNA probe. Hybridization standards correspond to 4, 16, and 64 copies of Inter-Alu per cell. High molecular weight DNA did not enter the gel or ran at the minimum mobility for DNA (◀). Hybridization to extrachromosomal DNA bands in advance of this is indicated by (△). (Reprinted by permission from Shmookler Reis, R.J., Lumpkin, C.K., McGill, J.R., Riabowol, K.T., and Goldstein, S. Extra chromosomal Circular Copies of an Inter-Alu Unstable Sequence in Human DNA are Amplified during in vitro and in vivo Ageing, *Nature 301*:394–398, Copyright © 1983 Macmillan Journals Limited.)

(integrated chromosomal) Inter-Alu band appeared at 3.4 kbp (Figure 2.7, a–f). The copy number of the genomic band in the various cell strains ranged from two to six per cell but remained approximately constant during serial passage in a given cell strain. Four of six cell strains showed discrete additional DNA bands either appearing for the first time or increasing at late passage (Figure 2.7, a–f), which likely represent extrachromosomal circular DNA. The sizes of these bands ranged from 1.6 to 8 kbp following digestion, and the degree of amplification also varied from strain to strain (Figure 2.7).

Each fibroblast strain examined here was derived by ourselves from skin biopsies and maintained in our laboratory. It is noteworthy that these cells preserved an essentially diploid karyotype throughout passage and are free of mycoplasma by a variety of assays. Furthermore, these strains have never been exposed to antibiotics which may lead to amplification of circular extrachromosomal DNA. Additionally, hybridization against pure mitochondrial DNA did not reveal homology to the Inter-Alu probe. This clearly indicates that the circular DNA molecules are not derived from the mitochondrial genome, itself a circular extrachromosomal molecule of 16.5 kbp (43).

Several different experiments were done to characterize these DNA sequences as extrachromosomal circular elements. When total DNA was run without restriction endonuclease digestion (Figure 2.7, a°–f°), late-passage fibroblasts showed an increased number and intensity of hybridizing bands running ahead of the high molecular weight linear DNA region. In concert with control reconstruction experiments using the circular plasmid pBR322, this strongly suggests that such circles can migrate freely ahead of the large chromosomal DNA and are in fact amplified extrachromosomal copies of Inter-Alu-containing DNA. Further studies on CsCl equilibrium density gradients containing ethidium bromide also confirmed the presence of these Inter-Alu sequences within covalently closed circular DNA molecules, which run at higher density than either nicked circles or linear molecules (42). Moreover, such extrachromosomal Inter-Alu sequences were greatly enriched in covalently closed circular DNA molecules isolated from CsCl/ethidium bromide gradients. Most important, these circular molecules were up to 10-fold more abundant in late-passage fibroblasts.

Cellular Aging *in Vivo*

To explore the occurrence of these extrachromosomal circular DNA species in other somatic cells, we examined peripheral blood lymphocytes from 18 young normal donors, age 21 to 31 years, and 24-year-old normal donors, age 61 to 91 years, all of whom were in apparent good health and living at home. We found that chromosomal Inter-Alu copies varied from 2 to 40 copies/cell with no obvious correlation to age of donor. However, a pronounced age correlation was found in the single additional band observed at 4.8 kbp (Figure 2.8, e–h), at levels of 4 to 40 copies/cell, in lymphocytes from old but not young donors. This band, appearing in samples from 16 of the 24-year-old donors but none of the 18 young donor lymphocytes, is apparently extrachromosomal since undigested DNA from precisely those 16 donors also showed two discrete hybridization bands electrophoresing in advance of the high molecular weight chromosomal linear DNA (Figure 2.8, e°–h°). These two bands are thought to correspond to covalently closed circular DNA (faster band) and nicked circular DNA (slower band). More recent experiments have localized the majority of these extrachromosomal DNA forms to B lymphocytes rather than T lymphocytes.

CIRCULAR DNAs IN HUMAN CELLS: IMPLICATIONS FOR DEVELOPMENT, AGING, AND AGE-DEPENDENT DISEASES

The data reviewed here add further impetus to the evidence of genomic plasticity in human somatic cells, and for the first time reveal remarkable correlations with cellular aging *in vitro* and *in vivo*. Developmentally, the most profound alterations in gene structure so far reported occur during B cell differentiation where combinatorial joining of several dispersed DNA segments leads simultaneously to immunoglobulin diversification and the

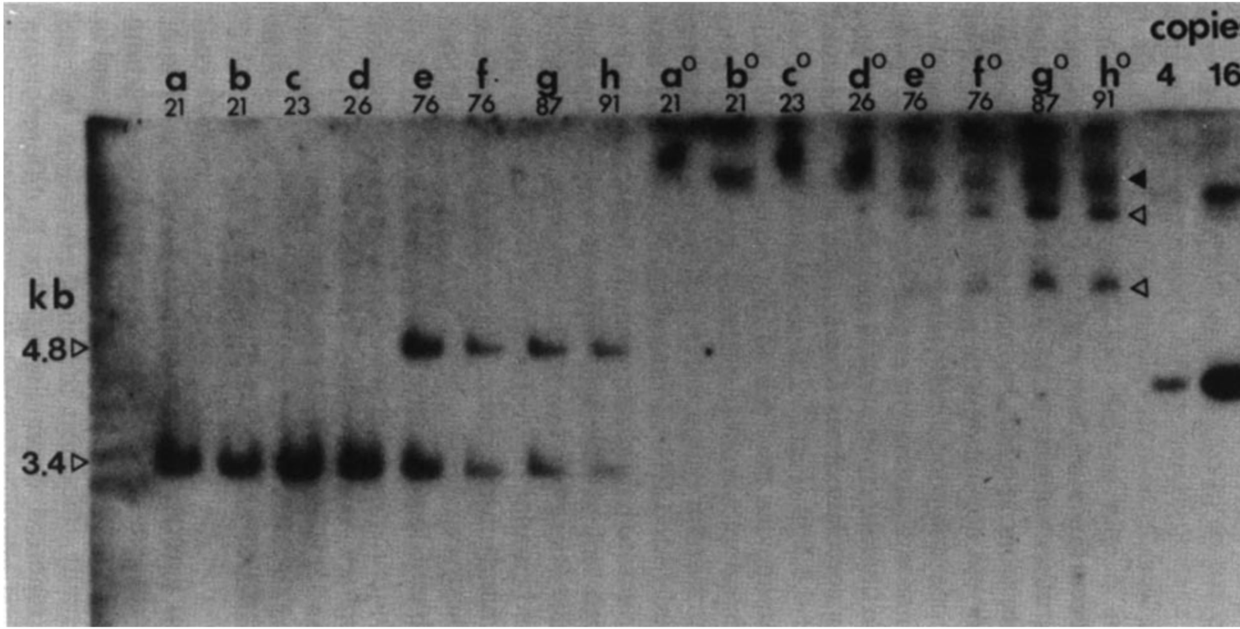

Figure 2.8. Integrated and extrachromosomal Inter-Alu copies in human lymphocyte DNA from young and old donors. DNA samples were derived from donors of ages indicated in years above each lane. Samples were digested with BamHI (a–h) or without digestion (a°–h°) and processed as in Figure 2.7. (Reprinted by permission from Shmookler Reis, R.J., Lumpkin, C.K., McGill, J.R., Riabowol, K.T., and Goldstein, S., Extrachromosomal Circular Copies of an Inter-Alu Unstable Sequence in Human DNA are Amplified during in vitro and in vivo Ageing, *Nature 301*:394–398, Copyright © 1983 Macmillan Journals Limited.)

specificity associated with major classes and individual clonal types (44). Indeed, it may well be that the immunoglobulin gene rearrangements during B cell ontogeny lead to the excision of specific segments and their appearance as circular DNA (45, 46). Experiments are underway to explore whether the circular DNA in old donor lymphocytes contains sequences homologous with immunoglobulin genes.

Apart from the striking rearrangements during ontogeny of immunoglobulin genes, however, there has been no evidence so far of DNA rearrangements in other aspects of vertebrate development. In this context, experiments on nuclear transplantation are of great interest, since nuclei of vertebrate somatic cells have been regarded as totipotent and therefore fundamentally similar to the germ line. But while normal animals can be produced after transplanting nuclei from embryonic tadpole midgut cells into a fertilized egg or early blastula, no one has ever succeeded in producing a normal animal using the nucleus taken from the somatic cell of an adult (47). Moreover, the maximal success rate for midgut nuclei directing tadpole embryogenesis is approximately 2 percent, which may correspond to the frequency of stem cell in this continuously proliferating tissue. Therefore, subtle gene rearrangements may occur during vertebrate development leading to irreversible commitment of somatic cells to a given line of gene expression with reciprocal loss of totipotent function.

By the same token, aging of somatic cells may proceed along the lines of terminal differentiation with progressive restriction of options. This would best fit a deterministic mechanism whereby DNA sequences such as the highly reiterated hRI and Alu I sequences are excised and/or rearranged in the genome, leading to progressive diminution in the functions thought to be subserved by their regulatory action, including initiation of DNA replication for Alu sequences (41) and perhaps mitotic regulation for centomeric arrays such as hRI (48). This is of immediate relevance to the "counter" which determines the critical replicative limit of fibroblasts and other intermittently or continuously mitotic cells *in vitro* and *in vivo*. In any case, genomic plasticity could contribute to the physiologic decline associated with cellular senescence. Moreover, appearance of DNA elements as extrachromosomal circles which can undergo autonomous replication would enable them to compete for limiting replicative factors, or ultimately to be reintroduced into the genome. This latter potential might produce the opportunity for random, aberrant insertion within a rare cell (rare in proportion to the vast number of somatic cells) leading to abnormal DNA replication which triggers the focal hyperplasias of aging (5). Similarly, in even rarer clones, the outcome could be malignant transformation, or even proliferation of smooth muscle cells in atherosclerotic plaques. But this randomness predicts that variability between tissues and between persons will increase, thus accounting for the age-dependent rise in variance for any given physiologic or pathologic parameter (49).

Other mechanisms will undoubtedly prove to be involved in senescence besides change in the repeat number of DNA sequences and their spatial configuration. For example, we and others have demonstrated imperfect transmission of DNA methylation patterns from cell generation to generation, particularly in the vicinity of the unique genes which code for specific proteins (34, 50, 51). Thus, if gene methylation is important in maintaining the repressed state (52), then demethylation may often lead to leaky expression of previously silent genes in individual clones even though the extent of leakiness for any given gene appears low when averaged over polyclonal cell populations. Future studies should elucidate the complex nature of genomic change during cellular senescence, its precise relationship to cytodifferentiation, and its intimate association with age-dependent diseases such as cancer and atherosclerosis.

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SECTION II

Clinical Practice

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CHAPTER 3

Multi-infarct Dementia

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INTRODUCTION

For many years, laymen associated "hardening of the arteries" with the slowly progressive loss of cognitive function commonly observed in the elderly, and the medical community seemed to agree (Fisher, 1968; Wells, 1978). However, ultrastructural analysis of neuritic plaques and neurofibrillary tangles (Terry, 1963, 1967; Terry et al., 1964), their lack of association with focal atherosclerosis (Corscillis, 1962; Rothchild, 1937, 1942), and the work of Tomlinson et al. (1968, 1970) demonstrating that degenerative neuropathologic changes correlated with dementia have led to the recognition of Alzheimer's disease or senile dementia of the Alzheimer type (SDAT) as the major cause of dementia in the elderly (Katzman, 1976). The question arises as to whether cerebrovascular disease is relevant to the problem of dementia in the elderly. Autopsy analysis of patients with dementia have revealed that about half showed change exclusively of SDAT, 20 percent revealed evidence exclusively of cerebrovascular disease or multi-infarct dementia (MID), and 12 percent revealed evidence of both disorders (MIX) concurrently (Tomlinson et al., 1970).

In recent years, conclusions based on these investigations have been challenged. It is well known that even patients with multiple small infarcts may not be demented (Fisher, 1965). How can one predict whether a specific pattern of infarcts is etiologically related to clinical dementia? Marsden and Harrison (1972) assigned the clinical diagnosis of vascular dementia to only 8 of 106 patients admitted to a neurologic ward for evaluation of presumed dementia. Wells (1978) compiled the data from a number of clinical studies (including Marsden's) and noted that vascular dementia accounted for only 8 percent of etiologic diagnosis in 222 patients. Conversely, Feigenson et al., (1977a, 1977b), in a study of poststroke rehabilitation, noted the presence of an organic mental syndrome in 27 percent of 318 patients admitted to a specialized stroke rehabilitation unit. Is cerebrovascular disease a frequent enough cause of dementia to warrant an extensive and expensive clinical evaluation of each patient presenting with this complaint?

We believe that the evidence is clear that vascular disease, while not the major etiology, is involved in a significant subset of elderly patients with dementia. It is an area where early diagnosis is crucial since appropriate intervention may arrest or prevent the ultimate development of dementia. This chapter will discuss clinical-pathologic and physiological (cerebral blood flow and metabolism) evidence concerning the role of vascular disease as a cause of dementia, the epidemiology of cerebrovascular disease diagnosis, and specific syndromes.

PHYSIOLOGICAL EVIDENCE: CEREBRAL BLOOD FLOW AND METABOLISM

The concept that dementia must be related to deficiencies in cerebral circulation has seemed logical to both medical and lay popular opinion. Since the initial description of techniques for measurement of cerebral blood flow (CBF) was made, there has been great enthusiasm for the use of CBF in the study of the dementing diseases, but results have been inconsistent (Sokoloff, 1978, 1981). Sokoloff (1966), using the nitrous oxide technique, reported that there was no significant change in CBF with aging in a nonhospitalized population of elite volunteers screened for disease and hypertension, while significant decreases in CBF were noted in elderly patients with dementia and in elderly controls with atherosclerotic disease. Most of the other investigations using xenon-133 inhalation have demonstrated a significant decrease in CBF in aging (McAlpine et al., 1981; Melamed et al., 1980; Naritomi et al., 1979; Obrist et al., 1975). Evaluation of CBF in dementia has also yielded conflicting results. While Obrist et al. (1975) using xenon-133 inhalation and Ingvar and Gustafson (1970) using intracarotid injection of xenon-133 found a decrease in blood flow to cortical areas in both SDAT and MID, Hachinski et al. (1975) and Harrison et al. (1979) using intracarotid xenon-133 reported decreased blood flow only for MID with normal blood flow in SDAT. Yamaguchi et al. (1980) using xenon-133 inhalation reported a uniform decrease in cortical blood in SDAT while MID showed a patchy reduction. They stated that blood flow was related to cerebral atrophy as identified by computed tomography (CT). Melamed et al. (1978) were unable to demonstrate a correlation, using the same technique, between cerebral blood flow and cerebral atrophy. Activation procedures which use specific tasks to increase regional cerebral blood flow in normal controls did not show similar increases of CBF in patients with dementia (Ingvar and Lassen, 1978; Yamaguchi et al., 1980). Difficulties with patient selection and technical considerations, particularly with the inhalation technique, compromise comparisons and conclusions from these studies (Rozenfeld and Wolfson, 1981).

A number of recent investigations have attempted to clarify the situation. Frackowiak et al. (1981) used the oxygen-15 label to measure regional cerebral blood flow (rCBF), mean cerebral oxygen utilization, and oxygen extraction fractions in patients with SDAT and MID and in age-matched controls. In patients with both SDAT and MID, regional blood flow and oxygen utilization were reduced in direct proportion to the severity of dementia. In both mild MID and SDAT, this reduction was most marked in the parietal lobes. In severe SDAT, there was a marked decrease in rCBF to the frontal lobes as well. Cerebral blood flow and oxygen utilization were closely correlated in all subjects. Most important, there was no evidence for increased oxygen extraction ratio in either MID or SDAT. Hence, these experiments rule out the presence of chronic cerebral ischemia in either of these forms of dementia. This implies as well that the decrease in cerebral blood flow in MID is related to decreased cerebral metabolism secondary to static cerebral infarcts and not to inadequate tissue perfusion. While it has been reported that cerebral ischemia will cause EEG changes when blood flow is decreased to 20 ml/100 gm/min (Ingvar and Lassen, 1978), there is no evidence that this occurs in the demented patient. Lagergren (1979) has demonstrated that memory may be improved in patients with severe bradycardia by correction of the rate abnormality. While in this situation, as well as in occasional cases of chronic atrial fibrillation, there is decreased cerebral perfusion (Lavy et al., 1980), use of the term "cardiogenic dementia" (Editorial, *Lancet,* 1977) to imply that a chronic dementia is generally secondary to chronic ischemia without cerebral infarcts is a misnomer. Such dysfunction is usually due to static lesions. Revascularization, if the tissue surrounding the infarct is well perfused, will not improve function in the area of the previous infarct. It is difficult to understand the recently reported improvement in memory and verbal skills reported after carotid endarterectomy for transient ischemia attacks (Kelly et al., 1980). It is curious that preoperative psychological evaluation in these patients with transient focal ischemia, but without stroke, was not different than a control group admitted for noncarotid peripheral vascular disease without cerebral symptoms. Another recent report has failed to note any improvement in cognition relevant to endarterectomy (Matarazzo et al., 1979).

Benson and his associates used F^{18}-deoxyglucose and positron emission tomography (PET) to measure patients with dementia. They noted a diffuse cortical depression of glucose metabolism in SDAT and patchy metabolic depression in MID. Abnormal cerebral glucose metabolism has been previously demonstrated in SDAT (Hoyer, 1978). Differences between the work of Frackowiak which indicated that MID was associated with diffuse abnormalities and the more focal abnormalities noted by Benson may be due to discrepanceies between oxygen utilization and glucose metabolism or due to the large areas (2.5 cm^2) used by Frackowiak for analysis.

The weight of the evidence today in this rapidly developing discipline indicates that cerebral blood flow is directly related to cerebral metabolism and that reduction in blood flow is due to reduced metabolic demand secondary to either degenerative or vascular disease of the brain. There is no reason to expect that vasodilator therapy would be of efficacy in SDAT or in most cases of MID as there is no evidence of active ischemia. In fact, in some patients who have focal brain ischemic lesion, there are indications that this could exacerbate the situation since their greatest effect would be on normal vasculature which would tend to steal blood from ischemic areas (Capon et al., 1977; Cook and James, 1981).

It has become possible to demonstrate, however, that chronic ischemia on a hemodynamic basis does occur in a minority of patients with cerebrovascular disease. This has been demonstrated by the use of positron emission tomography with measurement of the oxygen extration ratio (OER), a measure of the relationship of cerebral oxygen metabolism and cerebral blood flow. In most patients with stroke or multi-infarct dementia, there is no increase in OER (Gibbs et al., 1984). When there is an increase in OER, however, it becomes important to consider treatment such as surgical bypass procedure. Whether chronic ischemia contributes to dementia in multi-infarct dementia has not yet been determined.

CLINICAL PATHOLOGIC EVIDENCE: RELATIONSHIP OF DEMENTIA TO CEREBROVASCULAR DISEASE AND CEREBRAL INFARCTION

The evidence for the association between dementia and cerebral infarction is based in part upon the clinical pathologic correlations reported by Tomlinson, Blessed, and Roth (1968, 1970). These investigators carried out detailed neuropathologic examinations on the brains of 78 patients whose mental states had been established using standardized scoring systems during life. Fifty of the 78 had been demented: of these, 25 were found to have characteristic Alzheimer changes, 9 patients had multiple cerebral hemisphere vascular infarcts with the volume of the infarcts exceeding 100 grams, 4 patients had both Alzheimer's and infarcts, 3 had dementia probably related to infarcts, and 5 patients probably had both disorders. Thus, 18 patients (30 percent) had cognitive dysfunction, attributed in whole or part to cerebral infarcts of significant size. Forty-two additional subjects had small infarcts, but within this group, the number of subjects who were demented or not demented was about equal. In contrast, dementia occurred in 16 of 18 patients with infarcts greater than 50 ml and in all 9 patients with estimated infarct volumes of greater than 100 ml. The implication of this work is that the likelihood of developing dementia is related to the volume of cerebral hemisphere tissue infarcted. However, no correlation between infarct size and severity of dementia was reported.

In the Tomlinson study, the patients with vascular dementia had multiple infarcts involving both hemispheres. Specific bilateral focal lesions may produce severe memory impairment, e.g., bilateral hippocampal lesions (DeJong et al., 1969). Also, memory impairment plus confusion occurs with bilateral paramedian thalamic lesions (Castaigne et al., 1981). Bilateral hippocampal lesions were noted in four of the seven patients in the Tomlinson series with infarcts between 51 and 100 ml. The number of patients with paramedian thalamic infarcts was not specifically designated. In addition, it is possible that bilateral lesions of the nucleus basalis (the site of origin of cholinergic projections to the cerebral cortex) (Whitehouse et al., 1982) might contribute to confusion; the role of this nucleus was not known in 1968 and was not commented on.

Thus, the question of whether the dementias that occurred were simply a function of volume of tissue or due to the increased likelihood of involvement of specific structure with massive lesions is not yet resolved.

Few subsequent studies have examined vascular dementia in this detailed manner. Ladurner and Sager (1981) evaluated patients with multiple infarcts on CT scan and noted that dementia was much more common when infarcts were bilateral. Basso and associates (1981) analyzed intelligence as measured by the Raven Colored Progressive Scale in 183 patients with left hemisphere disease of which 159 were vascular lesions. Even when aphasia was factored out of the analysis, there was no significant correlation between lesion volume as measured by CT scan and cognition tests (r between -0.13 and -0.20), although patients with larger lesions tended to have poorer test scores. Further evaluation is necessary to assess the importance of infarct localization and size as determinant of dementia caused by cerebrovascular disease.

DIAGNOSIS

Dementia is defined by the 1980 *Diagnostic and Statistical Manual (DSM III)* of the American Psychiatric Association as intellectual deterioration sufficient to interfere with occupational and social function, memory impairment, and difficulties with either judgment, abstraction, aphasia, agnosia, or apraxia. Multi-infarct dementia (MID) includes dementia with stepwise deterioration, focal neurologic deficients, and evidence of significant vascular disease which is etiologically related to dementia. The term MID was initially reserved for dementia associated with multiple discrete cerebral infarction (Caplan, 1979) but has come to be used for all vascular causes of dementia (Hachiski et al., 1975; Rosen, 1979).

Confusion over the role of MID among the dementing diseases has arisen because dementia is defined in *DSM III* in response to the signs and clinical course of SDAT. While vascular disease is an uncommon cause of the slowly progressive difficulties seen in dementia of insidious onset (Wells, 1978) as typified by SDAT, it is also true that it is a major cause of mental impairment. Thirty-nine percent of over 1,000 patients referred to a stroke rehabilitation unit had perceptual difficulties of the type found in focal neurologic disease (e.g., neglect apraxia, aphasia, etc.) (Feigenson, 1978). While not sufficient for the formal diagnosis of dementia, such focal deficits of higher cortical function contribute to disability in the elderly and must be considered if one wishes to survey the cognitive deficiencies associated with stroke (Buller, 1981; Fisher, 1968).

The diagnosis of vascular dementia is readily apparent in the majority of patients because of the clinical history of several ischemic cerebral infarcts and the presence of focal findings on examination. Caplan (1979) noted three clinical characteristics of MID which should assist in differential diagnosis. One often finds focal, motor, sensory, and visual signs since these cerebral functions tend to be centered in the distribution of the major cerebral arteries and have poor opportunities for collateral flow. One would expect the cognitive deficits to parallel the typical clinical evolution of a stroke with abrupt onset and subsequent stabilization or improvement. Because vascular disease is rarely uniform, a patchy distribution of deficits in both sensorimotor and cognitive function would be expected. This is reflected by the spotty nature of the cognitive deficits reflected on formal psychometrics (Fuld, 1978; Perez et al., 1975).

Hachinski et al. (1975) developed an ischemic score based on the clinical features of vascular dementia as defined by Slater and Roth in a general psychiatry text (Mayer-Gross et al., 1969) (Table 3.1). Characteristics of history and examination were scored on an 18-point system to identify probable MID. Patients with SDAT by clinical criteria had scores of less than 7, while those presenting with MID had scores of greater than 7. This has held up reasonably well in a number of clinical reports (Frackowiak, 1981; Harrison et al., 1979). Rosen (Table 3.1) investigated the validity of an ischemic score, modified to eliminate features common to both diseases, with neuropathologic diagnosis obtained from autopsies of 14 elderly patients with moderate to severe dementia. She noted that SDAT was easily identified with scores of 0 to 2 but could not differentiate MID and MIX with scores greater than 4. While not useful clinically in a patient with obvious large vessel occlusions, this may prove useful in the evaluation of patients with a slowly progressive vascular dementia without evident strokes.

Other diagnostic tests have been helpful. The electroencephalogram may show patchy focal slow wave abnormalities (Harrison et al., 1979). New generation computed tomographic (CT) scans will reveal all but the smallest cerebral infarct

Table 3.1
Comparison of Ischemic Scores

Clinical Features	*Point Value*	*Hachinski et al. (1974)*	*Rosen et al. (1980)*
Abrupt onset	2	X	X
Stepwise deterioration	1	X	X
Fluctuating course	2	X	
Nocturnal confusion	1	X	
Relative preservation of personality	1	X	
Depression	1	X	
Somatic complaints	1	X	X
Emotional incontinence	1	X	X
History or presence of hypertension	1	X	X
History of strokes	2	X	X
Evidence of associated atherosclerosis	1	X	
Focal neurologic symptoms	2	X	X
Focal neurologic signs	2	X	X

(Weisberg, 1982). However, the demonstration of a focal cerebral infarction on CT scan of a demented patient is not sufficient to support the diagnosis of MID in the absence of the clinical criteria previously mentioned.

EPIDEMIOLOGY

While the prevalence of MID is uncertain, there is no question about the markedly increased frequency of cerebrovascular disease in the elderly resulting in large numbers of elderly survivors of multiple infarcts at risk for MID. Epidemiological studies reveal that the incidence of clinical stroke increases exponentially between the ages of 45 and 85 (Kurtzke, 1969; Robins and Baum, 1981). The average rate of increase doubles over each 10-year period, such that the incidence of strokes per 100,000 population per year ranges from 262.5 at ages 55 to 64 to 1,382 by ages 75 to 84. Survival at 5 years was 49.2 percent for the group under 65 and 21.9 percent for the 75 to 84 age-group.

Most of the excess mortality in both groups occurred during the first 6 months. Analysis of 5-year survival for 6-month survivors was 74.7 percent for those under 65 versus 41.8 percent for the 75 to 84 age-group (Robins and Baum, 1981).

The prevalence of the number of stroke survivors in the United States in 1976 was 1.7 million, or 794 per 100,000 (Baum and Robins, 1981). Seventy-five percent were between the ages of 55 and 84; 296,000 between 55 and 64; 468,000 between 75 and 84. Clearly, the population at risk for MID based on the prevalence of survivors of clinically diagnosed stroke is extensive, particularly in the older age-groups.

The evidence from pathologic examination indicates that the prevalence of cerebrovascular infarcts is even higher than the clinical studies would indicate. Jorgensen and Torvik (1966) noted that among 994 consecutive autopsies, there were 320 patients with ischemic cerebrovascular lesions and 65 patients with hemorrhagic vascular disease. (Forty-eight of those 65 also had ischemic disease.) A clinical diagnosis of stroke was made in only 196 of the 320 patients with postmortem evidence of ischemic disease. Fisher (1965) noted that in 88 of 114 patients with lacunar strokes found on postmortem examination, there had been neither a history of stroke nor any focal neurologic finding. It would appear that there is an appreciable incidence of subclinical cerebrovascular disease in the elderly, and this may contribute to the development of multi-infarct dementia even in the absence of clinically recognized stroke.

Identification of the risk factors associated with cerebrovascular disease would aid in diagnosis of multi-infarct dementia in those with subclinical infarcts. A profile of a candidate for cerebrovascular infarction has emerged from the Framingham study, a prospective epidemiological study of 5,200 residents of Framingham, Massachusetts, begun in 1949. The prime candidate is an elderly man or woman with hypertension, cardiac disease, diabetes mellitus, elevated hemoglobin, elevated serum cholesterol, and possibly a cigarette smoker (Dawber et al., 1977; Kannel, 1971; Kannel et al., 1972; Wolf et al., 1977, 1978a, 1978b).

Hypertensives have seven times as much cerebrovascular disease as a normotensive individual and the incidence is correlated to blood pressure. Even borderline elevations may double the incidence of stroke (Wolf et al., 1978a). There was no decrease in risk related to blood pressure as would have been the case if the disproportionate rise in systolic pressure frequently observed in the elderly was truly innocuous (Kannel, 1971; Wolf et al., 1977). Librach et al. (1977) has noted that hypertension remained a significant risk factor in the age range of 75 to 84.

The risk of stroke is increased by a factor of 3 in men and women in all age-groups with coronary heart disease (Wolf et al., 1978b). Even patients with chronic atrial fibrillation without rheumatic heart disease or mitral stenosis increase the risk of stroke by a factor of 8.5 (Wolf et al., 1978b). The presence of congestive heart failure, coronary artery disease, generalized cardiac enlargement, aortic calcification, and EKG abnormalities is associated with increased risk of stroke for all age-groups (Friedman et al., 1968; Wolf et al., 1978b).

Risk factor management may have already affected the incidence of multiple infarcts. In the well-studied population of Rochester, Minnesota, the incidence of stroke declined an average of 45 percent over 25 years. (Garraway et al., 1979a, 1979b). There has been an increase for age at onset of initial infarct from 72 to 75 years of age. The decline was largest for women and for the older age-groups. The decline in stroke incidence was not reflected appreciably as the statistic most relevant to MID: stroke prevalence. Prevalence remained unchanged for men and declined a bit for women, reflecting both increasing numbers of older individuals and decreased mortality from stroke as an additional 16 percent of all initial strokes will now survive five years as compared to the 1940s. The decline in mortality from both cerebrovascular and myocardial infarction is also confirmed by the Framingham study (Kannel, 1982). Forty-two percent of this decline occurred since 1972, a point in time when the therapy of borderline hypertension became more aggressive. In England, where risk factor manipulation has been less aggressive, this decline has not been seen. It would seem that this trend should continue as long as improvement in risk factor manipulation continues (Schoenberger, 1982) and should have important implication on the percentage of the elderly population at risk for the development of MID.

CLINICAL SYNDROMES

There are a number of definable clinical syndromes which are associated with vascular disease and cognitive dysfunction. Familiarity with their presentation would aid in recognition and diagnosis and permit intervention.

The most common stroke identified on examination of the brain at autopsy is the lacunar stroke. Lacunas are small cavities which represent healed infarcts, 0.5 to 15 mm in size, located in basal ganglia, thalamus, and surrounding white matter (Fisher, 1965b). Fisher demonstrated that they were caused by vascular occlusion of small perforating arteries which supplied the area of the lacuna, and was able to identify the occlusion in 45 out of 50 consecutive patients with lacunar strokes. Fisher (1965b) noted the presence of lacunas in 114 (11 percent) of 1,042 consecutive autopsies. There was a total 376 lacunas (33 lacunas per patient) and 9 patients had more than 10 lacunas. Jorgensen and Torvik (1966) in a series of 994 consecutive autopsies identified 155 brains with lacunas out of a total of 345 brains with evidence of cerebrovascular disease. Lacunas occur in the territories supplied by the lenticulostriates and thalamoperforant arteries (100 to 400 μ in diameter) which, if occluded, cause a wedge-shaped infarct 2 to 3 mm in size because of their lack of collaterals (Mohr, 1982). Fisher (1969) described the arterial lesion underlying lacunas as "segmental disorganization," localized fibrinoid necrosis of the vessel wall. Similar lesions have been seen in the arterioles and capillaries of the brain retina and kidneys in the setting of malignant hypertension and are believed to be a result of overdistension of the small vessel which lacks a muscular media layer (Chester et al., 1978; Mohr, 1982); but the vascular lesion underlying lacunas is found most commonly in the clinical setting of chronic nonmalignant elevation of blood pressure. The association between hypertension and lacunar strokes has been known for many years. Forty of 51 patients reported by Hughes et al. (1954) in a clinical study of vascular dementia were hypertensive. Evidence of hypertension was found in 111 of 114 patients with lacunas reported by Fisher (1965b). There is no evidence to suggest that these lesions may be secondary to unrecognized episodes of malignant hypertension. In hypertensive encephalopathy, infarcts are minute, but consist only of scans composed of reactive astrocyte and microglial cells which measure from 100 μ to as large as 1 mm and are not associated with focal findings (Chester et al., 1978). Focal signs, when they do occur as part of malignant hypertension, are secondary to large vessel involvement.

Among clinical syndromes associated with lacunar infarction are pure motor hemiplegia (Fisher and Curry, 1965), pure sensory stroke (Fisher, 1965b), and the clumsy hand dysarthria syndrome (Fisher, 1967). Diagnosis should be confirmed by CT as a majority of infarcts in patients who present with one of the lacunar syndromes can be visualized on the new generation scanners (Donnan et al., 1982; Pullicino et al., 1980; Weisberg, 1982). Occasionally, larger lesions have presented with a similar syndrome (Nelson et al., 1980).

However, most lacunas noted on neuropathologic examination have been asymptomatic during life. There was neither history of stroke nor evidence of neurologic deficits in 88 of 114 patients with lacunas reported by Fisher (1965b). In only 8 patients could a clear clinicopathologic correlation be shown. While lacunar strokes account for a third of all cerebrovascular disease of patients with neuropathologic diagnoses, only 19 percent of patients followed in the Harvard Stroke Registry were felt to have clinical presentations secondary to lacunar infarcts (Mohr et al., 1978). Even patients with greater than 10 lacunas did not have the picture of pseudobulbar palsy, short-stepped gait, or dysarthria as initially described by Marie (1901). Dementia, if noted, according to Fisher, is mild. Conversely, Hughes reported 51 patients with cognitive difficulties secondary to presumed lacunas, including 15 patients with neuropathologic verification of multiple lacunar infarcts. Jellinger (1976) states that lacunas were the most frequent type of infarct found in an autopsy series of over 1,000 patients, 22 percent of whom were felt to have a vascular dementia. Both Fisher (1968) and Tomlinson et al. (1970) did not consider lacunas important in their patients with vascular dementia. Dementia, however, sometimes does occur with lacunas (Earnest et al., 1974; Koto et al., 1977) and is usually of the subcortical variety described by Albert (1978) with psychomotor slowing and apathy.

Binswanger's disease, or "subacute arteriosclerotic encephalopathy," is a vascular syndrome with diffuse white matter involvement that results in a progressive dementia in over 90 percent of reported cases (Biemond, 1970; Burger et al., 1976; Caplan and Schoene, 1978; DeReuck et al., 1980; Loizou, 1981; Olszewski, 1962; Rosenberg et al., 1979; Zeumer et al., 1980). Binswanger's has attracted renewed medical attention since it has become evident that its characteristic pathology is reflected during life on the CT scan (Loizou, 1981; Rosenberg et al., 1979; Zeumer et al., 1980). Pathologically, the Binswanger brain shows demyelination and loss of white matter within the cerebrum with secondary gliosis, areas of cystic degeneration in white matter areas, lacunas in both white matter and basal ganglia area, and increased size of ventricles (Burger et al., 1976; Olszewski, 1962). On CT scan, low-density lesions are seen throughout the white matter in the cerebral hemispheres, but especially in the region of the centrum semiovale and in the frontal lobe, together with hydrocephalus. At autopsy, the CT scan findings correspond in a striking fashion with the pathology if the brain is cut in the same plane as the CT scan (Rosenberg et al., 1979). In addition to the white matter involvement, the lacunas, and the hydrocephalus, larger infarcts are often seen pathologically; these may not necessarily be evident on the CT scan.

The most typical clinical picture in Binswanger's is that of repeated acute focal deficits often associated with confusion and with a gradual increase in impairment so that the patient becomes severely demented, usually spastic, sometimes dysarthric, and pseudobulbar (Caplan and Schoene, 1978; Olszewski, 1962). Transient manic or paranoid states as well as agitation are not uncommon. Most patients have one or more frank strokes with hemiparesis. Rarely, however, motor deficits may not be evident and the disease may present as a relentlessly progressive dementia (Burger et al., 1976). The course is not a constant one, however, and plateaus will occur so that some patients will survive for ten years.

Now that diagnosis can be confirmed during life, the question arises as to whether further progression of the disease could be halted by medical intervention. Over 90 percent of patients with Binswanger's reported have been noted to be hypertensive and the underlying vascular lesion is arteriolar necrosis identical to that observed in the lacunar state. Certainly if diagnosed, rigid control of blood pressure would seem to be reasonable. We do not know, however, whether this would suffice. It is not at all apparent why only a small fraction of hypertensive individuals develop the specific vascular lesion leading to involvement of small arterioles feeding white matter. It is not a matter of degree of hypertension; often the blood pressure elevation is moderate and, in fact, Binswanger changes have not been reported in association with malignant hypertension. Evidently, another process is going on not at all understood; identification of the pathogenetic mechanism may be needed before this entity can be effectively treated.

A syndrome of dementia, visual disturbances, and motor neuron dysfunction is associated with multiple microinfarcts of the cortex. The disorder usually occurs in males in early middle age, and presents clinically as a gradual dementia but usually with a prior history of one or more episodes of frank stroke. Frequently, there are visual changes and in some patients evidence of motor neuron dysfunction. Pathologically, there is granular atrophy of the cortex due to coalescence of the microscopic lesions and fibrosis of small arteries and veins. The leptomeningeal vessels involved are quite small, less than 0.5 mm, but it has been suggested that involvement of the vessels is due to Berger's disease (Davis and Perret, 1946; Sourander and Wallinder, 1977; Torvick and Hognestad, 1965) or atherosclerosis (Fisher, 1957). In a recent review of the literature, and a series of our own cases (Kaplan et al., 1980), we have found that almost all of the affected patients have had valvular or ischemic heart disease, and in two cases, there is clear-cut evidence of embolization. Unfortunately, anticoagulant treatment has not altered the course of this disorder.

Watershed infarcts occurring in the border zone between the anterior, middle, and posterior cerebral arteries and associated with cardiac arrest, systemic hypertension, and carotid occlusion may cause a vascular dementia. Fisher (1968) has reported a 68-year-old man with a progressive dementia and focal motor abnormalities who on neuropathologic examination had multiple small infarcts in watershed areas.

Vasculitis

Cerebral vasculitis, which may cause widespread cerebral infarction with or without focal findings, has been reported as an unusual cause of dementia in the elderly. Ramos and Mandybur (1975) reported a 63-year-old patient with rheumatoid arthritis who presented with acalculia, alexia, finger agnosia, and loss of recent memory without focal motor signs, followed by dementia and cortical blindness. Autopsy revealed a necrotizing vasculitis confined to the brain. Generally, other cases have presented with focal finding and seizures. One of us (S.G.) has recently seen a patient with rheumatoid arthritis develop a rapidly progressive dementia with paranoid ideations without focal findings with a Westergen Sedimentation Rate of 44 mm/hr and high serum titers of rheumatoid factor. Skin and muscle biopsy revealed evidence of a chronic vasculopathy with intimal thickening and perivascular cuffing. Steroids were begun in high doses with a rapid improvement in mental status.

Similar presentations may be seen with granulomatosis arteritis, a noninfectious inflammatory vasculitis almost entirely confined to the vessels of the central nervous system which presents in adults in the fifth to eighth decade with mental changes, focal neurologic dysfunction, and signs of increased intracranial pressure (Burger et al., 1977; Kolodny et al., 1968). Kolodny et al. (1968) reported a 54-year-old woman with headaches, mental slowness, and lethargy who was noted to have lost interest in her usual activities. There were no focal findings on examination. Autopsy revealed inflammatory vasculitis with vessel wall necrosis, lymphocyte infiltration, and multinuclear giant cells in all areas examined. Patients frequently present with seizures and lethargy, but mental changes, including alteration in personality and confusion as well as somnolence, were seen in 12 of 16 patients reviewed by Kolodny et al. (1968). Neuropathologic examination reveals involvement of small arteries and veins of less than 200 μ. Parenchymal changes include both ischemic and hemorrhagic infarcts. The disease is thought to be autoimmune in etiology and steroids are said to be effective. Other diseases of the cerebrovascular system which may present with cognitive dysfunction include temporal arteritis (Hamilton et al., 1971), systemic lupus erythmatosis (Petz, 1977), Takayasu's arteritis, Moya Moya disease, and fibromuscular dysphasia (Scheinberg, 1978).

Focal Cerebral Vascular Lesions That May Present as Dementia

While disorders of higher cortical function are common even with small focal infarcts, dementia in this setting is unusual, except for a number of specific situations. It is well known, predominantly from work in the surgical control of epilepsy, that *bilateral temporal lobe lesions* produce memory loss (Penfield and Jasper, 1954). It is postulated that this is because of involvement of the medial temporal lobe, particularly the hippocampus (Victor et al., 1961). Blood flow to the hippocampus is by way of branches of the posterior cerebral arteries which both arise from the head of the basilar artery. Thrombosis at the basilar artery tip or general circulatory compromise may impair blood flow to both mesial temporal lobes (Caplan, 1980) at once, which could cause acute short-term memory loss. Muramoto et al. (1979) have reported a 59-year-old man who developed a severe short-term deficit during anesthesia for a minor surgical procedure. Pneumoencephalography revealed bilateral hippocampal damage. De Jong reported a 44-year-old man with a very similar situation in whom postmortem revealed ischemic necrosis of both hippocampi. Trillet et al. (1980) have collected 30 patients with acute onset of a memory disorder and evidence of posterior cerebral-artery ischemia.

Castaigne et al. (1981) have demonstrated that bilateral focal *paramedian thalamic infarction* may cause a profound disturbance in memory. Among patients described was a 78-year-old hypertensive woman who developed agitation, disorientation, and insomnia with a marked disturbance in memory. Pathologic examination revealed recent bilateral paramedian thalamic infarcts.

Frontal lobe lesions have been associated with a number of behavioral abnormalities (Luria, 1969, 1973, 1980). Large bilateral lesions in this area lead to a generalized disturbance of cortical regulation of attention and activation, presenting with apathy, akinesia, and abulia. Difficulties in intellectual processes relate to impulsiveness and inability to follow a course to a conclusion. Problem solving for simple arithmetic is normal, but patients are unable to solve problems where the solution requires formulation and testing of a hypothesis or choice between two methods of solution.

Focal dominant hemisphere lesions, especially in parietal and temporal areas, may lead to aphasias and agnosias. In the nondominant hemisphere, parietal lesions often result in spatial disorientation and constructional apraxias. Aphasia is perhaps the major problem resulting from stroke, contributing to cognitive dysfunction in the elderly.

Brust et al. (1976) have reported that among a group of 850 acute stroke patients, 177 (21 percent) were aphasic. Fifty-seven patients had a fluent aphasia and 120 were nonfluent. Fluent aphasia is associated with disease in Wernicke's area, the posterior portion of the superior gyrus of the dominant temporal lobe. Nonfluent aphasics tend to have involvement of Broca's area in the posterior portion of the inferior frontal gyrus of the dominant hemisphere (Kertesz et al., 1977; Naeser and Hayward, 1978). Many other less well-defined syndromes occur with deeper lesion of the dominant hemisphere involving the arcuate fasciculus (Benson et al., 1973) and other white matter tracts as well as the striatum (Damasio et al., 1982; Naeser et al., 1982).

A number of recent reports has discussed the development of acute confusional states after focal cerebrovascular infarcts of the nondominant hemisphere. Mesulam et al. (1976) reported several patients, among whom was a 74-year-old man admitted for evaluation of sudden mental deterioration. He was inattentive, agitated, and disoriented to all spheres. There were no focal motor or sensory abnormalities. CT scan revealed an infarction in inferior frontal gyrus of the right hemisphere (Mesulam et al., 1976). Medina et al. (1977) have emphasized the association with acute visual loss and believe similar manifestations may occur with infarction of either medial temporal occipital area. Fisher (1982) has recently reported disorientation for place as a manifestation of nondominant occipitoparietal infarction. Any of these focal cognitive abnormalities may cause functional difficulties for the elderly and mimic parts of the "dementia syndrome."

CONCLUSION

Cerebrovascular disease accounts for a substantial minority of elderly patients with dementing disorders. While an incidence of 8 percent has been noted in clinical studies of patients presenting for evaluation of dementia, it is likely that the actual incidence is better approximated by the autopsy study figures of 20 percent or more. Most patients with multiple strokes and dementia will not be referred by their physician for further diagnostic evaluation of cognitive dysfunction since diagnosis seems obvious.

MID may occur with either several large cerebral infarcts or with many small infarcts. It is usually seen when infarctions are bihemispheral and multiple, but may occur with bilateral infarction of specific strategic foci. Diagnosis is aided by the criteria noted in the modified Hachinski scale (Rosen et al., 1980) and the recognition of specific clinical syndromes.

Since MID occurs after brain tissue destruction, therapeutic intervention must be directed toward early recognition and the prevention of stroke. Stroke is related to the underlying disease processes, such as hypertension, heart disease, and blood lipid abnormalities and their causes, which serve as risk factors for stroke and MID. The marked decrease in incidence and mortality of stroke indicates that risk factor management has been successful. Further research is needed to investigate risk factors specific to the elderly (previous studies have been primarily in subjects under 75) and the effect on intervention in reducing this risk in persons over 75.

The 20 percent reduction in mortality in the elderly during the last decade resulted largely from reduction in heart disease and stroke. This is an opportune time to try to eliminate multi-infarct dementia and save a small but significant portion of the elderly from the devastating disability of this disorder.

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CHAPTER 4

Normal and Abnormal Oral Status in Aging

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The oral cavity is the main portal of entry for foreign matter into the body, and many specialized tissues and functions have developed in the mouth to meet the demands of such a passageway (1). The need for various sensing and detecting devices has resulted in sensory organs for taste, tactile discrimination, thermal detection, and pain recognition. Defense mechanisms would be useful for protection from potentially harmful microorganisms, and many enzymatic and nonenzymatic antibacterial systems are found in saliva. Since food consumption is by mouth, systems would be required to process (or begin to process) foodstuffs for extraction of their nutritional value. Thus teeth and their supporting structure (periodontium) and muscles for mastication and swallowing are found, along with a complement of digestive enzymes from various secretions. Finally some sort of maintenance facility, able to preserve the homeostasis of the intra-oral milieu, would be desirable. Saliva, which lubricates the oral mucosal tissues and can remineralize teeth, fulfills this need. The result is a fascinating and complex environment which has provided physiologists with many models for study, and clinicians, many areas for concern.

Should a gerontologist/geriatrician have concerns about oral physiology and oral health? Unquestionably yes! Alterations in any of the general oral functions described above, though not typically of a nature to be acutely threatening to life, have considerable influence on the quality of an individual's existence. Lack of awareness of such problems by clinicians likely will frustrate the elderly patient.

It is the purpose of this chapter to provide the interested clinician with a current description of the oral health status of the older individual. Emphasis will be placed on distinguishing "normal" from "abnormal" oral status. Normal, as used here, will refer to observations made in generally healthy persons (defined as not using prescription medication), while abnormal will focus on the influence of disease and its therapeutic treatment on the oral condition. It is hoped that this approach will illuminate areas of practical importance to the clinician.

EXOCRINE (SALIVARY) GLANDS

There are three pairs of major salivary glands (parotid, submandibular, sublingual), which together produce ~95 percent of the daily volume of saliva. The remaining saliva results from secretions of many minor glands scattered throughout the oral cavity (e.g., buccal, labial, palatal, lingual). The minor and sublingual glands are made principally of mucous cells and secrete, as a primary feature, mucous glycoproteins (mucins) having a very high carbohydrate:protein ratio. The submandibular gland is a "mixed" gland, containing both mucus and serous acinar cells. Serous cells secrete a more watery, less viscous fluid with a much lower carbohydrate:protein ratio than mucous cells. In addition serous cells produce and release many other proteins with important oral biological roles (see below). The mucous cells of the submandibular gland secrete mucous glycoproteins, though chemically distinct from those produced by other glands. The parotid gland is composed principally of serous cells, which function like those of the submandibular gland. Salivary gland secretion is regulated by the autonomic nervous system—cells being responsive to various adrenergic, cholinergic, and certain peptidergic neurotransmitters.

Salivary glands have a similar architecture. They contain a "secretory endpiece" and a "duct system" in which saliva is carried to the mouth. The generally accepted theory of saliva formation is based on the original observations of Thaysen et al. (2) (Fig. 4.1). In the most distal portion of a salivary gland (endpiece and initial duct segments), the fluid and electrolyte "base" of gland saliva is formed, essentially as a filtrate of serum termed a "primary fluid" (serum proteins are removed). Most exocrine proteins are added in the secretory endpiece region, though different duct cells clearly contribute to the final macromolecular content of gland saliva, as well as to its electrolyte composition. Each type of salivary gland makes a generally similar, but unique secretion. These individual gland salivas mix in the mouth, yielding what is termed whole saliva. Whole saliva is not just the simple additive sum of the individual gland secretions. Once a gland saliva enters the mouth, its composition undergoes many changes, e.g., some proteins adhere to teeth or mucosa, others are degraded. In addition, many nongland factors are found in whole saliva, including food debris, desquamated cells, bacterial products, etc. The principal function of saliva is to maintain the "health" of oral tissues. Table 4.1 enumerates the major roles that salivary constituents play in oral physiology. This summary makes clear that alterations in salivary gland physiology are likely to have considerable impact on the status of oral tissues.

Although a common generalization about aging is that salivary gland function is reduced and that older persons suffer frequently from xerostomia (a dry mouth), little systematic examination of salivary gland function across the human life span has been done. Recent, careful evaluations of saliva output in healthy persons have suggested that there is no generalized age-related deterioration in gland function, but some specific alterations do occur. Currently the study of salivary gland physiology is difficult. Normal values for constituent concentrations are not established; reported data vary widely and there is some controversy simply over ways to express data.

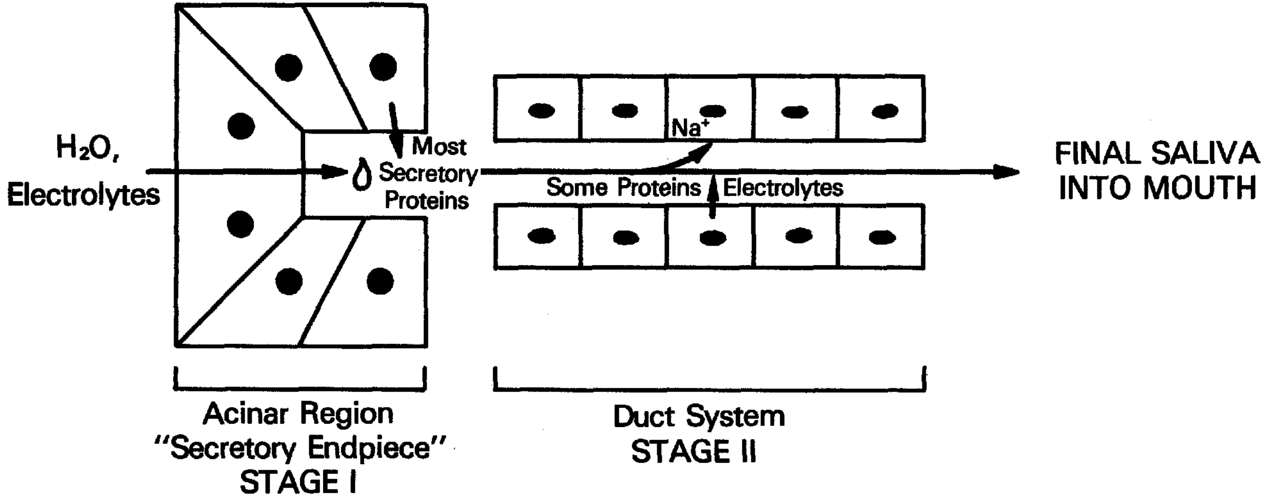

Figure 4.1. Schematic representation of the theory of saliva formation (2). Saliva formation occurs in two stages. Stage I takes place in the most distal portion of a salivary gland (acinus and initial duct segments). An ultrafiltrate of serum is produced in the gland cells and basal lamina; serum proteins are retarded and a fluid (termed "primary fluid") enters the initial duct lumen. The primary fluid has serumlike electrolyte concentrations. Exocrine proteins found in the final saliva are principally secreted in the secretory endpiece via exocytosis of secretory granules from acinar cells. Stage II of saliva formation occurs in the duct system of the gland. Considerable electrolyte flux occurs here, and some proteins are added as well. Particularly interesting is the way Na^+ is handled by the gland. The Na^+ concentration in primary fluid is approximately 140 mM. By the time final saliva enters the mouth, the Na^+ concentration is approximately 30 mM. Considerable Na^+ reabsorption occurs in the duct system. It is felt (though not unequivocally proven) that water enters the gland only in the endpiece. Saliva is thus a hypotonic secretion. The extent of Na^+ reabsorption is dependent on the contract time of saliva with the luminal membranes of duct cells. For example, the higher the flow rate of saliva, the less contact time with the duct and the higher the Na^+ content of the final saliva.

Table 4.1
Major Roles for Saliva in the Maintenance of Oral Health

Lubrication of oral mucosa
Buffering acid produced by oral bacteria
Antibacterial properties
Mechanical cleansing
Mediation of taste acuity
Remineralization of teeth

Many factors influence salivary gland secretion, a situation which probably accounts for much of the variability observed. For example, the concentration of many components (1) shows extreme diurnal variations, (2) is related to flow rate (thus flow must be considered in data analysis), (3) may be influenced by medications being used, and (4) is affected by the method of stimulation chosen.

Most work presently under way evaluates single-gland saliva, typically from the parotid gland. Earlier studies have frequently utilized whole saliva, which complicates analysis and interpretation. Figure 4.2 shows the results of stimulated parotid saliva flow rate obtained from 95 nonmedicated men, 23 to 88 years of age (3). There are no differences across the age spectrum in volume of secreted parotid fluid. A quite similar result was found among female subjects. When acinar cell protein exocytosis is measured (as secretion of anionic proline-rich proteins in mg% or percent of total protein released) again constant values are observed across different age-groups (4). Conversely, Na^+ handling by the parotid gland is significantly different with increased age (5, 6). Na^+ secretion levels must first be corrected for flow rate variations and only then analyzed against age. For both nonmedicated men and women, lower concentrations of Na^+ were secreted with increased age (i.e., Na^+ ductal resorption presumably being greater, see Fig. 4.1). Mean Na^+ concentrations, independent of flow rate, in secretions from younger persons are about twice that of their older counterparts.

While the meaning of this last observation is as yet unclear, the findings described here emphasize that there is no uniform decremental change in salivary gland function with age. In a

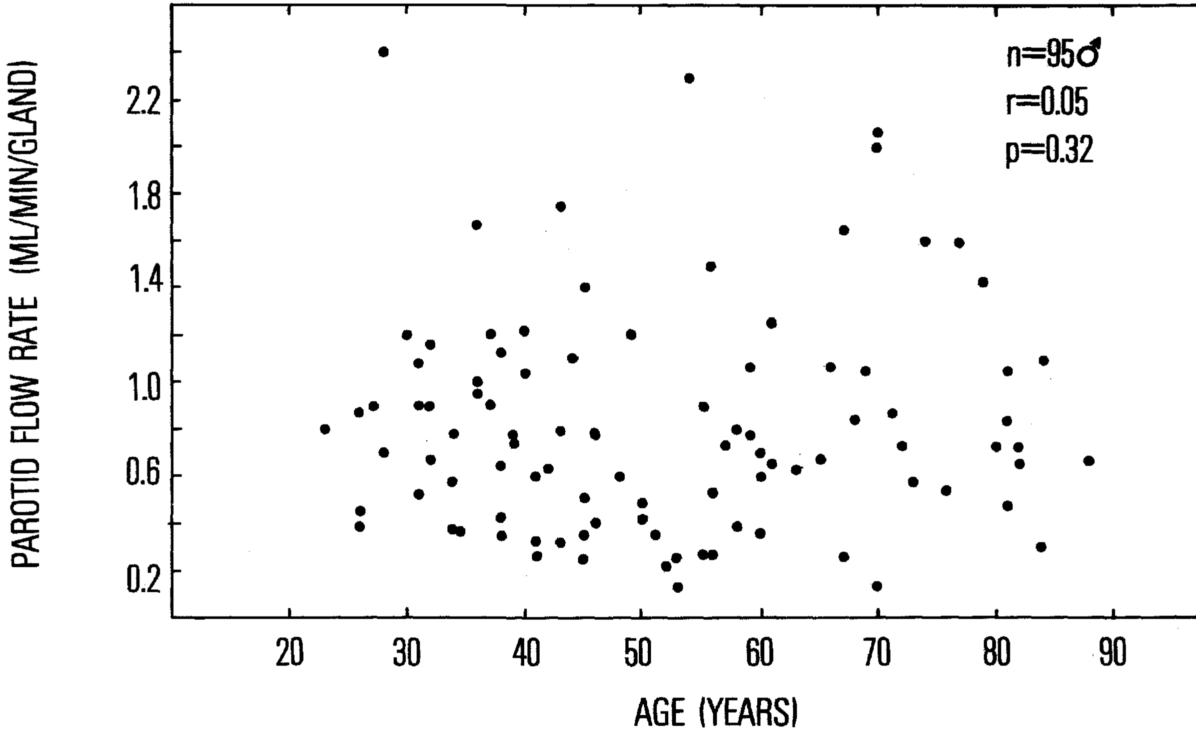

Figure 4.2. The distribution of 2 percent citrate-stimulated parotid saliva flow rates among 95 nonmedicated men aged 23 to 88 years. Each data point represents the flow rate from a single subject. Note that there is about a 10-fold range in "normal" values obtained for stimulated parotid fluid output. There is no significant relationship between the age of subject and stimulated parotid saliva flow rate observed. (Reprinted with permission from Baum, B.J., Evaluation of Stimulated Parotid Saliva Flow Rate in Different Age Groups, *Journal of Dental Research 60*:1291, 1981.)

healthy unmedicated population, most stimulated parotid gland responsivity should be maintained with age.

Salivary gland secretion is considerably affected by systemic disease and its treatment. Many conditions relatively common among older persons may potentially influence saliva formation and thus may have secondary, negative manifestations in the oral cavity. A few examples of abnormal salivary gland functional states, of likely interest to the gerontologist, will be cited rather than recapitulating an exhaustive review (7).

An extreme case of diminished salivary gland function is produced by therapeutic radiation to the head and neck. About 6 percent of all malignancies occur in this region and most are carcinomas, usually treated by radiation. Salivary glands, when exposed, suffer considerable damage; apparently serous cells are more vulnerable than mucous cells. Salivary flow rates are considerably reduced and patients are prone to rampant dental caries and a severe mucositis. Mastication and food consumption can be difficult. Such severe sequelae are not surprising in view of the multiple important roles saliva fulfills in the mouth (Table 4.1).

A number of drugs commonly used by older persons are known to affect salivary gland secretions, including sympathomimetics and parasympathomimetics and antidepressants of the tricyclic and MAO-inhibitor variety. The usual focus in drug-induced salivary functional alteration is on flow rate (increased or decreased); however, compositional changes in saliva can also be induced and, based on recent animal studies, structural (and thus probably functional) alterations in certain proteins are possible. For example, rats subjected to chronic administration of β-adrenergic agonists show markedly different patterns of salivary proteins on evaluation by polyacrylamide gel electrophoresis (8). Any perturbation in gland physiology can produce a spectrum of ramifications (e.g., altered taste, dryness, increased caries). Clinicians dealing with patients taking drugs frequently, like the elderly, must be cognizant of the multiple disturbances to oral homeostasis which can result from drug-induced changes in saliva.

Salivary secretions have a broad influence on an individual's state of oral health. Generalized disturbances in human salivary gland physiology should not be viewed as a normal sequela of old age. To the clinician, such salivary pathology should indicate an adverse drug effect or a symptom of systemic disease. However, if gland alterations exist, whether primary or secondary in origin, the gerontologist should be prepared to recognize multiple intraoral manifestations.

SENSORY FUNCTION

A number of important sensory systems are in the mouth (e.g., taste, touch, temperature, pain), but only the impact of taste on the oral status of the elderly has been well studied. As noted previously, functional detection systems are essential, given the role of the oral cavity as the "entrance" into the body. Each modality mentioned functions as part of a warning system.

This section will focus on taste as the most thoroughly studied sensory function in the oral cavity of older persons. Other sensory functions are no less important; adequate data have not yet been collected.

Many reports suggest that gustatory function (and thus food enjoyment) is substantially reduced among older persons. Recently, however, such data have been seriously questioned (9). Because of methodological advances in measuring the ability to taste, much of the data upon which such generalizations are based may be now considered inaccurate (9, 10).

Taste is a complex modality to assess, for "registration" involves true taste receptors (taste buds), neural transmission pathways and central integrative functions, and the influence of olfactory receptors. Taste buds are distributed throughout the oropharyngeal region, but are concentrated in three types of tongue papillae (fungiform, circumvallate, and foliate). Very early studies by Arey and co-workers (11) reported an age-associated decrease in the number of taste buds on circumvallate papillae. This work, however, has never been confirmed, and Arvidson, examining taste buds on fungiform papillae, recently has shown no change in the number of taste buds per papilla with age (12).

Functional measurements of gustatory ability may fall broadly into two categories: threshold, involving the detection of very low concentrations of tastants such that one can merely distinguish that something other than water is tasted (i.e., this may be viewed as a molecular-level event); and suprathreshold, involving tastant concentrations approximately 100 to 200 times greater than those evaluated with thresholds and in a range relevant to real world taste experiences (i.e., a clinical-level event). Suprathreshold approaches may be used to evaluate not only intensity differences between concentrations (i.e., strength of stimuli), but also an hedonic component (degrees of pleasantness). Typically, four general taste qualities are evaluated: sweet, sour, salty, and bitter.

Virtually all data available are of the threshold type. Though worthwhile, threshold data may not be fully relevant to daily life gustatory function, and broad generalizations concerning changes in taste function with aging based on such data are tenuous. Recent studies of four quality-detection thresholds in healthy persons across the human life span suggest that there is no general deterioration in this type of gustatory function with increased age. Rather, specific changes have been noted which are modest in degree (9, 10). For example, older persons show a small, though significant elevation of threshold for sodium chloride, i.e., they require higher concentrations to detect salt taste than younger individuals (Fig. 4.3); but they show no difference in thresholds for sucrose. Interestingly, this same general conclusion may be drawn from the limited, available, suprathreshold data, i.e., modest quality-specific changes with age (13).

Based on these recent results, as well as careful evaluations of past studies of taste change with age, it seems that many gross abnormalities in gustatory function previously associated with aging may be due to systemic disease, therapeutic drug use, or compromised dental and periodontal health. The considerable influence of disease and its drug treatment on salivary glands, and thus indirectly on taste, becomes apparent. Poor oral hygiene and dental disease can also directly impair gustation in an older person. If food debris is inadequately removed from about teeth or prosthetic devices, oral bacteria, by digesting them, can produce noxious products which might adversely influence taste

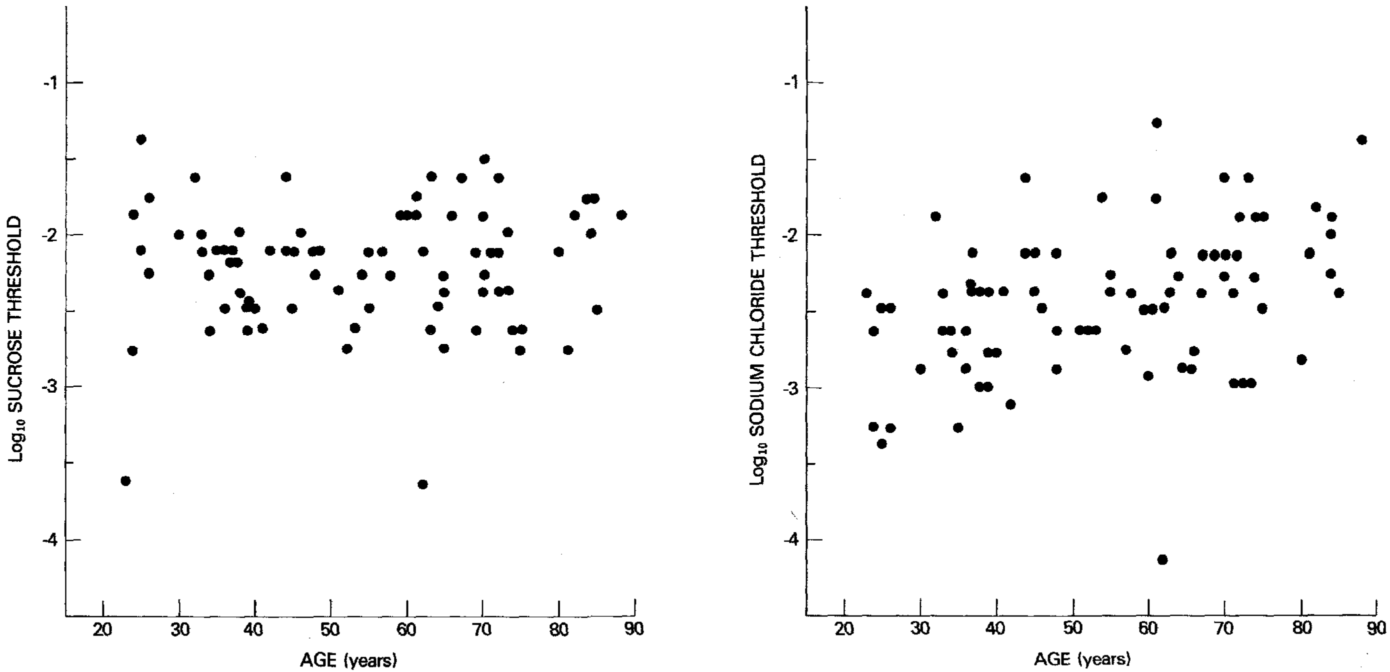

Figure 4.3. The distribution of taste detection thresholds for sodium chloride (left panel) and sucrose (right panel) among 81 men and women. Data were obtained by a series of two alternatives (water or tastant), forced-choice (response required) trials according to a predetermined random schedule. For sodium chloride a modest increase in detection threshold was seen with age ($r = 0.38$, $p < 0.001$), while for sucrose no such difference was found ($r = 0.05$, not significant). (Reprinted with permission from Weiffenbach, J.H., Baum, B.J., and Burghauser, R., Taste Thresholds: Quality Specific Variation with Human Aging, *Journal of Gerontology 37*:372, 1982.)

perception. Also, chronic dental or periodontal infections might result in the continuous discharge of purulent matter into the mouth, creating constant unpleasant taste.

ORAL MOTOR FUNCTION

Oral motor function refers to the coordinated operation of the neuromuscular units of the face and oral cavity. It includes many physiologic activities important to all age-groups, such as speech, posture, mastication, and swallowing. In addition, adequate dental prosthetic retention and function do require a contribution by the oral musculature. The oral motor complex is also involved in a number of pathologic states including paralysis, bruxing, spasm, and trismus. Surprisingly, little study of normal or abnormal oral motor function in older persons has occurred despite its clear importance. The principal focus of this section will be on normal physiologic activities of the orofacial musculature. However, a brief comment will be made on pathologic states related to temporomandibular joint (TMJ) disorders.

Recent studies of substantially healthy and dentate persons have identified certain types of oral motor dysfunction associated with increased age. Feldman et al. (14) have shown in men that while direct measures of masticatory efficiency (ability to chew "completely" a food bolus) are unaltered with age, both the time required for older persons to prepare food for swallowing and the average particle size of food an older person is willing to swallow are significantly increased compared with younger adults. By separate methods this general conclusion has been supported and extended to include women (15). Inadequate ability to prepare food by chewing could influence food selection by an older person or could impede actual swallowing.

There is also evidence that the postural role of the circumoral muscles may be compromised with increased age (Fig. 4.4). This may be a contributory factor in the occurrence of labial spill of saliva (drooling) among older persons. Drooling appears to be a fairly common complaint of the elderly and may cause considerable embarrassment and annoyance. Assessments of

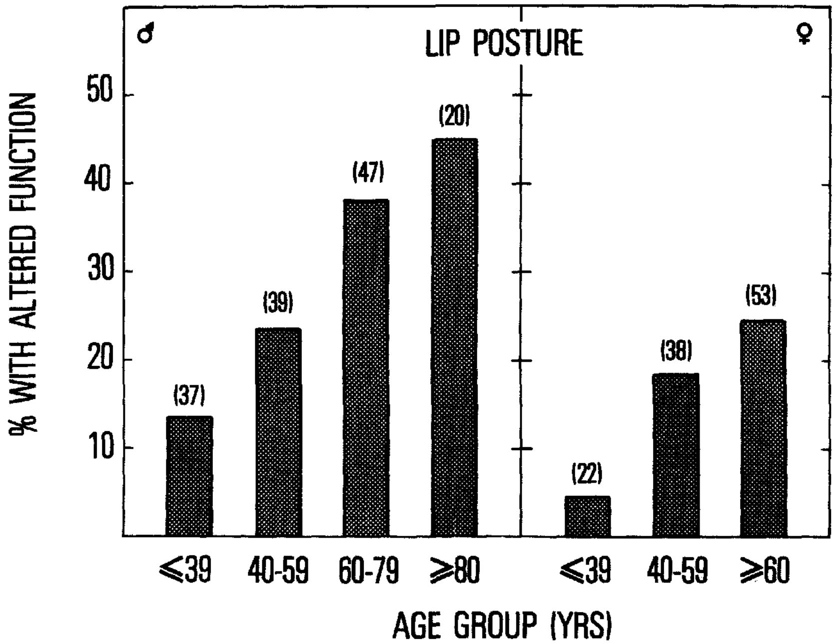

Figure 4.4 Frequency of subjects presenting with alterations in the Lip Posture Index as a function of age. This index evaluates five parameters: tonus of the circumoral muscles; posture of the lips; history of either daytime *or* nocturnal drool of saliva; and ability to purse the lips symmetrically for whistling. For males a steady significant progression in the prevalence of altered function was seen with increasing age ($X^2 = 9.51$, $p < 0.05$). For females, the differences between youngest and oldest age-groups were also significant ($X^2 = 4.52$, $p < 0.05$). The number of persons considered in each age category is given in parentheses. (Reprinted with permission from Baum, B.J., and Bodner, L., Aging and Oral Motor Function: Evidence for Altered Performance among Older Persons, *Journal of Dental Research* 62:2–6, 1983.)

tongue function have also suggested some impairment with age. Interestingly, an increased prevalence of "dysfunction" of the tongue suspensory muscles was observed among men but not women (15). The consequences of such disturbances could range from annoyance (speech alterations, traumatic bite injury, regurgitation) to disaster (choking, laryngeal obstruction).

The above findings were based on observations of healthy older persons and thus may not be representative of the general elderly population with its disease burden. Since systemic disease and therapeutic drug use are increasingly common with age, oral motor functional abnormalities among the "well-elderly" underestimate rates of dysfunction in the unselected elderly population. Many therapeutic drugs are known to induce motor disturbances, especially in the orofacial region (i.e., tardive dyskinesia caused by phenothiazines), including frank movement disorders as well as diminished performance. In one study of the motor activities related to swallowing in different aged persons, while no separate effect of age on swallowing was observed among nonmedicated persons, a significant increase in the prevalence of dysfunction was seen among older persons utilizing prescription medications (15).

The oral motor complex is involved in certain pathologic activities, most commonly associated with TMJ disorders, although it is unclear as to whether such pathology is age-related. The TMJ is located between the glenoid fossa and the condylar process of the mandible. It displays a gliding hingelike movement and has been the focus of a variety of craniofacial pain disorders. TMJ disorders may be described in two general categories (16): (1) *articular*—related to pathology of the joint; and (2) *nonarticular*—pathology in unrelated structures but causing similar symptomatology (such as oral motor disturbances). Reports (see ref. 17) suggesting that this joint undergoes degenerative changes with increased age (e.g., erosion, osseous remodeling) typically have come from histologic or radiologic studies, and there is little investigation actually correlating joint changes with symptomatology.

The most common nonarticular joint disorder is the myofascial pain dysfunction (MPD) syndrome. Clinical complaints can mimic those of true joint changes and may include pain, tenderness, swelling, and limited jaw movement. Most cases of MPD are felt to be psychophysiologic in origin (for example, jaw clenching or tooth grinding produced by tension), with subsequent fatigue and spasm of orofacial muscles. Ill-fitting dental prostheses have been implicated among adult populations, though little firm support for such a conclusion exists.

DENTAL (CARIOUS AND PERIODONTAL) DISEASE

The typical adult dentition consists of 28 teeth (excluding the 4 third molars or "wisdom teeth"), each with a crown and root portion (Fig. 4.5). The crown (the portion exposed to the oral milieu) consists of an outer layer of enamel and inner layer of dentin. Enamel is the hardest body substance (~90 percent mineral), while dentin is somewhat less mineralized (~70 percent). The root portion consists of a thin outer layer of cementum (~50 percent mineral) over the inner dentin. The vascular and neural supply of the tooth are enclosed within the pulpal connective tissue and enter the tooth through an apical orifice. The tooth is embedded in the alveolar bone of the jaw, firmly attached by means of a periodontal ligament. The term "periodontium" refers to the supporting structures of the tooth and

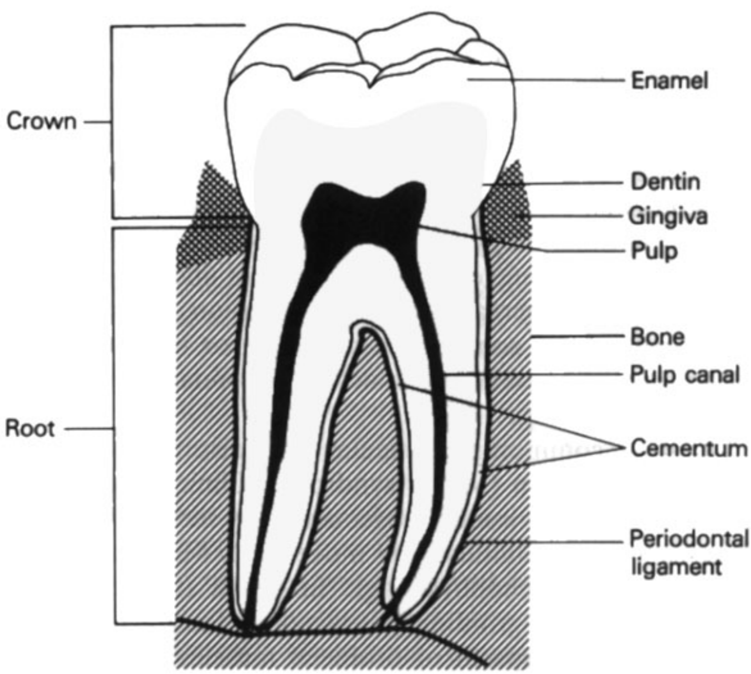

Figure 4.5. Schematic diagram of a tooth and its investing tissues. Modified from Baum, in Andres et al., (Eds.), *Principles of Geriatric Medicine*, New York: McGraw-Hill, in press.

includes alveolar bone, the covering gingiva (gum), the periodontal ligament, and cementum.

Tooth loss is commonly considered a sequela of aging, and a majority of persons over 65 in the United States have at least one edentulous jaw (18). In recent years, advances in dental treatment and disease prevention (especially fluoridation) have prolonged tooth retention, and edentulous jaws will probably become less common in a generation or two. Future older individuals, beneficiaries of these achievements, will therefore experience dental caries (tooth decay) and its treatment.

Dental caries is an infectious disease which will result in complete destruction of an affected tooth if not treated. It may be viewed as a two-stage process: an initial demineralization of the inorganic phase and a secondary dissolution of the organic matrix (19). The principal etiologic agents of caries are acidogenic bacteria. To be virulent, bacteria must be attached to the tooth surface, and dental plaque is principally a mass of bacteria, adherent to the tooth. Plaque bacteria metabolize available carbohydrates and produce acid, which in turn dissolves the hydroxyapatite mineral of a tooth. The caries process is also influenced by diet (level and frequency of carbohydrate intake especially), oral hygiene habits, and host defense factors in saliva.

Most studies on caries focus on the disease as affecting the coronal portions of teeth. Indeed in adolescents and young adults, caries is primarily a disease of the tooth crown. The principal (though not exclusive) coronal caries causing microorganism is *Streptococcus mutans*. The prevalence of coronal caries in persons from about age 35 through old age is stable and well below that observed in younger populations.

With age, gingival recession occurs and portions of the root of a tooth become exposed to the mouth, i.e., the *clinical* crown of a tooth enlarges to include more than the *anatomic* crown. The root surface is covered by cementum, which, as noted above, is less hard than enamel. Caries of exposed root surfaces (cervical caries) are apparently more prevalent with increased age. Prevalence data, based mainly on hospitalized populations, suggest that persons over 60 years of age have approximately three to four times more cervical caries than those younger than 40 years. There are no good prevalence figures for cervical caries with an epidemiologically valid population base and there are no incidence figures at all. Furthermore, little is known about prevention of caries on root surfaces or about the bacterial species involved.

Like dental caries, periodontal disease has as its primary etiologic agents bacteria and their products. Macromolecular bacterial factors are thought to leach out of dental plaque, cross the gingival epithelium, and enter the subepithelial connective tissues. These substances activate specific cell-mediated, immune host-defense mechanisms which initially seek to limit and eliminate disease in the manner of a classic inflammatory response. Chronic insult to periodontal tissues (e.g., through inadequate removal of plaque bacteria by poor hygiene) will result in a chronic inflammatory response where host-defense mechanisms are activated and tissue destruction results. Periodontal disease is a cellular-immunopathologic disorder of connective tissues yielding destruction of both soft connective tissue (i.e., collagen, fibronectin) and bone (20).

Little study of periodontal disease among older persons has occurred. Most reports evaluate the disease in the 20 to 50 age-group, and it is not at all clear whether increased periodontal disease is associated with senescence. It may be that periodontal disease is a disorder of middle age and the diagnosable disease seen among the elderly is merely the end result of a process active in previous years but quiescient at present. Clinically the diagnosis of periodontal disease is based on classic signs of inflammation; the signs being the result of activities of the cell-mediated immune response. There are substantial data supporting the concept that alterations in cellular immune response occur with increased age. Conceivably then the very criteria dentists utilize to diagnose active disease may be improper when applied to elderly populations.

For both the major dental disorders, caries and periodontal disease, adequate epidemiologic and biologic data on disease processes as they pertain to older persons are presently lacking. With the clear prospect of more individuals retaining their teeth throughout life, dental (i.e., tooth related) disease likely will become, for the elderly, an important public health problem.

ORAL MUCOSA

The oral mucosal tissues may be grouped in three broad categories: (1) slightly keratinized and freely movable tissue like the labial and buccal mucosa and the floor of the mouth; (2) well-keratinized tissue, firmly adherent to underlying bone like gingiva and palatal mucosa; and (3) specialized tissue like the dorsum of the tongue. The function of this oral lining (exclusive of special features like taste buds) is to protect the mouth from desiccation, infection, detrimental chemicals, and thermal shock.

The health and integrity of the oral mucosa may be compromised by a number of pathologic situations. For example, many systemic disorders have oral manifestations (e.g., blood dyscrasias, endocrinopathies). Also traumatic injuries may be caused by sharp, irregular food products, hot foods, and tooth bites. Bacterial (e.g., acute necrotizing ulcerative gingivitis) or viral (e.g., acute herpetic gingivostomatitis) infections may also be of concern. Among debilitated persons with poor oral hygiene, infections due to *Candida albicans* may often be observed. In addition, oral cancers represent about 6 percent of all neoplasms; by far the most frequent form of malignancy observed is a squamous cell carcinoma.

Although commonly it is believed that atrophic changes (dryness, friability) in the oral mucosa accompany aging, there are few scientific data to support the claim. Such alterations may occur among older persons, but they are not typical and are more likely related to disease states, poor nutritional status, or pharmacological side effects. Many earlier reports on this subject offer conflicting results and use inadequately described population groups. At present it is difficult to say whether aging per se has any influence on the oral mucosal condition.

Although not normal sequelae of aging, two of the pathologic situations mentioned above are especially relevant to elderly populations. First, traumatic injury due to poorly fitting and/or poorly cleaned dental prostheses may be fairly common, given the current frequency of denture utilization. This may result in a wide range of ulcerative damage to the mucosa. Also, chronic irritation from dentures can result in hyperplastic and erythematous tissue changes, as well as hyperkeratotic lesions. Second, neoplasms, which present with a very heterogeneous appearance, are of major concern. Carcinoma should be included in a differential diagnosis of all unknown oral lesions.

More study of the oral mucosa in generally healthy older persons is needed. Further, more rational means to assess mucosal health status (i.e., How does one objectively gauge abradability or atrophy?) need to be developed. This epithelial lining tissue is very important for normal oral function, and it is necessary to have a better understanding of its status through the human life span.

CONCLUSIONS

Only a small amount of firmly established information exists on the normal health status of oral tissues with increased age. However, what we do know unequivocally negates the stereotypic picture of wholesale degenerative changes in oral tissues and oral functions with increased age.

The oral cavity offers many challenges for gerontology. Surely more epidemiological descriptions are needed, but currently identified problems also require solutions. This "gateway to the body" has been a storehouse of useful diagnostic information for the traditional clinician, and it likely will be for the gerontologist/geriatrician as well.

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CHAPTER 5

Management of Oral Problems in the Elderly

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INTRODUCTION

The purpose of this review is to discuss recent advances in geriatric dentistry, particularly developments in the management of oral problems in the elderly. The field of geriatric dentistry is not new. General dentists have treated aged patients in the community, in nursing homes, and in hospitals for many years. But systematic examinations of the special dental needs of aged patients and considerations in treatment planning for this segment of the population have only recently been undertaken. Thus, we are only now beginning to distinguish normal, age-related oral changes from changes in oral physiology and function which are a result of disease (see chapter by Baum in this volume). Principles of diagnosis and treatment planning have only recently been discussed (Ettinger and Beck, 1983; Milgrom et al., 1981). Another issue of growing concern is the maintenance of oral health in the later years. The increasing number of persons living to a very old age, together with scientific and technological developments in dentistry over the last 30 years, have created a situation of more elderly retaining more of their natural teeth. Systemic diseases and inadequate oral health maintenance in the middle and later years result in severely compromised dentition and diseases of the soft tissue in old age.

The impact of these conditions on the quality of life of older persons, and how these problems may be prevented and treated through an interdisciplinary health care approach, are the focus of this chapter. We will first review the epidemiology of dental diseases in the later years and discuss the implications of these conditions for treatment needs. The psychological aspects of oral health behaviors among the elderly will be presented, followed by a discussion of the need for preventive dental care for older persons.

DENTAL DISEASE IN THE ELDERLY

Coronal Caries

Both national and international surveys have pointed to a reduction in caries rates among children over the last ten years (Beck et al., 1982; Infirri and Barmes, 1979; National Caries Program, 1981). The widespread use of fluoride appears to be a major reason for this trend. There are fewer studies of caries in adults, but surveys in Iowa (Beck et al., 1982) and in North Carolina (Hughes, Rozier, and Rumsey, 1982) suggest that the prevalence of coronal caries remains high in this age-group. As Beck (1984) states, in an excellent review of the epidemiology of dental diseases in the elderly, it is difficult to infer from these prevalence surveys whether the incidence of caries is also greater in adults, or whether the observed differences are due to historical factors, i.e., that the older person has accumulated more untreated caries over time which will also be seen in today's children when they are older. Very few studies are available on coronal caries among the elderly, but in their investigations of dental status among healthy adult males, Chauncey and colleagues (1978) found that males aged 65 to 74 were not significantly different in the number of decayed teeth, but had more secondary caries (i.e., previously restored teeth with new decay) than any other age-group.

Root Caries

Turning to cervical or root surface caries, a condition which is generally more difficult to restore than coronal caries, and which can lead to tooth loss in the later years, few researchers have examined its prevalence or incidence. Beck (1984) has reviewed these studies and concludes that the prevalence data show an increase with age. These studies examined healthy persons varying widely in age, but rarely above 60 (Hazen et al., 1974; Hix and O'Leary, 1976; Sumney et al., 1973). Surveys which included older persons have shown even greater prevalence rates. Thus, Ravald and Hamp (1981) found that 87.9 percent of their periodontally treated subjects aged 34 to 74 had some root caries. Baum (1981) found persons over age 60 had four times the root caries rate of those under age 40. Subjects in this case were healthy males who were enrolled in the Baltimore Longitudinal Study. In a larger study of a fluoridated and a nonfluoridated community, Stamm and Banting (1980) found increased rates of root caries with age, but the older residents of the nonfluoridated community had twice as many untreated and filled root surface lesions.

Although there is strong research and clinical evidence for increased rates of root caries with age, it is often difficult to determine this with great accuracy. Some investigators have argued that gingival recession must be present for root caries to occur, but they have not always taken this into account in their measurement methods. The Root Caries Index (RCI) developed by Katz (1980) measures the percent of teeth with root caries per number of teeth with gingival recession. Using this index, Katz et al. (1982) found that persons aged 60 to 64 had lower RCI scores than those in the 50 to 59 age-group. Both groups in turn have been shown to have significantly higher RCI scores than younger populations.

In a recent study (Kitamura et al., unpublished manuscript), RCI scores among 49 persons aged 55 to 95 were found to be slightly higher than in Katz's study (17.7 vs. 17.2). In an attempt to determine what factors might be associated with root caries, the investigators obtained data from patient records regarding any medications the individual was currently taking. All subjects were on at least one prescription drug. Those using medications which were known to have xerostomic side effects were compared with persons whose medications had no xerostomic side effects. A significant difference emerged between the RCI scores of these two groups, with mean root caries scores of 23.1 for the former and 7.4 for the latter. The presence and extent of plaque and calculus were correlated with RCI scores. Finally, nursing home residents in this study had significantly higher RCI scores than did community elderly (RCI = 25 vs. 10, respectively). This is consistent with a study of 59 institutionalized elderly by Banting et al. (1980), who found that 44 residents had at least one decayed or restored root surface lesion. It is clearly not the environment of the nursing home per se which explains the greater occurrence of root surface caries in institutionalized elderly. Instead, it is the complex interaction between multiple medical conditions, medications to treat these conditions, and the oral hygiene status of residents of nursing homes which renders them more vulnerable to developing root caries.

Despite the growing recognition of root caries as a major dental problem in the elderly, particularly the institutionalized elderly, research on the most effective preventive and treatment modalities is lacking. Recent attempts to apply topical fluorides to aged patients in dental offices have shown some promise, but longitudinal studies are lacking. If the efficacy of topical applications and/or fluoride mouth rinses can be proven, it may be easier for the independent older person to prevent the development of caries; it may also be easier to maintain the oral health of frail elderly. Restorative materials and the procedures which are most effective in treating root caries have not been explored either, although clinical trials of several bonding products have recently been undertaken at many universities. An extensive discussion of restorative methods for root caries is presented by Banting (1984).

Unfortunately, no matter how effective the restorative material, dentists cannot successfully treat a lesion which has attacked multiple surfaces and is in the subgingival region. These cavities are often too advanced, and result in broken root tips or the necessity to extract the teeth. Root surface lesions generally produce less pain than do coronal caries. It behooves the older person to seek regular dental care, and for other gerontological health care providers to look for signs of root caries in examining their older patients, particularly those who are on long-term treatment regimens with drugs known to have xerostomic side effects.

Periodontal Disease

Diseases of the periodontium also occur with greater frequency in the later years. Gingivitis and the more advanced condition of periodontitis are significant predictors of tooth loss in adulthood (Page, 1984; Page and Schroeder, 1982). Adult-onset periodontitis often begins at age 30 or later, increasing in incidence and severity with age. It appears that older persons develop greater susceptibility to microbial plaque than the young, resulting in rapid and severe gingival inflammation, based on research by Holm-Pederson et al. (1975). This may be associated with senescence of the immune system, which reduces the effectiveness of host defenses dependent on T-cell function. But, as Page (1984) has pointed out, the correlation between immune system senescence and the prevalence of periodonitis is weak. Given that periodontitis is caused by bacteria and that T-cell dysfunction does not influence susceptibility to bacterial infections, this is unlikely to be an important factor in the increased occurrence of periodontitis in old age. There may be defects in the functional capacity of phagocytic cells with age, and these cells are believed to be responsible for defending against microbial attacks around the teeth and periodontium.

There are recent, large-scale epidemiological studies of periodontal diseases in the United States. Douglass et al. (1983) have reviewed periodontal status data obtained in two nationwide health surveys of persons aged 18 to 70 conducted by the National Center for Health Statistics. Both males and females were observed to have a greater prevalence of periodontitis with age, such that in the 1971–1974 survey, 58.9 percent of men and 42.9 percent of women aged 65 to 74 had periodontal pockets. But in comparing prevalence data from the 1960–1962 survey with that from 1971–1974, Douglass and colleagues found significant reductions in persons aged 18 to 34, and more persons without any form of inflammatory periodontal disease. This provides some indication that periodontal disease will be much less of a widespread problem in future cohorts of elderly.

Two large statewide surveys were conducted in North Carolina during 1960–1963 and 1976–1977 (Fulton et al., 1965; Hughes et al., 1982; Rozier et al., 1981). In the first survey, 7,236 adults were examined; 3,454 were studied in the second. Comparisons were made between males and females, whites and nonwhites in their oral health status. Some sex differences emerged, and racial differences in Periodontal Index (PI) scores were minor in the 1960–1963 assessment. However, significant differences emerged between whites and nonwhites in the second survey, such that the latter obtained PI scores almost twice that of the former. Nonwhites examined in this survey were found to have an earlier onset of periodontal disease, with nonwhite males aged 60 and older showing the highest rates of advanced periodontitis.

Data from the Iowa Survey of Oral Health (Beck et al., 1982) suggest that periodontal disease may in fact be a disease of middle-age which does not become more servere in old age, but in fact remains quiescent. In their survey of 935 dentate persons above age 5, Beck and colleagues found that the proportion of persons with periodontal pockets 3–6 mm in depth increased to age 45, then remained steady among the older groups. It is also noteworthy that the proportion of persons with severe periodontitis (pockets over 6 mm) was highest in the 45 to 54 age-group, and very low in the older groups. The lack of longitudinal data precludes a conclusive explanation for this phenomenon, but it may be that severe cases of periodontitis are treated in the middle years or that they result in tooth loss, so that the individual aged 65+ has already passed through the most susceptible years.

Tooth Loss

The ultimate goal of therapeutic dentistry is the retention of natural teeth. There is considerable evidence that more people are retaining their teeth into old age. A comparison of 1960 vs.

1970 survey results from the National Center for Health Statistics reveals that edentulism has decreased significantly since 1960. In that first survey, 45 percent of males and 52.9 percent of females aged 65 to 74 were found to be totally edentulous. The proportions had dropped to 43.6 percent and 47 percent, respectively, in the 1971–1974 survey. These trends are particularly significant among older black males, whose rates of edentulism dropped from 36 percent in 1960 to 28 percent in 1970. It should be noted that the retention of natural teeth does not necessarily imply better oral health or improved oral hygiene. In fact, as we saw above, elderly black males have the highest rates of periodontal disease when compared to their cohorts who are white or to females.

UTILIZATION OF DENTAL SERVICES*

There is considerable evidence to support the value of regular dental care in the prevention of oral diseases. Thus for example, results of the Iowa Survey of Oral Health (Beck et al., 1982) revealed an association between gingival bleeding, calculus, periodontal pockets, and not seeking dental care in three or more years. To the extent that one makes asymptomatic visits to the dental office for an examination and professional prophylaxis, the likelihood of preventing caries and periodontal disease and detecting oral cancers in the early states increases. Studies by Douglass and Cole (1979) and Moen and Poetsch (1970) have shown increased utilization of dental services by the younger population. The former compared the proportion of persons visiting a dentist within the past two years in 1963–1964 with those who reported doing so in the 1975 National Health Survey. The rates had risen from 54.5 percent to 61.2 percent. Moen and Poetsch (1970) found a significant increase in the proportion seeking preventive services between 1959 and 1969, paralleling the historical growth of awareness of the value of preventive dentistry.

* Material for this section comes from a review of dental service utilization patterns recently completed by the author (Kiyak, 1984).

Although there has been some increase in utilization of dental services by persons over age 65, this increase is not as great as it is by younger persons. It is also selective by race, education, and availability of third-party payments. In a comparison of 1964 and 1974 utilization rates by the Health Resources Administration (1977), it is clear that older persons with less than a high school education continued to be the lowest utilizers of professional dental services in 1974. Nonwhite elderly and those with no third-party coverage for dental care are least likely to seek dental care, but elderly of all racial and educational groups tend to be less likely than the young to seek professional dental care. This is contrary to the use of other health services by the elderly. Thus for example, elderly in the United States represented 11.8 percent of the population in 1982, but accounted for 27 percent of all health expenditures. They make twice as many visits as do the young to a physician's office, with an average of 6.5 visits per year. The elderly are hospitalized twice as often and stay at least two times longer than individuals in the 20- to 40-year-old group (Hammerman, 1974; SSA, 1976). Furthermore, older persons purchase 25 percent of all medications sold in this country. It should be noted that the health services used by older patients (e.g., diagnostic tests, intensive care hospital stays, nursing home services) are among the most expensive of all health care costs. As a result, per capita nondental health expenditures for older persons were $1,521 in 1975 (SSA, 1976), the most recent data available. In contrast to this disproportionately high use of medical services, individuals over age 65 have the lowest utilization rates for dental services, with the possible exception of children under age 6. For example, only $32 (21 percent) of older persons' per capita health expenditures went for dental care in 1975. In fact, for some elderly, this figure is zero. Although the proportion using dental services in 1975 was double that of 1957 (32 percent vs. 16.2 percent), almost 50 percent of all elderly have not used dental services in more than five years. Utilization rates are even lower for the edentulous population; 72 percent of edentulous elderly in 1974 had not sought dental care in more than five years, as revealed by a national survey conducted by NCHS (1975). This is particularly disconcerting when one considers the greater needs of older persons for more frequent recall appointments because of the need to control gingivitis and periodontal disease, and the potentially rapid development of root caries. Mulligan (1984) suggests a recall interval of three months for most elderly, six months in others.

Why do elderly use dental services at a much lower rate than they use medical services and less than the young? Surely it is not for lack of dental disease. As described above, the incidence of coronal and cervical caries, as well as periodontal diseases and benign and malignant tumors of the oral cavity, increases with age. In this section we will review some factors which have been examined by other researchers as predictors of utilization. The author's own research in this area, which examined psychosocial variables associated with utilization behavior among the elderly, will also be discussed as an alternative method of predicting utilization.

Environmental and Demographic Constraints on Utilization

Health care providers, planners, and advocates of Medicare reform have pointed to cost as the primary barrier to seeking dental care by older persons. They draw attention to the fact that Medicare pays for medical but not dental services. This may in part be true, but even with Medicare, the elderly must pay 20 to 50 percent of their medical expenses out-of-pocket. This has not significantly reduced older persons' medical service utilization rates, as described earlier.

Further evidence for the insufficiency of the cost argument is provided by utilization data for low-cost or free dental services which have emerged to treat the elderly. These include programs through public health departments, federally funded programs such as Triage in Connecticut (Doherty and Segal, 1978), Senior Dent in Minnesota (Portnoy and Yellowitz, 1977), and the Community Health Board's federally funded dental program in Seattle for low-income persons of all ages (Kiyak and Miller, 1982). Despite the proliferation of these programs in the 1960s and 1970s, utilization rates have not improved dramatically.

There is often an increase in demand for emergency dental services and new dentures, but the use of maintenance of preventive services does not change. Thus for example, after 2½ years of a reduced-fee program for elderly by the Dental Delivery System of Vermont, the application rate was 8 percent and the utilization rate was 5 percent of all eligible elderly (Taylor, 1980). Taylor points out that even in states where dental services are covered by Medicaid, utilization is still only one-half that of younger persons. As further evidence for the inadequacy of the cost hypothesis, a survey conducted by the ADA in 1978 revealed that very few respondents over age 60 perceived dental costs to be a barrier to seeking care; 30 percent believed that dental costs were too high, whereas only 18 percent of elderly with natural teeth agreed with the statement.

If cost alone is not the critical barrier, what is? The model of health service utilization proposed by Anderson and Newman (1973) has been tested widely in dental services with mixed success (Evashwick et al., 1982; NCHS, 1975). This model suggests that three conditions must exist if individuals are to seek health care. These are classified as predisposing, enabling, and need variables. The first, predisposing conditions, consists primarily of demographic characteristics such as age, sex, race, education, and occupation of household head. Sex differences are more important in younger populations, where females make 10 to 25 percent more visits to dental providers than do males. But in the elderly, this difference is insignificant. In fact, the 1974 survey by NCHS revealed that males over age 65 actually made *more* visits than females (NCHS, 1975).

Racial differences are more dramatic, with nonwhites making one-third to one-half the number of dental visits made by whites. This racial difference may be related to other factors such as residence, access to dental services, socioeconomic status, and availability of a regular source of dental care. Unfortunately, the reports available on national surveys provide information only on main effects, not interactions.

Education of the household head is an important predisposing variable across all age-groups. Families headed by college graduates are two to three times more likely to seek dental services than those headed by an individual with eight years or less of education (HRA, 1977). Older persons with college degrees were twice as likely to use dental services as those with some college education in 1974, and almost four times as likely as the least educated. The author recently completed a small survey of retired university faculty which provides further support for the effect of education, occupation, and income status on dental service utilization (Kiyak, 1984). All 20 respondents in that study had been to a dentist in the previous year, although seven persons reported that their usual frequency was once every two years. All had a private dentist, generally one they had visited regularly for the past 20 to 30 years. In most cases, this elite group of elderly sought dental care to prevent tooth loss and to maintain "teeth that feel clean."

The benefits of these lifelong preventive dental behaviors were revealed by the fact that all respondents had maintained most of their natural teeth. These results would suggest that future cohorts of elderly who will have more years of education and higher retirement income than the current cohort will be more likely to seek dental care. But the problem of low utilization by elderly today, who on the average have less than a high school education, cannot be ignored in anticipation of future generations.

What is the effect of a related socioeconomic concept, occupational status, on utilization rates? Not surprisingly, families headed by persons in the highest occupational groups are two to three times more likely to seek dental services than those in the lowest (HRA, 1977). However, differences for the extreme groups among the elderly are not as dramatic as differences between extreme groups on educational level.

The second category of variables associated with health services utilization is enabling variables. These include family income, ability to pay for services, dental insurance, and community resources. The difference in dental service utilization by elderly in the lowest and highest income categories has become more significant in 1974 compared to 1964. Even those who are earning the median income are seven to eight times more likely than the poorest elderly to use dental services. Ability to pay and insurance coverage also play an important role in the use of dental services, as revealed by the NCHS surveys. Regardless of income status, individuals who feel they cannot afford dental treatment will not obtain it. Differences of a factor of two to three are evident at all ages. As one might expect, insurance coverage increases the likelihood of using dental services by 50 to 100 percent. But respondents over age 65 in the NCHS survey continued to be the lowest utilizers, whether or not they had dental insurance. Utilization rates for elderly with dental coverage approach those of younger age-groups *without* insurance. The effect of community resources has been adequately examined for the elderly, but it appears that a similar pattern exists across age-groups. That is, individuals in urban communities, in areas with a high dentist-to-population ratio, and with several easily accessible dental services are more likely to use dental services than those who do not live in such communities, but there are few studies available on the interaction of age × environment.

Another predisposing condition is familiarity with the health care system. Previous experience with a particular illness and with specialists to treat the illness has been found to result in higher utilization rates subsequently (ADA, 1978; Bernstein and Berk, 1982). But none of these variables seems to be adequate for explaining dental service utilization. In a secondary analysis of the 1977 Health Interview Survey for 2,287 elderly persons, Eve et al. (1980) entered the available predisposing, enabling, and self-reported illness variables into a regression analysis to predict dental service utilization. They found that these variables could explain only 9 percent of the variance in number of dental visits and 15 percent of the variance in interval since last dental visit. It is unfortunate that this large data set did not include questions on health attitudes and perceived and objective need for treatment.

One of the most difficult areas of health service utilization to study systematically is the need variable. Particularly in large-scale national surveys, it is difficult to assess perceived and objective needs with more than just a cursory questionnaire and/or examination. Yet these are precisely the variables which play the greatest role in older persons' utilization of dental services, as shown by several researchers (ADA, 1978; Beck et al., 1982; Kiyak and Miller, 1982). In their 1978 survey, researchers at the

ADA found that nearly half (47.4 percent) of their respondents over age 60 had not sought dental care in more than three years, but only 39 percent were dissatisfied with their oral health. Among those who had not sought dental care recently, only 12 percent cited cost as a barrier; 79 percent indicated that they felt no need. When the investigators distinguished between denture wearers and those with some natural teeth, 90 percent of the former and 52 percent of the latter felt no need. Despite the popular belief among young and old that denture wearers do not need professional dental care, the increased incidence of diseases of the soft tissue and changes in the underlying bone supporting dentures demand periodic examination in the dental office.

In the Iowa Survey of Oral Health (Beck et al., 1982), a stepwise regression analysis was conducted on the interval since last dental visit. It included nine attitude statements regarding dentistry and dental problems, respondent's education, income, and satisfaction with dental fees. The first four items which entered the equation were attitude variables; the fifth was education. These five items could account for 14 percent of the variance in interval since last dental visit.

The importance of considering patients' perceived needs is supported by the work of Evashwick and colleagues (1982), who interviewed persons aged 62 or older who were living in apartments for low-income elderly. Using a set of predisposing, enabling, and need variables to predict recency of dental visit and number of dental visits during the past year, they found that the perceived number of dental problems was the best predictor of both dependent variables. It should be noted that this sample had a restricted range of income and education, so the lack of significant effects for these variables may not be applicable to other populations of elderly.

This review of the major studies in dental service utilization which have examined predisposing, enabling, and need variables may be summarized as follows. Although demographic variables such as education, occupation, and income status may differentiate between regular and infrequent utilizers of dental services, these factors do not necessarily imply a greater availability of financial resources. As we have seen, the cost of dental services is not cited as a barrier even by respondents in the lowest income groups. Instead, it appears that these three socioeconomic status indicators represent a greater awareness of and concern with oral health. If this is in fact true, then we may not have to wait for future cohorts of more educated and financially more secure elderly to seek dental care. It may be possible to change some of these psychosocial aspects of the individual such that oral health becomes a more salient aspect of well-being and part of the individual's total health-seeking behaviors.

Psychosocial Predictors of Utilization

The major advantage of the psychosocial or individual differences approach to assessing health care behavior is that it examines the *subjective world of the individual* (one's values, beliefs, desires, and interpersonal network) as it exerts a force upon the individual to seek health care. Psychological factors have been described as "variables affecting the perception of symptoms" (Kegeles, 1969; Mechanic, 1969). The specific steps by which an individual decides to utilize health services have been described within this psychological framework by Mechanic (1969) and Suchman (1965). Other investigators have found psychological factors to contribute significantly to utilization. Richard's (1975) study of nonusers of medical services in Canada revealed that factors such as self-reliance and favorable assessment of one's own health played an important role in not utilizing medical services.

Kegeles (1969) has proposed "saliency" or priority of health care relative to other activities as an explanatory variable. Kegeles found that knowledge alone does not improve utilization because most people are already aware of the need for yearly dental visits. Instead, respondents in his study who felt vulnerable but whose feeling of helplessness could be converted to a sense of being able to do something to prevent dental disease were more likely to subsequently use dental services. The work of Langlie (1977) has contributed to the importance of psychosocial variables in seeking health care. Personality factors such as the perception of control over one's own health, as well as interpersonal variables such as social network and social isolation, were found to distinguish between those who believed in preventive health behavior (e.g., seeking medical and dental care, exercise and good nutrition) vs. those who did not.

These findings suggest that an attitudinal framework which incorporates health beliefs and values held toward these beliefs may be a beneficial one for examining dental service utilization. The author and colleagues have conducted a series of studies to examine utilization behavior within the theoretical framework proposed by Fishbein (1967, 1975) in his "summation theory of attitudes" (Diehnelt and Kiyak, 1984; Kiyak and Miller, 1982; Gilmore and Kiyak, 1984). This concept has been extensively tested and found to be a useful approach to predicting diverse behaviors (Fishbein and Ajzen, 1972; Fishbein and Hunter, 1974; Wicker, 1971; Wyer, 1968), but until recently it had not been applied to dentistry. According to this theory, attitudes may be defined as "feelings or affect toward an object or behavior." In other words, attitudes consist of a set of beliefs and the individual's evaluation of these beliefs. Each belief is weighted by the importance or affect attributed to it by the individual. These scores are then summed across all the items to obtain a total attitude score toward a particular object or behavior.

The summation theory was first applied to dental behavior in a study of regular vs. emergency utilizers vs. nonutilizers of dental services (Kiyak and Miller, 1982). Low-income residents of central Seattle who qualified for and had been enrolled in a federally funded, free dental service for at least one year were interviewed. Despite the availability of free transportation and choice of health providers, utilization patterns remained low, particularly among persons over age 65 and those who were edentulous.

A series of beliefs related to oral health were obtained through open-ended interviews with another comparable sample. The 15 most frequently mentioned beliefs were then translated into Fishbein's model, i.e., the research sample was asked to assign a *subjective probability* to each belief item. The evaluation of each belief was determined by asking the respondent to indicate how *important–unimportant* that event was to him or her, and how *good or bad* the outcome of that event would be for him or her. Both sets of evaluation questions used a five-point Likert Scale. Attitude scores could then be derived in two ways, operationalizing evaluations as importance or affect. Results revealed significant differences between elderly utilizers and nonutilizers on the importance and affect dimensions of attitudes, but not on the belief component. That is, both groups held favorable beliefs about oral health (e.g., brushing three times daily will reduce tooth decay, regular dental care by a professional will prevent tooth loss), reflecting the influence of TV and radio commercials for dental care. But nonutilizers had apparently not integrated these beliefs into their personal value systems, resulting in less importance attributed to these beliefs for the individual compared to those who were regular utilizers.

In a second study, we sought to determine the relative effects of these attitude variables, locus of control, and ethnic factors in seeking dental care (Diehnelt and Kiyak, 1984). A sample of 52 Japanese-American elderly living in the community were interviewed, one-half of whom had immigrated to the United States as youths. The other half were second-generation Americans. The interval since last dental visit ranged from one day to 40 years. The best predictors of recency of last dental visit for the first-generation Japanese were total attitude scores, importance, and belief scores. Locus of control scores and education added slightly to the explanation of variance (R^2 = 47 for all five variables). The second-generation Japanese-American elderly revealed a pattern similar to that found in Caucasian and black elderly in the study described above. Scores on the importance component emerged as the best predictor and could explain 41 percent of the variance in utilization interval. Beliefs and locus of control added slightly to this equation (R^2 = 45).

These results suggest that attitudes toward oral health, composed of the individual's beliefs and the degree of personal importance or salience attached to these beliefs, may be better predictors of older persons' utilization of dental services than the predisposing, enabling, and need variables which have traditionally been used in studies of utilization. As described earlier, previous researchers rarely have been able to explain more than 15 percent of the variance with these variables. However, attitudes have emerged as powerful predictors of utilization when this variable is operationalized as interval since last dental visit.

Education level and locus of control contributed slightly to the variance explained by these predictors.

Further research is needed to determine the association between attitudes, income level, insurance coverage, perceived ability to pay for dentistry, *and* other health, social, and recreational services relative to their perceived usefulness. It may be that expanding Medicare to cover dental costs, no matter how extensive the coverage, will not significantly enhance utilization except for immediate, long-standing needs and emergency services. But what are the relative effects of improved dental coverage, priorities for dental vs. other needs, and income status on older persons' desire to seek dental care and actual behavior in seeking it? These and other characteristics of the individual should be tested within different populations of elderly such as those in nursing homes vs. independent living situations. The serious problem of severe underutilization by nonwhite elderly populations must also be examined. Previous research provides some indication that differences in health beliefs and the importance attributed to oral health may influence utilization patterns. Programs to address these differences should be developed and tested, with the goal of a more equitable demand for dental services. Finally, research is needed regarding the impact of dental care on other aspects of the older person's life. That is, by improving oral self-care and increasing dental service utilization, can we enhance the functional health, psychological well-being, and overall quality of life among the elderly population? Only through more intensive studies of this sort which go beyond the traditional descriptive research of the past can we hope to improve dental behaviors and oral health of the elderly and perhaps even to enhance the quality of their lives.

PREVENTIVE DENTISTRY FOR THE ELDERLY

The concept of oral health promotion or preventive dentistry for the elderly seems anomalous to both dental practitioners and older persons themselves. It is often assumed that dental disease and tooth loss are natural concomitants of aging. Furthermore, these persons ask, once the individual has lost many teeth from poor dental health in the middle years, what is there to prevent? Even in current journal articles and books on health promotion for the elderly, recognition of the need for oral health promotion is lacking. Thus for example, two recent publications on this topic (Hickey, 1980; Wells, 1982), both of which cover a broad spectrum of health, include no references to oral health.

In this section, we will examine the nature and benefits of preventive dentistry for the elderly, and its value for the overall health of older persons. Two experiments to enhance oral health self-care in the elderly will be discussed. It has been argued that health promotion and disease prevention can enhance the quality of life for the individual. Because oral health is a critical factor in nutrition, speech, and esthetics, we would argue that the prevention of oral disease has an even greater impact on the quality of life for older persons. The concept of preventive dentistry encompasses periodic examination of the dentition, soft tissue, and supporting structures, as well as a professional prophylaxis, fluoride application, and education in appropriate home care behaviors for the individual's particular needs. This becomes particularly important in the elderly who, because of normal physiological changes, multiple chronic illnesses, and a high consumption of medications, often experience changes in the oral cavity and its functions. These include a change in the ridge which supports dentures, xerostomia (dry mouth), inflammation, and diseases of the soft tissue. Furthermore, it is important to provide the older person with up-to-date information on home care relevant to his or her current oral status. Hence, regular interaction with the dental team is a critical component of preventive dentistry for the elderly. Older persons can benefit significantly from a combined program of periodic oral examination by a dentist and an interactive educational approach to teach them home care techniques.

Research on Preventive Dentistry for the Elderly

The author has recently completed two studies of enhancing self-care in dentistry among the elderly (Kiyak, 1979; Price and Kiyak, 1981). This research was based on the premise that older persons, whether institutionalized or living independently in the community, can learn techniques of preventive dentistry which will improve oral hygiene, prevent further disease, and have a significant impact on their psychological well-being. That is, by experiencing improved oral health through his or her own efforts, the older person's personal responsibility for health and competence will increase and learned helplessness will decrease, resulting in improved perceptions of general health and increased self-esteem.

It should be noted at the outset that preventive dentistry for the elderly was defined differently for these studies than the traditional concept of preventive dentistry. In the younger population, prevention implies freedom from disease and maintenance of all adult teeth. For older persons, particularly those who have lost some or all of their natural dentition, preventive dentistry must focus on the prevention of *further* disease, particularly iatrogenic disease caused by poorly fitting dental prostheses and prescribed regimens for medical conditions. The comfort and maximization of oral functions such as mastication and speech must be the goal of any preventive dentistry program for the elderly.

Both studies utilized techniques from behavioral psychology which have successfully been applied to gerontology. Among the various behavior-change programs, perhaps the most successful are those which have been used with institutionalized elderly. Verbal communication increased significantly among elderly mental hospital patients in two studies which used operant procedures (Hoyer et al., 1975; Mueller and Atlas, 1975). Token economy programs have been successful with the elderly in increasing their exercise behavior (Libb and Clements, 1969), in reducing bizarre and dependent behavior while at the same time increasing meaningful social interactions (Mishara, 1978), and in improving performance on experimental tasks (Swenson, 1971). The use of positive reinforcement in the form of material or verbal rewards has proven successful with diverse elderly (Meichenbaum, 1974; Sachs, 1975), but few investigators have attempted to change dental behaviors among older persons.

One of the disadvantages of many behavioral-change programs is their reliance on an external change agent. The researcher or an assistant monitors the individual's behavior and controls the reinforcement. This may be one reason why many behavior-change programs do not produce long-term effects. One of the few studies which utilized a self-management approach with the elderly was conducted by Meichenbaum (1974). The success of this technique suggests that it might be more effective in motivating the elderly, enhancing their perception of control over their life space, and producing long-term changes. A self-management approach should be particularly effective in improving oral health behavior. The behavior is within the direct control of the individual. It can easily be recorded by the performer, and even minor improvements are clearly detectable. This technique was therefore selected as the behavioral change approach to be tested in the author's own research.

It was hypothesized in both studies that a self-monitoring system based on principles of behavior management (Hoyer et al., 1975; Mishara, 1978; Sachs, 1975; Skinner, 1953; Weinstein and Getz, 1979) would be better than a traditional educational program in oral health. This approach should reduce oral disease conditions and improve the self-sufficiency of the elderly. It was anticipated that this self-sufficiency would spill over into other areas of the aged individual's functioning, thereby increasing his or her perception of active mastery. The combined effects of better oral health and increased self-sufficiency should improve the morale, self-esteem, and perceived health status of participants in such a program. The effectiveness of self-monitoring for both immediate and long-term change was compared with an education-only program. These two approaches were each combined with periodic oral examinations. A control group received no intervention. Both short-term and long-term changes in objectively assessed oral health status, perceived health status, morale, and self-esteem were measured.

The first study applied this model to a sample of older persons residing in a nursing home (Kiyak, 1979). Residents who were free of dementing illness and were physically capable of oral self-maintenance (i.e., manual dexterity not seriously impaired) were selected to participate in this study. Even in this skilled-care facility, 76 of the 128 residents fulfilled these research criteria. Among the potential list of 76 persons, 68 nursing home residents whose mean age was 82.8 completed the study.

In the second study (Price and Kiyak, 1981), we sought to replicate the nursing home experiment with elderly who were living in the community and to compare ethnic differences in response to this preventive dentistry intervention. The experiment was conducted in two local senior centers; one where the elderly were primarily Caucasians, the second where they were all Japanese. In the latter setting, the educational program was conducted in Japanese by the senior author (S.P.). Twenty-seven elderly participated in the former, 33 in the latter. As one might expect, the mean age for this sample was lower than the nursing home sample (74.6 vs. 82.8). This provided an opportunity to test the efficacy of a dental health promotion program for both "young-old" and "old-old," for institutionalized as well as community elderly, and for two ethnic groups.

Interviews and baseline tooth and denture cleaning were conducted with all participants two weeks before the experimental interventions. Elderly who had been randomly assigned to the two experimental conditions were assessed for plaque levels just before the interventions. These methods are described in Kiyak (1979) and Price and Kiyak (1981). The educational interventions were conducted separately for the two groups during the subsequent three weeks. The content of these two health education programs was identical; techniques of denture and natural teeth maintenance, nutritional needs, and the procedures for daily and professional oral health care were presented during the six sessions for each group. Correct oral home care behaviors were modeled. Each session lasted 25 to 30 minutes, with ample time for one-to-one interactions with the course instructor. The lack of published material for oral health education of the elderly made it difficult to give appropriate handouts. Nevertheless, brief instructions with diagrams were given to participants, who were eager for such material to take back with them.[†] It was important to provide participants with appropri-

[†] The lack of material in this area has prompted the author to produce written and audiovisual information specifically for the elderly. Two booklets on caring for natural teeth and dentures were developed specifically for the elderly with a grant from the Jenny Baker Foundation. A subsequent grant from the American Fund for Dental Health has allowed the author to produce five slide-tapes and three videotapes on preventive dentistry issues for the elderly. Information about these materials may be obtained from the author.

ate preventive dentistry materials at the start of the intervention, in order to reduce the bias of varied preventive aids. Hence, each older person was provided with a new toothbrush and/or denture brush, toothpaste, floss and floss holders for those with natural teeth, and toothbrushes with special grips for those with manual dexterity problems.

Participants in the self-monitoring condition were given charts at the start of each week. Separate charts were designed for denture wearers and for those with natural teeth. The former group was asked to note their frequency of washing and brushing dentures each day, and whether the dentures had been removed each night before retiring. Those with natural teeth were asked to record frequency of brushing and flossing each day on a simple chart provided to them at the start of each week.

Participants brought their charts to each session; their progress and areas where no change had occurred were discussed in the group. Positive verbal reinforcement was provided by the instructor and other members when an individual showed improvement from week to week. It was decided that material reinforcements would not be used. In this manner, we could conclude that an effective intervention was clearly attributable to self-monitoring. Furthermore, future applications of this approach in settings for the elderly would probably not include material reinforcers.

Each participant in the two nursing home experimental groups was assessed for plaque levels immediately after the educational intervention, 5 weeks later, and 4 months later. In the community sample, time constraints precluded a 4-month assessment. The control group was assessed for plaque levels at baseline and again 12 weeks later.

Group comparisons in the nursing home study revealed significant differences at the pre-intervention, immediate post-intervention, and the 12-week assessments. Although the self-monitoring group had the *highest* plaque levels before the intervention, they showed a significant and steady decline to 12-weeks post-intervention. Their plaque levels then stabilized in the subsequent 4 months, but did not decline further. This was particularly true for denture wearers. There was no reduction in plaque levels for the education-only and control groups. This supports the need for a self-monitoring program if preventive dentistry education is to reduce plaque levels in the elderly.

A follow-up interview was conducted with all subjects at the 12-week assessment, to determine whether any changes had occurred in self-reports of oral health maintenance, perceived health, morale, and self-esteem. Significantly more elderly in the self-monitoring group reported using the correct procedures for oral hygiene (e.g., soaking dentures, frequent brushing of teeth and dentures) at follow-up than did the education-only group. That the former group did indeed perform better and more frequent oral hygiene behaviors is supported by their improved plaque scores. Consistent with these findings, the former group rated themselves highest on perceived health at the post-intervention interview. Although the education-only groups also showed some improvement, the change was nonsignificant. Self-esteem did not change for any group, but elderly in the self-monitoring condition showed higher morale at the post-intervention interview than at pre-intervention, and the highest of any group.

In the community study, we found no differences at pre-intervention between Japanese and Caucasian elderly in plaque levels, self-reports of oral health behavior, and oral hygiene status. At the immediate post-intervention assessment, both the self-monitoring and education-only groups showed significantly lower plaque levels than the control group in the Japanese *and* Caucasian centers. The second follow-up revealed that the plaque levels for those receiving self-monitoring remained stable, but that it *increased* for those in the education-only and control groups. This effect was particularly pronounced in the Japanese center. Perceived oral hygiene improved significantly only for this latter group at the follow-up interview. Significant improvements in dental beliefs and dental behaviors were found in both self-monitoring groups, but Caucasian elderly in the lessons-only group also showed improvements in dental beliefs.

The Effect of Manual Dexterity

The mechanism of skilled activity consists of *receptor* processes (i.e., the interpretation of an incoming stimulus via sensory and cognitive modes) and *effector* processes (i.e., the motor aspects of skill), according to research by Welford (1968, 1977). What happens in skilled motor activities such as oral hygiene behaviors as the individual ages? To the extent that motor control deteriorates with aging, oral self-care will become a problem, resulting in a need to modify home care regimens in an effective preventive dentistry program for older persons. In order to determine whether modifications in recommended self-care procedures were necessary in our study of nursing home elderly, we assessed each subject's manual dexterity, using the Jebsen Hand Function Test (1970), which measures various motor skills necessary for activities of daily living (writing, turning over cards, picking up small objects, simulated feeding, stacking small objects). Time to complete each task with the dominant and nondominant hand was measured. However, neither this nor any other test of motor functioning simulates the movements in cleaning dentures, a skill requiring manual and finger dexterity in both hands. For this reason, we devised a simulated denture-brushing exercise and administered it together with the Jebsen test. As with other Jebsen subtests, time to complete the task with each hand was measured.

In an attempt to assess the elderly participant's cognitive capacity to learn the skills necessary for oral hygiene, we administered the Mini-Mental Status Questionnaire (Folstein et al., 1975). In order to reduce situational variability on task performance, the same interviewer administered both the manual dexterity and mental status tests to all participants.

In terms of receptor processes, all subjects in the nursing home experiment showed signs of visual and auditory decline, and one-third had serious decline in one or both sensory modes (e.g., cataracts, blindness in one eye, total hearing loss). Scores on the Mini-Mental Status Questionnaire ranged from 10 to 26 (maximum possible = 31). The median score was 17, similar to the norms reported for this age-group by Folstein. This suggests that participants in this program had some limitations in receptor processes, although the primary problem was in sensory mechanisms, not cognitive.

Turning to effector processes, we found two aspects of these processes to be critical mediators of task performance. The first was *motor functioning*. Medical charts of each participant revealed that 60 percent had some disease of the neuromuscular system, including senile osteoporosis, degenerative joint disease, and rheumatoid arthritis. In addition, five persons had experienced cerebral vascular accidents which affected their upper extremity function. There was a significant correlation between these medical diagnoses of motor dysfunction and time to complete the denture-cleaning simulation subtest ($r_{pb} = 0.51$, $p < 0.11$). The relationship between motor dysfunction and the simulated feeding subtest of the Jebsen test were also in the expected direction, although the values were not significant ($r_{bs} = 0.11$). Not surprisingly, elderly who had neuromuscular diseases generally took longer to perform these subtests than did those who had no signs of motor dysfunction. When compared to Jebsen's sample of normal elderly (60 to 94 years), the mean time to complete each of the subtests with each hand was consistently lower for the present sample. Reasons for this difference are not readily apparent.

Although these results point to the importance of effective motor functioning for successful oral self-care, it should be pointed out that motivation plays a significant role also. Based on the results of this study, we would argue that motivated elderly can benefit from preventive dentistry programs, regardless of poor manual dexterity or problems in cognitive and sensory functions. For many participants in this study, oral hygiene had been performed for them by staff of the facility. At most, they removed and inserted their dentures; many had not performed personal oral hygiene since entering the facility. The relearning of an earlier skill, and in some cases a totally different skill, was often independent of motor or cognitive functioning. Instead, motivation appeared to be a key determinant of success in this program. Elderly participants who felt they had something to gain from classes in oral hygiene did indeed make an active attempt to acquire both the didactic knowledge and the specific manual skills necessary in personal oral hygiene. They were motivated to try the individualized techniques we designed for cleaning their dentures and/or natural dentition. Even those who had severe motor limitations learned these techniques, albeit somewhat more slowly, if they were motivated and made an active attempt to acquire these new skills. Thus, the learning of new movements demands more than motor, sensory, and cognitive capacities in the elderly. As stated by Welford (1951, 1977), motivation is a critical element in learning a new task.

Implications for Oral Health Promotion for Elderly

These results provide dramatic support for the value of a behavioral approach to preventive dentistry education for the elderly. Long-term improvements are particularly impressive with self-monitoring techniques, although short-term change is possible with an education-only approach for community elderly. It is worth noting that self-monitoring techniques have a powerful impact on many aspects of preventive dentistry such as home care, plaque levels, perceived health in general, beliefs about the importance of oral health, and psychological well-being as measured by morale. When one considers the role of beliefs in motivating the elderly to seek dental care, the finding that a self-monitoring approach can change dental beliefs is in itself a strong justification for using this technique in any health-promotion program for the elderly. Furthermore, the success of this technique with two very different ethnic groups suggests that it may be a universally superior approach to a program which uses information dissemination alone. Elderly living independently in the community and those with multiple chronic illnesses in nursing homes may benefit from active participation in oral health education. A few principles must, however, be kept in mind when designing oral health promotion programs for the elderly. A detailed discussion of learning ability in the elderly and implications for health education are described by Whitbourne and Sperbeck (1982). The principles described below grew out of the author's own experiences with preventive dentistry for the elderly:

1. Learning occurs more slowly in old age, and the rate of recall is slower. Hence, any information presented to the older learner must be repeated several times and reinforced both visually and aurally. Thus, for example,

slides and films to describe graphically the information presented in a lecture, as well as booklets, pamphlets, or other handouts, should be used.

2. Active learning techniques are generally better than passive learning for all age-groups, but particularly for the elderly. Because of changing learning styles with aging, a self-monitoring program where the individual actively participates in his or her learning progress is more effective than a lecture-only approach.
3. Because of sensory changes with aging, written material must be presented in large-format print with contrasting figure-ground relations. Photos and charts must be simple and of high visual quality.
4. Because fatigue occurs more rapidly for the elderly, it is important to keep information sessions brief, preferably less than 45 minutes. Frequent and brief sessions are far superior to a few sessions which last one hour or longer.
5. A professional dental practitioner or health educator is not necessary in presenting an effective oral health promotion program. A volunteer or paraprofessional can present the necessary information after developing the key concepts and design with a professional.
6. Motivation will be significantly enhanced with regular feedback to participants regarding their success in achieving predetermined oral health goals. To the extent that older persons received individual feedback and praise from the educator in our experimental programs, they were more likely to take an active role in their change program and less likely to drop out.

By keeping in mind these principles of health education and applying them to any oral health promotion program, future program developers will increase the potential of successful outcomes. As we have shown, older persons of diverse functional capacity and ethnic groups can benefit from a well-designed program to promote individual responsibility and self-care in oral health.

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CHAPTER 6

The Management of the "Chronic" Patient

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The planning and management of services for chronically sick old people has assumed greater importance in the last decade, both because of the expansion of geriatrics as a profession, and because of the increase of the elderly population. Beginning with voluntary endeavor and often with a religious focus during the Middle Ages, the care of the disabled aged has emerged as an integral part of the social structure of many countries, demanding a substantial outlay of the national income (Sheldon, 1971; Adams, 1975; Cape, 1978). In many Western countries, the percentage of pensioners has risen to between 13 and 14 percent in the last 20 years. At the time of the foundation of the State of Israel in 1948, the percentage of pensioners was 3 percent and it has risen in the last 15 years from 6.5 percent to 9.5 percent. The rise in number of elderly has brought with it a rise in morbidity in very old people—the "old" old people. It is timely, therefore, to examine our concept of chronic care with respect to the roots of the problem, the composition of the "chronic" population, the aims that one should set, and the achievement or lack of it in our present amenities.

THE "CHRONIC" PATIENT

A chronic patient can be defined as one who is disabled as a result of a disease that has occurred in the past and left the patient impaired; or that is still present, causing continuing disability, which might still progress. The word "chronic," in the sense of prolongation, implies one or both of two meanings. It might refer to continued activity of a disease process or it can reflect a prolonged period of functional disability. The distinction is of diagnostic and therapeutic importance. In the first case, the disease process can and must be defined, criteria of activity stipulated and proven, and appropriate treatment given, with follow-up designed to check whether the disease has been brought under control. The person's functional disability may be more or less paralleled by the degree of disease activity. Common examples of this type of chronic patient are to be found in any hospital outpatient clinic. These include patients with ischemic heart disease that may be controlled with a variety of vasodilators, beta blockers, and inotropic drugs; peptic ulcer disease controlled by antacids or histamine 2 receptor blockers; and bipolar depression controllable by drug regimens, such as lithium or polycyclic antidepressants. In these cases, function and dysfunction parallel remission or relapse of the disease and medical interference is of supreme importance in the rehabilitation of the patient.

The second group conforms more closely to the accepted image of the chronic patient. Here there is partial or total loss of independent function in daily living activities, including occupational activity; this impairment may be unrelated to any active pathologic process remaining from the original disease. The functional disability may or may not be susceptible to improvement through rehabilitation techniques. Reactivation of the original disease or the occurrence of other diseases will cause a deterioration of the functional status. Examples of this type of chronic patient are hemiplegics who retain some measure of response to mobility training, but whose neurological deficit remains static; a further stroke as evidence of continued vascular occlusive disease will worsen whatever improvement was previously achieved. Further examples are patients with dementia who show an incapability of independent coping which will remain for the rest of their lives; this can be exaggerated by intercurrent acute illness or superimposed confusional states or psychosis.

Broadly, the distinction between the two groups of chronic patients is that in the first, the emphasis is on the disease, with its secondary effect on function; in the second, the emphasis is on dysfunction, with the primary disease exercising a background role and other disease acting as exacerbating secondary phenomena. Similarly, the facilities that deal with the first group are usually in a general acute care setting, and less than adequate attention may be paid to the functional and psychological consequences of the disease. The second group of patients are dealt with at best in rehabilitation facilities, often for only a limited period, and thereafter the necessary diagnostic and therapeutic integration may be sadly lacking in the chronic care facility to which the patient is assigned. It is evident that patients from the first group may, at some stage, require the facilities provided for the second group in the form of community or outpatient rehabilitation services. Patients from the second group will sometimes need acute care facilities and general medical follow-up within the institution or hospital framework.

Hospital management of chronic disease has evolved on the basis of advances in medical thinking and technology that have rendered more and more groups of patients and diseases susceptible to treatment. Examples are the post-myocardial infarct rehabilitation programs, dialysis units, and day-care oncology services. The need for supplementary management of psychological, occupational, and family problems may be dealt with also in facilities existing outside the hospital. Medical advances, together with rising costs, will continually demand more ambulatory procedures, with services from the hospital integrated with those of the community in the follow-up of chronic disease patients. Present examples are the programs for the treatment of hypertension (see Hypertension Detection and Follow-up Program Cooperative Group, 1979), and some of the population screening designs for diabetes (e.g., the Birmingham Diabetes Survey of 1962 [Royal College of General Practitioners, 1970]) or for disability (Warren, 1974). These developments are in tune with the dynamism of medical advances. Not so the more pedestrian concept of the chronic patients of the second group, where the emphasis on dependency and institutional treatment confers an air of medical stagnation as well as the impression of a crushing economic burden. It is with this group that the rest of this survey will be concerned.

ASSESSMENT AND MEASUREMENT OF NEEDS FOR CHRONIC CARE

The needs of the chronic patients of the second group may be determined by two factors: (1) the type of loss of independence and its severity; and (2) the relationship between the degree of dependency and the number of hours per day that the person needs care or supervision. Social circumstances are not a cause for dependency but are related to the solution of that problem. At the same time, the factors involved in the type of dependency and the time required for treatment during the day take account of psychological as well as physical causes for the patient's disability. Table 6.1 outlines the chief categories of disabilities and disorders that may require chronic care outside the acute care facilities of a hospital.

A patient's need for chronic care may become evident in one of three ways:

1. Recurring illnesses with progressive deterioration in function may weigh increasingly on the family until they can no longer provide unaided support. Examples are those with progressive impairment of mobility due to recurrent strokes or deteriorating joint function, or the increasing nursing burden presented by advanced cardiac failure.
2. A previously well patient may be stricken suddenly with an impairment that permanently interferes with independence. Examples are automobile accidents or a major stroke that leave permanent brain damage.
3. A patient with a degree of disability and dependency may be well cared for until social supports are suddenly removed by the illness, death, or change in social circumstances of the patient's caregiver.

Table 6.1
Categories of Disability Leading to Need for Chronic Care

Disability	*Type of Impairment*	*Type of Disease*
Locomotor	Impaired mobility	Cerebrovascular—strokes, either major (hemiplegia), or minor (paresis, dysequilibrium)
		Other neurological diseases—parkinsonism, multiple sclerosis, motor neurone disease, myelopathies, neuropathies
		Skeletal injury, osteoporosis—fracture of femoral neck, vertebral fracture, traffic accidents
	Pain and stiffness causing immobility	Joint disease—chronic inflammatory, chronic degenerative
Mental	Cognitive impairment Confusional states	Dementias—Alzheimer's, arteriosclerotic (multi-infarct), parkinsonism
Psychiatric	Personality and behavior impairment	Chronic depression Neurosis Paranoid states
Impairment of special senses	Blindness	Cataract, diabetic retinopathy, macular degeneration
	Deafness	Ostosclerosis
	Aphasia	Strokes, degenerative brain disease
Loss of sphincter control	Incontinence	Dementia Diffuse cerebrovascular disease Paraplegia Severe prolapse of bladder or rectum

(continued)

Table 6.1 (continued)

Disability	*Type of Impairment*	*Type of Disease*
Chronic system failure	Breathlessness weakness and symptoms specific to system involved	Chronic lung disease (obstructive, restrictive) Cardiac failure Decompensated cirrhosis End-stage renal failure Metabolic failure, e.g., uncontrolled diabetes, electrolyte disturbances Immunological disorders
Malignant disease	Variety of symptons—bed-ridden pain, weakness, anorexia, organ dysfunction	Carcinoma Sarcoma Lymphoproliferative diseases Leukemias
Prolonged severe global cerebral dysfunction	Vegetative state or complete dependency	Post-head injury Irreversible brain damage from drug intoxication, anesthetic accident Hypoglycemia

In each of the above categories, it is important to make the following assessments:

1. A definitive medical diagnosis and an estimated prognosis of recovery or deterioration with some reference to the duration of expected treatment and duration of survival.
2. Assessment of deficiency of function causing dependency (e.g., determining which parameters of mobility are lacking—can the patient walk out-of-doors or on stairs? Can he or she get in and out of bed unaided?).
3. The relation of the physical, psychological, and social needs to the environmental resources. What family is available? How near are they? For what periods during the day are they available?
4. Assessment of the physical abilities and emotional attitudes of the caregiver.

With the above comprehensive assessment, one is in a good position to define what needs are unfulfilled by the home environment, whether these can be supplied by community facilities, or whether the gap between needs and resources is so wide as to necessitate referral to an institution.

Isaacs and Neville (1976) described a standard protocol for measuring needs of dependent old people which referred to four variables:

1. The disability and the kind of help required to compensate for it.
2. The frequency of help required per 24 hours and the duration on each occasion.
3. The amount of time and the number of periods per 24 hours that the patient was unsupported—that is, bereft of help.
4. The availability of adequate and appropriate help and the duration of its availability.

This formula thus related need for help to the estimated response to this need, and associated each with the element of time. This kind of practical geriatric assessment can demonstrate in a given situation whether frequent needs of a patient are compatible with the potential help available, and can define clearly the absolute indications for admission to a nursing facility. An important conclusion from the above study was that the number of beds existing in residential accommodation in the areas studied in Scotland matched the requirements, but the domiciliary services of nursing, "home helps" and "good neighbors," were short by 50 to 70 percent.

Estimating need as mentioned above takes account of any factor depriving the old person of independent function. This approach, which measures the negative side, should be supplemented by the positive question of whether all the foundations of a satisfactory old age are present in the given case. These cornerstones of satisfaction include:

1. A comfortable environment with reasonable space, domestic facilities, warmth, and security.
2. Availability of good nutrition—access to shops, and ability to purchase, select, cook, and eat the food.
3. Economic stability, with a reasonable income.
4. Personal security against ill health, and against physical attack.
5. Availability of appropriate social interaction.
6. A purpose in living—with regard to the general outlook and occupational activity (see Kennie & Arnott, 1973).

Standards of satisfaction vary according to the personality, education, and cultural background of the individual, as well as previous social interactions. The lifestyle of the old person should conform to acceptable standards of cleanliness, function, and behavior. However, the "authorities" do not necessarily change an old person's lot for the better by moving him or her from an outdated, primitive apartment to a brand new urban development where social isolation may be more likely. On the other hand, the patient may not always be right. The description of the self-destructive or self-hating old person—the Diogenes syndrome, as described by Clark (1975)—is the other extreme, but no rarity. These people are very neglected and make little or no attempt at self care, although in many cases they are not demented. They pose a great problem for social and medical authorities by their refusal to be helped, even when their health is severely threatened by their self-neglect. The most meticulous plan for their care—in an institution or in their own home—is often fruitless due to a steadfast refusal to cooperate.

CARE IN THE COMMUNITY

With the vast majority of old people, the assumption can be made that the person's own home is his or her natural environment even if the person is living alone. "Aloneness" is compatible with a stable lifestyle, provided the old person has enough personal, cultural, and spiritual resources to allow a healthy independence. "Loneliness," on the other hand, is a state of mind often but not always induced by the situation of being alone. It is really an attitude born of the feeling of being left out of things. The social incompatibility of an old person with the environment, whether in his or her family or in a Home, can induce deep feelings of loneliness to the point of depression. It is relevant, therefore, to consider what kinds of help are available from the community to an old person living at home. The broad principles are similar in most countries, with points of novelty in some places or differences in accent in other. The division (and overlap) of responsibility among various authorities may also vary from country to country. Table 6.2 summarizes the chief classes of help with an indication of the authority under whose auspices the help is provided.

Types of Community Services

Although health and welfare services as shown in Table 6.2 indicate an advance in social thinking and responsibility, two points of criticism are relevant at the present time. A service is an intrusion and an act of interference in the life of the old person. As such, one must be sure that the interference is necessary and appropriate to the person's defined needs. Community

Table 6.2
Types of Help in the Community Available to Old People at Home

Health	Physician—family practitioner, specialist clinics.
	Home nursing.
	Physiotherapy, occupational therapy at home.
	Public health screening programs.
	Home-care team.
	Meals-on-Wheels.
	Incontinent laundry service.
	Geriatric clinics in hospital or in community.
Social	District social worker, geriatric social worker.
	Community centers with special programs for elderly and disabled.
	"Good neighbor" supervision.
Housing	Special housing for the elderly.
	Alterations to existing house to meet disability needs of aged.
	Sheltered housing schemes.
Finance	Pension schemes, supplementary allowances.
	Advisory services about rights of the elderly.
Voluntary	Visiting schemes.
	Transport, clubs, advisory bureau.
	Education and occupational activity.

services should not be seen as a substitute for the family, but rather as a supplement, and often as a recognition of help needed by the family to assist them with the old person's management. The case is known of a daughter who complained that her function was supplanted when a Meals-on-Wheels service was provided for her mother, since she had spent an hour every day giving her mother lunch. Second, it is not enough that services exist—there must be proper coordination to ensure that the correct needs are dealt with in time by the correct services. For this, a well-coordinated diagnostic service—a nurse, a social worker, and a doctor—must be able to make proper contact with the providing authorities. The organizational difficulties are not inconsiderable when services are supplied from a number of sources, such as the local health authority or welfare department, government or state agencies, or countrywide federal services. Ideally, the general practitioner with a team of nurse, health visitor, and social worker should be responsible for a particular patient population and should have appropriate contacts with regional geriatric centers and local authority facilities. Not every general practice, however, has such a team or the facilities to recognize or assess geriatric problems. An alternative wider-based organization is the regional geriatric hospital department, with its outreach to the community enabling it to make contact with general practitioners and the relevant social services. A number of such hospital-based home care schemes have operated in the United States in the last 20 years. One of the first was the Montefiore Hospital Home-Care Service in New York, set up by Dr. Cherkesky in 1961. There, a clientele of patients discharged from the hospital was built. An after-care program has included group activities and an extended-care program has provided medical and nursing care, occupational and physical therapy, health aids and various kinds of social aids, and help in the home (Cohen et al., 1984; see Rossman, 1981). A similar hospital-based home-care service has been provided by the geriatric unit in Beersheva, Israel, where the hospital is the only one in an area serving a large population, and the service is run on a multidisciplinary basis with consultant and assistant physicians, nurses, physiotherapists, social workers, and occupational therapists (Galinsky et al., 1983). A community-based home-care service based on a regional responsibility was started in Israel ten years ago, by the health service of the Confederation of Labour (Kupat Holim) in order to meet after-care needs of patients discharged from hospitals and, in many cases, afforded pre-admission assessment or avoided hospital admission altogether. The cases were coordinated at a central regional office by the home-care team who were in contact with the family health clinic throughout the region (Alkalay, 1976; Alkalay & Wasserman, 1983). The success and impact of such a service is dependent on close coordination between the primary physician in the health clinic and the regional team, with both maintaining adequate contact with the area hospital.

Despite the many medical and functional deficiencies occurring in the elderly living at home, the mere existence of services to "cure" or to help is not always relevant to the true needs of those people. For example, provision of dentures to the edentulous or hearing aids to the deaf is not always accompanied by a high degree of compliance. The effectiveness of community services must demonstrate a positive advantage to the aged person living in his home as distinct from going into care in an institution, together with a saving in cost. It must also plan to keep the cost of such services from rising disproportionately to services given in other sectors.

An example of geriatric planning illustrating the above point is that of dealing with the patient at home who plays the "sick role," that is, who fails to realize his or her full rehabilitation potential. The question posed to the team arranging services is not merely what the disability is. In considering the patient's personality, cultural background, motivation, and environment, the team should judge whether he or she is likely to resume useful, independent function, or whether to allow the patient to continue playing the sick role of receiver and let the family play the active role of giver. The difference in type of service and cost between these two approaches is important, just as is the eventual result. Moreover, for the individual who plays the "sick role," it may be important in one case to provide only a "good neighbor" who will cater to the patient's need for attention without employing more expensive services or undertaking extensive medical investigations (Shuval, 1972; Kovar, 1980). In another case, the very dependency exhibited by the patient at home as distinct from a normal behavior pattern in hospital may itself indicate a cry from the patient asking to arrange for entry into an institutional setting. Boyd (1978) described this alteration of behavior between nonfunction at home and independent function in the hospital as the "Jekyll and Hyde" syndrome. In such cases, proper recognition of the patient's need and desire for an organized framework rather than a shaky independence at home should result in a correct placement in an institution and improvement in the quality of the patient's life.

Preventive Community Services

The first step in the development of geriatrics in Britain since the 1940s was the emphasis on assessing the patient as a whole, including the functional and social aspects. The second step saw the establishment of regional geriatric departments and the flowering of the specialty, with more detailed attention to the management of vague areas in medical practice such as incontinence, falls, and confusion. The third step was an ongoing connection with the community by pre-admission assessment of the patient at home, as well as increasing after-care services (see Williamson, 1979). The next step logically was the nurturing of preventive services such as clinics for the well aged (Anderson & Cohen, 1955; Lowther, Macleod & Williamson, 1970), screening procedures (Warren, 1974; Rosin & Galinsky, 1975), health education, proper ways of living, nutrition, activity, and preventing illness. A further extension has been the proliferation of preretirement programs with a view to preventing some of the physical and psychological ills of old age (Anderson, 1967; Nusberg, 1981; Kremer & Harpaz, 1982a, 1982b).

These welcome developments must be tempered with the question of what we are trying to do and why. Preventive medicine with the elderly is more than avoiding acute complications of a long-standing disease like hypertension. It is rather an attempt to detect disability early, to prevent a spiraling downward with accelerating accumulation of secondary disease. If successfully applied, preventive medicine in the community should allow old people to continue to function although they will also be at risk and vulnerable to further bodily or mental insults for a longer period of life. The ideal is to detect and treat in the early stages conditions that, if untreated, would bring about a state of irremedial disability. But, whereas the end result might be a terminal illness that is short and acute, such treatment may also lead to older, more frail individuals who will succumb to the chronic diseases of very old age. Evaluation and end points of successful preventive medicine are difficult to measure, because its positive end point must be measured in parameters other than survival. Although preventive medicine may improve the quality of life, and possibly increase its length, it may not, however, necessarily decrease the need for community or institutional services. Rather, it might shift the emphasis to greater help from the community, and it might postpone the age at which institutionalization will become mandatory.

Community preventive services for the elderly are still patchy and not always structured uniformly or efficiently. Multiphasic screening, for example, has been recommended (Garfield, 1970), but we agree with Williamson (1981), that this is an inefficient and costly way of trying to reach a selected population. Those at risk who should be screened and sought out are the following groups:

1. Recently widowed.
2. Recently discharged from the hospital.
3. Those with known mental failure (for example, forgetfulness and other signs of incipient dementia).
4. People who fall, especially if living alone.
5. Very old people.
6. Those who have recently moved.
7. People with sensory deprivation (that is, poor sight, hearing, speech, and facility of communication with society).
8. Patients who are taking multiple medications (see Williamson, 1981).

Experience has shown that preventive screening or case finding may be carried out by nurses, with only special referrals of problem cases to physicians. Such tasks involving clinical judgment as well as functional assessment are in tune with the increasing responsibility being assumed by nurses and allied health professionals such as physiotherapists and occupational therapists. Protocol testing, such as the Royal College of Physicians' mental status questionnaire (Hodkinson, 1972, 1973; Stonier, 1974) or the Kilsyth questionnaire (Powell & Crombie, 1974), standardize the screening procedures, which can also be applied to the follow-up of disability occurring in the old people discharged from hospital. Thus, two 3-year follow-up studies of stroke patients who were successfully discharged from geriatric rehabilitation units revealed that few went out of doors, many were heavily dependent on spouse and family, and the strain at home became progressively greater with time (Isaacs, Neville & Rushford, 1976; Lawrence & Christie, 1979).

A most important part of community preventive services is supportive treatment for caregivers, spouses, and children, and those who help from the neighborhood. A review of the difficulties of caregivers with patients afflicted with mobility problems pointed to health and finance as two crucial areas in determining the success of coping (Fengler & Goodrich, 1979). The emotions of the caregiver may vary from extreme mercy and compassion to resentment and wishing the patient dead; from empathy and concern to guilt and depression. A variety of emotional reactions may be exhibited by the relative in varying proportions and at different times. As the caregiver is often the most important element supporting the patient, help supplied to him or her by the community for the patient's sake is often economically more worthwhile than transferring the patient to an institution. Support can take the form of case work, home-care services, or day care in the community for the patient, while keeping contact with the relative; as well as the provision of clubs and outings for relatives. The stroke club model in Great Britain allows some social relaxation as well as discussion of mutual problems by the relatives. A further boon to caregivers is the scheme of holiday admissions to a hospital or a Home. This scheme plans the admission of the patient to the facility for a limited period in order to allow the relative to take a holiday or a rest, and thereby renew the care of the patient at home with increased vigor (Crossman, London & Berry, 1981).

Day Care in the Community

Reference has been made to day care facilities as part of the services available for maintaining disabled aged people at home. Farndale (1961), summarizing the day hospital movement in Britain, pointed to the psychiatric day hospital as an important adjunct to inpatient treatment, and described a small number of geriatric day hospitals, the practice of which was still at an early stage. Since then, day hospitals as an integral part of geriatric departments have become the rule in Britain, and the Department of Health and Social Security has recommended 2 places per 1,000 elderly in the population. The emphasis of their role, function, patient intake, and staff varies from place to place. Generally, their function is as a supplement to inpatient care rather than a replacement. Their role is mainly in the rehabilitative and physical treatment areas, including occupational therapy, with much emphasis on combating social problems connected with the patient's disability and disease. Patients may be more fully assessed prior to admission, or as an extended kind of outpatient check-up. Brocklehurst and Tucker (1980) have summarized the present position in Britain through an extensive survey of over three-fourths of the day hospitals in the country. In some, the leading figure is a nurse, in others an occupational therapist. The emphasis is on active maintenance, and as a hospital function, the survey showed that patients were discharged when they were sufficiently improved (50 percent), or when they deteriorated or died, when they were admitted to a hospital (32 percent), or when they did not continue attending (10 percent). The duration of attendance in these kinds of day hospitals varies between an average of six weeks to about three years, the longer treatment being occasioned by maintenance of physical fitness, or in order to give some relief to the overcrowded family.

The proportions of patients requiring transport may be up to 90 percent, according to the frailty of the population. Without guaranteed transport by the local ambulance service, voluntary services, or by a hospital-manned vehicle, most day hospitals would lose their essential therapeutic function and become converted to heterogenous social centers.

The addition of day care to a residential facility such as an old-age home for healthy aged, or a Home with rehabilitation and nursing facilities, is becoming a practice in some places. The advantages are those of exposing a resident, static population to a mobile one, as well as the use of ready-made facilities for the aged of the community, and the integration of the Home into the communal framework. This is an economic way to develop day care for the healthy ambulatory aged. Up to a point, the same principle can be applied to infirm aged in the community, and a limited number can be brought into a geriatric ward, where they can be integrated into the occupational and physical activities of the ward. Such a scheme was run without any extra budget in three geriatric wards (Rosin, 1965). Conversely, many day hospitals were used as the rehabilitation and occupational therapy facility for the inpatients of the geriatric unit. An interesting prospective survey on the dynamics of a day hospital concludes that the goals of the program of acute assessment, work-up, rehabilitation, social integration, and maintenance should be clearly defined (Martinez, Carpenter & Williamson, 1984). Careful categorization of the attending population should maintain a small number of "chronic" attenders, and a large number of new patients for a small number of visits, so that the day hospital can respond quickly and comprehensively to the demands by the community doctors. This study found that one-tenth of the patients were referred to as recent discharges from the geriatric wards, about one-third were new patients, and another fifth attended only once for diagnosis or assessment. "Chronic" attenders constituted about 11 percent. This scheme sees the day hospital less as a community facility and more as a part of the hospital service. Therefore, there must be an ongoing discharge—either home, or to a club, or to a home-care scheme (such as municipally funded assistance from "good neighbors").

In summary, the management of chronically ill old people in the community, as distinct from institutional care, must first define what losses and deficiencies adversely affect the smooth conduct of the old person's life at home, and then build compensatory support services. The latter should be aimed, if possible, at directly replacing the deficiency (for example, environmental problems such as heating, or financial stress). Second, support and encouragement to enable the family to give appropriate help is required, together with adequate counseling of intergenerational problems or actual marriage counseling of the elderly themselves. The third category of help is actual service rendered in the form of medical or nursing treatment, or social and occupational rehabilitation. Greater emphasis or properly focused community services could probably keep many old people in their own homes at less cost than nursing beds, with much less subjective burden on the families (Ikegami, 1982). Even if the home care needs are not much less expensive than removal to an institution, a welfare-oriented society should consider the needs and the relevance of the service to the patient, instead of estimating how much cheaper it is than residential accommodation (Opit, 1977; Clarfield, 1983a)

INSTITUTIONAL CARE

If after adequate examination and analysis of the dependency problems of the aged person it is clear that he or she cannot or will not be maintained at home, then recourse must be had to some form of institutional care. A critical approach to placement of an old person outside his or her home should take account of the person's ability to function or degree of dependency, and the expected contribution that the institutional setting could make toward relieving his or her problem. Table 6.3 summarizes the various kinds of frameworks of institutional living with the types of facilities each is supposed to supply. Many surveys (e.g., Silberstein et al., 1970) have indicated how inadequate assessment does not permit a correct choice of facility. Commercial interests and the area of private practice are additional factors that encourage preferential admission of those who can pay more, and mitigate against placement according to real medical or functional need (Vladeck, 1982).

Reasons for Entering a Home or Institution

Table 6.4 summarizes the categories of reasons given by old people or analyzed by those working with them for entering residential accommodation. It might be expected that social norms and economic circumstances could cause a variety of reasons for old people to enter a Home. A comprehensive survey of a heterogenous population in Israel (Weihl & Beber, 1978) showed, however, that the single most frequent reason was a concern by the old person of what would happen if his or her health failed in the future. One-third of the respondents gave this as the only reason, and over one-half included it in

Table 6.3
"Institutional" Settings and Their Characteristics

Framework	*Facilities Supplied*
Hotel, hostel, foster family	Board and lodging. Minimal personal supervision.
Sheltered housing ("almshouses" in U.K.)	Independent living. Domestic, on-call help. Warden or housemother.
Home for the aged (senior citizens' home)	Board, lodging, communal social facilities; on-call personal help usually available. Minimum of medical/nursing services.
Home for the infirm aged.	As above, plus nursing supervision and nonskilled personal help.
Nursing home (skilled nursing facility), chronic diseases hospital	Varying degree of medical service, plus day and night nursing help.
Multitier home—independent, infirm, nursing, and psychogeriatric sections	Graded levels of care, from minimal personal supervision to full nursing; closed section for demented patients. Social and activity programs as indicated by patients' needs.
Intermittent (holiday) admission	Arranged admission for limited period, to give family a rest; all facilities available in the Home or hospital.
General hospital	Acute departments. Geriatric service or unit.
Rehabilitation hospital	Short-term or long-term admissions.
Psychiatric hospital	Short-term or long-term admissions.
Hospice	Care for the dying. Elective admissions. Full nursing care. Medical and psychosocial programs of therapy.

Table 6.4
Reasons for Old People to Enter a Home for the Aged

Functional	Physical decrepitude and infirmity.
	Difficulty of coping physically with self-care.
	Difficulty in caring for spouse.
	Tired of coping in own home.
Psychological	Fear of the future, particularly the prospect of dependency.
	Anxiety, uncertainty, and insecurity in own home.
	Pressure from the family to leave own home.
Environmental	Poor physical conditions, area redevelopment, pressure from neighbors.
	Bereavement.
	Social isolation and wish to have company.
	Isolation or separation from children.

their motivation for entering a Home. Reactions to widowhood and lonesomeness formed the second largest group; about one-third included this among their reasons, and one-eighth stated it as the sole reason. Conditions of the house and difficulties managing it were among the reasons stated by one-fifth, and one-tenth had problems within the family that impelled them to seek residential accommodation.

This research confirmed what many physicians and social workers have seen or felt. An important motivating influence to enter a Home is the subjective feeling of potential ill-health, which stands in contrast to objective well-being. This occurred in more people who felt that a change of health had taken place in the previous five years. Pressure from children was detected in only ten percent. This fact finds support in surveys showing that rejection of ailing parents by children is relatively uncommon, and is balanced by more than expected care given by an almost equal number of children in the population (Isaacs, 1971). On the other hand, almost two-thirds hoped to solve the problems of loneliness caused by widowhood by entering a residential home.

The basic problem raised by this research is the extent to which institutional care of any kind can answer the needs and the expectations of the old person who enters it. The specter of misplacement of the elderly, whether in an institution (such as Peter Townsend described in "The Last Refuge"), or the arbitrary admission of old people to mental hospitals because there was nowhere else for them to go (McKeown, MacKintosh & Lowe, 1961; Kidd, 1962), has dented the conscience of planners for old people's services. It is relevant, therefore, to consider the different types of institutional care available nowadays, and what each type purports to do in serving its residents. Residential accommodation for the elderly is designed to provide one or more of the following items, and the needs of the potential dweller should be seen to in terms of the services provided.

Hotel Services. These include bed, bathroom facilities, heating or air conditioning, usually cleaning, food or facilities for preparing it, and sometimes laundry. This is provided in most kinds of sheltered housing, although independence in cleaning and attention to laundry may be expected of the dweller. They are also provided in all other kinds of accommodation—from hotels and hostels to nursing homes. Sometimes these environmental facilities are reduced in order to cut costs, so that the physical standards are low.

Social Activities. These may vary from occasional passive activities, such as a film, to a constructive program of graded activities of independence, hobbies, and programs aimed at integration and social support given by one dweller to another. The social program may also be therapeutically oriented, as in group discussions popularized by Irene Burnside in a nursing home setting (Burnside, 1976). Some homes also employ social workers and/or psychologists who provide counseling either as an exercise in integration, or as a psychosocial support against the trauma of separation from home, family, or possessions (Harel, 1981). This kind of service is sadly lacking in many senior citizen residences or old age homes, and especially in nursing home facilities. Not a little of the induction of institutional neurosis can be attributed to boredom, consequent on the lack of organized social activity, together with the deficiency in integration of the residents (Seligman, 1975).

Personal Assistance. This includes a more specific kind of help in the face of disability, such as supervision of clothes changes, cleaning, some physical assistance in getting in and out of bed, and also personal advice in dealing with small administrative problems in finance or communal agencies. Here the role demanded is that of housemother, or personal attendant or nurse. Such assistance is often lacking for old people living in the "independent" section of an old age home, and is only available if they move or are moved to a nursing facility. This intermediate grade of disability is recognized in some Homes where a department for "frail elderly" is provided, giving the dwellers nonprofessional domestic assistance, which allows them to remain out of the category of nursing cases.

Nursing Services. These may vary from a part-time supervisory nurse, such as is provided in sheltered housing, to a well-staffed ward for bed- or chairridden permanent patients within the confines of a residential home. One of the measures of quality of skilled nursing facilities is the number of nursing hours according to each dweller or patient per day or per week (Fottler et al., 1981). The quantity and quality of nursing should be determined by the type of patient expected to be admitted to the facility. Unfortunately, the determining factor is more often financial, and the easiest way of cutting costs is often by reducing numbers of staff, especially qualified personnel. The relatively low payments for Medicaid patients compared to the high expenditure demanded by the needs of heavy nursing is a most important factor mitigating against good nursing care in many proprietary nursing homes in the United States (Kane & Kane, 1978; Fottler & James, 1981; Rango, 1982). However, the aim should be to obtain good service by efficient deployment of smaller numbers of good staff, or efficiency of organization without great increases in costs in optimally sized facilities of about 100 beds (Weihl, 1981; Rango, 1982; Vladeck, 1982).

Paramedical Services. This includes physiotherapy, occupational therapy and recreational activity, chiropody, and psychological counseling. The practice of rehabilitation is often thought to be unnecessary or superfluous after an old person enters a nursing home. There are three good reasons why physiotherapy should be provided: (1) Some patients are rehabilitatable, and others develop conditions while in the Home, such as falls (Gryfe, Amies & Ashley, 1977; Ashley, Gryfe & Amies, 1977), strokes, or loss of confidence in balance, that require specific rehabilitation techniques. (2) Maintenance treatment may allow some patients to remain mobile, who would otherwise stay in bed, and the psychological benefit of mobility is enormous. (3) Organization of group exercises is an efficient way of promoting well-being and communication, and of serving a number of clients at the same time. Similarly, occupational activity can be considered as a therapy in the task of providing an aim in life—the lack of which is a component of the institutional neurosis complex. Art therapy is a creative form of nonverbal expression, which can enliven even those who were hitherto unacquainted with techniques or knowledge of the subject (Pouldon & Rosin, 1967).

Many such programs are not to be found in facilities that have little else to offer patients who are markedly dependent and impaired. It is noteworthy that in those Homes and nursing facilities where such programs exist, the level of awareness and awakefulness of the dwellers seems to be enhanced with corresponding staff enthusiasm, which is transmitted to the patients.

Physician Services. These vary from occasional mandatory visits (e.g., once in 30 days in the first 3 months of stay in a skilled nursing facility—according to federal guidelines) to appointed physicians as permanent staff members. In between are the Homes or nursing facilities with general practitioner care on a permanent basis, and medical visits several times weekly. It is a fallacy to think that because a patient requires from the nursing home a once-and-for-all solution to his or her living problems due to disease or disability, that the patient's medical care needs are also static, with little change or improvement likely to occur. Experience in chronic-disease hospitals has shown that inadequate pre-admission screening not infrequently allows the label of wrong diagnoses to remain on the patient. Moreover, the extensive morbidity of those patients is often amenable to symptomatic relief, and the patient's lot can be ameliorated through intelligent management by a general practitioner. A common result of inadequacy of medical treatment is the polypharmacy or the lack of monitoring of psychoactive drugs prescribed. Lack of financial and professional motivation is often at the root of the inadequate medical service provided (Rabin, 1981), but medical education with correct focusing of perspectives on what can be achieved in those patients may go far in solving the lack of physician services in nursing homes (Solon, 1974; see Eisdorfer's review, 1981).

The Nursing Home "Model"

The ideal arrangement is one that will cater to all contingencies in the lives of old people, and will consider their needs, which may vary from time to time in the types and intensity of service required. The old workhouse system in Britain with its chronic sick ward led to the disposition of many infirm people in improperly staffed facilities, lacking equipment. The traditional division between health and welfare authorities may also cause misplacement when the functional status of an old person in residential accommodation changes. A model that has become popular in Israel is the multitiered Home with one section for the independent ambulant, one for frail ambulants who need assistance with daily living activities, one for patients who become dependent, and a section for demented patients. It is convenient if these sections are all housed in the same building, but the presence of wards may spoil a homey atmosphere in the facility. On the other hand, separate buildings may confer a sense of leaving and longing when a person is moved to a more dependent section. Although a large complex along these lines was set up as part of the medical services for immigrants many years ago, containing over 1,000 beds (Hart & Schadel, 1972), most such facilities nowadays operate with 100 to 150 beds, a number that has been shown to be optimal in terms of cost and human relationships (Ullman, 1981; Weihl, 1981). Whatever the arrangement, our opinion is that there should be a close association with a local general hospital, preferably with a geriatric department. The flow of patients and correct placement can thus be facilitated, appropriate consultation services supplied, and a correct standard of medical practice maintained in the hospital or in the nursing facility. Moreover, the latter can be utilized for teaching purposes, with beneficial orientation for students and doctors alike (Breichtenbucher & Schultz, 1983; Clarfield, 1983b).

Evaluation of the quality of care in a nursing facility is made difficult by the necessity of relating the extent and intensity of the medical and nursing problems to the facilities provided. Thus, one Home might create a favorable impression by selecting its patients to exclude heavy nursing cases, although their needs might be the most urgent; while another Home that tries to cope with them is found wanting because of lack of correct facilities. Of the methods for evaluation that have evolved, mention had been made of calculating the number of nursing hours afforded per patient, and this can then be related by a semi-quantitative scale to the patients' disability status. Another novel method is the use of tracers, whereby all aspects of a common, easily defined disease or disability are examined, and the impact of the institution is assessed at all levels of care and follow-up (Kessner, Kalk & Singer, 1973; Nutting, Shorr & Burkhalter, 1981).

Recently, questions have been asked in the United States regarding the role of the general hospital in the care of the chronic sick (Campion, Bank & May, 1983). If, the argument runs, many beds are occupied by old people with multiple pathology, and their stay prolonged because of inadequate facilities outside to care for them, then why should the general hospital not take a more active preempting role in dealing with the problem (Somers, 1982). The author suggests reimbursement by Medicare, community programs associated with the hospital staff, and the practice of professional criteria for the allocations of resources to chronic as well as acute cases of illness. This kind of practice has been in vogue in the United Kingdom with the development of comprehensive geriatric departments in which acute illness and rehabilitation problems are dealt with by the same team that also has responsibility for a large backup of long-stay beds. Such units under one medical team may have up to 200 beds as well as having consultative responsibilities to the Welfare Department beds for custodial care of well or infirm old people. It is common for the rehabilitation and extended-care beds to be situated outside the acute main hospital, with consequent saving of overhead costs. The concentration of administrative responsibility allows a proper practice of progressive patient care, while maintaining necessary links with the full facilities of a general hospital.

SERVICES FOR THE DEMENTED

Much of the foregoing is relevant to community and institutional care of the demented; but the behavioral, cognitive, psychiatric, and social problems of these patients have resulted in the evolution of new systems and approaches (Arie, 1973, 1981; Campbell et al., 1983). Table 6.5 summarizes the range of services that, individually or generally, may be required at different times during the long years of the illness. Awareness of the different etiologies of senile dementia, and strict diagnostic criteria, enable more precise delineation of characteristics of different types of the condition, such as subcortical and parkinsonian dementias. A clinical and investigative service is important to pick out those patients suffering from iatrogenic causes such as drugs or alcohol, as well as the less common and more specific causes for senile dementia.

Beyond the acute, short-lived interest in making the diagnosis in amply equipped facilities, continuation treatment has often been sadly lacking until end-stage institutionalization. Joint assessment units shared by geriatric physicians and psychiatrists have been one type of model for comprehensive diagnosis and referral for further care (Morton, Barker & MacMillan, 1968). The introduction of psychogeriatrics as a specialty in the United Kingdom also ensured a more accessible and comprehensive service in areas where such a specialist functioned, with proper appreciation of the combination of psychiatric and organic physical compounds of the illness (Copeland et al., 1975; Jolley & Arie, 1978). Some psychogeriatric programs deal only with the demented; some treat the whole area of psychiatry in old age, while others see their specialized function as caring for the interface between geriatrics and psychiatry. Psychogeriatric programs in the community have been sporadic and methodological difficulties of evaluation could only demonstrate a few improved

Table 6.5
Range of Services Required for Management of Dementia

Diagnostic	General hospital.
	Psychiatric clinic.
	Community screening—"at-risk" subjects, prevalence survey.
Follow-up	Home visit by general practitioner/specialist, or clinic visit for medical/psychiatric appraisal; safety measures to protect patient.
	Social assessment of patient vis-à-vis home environment.
	Legal service regarding patient's competence.
Treatment	Psychoactive drugs where indicated—geriatric and/or psychiatric service.
	Psychiatric specific treatment, e.g., group therapy.
	Social support to family, e.g., support groups.
	Daycare in special community clubs or day hospitals.
Institution	General hospital—temporary admissions.
	Foster home.
	Geriatric long-stay facility—preferably attached to general or geriatric hospital.

indices of life contentment (Nielsen, Blenker & Bloom, 1972). What appears of paramount importance is to try and fit the environment to the patient, who finds the normal social scene too complicated, and who cannot stand up to accepted interpersonal activity. For demented people, a special framework is required, either as a community club geared to their needs, or in the context of a day hospital (Jolley & Arie, 1978). We have found that a day center to which transport is provided has a meaningful, stimulating influence when its program is structured with planned activity, both physical and social, including reality orientation; and is run along lines designed to involve the participants to the maximum of their ability. These programs have had an impact on the patients, who look forward to their trip to the local community center, as well as providing some respite for the family. Despite moving the patient from home to the club or day center, the possibility of increased confusion has been combatted by the regularity of the program and the limited nature of the circle—usually about 15 in all.

The formation of Alzheimer groups has been an important advance in fostering the main therapeutic support for the patient—his or her immediate family. Discussions with families of demented patients have highlighted the dilemmas beyond the decision to "put their relative away." Even though patients' failure to recognize their relatives or their home, incontinence, and erratic behavior are reasonable indications for recommending an institution, many families prefer to try and continue the care of their relative at home. Such cases are deserving of as much community support as possible to help them physically cope with the burden, as well as the emotional lift given by family support groups (Sheldon, 1982; Levine, Dastoor & Gendrom, 1983).

Perhaps the main problem of today's institutions for patients with senile dementia is the lack of a program, often because it is felt that the residents are incapable of conforming to structured activity. We have found this not to be so, and modified physical exercise, even dancing, music, and movement, and painting are all devices that can improve communication with cognitively impaired patients. Learned helplessness can occur even more with demented patients in institutions that with other types of patients, and active programs of stimulation with due attention to the patients' problems, rather than the specific diagnosis, may result in improved social behavior (Lieff & Brown, 1981).

CARE OF THE DYING

One area of health care in which a humanizing influence has become prominent is the organization and practice of treatment of the dying. The philosophy of the hospice movement has brought about a more positive approach to palliative care, both in and outside of hospices, than has hitherto been evident on the medical scene (Kutscher et al., 1983). This approach has tried to overcome the sense of failure in managing a patient who is destined to die within a short time. The physician has to consider not only the specific treatment for the underlying disease, or acute intercurrent emergencies such as infections, but also to concentrate on control of the patient's symptoms during the last days or weeks. The specific problems of the dying have not always been considered as such, and the hospice movement has sharpened our awareness of successful management of the distress of chronic pain, breathlessness, nausea, and other discomforts of the terminal state (Saunders, 1978; West, 1978; Saunders, Summers & Teller, 1981).

There are parallels in the approach to the treatment of the geriatric patient and that of the dying. Teamwork is essential in each, with involvement of the family both as a partner in treatment and as those in need of treatment (Greer, 1983). There is emphasis on quality of life and on providing comfort and cure rather than an extreme solution to the problem of patient distress (Fulton & Owen, 1981). Education of the staff is an important part of management in promoting perceptive care of the individual, as well as of the patient's disease.

One reason why this area of medical care was relegated to the backwaters of nonconformist institutions was the apparent incompatibility of symptom control as the mainspring of treatment with the intensive demands of a general hospital ward. The hospice has tried to create an environment different from that of investigative medicine, but appropriate to all-embracing care. Attempts to recreate this in a general hospital have also been made. Mount (1976) described the setting up of a palliative care team in a 12-bed unit in a general hospital, staffed by a multidisciplinary team. Full cooperation was sought with the families, who were also followed up for several weeks after bereavement. Mount concluded that the unit resulted "less from the discovery of new techniques for treating the dying than from the assertion of a positive creative approach to death and bereavement" (p. 121). We have also found that a geriatric ward or a chronic disease ward can serve as suitable settings for looking after the dying, provided that proper in-service training is given to the staff in the form of ventilation talks and case conferences (Rosin, Wallach, & Assael, 1982; Greer, 1983; Rosin & van Dijk, 1984).

A comparison of the suitability of different places for the optimal management of the dying patient was carried out by Hinton (1979). He personally interviewed dying patients in four settings: a radiotherapy ward in a general hospital; a residential home devoted to the care of the dying; a hospice; and hospice outpatients being cared for in a home-care program. The hospice patients were less depressed than the others, and there was more staff communication with them. However, although the patients in the hospice home-care treatment exhibited most anxiety, they were the group most satisfied with medical treatment. It emerges from Hinton's work that perhaps the conscious effort itself to manage the state of dying is the most important feature, rather than any particular setting. The general hospital ward might also be an equally appropriate place for the dying, if due attention is paid to the physical and psychological aspects of the dying process.

Estimates of the numbers of beds and costs for institutional care of one type or another are difficult to make because of varying policies of placement, and because of a certain number of people who die at home. For example, Wilkes (1965), a general practitioner from England, surveyed deaths from malignant disease in a large city, and noted that 55 percent had died at home. However, the trend since then, especially in the United States, appears to show a rise in the number and percentage of people who die in institutions, or come to them in order to die (Lerner, 1970). A survey in the United Kingdom showed that there was a large variation in disposition of services for the dying in different districts throughout the country. Only a few places came up to the recommended standard of 40 to 50 beds per million inhabitants (Lunt & Hillier, 1981). Great stress was laid on home-care teams and how such a service can reach large numbers in an efficient manner.

Efficient home-care for malignant disease is dependent on the ability of the family to cope physically and emotionally, and on adequate nursing and social support being available. Nevertheless, some patients have preferred to remain in hospitals, because of the therapeutic security it gives them, and because their families are shielded from the stress of caring for them. However, the teamwork of a home-care service has been shown to alleviate patients' anxiety, and has also significantly reduced the days of hospitalization in the terminal phase by delaying the families' requests for admission to hospitals or hospices (Parkes, 1980). The physical stress and nursing needs imposed on the home were not necessarily diminished by the help afforded by the advisory service of the team. The advisory service pointed to the necessary community facilities, which should be supplied to the family by statutory services in the district, and acted as an emotional sounding board for the family.

The care of the dying extends also to the period of bereavement. The purpose of the caring team is supportive in the face of a crisis of acute family change, and also to prevent the accelerated morbidity and mortality that commonly occur in spouses not long after the death of their life-partners. The prospective studies of Parkes (1977) in St. Christopher's Hospice, London, have confirmed the emotional value as well as the humaneness of the after-care supplied by the home-care counseling service.

THE PRESENT AND FUTURE IN LONG-TERM CARE

Chronic disease and its management are commanding increasing attention both in health planning and in medical education (Weksler, Durmaskin & Kodner, 1983). Legitimization of the subject as worthy of physician attention is still, however, fraught with difficulty, as long as the medical approach is disease oriented and not person oriented. This philosophy of considering and being responsible for all aspects of patient care, including the assessment of interpersonal problems affecting the old person's health, is one that has been accepted by most physicians who practive geriatrics, and is embodied in a number of statements issued in recent years (Editorial, 1977). The Royal College of Physicians working party on medical care of the elderly (1977) stated that geriatrics should be accepted as a true specialty of medicine, and is particularly concerned with:

1. "The development and management of a system of patient care to deal with the complex multiple disabilities and socio-medical problems in old people . . . acutely or

due to breakdown of their independent living. . ." (p. 2).

2. "To return as many elderly people to the community and support them there."
3. "Development and management of long-term hospital care for those old people who need it."

The British Geriatric Society has stated that they are seeking to ensure provision of centralized departments of geriatric medicine with a full spectrum of investigatory services, and adequate day-hospital services for assessment and support of elderly patients with mental illness. There is no doubt that the statutory uniform district responsibility in the United Kingdom has assured a certain homogeneity of services with built-in coordination with the Welfare Department accommodation for well and infirm aged. The private and nonprofit voluntary institutions vary in numbers in different districts, and are in the minority. In the United States, the nursing home is the main prop of the system of institutions, and is still seeking its role and definition (Kane & Kane, 1978; Report of National Committee on Vital and Health Statistics, 1980). The integration of the skilled nursing facility into conventional medical frameworks has begun (e.g., Breichtenbucher & Schultz, 1983), but in many places problems of cost, inefficiency, and financial considerations, rather than patient needs, still dictate policy. Planning on a state or federal basis will have to solve this problem by integrating services for old age, including acute and chronic care, under a coordinated authority such as local authority management organizations (Ruchlin, Morris, & Eggert, 1982), or Elderplan (Weksler et al., 1983). In Israel, there is a gradual move toward coordinating services both in community and institutional care through local health authorities. However, the plethora of private institutions, which contain 47 percent of all the long-term nursing beds, makes a uniform policy of care difficult, although measures of introducing quality control of management are being investigated and developed (Factor, Guttman & Shmueli, 1982).

In most countries, it is admitted that community services have to be developed more extensively in order to prevent unnecessary institutionalization and also to raise the standard of care. However, good comprehensive home care can be expensive, and this may negate much of the savings of avoiding institutionalization. Nevertheless, the outlook underlying this trend is a welcome one, because it implies greater attention to the individual. This is counter to the impersonality associated with waiting lists and allocation to long-term facilities. In this connection, research must be directed toward the iatrogenic illnesses of institutionalization. The "learned helplessness" that envelops relatively healthy old people who enter a Home, the exaggerated passivity encouraged by care given by attendants, albeit with good intentions, without adequate participation of the residents themselves—these are negative features that well-trained staff and correct orientation can do much to avoid (Avorn & Langer, 1982; see review by Clough, 1981). The borderline between dependency requiring help from others and acquired dependency that is exaggerated by giving help is a fine one, and diagnosis of the individual problem through adequate psychosocial assessment within the institution is one of the growing points of progress in long-term care (Graham, 1983). Future research will also have to concentrate on the methodology of evaluating the quality of community and institutional services; the construction of suitable instruments of validity (Jette, 1980); and the determination of practical priorities of care, among which the training of a wide spectrum of manpower for treating the elderly is mandatory.

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CHAPTER 7

Use of Antipsychotic Medication in the Elderly

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INTRODUCTION

This review explores recent progress in antipsychotic medication usage in the elderly and focuses on some of the problems in appropriate and effective prescription of drugs to treat mental illness in this age-group.

Two important and relevant points that have direct impact on antipsychotic drug usage must be considered at the outset.

1. There is a myth that antipsychotic medications do not work as well in older patients as they do in younger ones. This frequently leads to a nihilistic attitude regarding treatment for the elderly psychotic patient, despite the well-known fact that the number of medications overall increases in direct proportion to increasing age.
2. In recent years few novel antipsychotic drugs have been developed. The last two new molecules, marketed in the early 1970s, were the molindones (Moban®; Lidone®; and the loxapines (Loxitane®; Daxolin®), neither of

which has been extensively used by the psychiatric community, despite ample evidence of their efficacy.

Present antipsychotic development involves expanding dosage choices and modes of administration, e.g., concentrates and higher-potency injectables, rather than developing new compounds.

Also, experimentation continues that combines antipsychotics with various salts to produce longer action and thus increase time between doses (similar to the fluphenazine decanoate prototype introduced in the early 1970s). This lack of development of new antipsychotic compounds is unlike the antidepressants, now entering an era of new compounds, each molecule tailored differently than the next in terms of action, efficacy, and side effect profile. The increase in medications for depression coincided with the elaboration of revised theories on the physiologic mechanism of depression put forth by the psychiatric community (Charney, Menkes, and Heninger, 1981). New antipsychotic compounds from the drug companies may await the development of newer theories of psychosis than the present concept of excess dopamine in specific CNS pathways.

Two specific issues have arisen recently which are of special interest for elderly patients. One is site specificity of antipsychotic compounds. There is a claim that at least one antipsychotic acts primarily in the mesolimbic dopamine pathways, where presumably psychotic symptoms arise, with minimal activity in the nigrostriatal dopamine pathway, thereby causing minimal extrapyramidal system stimulation (Borison, 1980). Although the concept of varied thresholds of stimulation for the postulated postsynaptic membrane dopamine receptors in an individual brain is an exciting one (Waziri, 1980), and would be important in developing future antipsychotic compounds, it seems premature to assume clinical utility with minimal human data. This is especially true for elderly patients, in whom data on number and sensitivity of CNS receptors are just beginning to appear and suggest a complex interaction between anatomic and physiologic changes in the aging brain.

Extrapyramidal side effects (EPS) are another important problem in elderly patients. EPSs are seen with virtually all antipsychotic compounds, and there is a question as to whether a higher incidence of EPS can directly be related to an increased incidence of tardive dyskinesia (TD), especially in older patients on antipsychotic medications. This issue will be discussed later under long-term effects of antipsychotic compounds, but here it may be stated that there is no unequivocal evidence that provides a direct link between an increased prevalence in EPS and an increased prevalence of TD.

Psychotropic Dose

The need for information concerning the use in the elderly of medications in general, and antipsychotics in particular, grows in direct proportion to the well-known substantially increased consumption of medications by older individuals (Vestal, 1978).

The present 11.7 percent of the U.S. population over 65 use more than 25 percent, i.e., 200 million prescriptions, of the total drugs prescribed annually (Ray, Federspiel, and Schaffner, 1980). Many of these individuals take medications on a regular basis, and fewer than 5 percent abstain entirely from medicines. The elderly receive an average of 13 prescriptions per year compared with 4 for younger adults; and those over age 60 take, at any one time, an average of 5 different drugs. Elderly hospitalized inpatients are often given 8 to 10 concomitant medications. One study suggests that 85 percent of the elderly population takes at least one prescription drug (Lamy, 1980). Of the enormous number of drugs utilized, upwards of three-quarters of them act in some manner on the central nervous system, i.e., are psychotropic medications (Maletta, 1980). Three-quarters of the 5 percent of individuals over 65 residing in nursing homes are receiving one or more psychotropic medications (Ray, Federspiel, and Schaffner, 1980). Upwards of 40 percent of all medications used in the institutionalized elderly either directly or indirectly affect central nervous system function (Maletta, 1980; Raskind and Eisdorfer, 1976).

To underscore the magnitude of medication usage in the elderly, the data may be reviewed from a financial aspect. Older people represent 11.7 percent of U.S. population and account for 30 percent ($48 billion) of the total personal health care costs and 50 percent of the $40 billion federal health budget (Besdine, 1982). One-third of this amount is paid by private sources, and two-thirds by Medicare, Medicaid, and other state and federal programs (Libow and Sherman, 1981; Report of Comptroller General, 1977). Almost 75 percent of that personal health dollar amount is spent for medications. Whether or not the increased number of medications prescribed for the elderly is justified is an issue for discussion.

The prevalence of disease rises sharply with age. Greater than 50 percent of those over 65 have one or more chronic medical conditions, and 17 percent of noninstitutionalized elderly have a limited ability to work or care for themselves, compared with 7 percent for younger age-groups (Shanas, 1980). Older people make 40 to 50 percent more outpatient visits and are 2½ times more likely to be admitted to a hospital (where they spend 70 percent more time compared to younger patients). Thus, per capita, the aged accumulate three times more hospital bed days than the young, and comprise greater than 90 percent of long-term care patients. Long-term care patients occupy more beds than all the general hospital beds in the U.S. combined (1.4 million nursing home beds vs. 800,000 acute beds) at an annual cost in 1980 greater than $20 billion (Raskind and Eisdorfer, 1976).

Mental illness among the elderly is a particularly serious problem. Eighty-five percent of their mental health needs are inadequately met by our current system. Psychopathology is high among the aged, e.g., psychosis, severe anxiety, depression, dementia, and alcohol abuse. Although there are certainly opiate, barbiturate, and other drug abusers in the elderly population, there are no good data available in these areas at this time.

The breakdown by age of prescription drug utilization is a particularly informative statistic. As an example Table 7.1 lists those drugs prescribed for the Minnesota Medicaid population during the month of November 1980. Several points can be gleaned from these numbers. First, the average number of prescriptions per recipient increases steadily after age 50, having remained constant from age 30 to age 50. The average number of prescription medicines used by an 80-year-old is approxi-

Table 7.1
Prescriptions Reported for the Minnesota Medicaid Population, November 1980

	Number of Prescriptions			*Recipients*			*Average Prescriptions per Recipient*
Age	*Male*	*Female*	*Total*	*Male*	*Female*	*Total*	
0–9	8,731	7,924	16,655	5,455	5,276	10,731	1.55
10–19	4,244	7,397	11,641	2,146	3,890	6,036	1.93
20–29	6,904	22,343	29,247	2,380	10,012	12,392	2.36
30–39	5,706	16,524	22,230	1,854	5,423	7,277	3.05
40–49	4,635	11,166	15,801	1,303	2,925	4,278	3.74
50–59	6,285	15,127	21,412	1,549	4,876	6,425	3.33
60–69	10,219	21,988	32,207	2,303	4,526	6,829	4.72
70–79	16,353	35,088	51,441	3,333	6,686	10,019	5.13
80&Up	21,488	72,717	94,165	4,102	13,772	17,874	5.27
All	84,565	210,256	294,821	24,425	57,386	81,811	3.60

mately 5.3, compared with a low of 1.6 between ages 0 to 9. Separating out data for the age-groups over 60 from total numbers of prescriptions, the number for males is 48,020, out of a total of 84,565 (56 percent). This group of over-60 males make up only 40 percent of the total prescription recipients. The number of prescriptions for females is 129,793 out of a total of 210,256 (62 percent). This group of over-60 females makes up only 43 percent of the total prescription recipients.

Also noteworthy is the large ratio of female to male recipients of prescriptions, at both the 20 to 29 and 80 and up age-groups. This bimodal distribution probably reflects the substantial use of gynecologic prescriptions in the younger women, and the longer survival of women to actually receive prescriptions in the 80 and up age-group. Additionally, psychotropic medications are given to women of all ages more often than to men, reflecting the fact that more women than men seek help for psychiatric problems.

Tables 7.2 and 7.3 list the numbers of prescriptions written for antipsychotics and antianxiety agents for the Minnesota Medicaid population during the month of November 1980. The numbers are categorized by age of recipient, in 10-year cohorts, from 20 through 29 and up.

Table 7.2
Prescriptions for Antipsychotics Reported for the Minnesota Medicaid Population, November 1980

	Number of Prescriptions by Age of Recipients					
Medication	*20–29*	*40–49*	*60–69*	*70–79*	*80 & Up*	*All Ages*[a]
Mellaril®	209	305	641	773	1,419	4,097
Haldol®	126	174	245	488	978	2,444
Thorazine®	107	137	331	388	523	1,858
Navane®	172	100	125	152	298	1,129
Stelazine®	102	88	140	107	59	737
Compazine®	58	21	72	93	161	520
Trilafon®	87	66	49	50	30	411
Prolixin®	79	63	60	35	28	382
Loxitane®	48	47	20	24	22	275
Serentil®	20	20	28	21	37	185
All antipsychotics	1,008	1,021	1,711	2,131	3,555	12,038

[a]Includes drugs reported but not listed here.

Among antipsychotic groups (Table 7.2), Haldol®, Mellaril®, and Thorazin® use increases substantially in the older age-groups. These drugs (especially Mellaril® and Thorazine®) have long been promoted as particularly efficacious for use in the elderly, primarily because of their sedating side effects, and their low incidence of extrapyramidal side effects. However, they have substantial anticholinergic side effects, both peripheral and central, which can be troublesome for the elderly. Navane® usage increases substantially in the "old-old" age groups (80 and up), while those antipsychotics that were appropriately labeled "energizing drugs," e.g., Stelazine®, Trilafron®, and Prolixin®, actually are used less in the older age-groups. No important changes are noted in use of the other antipsychotic medications (although Compazine® is a phenothiazine and is listed for purposes of completeness, its efficacy as an antipsychotic medication is negligible).

In Table 7.3, the usage for all antianxiety agents listed, be they benzodiazepines (Valium®, Librium®, Serax®, Ativan®, Tranxene®), hydroxyzines (Atarax®, Vistaril®), or meprobamate, increases with the patients' age. Valium® is the most fre-

Table 7.3
Prescriptions for Antianxiety Agents Reported for the Minnesota Medicaid Population, November 1980

	Number of Prescriptions by Age of Recipients					
Medication	*20–29*	*40–49*	*60–69*	*70–79*	*80 & Up*	*All Ages*[a]
Valium®	349	364	473	504	764	3,323
Librium®	40	98	143	132	172	792
Atarax®	76	47	79	122	250	768
Tranxene®	76	81	111	105	129	709
Vistaril®	43	39	70	95	171	508
Serax®	26	22	64	97	175	482
Ativan®	45	44	81	76	74	459
Meprobamate	17	29	60	81	99	366
All	672	724	1,081	1,212	1,834	7,407

[a]Includes drugs reported but not listed here.

quently prescribed antianxiety agent despite its pharmacokinetic disadvantages (see below).

Meprobamate, because of the relatively small difference between therapeutic and toxic dose, is more dangerous than other antianxiety agents in the elderly, in whom optimal dose is more difficult to ascertain. It is also addicting and can produce withdrawal seizures. For these reasons, meprobamate should not be used in the elderly.

Among the benzodiazepines, some are promoted for use in the elderly patient because of the absence of any active metabolites of the parent compound, and therefore their relative safety (Serax®, Ativan®). Others, producing active metabolites, are promoted because of the gradual decline of their serum levels following discontinuation, thus allegedly allowing more time for return to nondrug homeostasis. These high-powered, conflicting, advertising campaigns underscore the enormous competition underway for the increasing, multiple-medication-using, elderly population market. On balance, the short half-life compounds without active metabolites seem most appropriate for elderly patients.

Table 7.4 lists prescriptions by drug class for three representative age-groups, beginning with patients age 40.

Table 7.4
Prescriptions by Drug Class for Three Age-Groups Within the Minnesota Medicaid Population, November 1980

	Prescriptions by Age-Group[a]		
Drug Class	*40–49*	*60–69*	*80 & Up*
Antipsychotics and Anxiolytics	1,872 (11.8%)	3,024 (09.4%)	5,579 (05.9%)
Antidepressants	561 (03.5%)	745 (02.3%)	1,457 (01.5%)
Sedative-hypnotics	615 (03.9%)	994 (03.1%)	1,718 (01.8%)
Analgesics and antiarthritics	1,671 (10.6%)	3,001 (09.3%)	8,340 (08.9%)
Cardiac Drugs	347 (02.2%)	1,392 (04.3%)	5,342 (05.7%)
Vasodilators	155 (00.9%)	641 (02.0%)	2,001 (02.1%)
Diuretics	708 (04.5%)	2,235 (06.9%)	8,621 (09.2%)
Other Drugs	9,872 (62.5%)	20,175 (62.6%)	61,107 (64.9%)

[a]Percentage figure represents the prescriptions in each drug class as part of all the prescriptions in each age-group.

Among those age 60 to 69, use of antipsychotic-antianxiety agents is highest, exceeding the use of analgesic-antiarthritic drugs (9.4 percent to 9.3 percent). In those over 80, although absolute numbers of psychotropic drugs increase, the percentage decreases to 5.9 percent, while diuretics (9.2 percent) and analgesics (8.9 percent) increase even further.

Cardiac drugs (5.7 percent) run a close second to the antipsychotic-antianxiety drugs. Thus, even though there is an absolute increase in numbers of antipsychotic drugs used in the old-old population, there is a relative decrease in percentage when compared with cardiovascular drugs.

The increased consumption of prescription medications by the older population may be secondary to the increased prevalence of diseases (80 percent of people over 65 have at least one chronic disease, compared with 40 percent for those under 65). Also, the relative decreased use of antipsychotics-antianxiety agents in old individuals (11.8 percent down to 5.9 percent) may well reflect a therapeutic nihilism in treating mental illness in the elderly. There is an expectation by some that because a small decline in some cognitive functions occurs with aging, along with an increase in depression and disability, little effective treatment exists. Many good data invalidate this viewpoint.

Elderly Do Get Mentally Ill

There is a well-documented increase in psychiatric disorders among those individuals 65 years and older (Kramer, Tauber, and Redick, 1973). Older people are most likely to develop signs and symptoms of major psychopathology. Determining the true prevalence of psychiatric disorders among the elderly is difficult. There is increased tolerance for a longer time of deviant behavior in older people, and a reluctance to identify disturbed behavior in the elderly as a "psychiatric problem."

In those 95 percent of individuals over 65 living in the community, estimates of psychiatric disease range from 20 to 45 percent, while the prevalence among those elderly individuals residing in nursing homes (who occupy about 85 percent of the 1.4 million extended-care beds) is much higher (Raskind and Eisdorfer, 1976). The explanation for the high prevalence is not known, but both physiological and environmental factors probably play a role. The increase in adverse environmental stresses for the elderly, frequently manifest as unplanned loss, probably contributes to this increased prevalence of mental illness. It is additionally likely that age-related degenerative changes in the nervous system (Terry, 1978) play an integral role in the increased prevalence of psychiatric disorders with aging.

Changes in Morphology and Chemistry in the Aging Brain

Substantial morphologic and biochemical brain changes occur with normal aging (Brizzee, 1981; Brody, 1980; Terry, 1978; Timiras and Vernadakis, 1972). The brain is metabolically a very active organ, comprising only about 2 percent of total body weight, but at any given time using approximately 20 percent of the oxygen and 65 percent of the glucose in the circulation. Also, brain blood flow, at the rate of about one liter/minute, is disproportionately great by weight. There is some decrease in cerebral blood flow with aging, from approximately 65 ml/min/100 mg tissue at age 25 to 51 ml/min/100 mg tissue at age 70. It is thought that this decrease is secondary to a loss of neurons in certain brain areas, leading to gradual cerebral atrophy with a concomitant decreased blood flow. Not much is known about changes in the blood–brain barrier, and no breakdown has been documented in normal human aging.

The human brain undergoes gradual shrinkage with aging, from about 1,390 gm at ages 20 to 29 to about 1,250 gm at ages 70 to 79. Brain atrophy is grossly obvious by the narrowed gyri and widened sulci seen in brains from older individuals. The major cause of this decrease in brain weight with aging is the loss of neurons in certain brain areas (frontal, superior temporal, precentral, and visual cortex; locus coeruleus; putamen; substantia nigra; hippocampal pyramidal cells; and Purkinje cells in cerebellum). This neuron loss is not a general phenomenon throughout the entire brain. Concomitant with this neuronal loss is a progressive loss of dendrites and dendritic spines in the remaining neurons, the spine changes reflecting loss of central axodendritic synapses. This dendritic loss results in a decrease of basilar dendrites, as well as a decrease in number of horizontal and oblique branches of the apical dendrites. These structural changes in intracortical circuitry may lead to functional impairment.

Synaptic changes with aging occur as declines in activity of enzymes responsible for the synthesis and hydrolysis of some CNS neurotransmitters (Samorojski, 1977; Selkoe, 1982).

Glutamate decarboxylase, the enzyme responsible for synthesis of gamma aminobutyric acid (GABA), a putative CNS inhibitory transmitter, decreases in activity in some brain areas with aging. GABA transaminase, the enzyme responsible for hydrolysis of GABA, may not change with age.

Monoamine oxidases, a group of isoenzymes responsible for hydrolysis of catecholamine neurotransmitters (norepinephrine, dopamine), show an increase in activity with aging in some brain areas. Activity of the synthetic enzymes for catecholamines (dopa decarboxylase and dopamine-beta oxidase) may not change with aging.

It is well established that there is a decrease in some brain areas in choline acetyltransferase and acetylcholinesterase, the synthesizing and hydrolyzing enzymes of acetylcholine, respectively, in patients with Alzheimer's disease (Terry and Davies, 1980); but there is currently no evidence for changes in enzyme activity in older individuals without clinical disease.

Attempts to relate biochemical changes with CNS functional activity is presently a rich area of research interest.

Neurofibrillary tangles (NT), found only in humans, are seen in an increasing number of normal individuals after age 60, and in almost everyone after age 80. They are found especially in frontal, temporal, and hippocampal cortex (Terry, 1978). There is a clear, quantitative threshold for NT in Alzheimer's disease such that victims can be identified by more numerous tangles in hippocampus and neocortex. NT are also seen in postencephalitic Parkinson's disease, aging adults with Down's syndrome, Guam-Parkinson dementia, subacute sclerosing panencephalitis (Dawson's disease), and dementia pugilistica.

Unlike NT, neuritic plaques (NP) are not unique to humans and are seen also in monkey and dog. They are found only in the gray matter in both normal elderly brains and, in much greater quantity, in brains of demented patients. There seems to be a direct relationship between the numbers of plaques and the degree of dementia, and the NP count seems more reliable than trying to correlate the amount of NT with the degree of dementia (Terry, 1978).

Several chemical components decline in the aging brain. Total protein decreases from 12 percent from ages 19 to 55 to 8 percent by age 75. Total DNA decreases, reflecting a decrease in cell number, since nuclear DNA remains the same. There is a decrease in some lipids (cholesterol, phospholipids, and cerebrosides, all constituents of myelin), in sulfur, and in potassium, with a concomitant increase in extracellular H_2O (90 percent at birth, quickly decreasing to 75 percent until age 65 to 70, and then increasing to 78 percent). Sodium and chloride both increase with aging.

Changes in resting ionic equilibrium, along with the biochemical alterations and possible myelin degeneration, coupled with the structural changes outlined, may be responsible in large part for the functional changes seen in the elderly individual. Along with a decrease in reflex activity, decreases are seen in response time to stimuli, memory, motor performance, sensory acuity, and thermoregulation. Movement impairment and gross EEG changes are also seen with aging, and it is tempting to speculate that the increase in psychiatric disorders may be due, in part, to the same changes that alter other CNS functions.

Antipsychotic Drugs Are Effective in the Elderly

Many well-controlled, double-blind studies have demonstrated the beneficial therapeutic effect of antipsychotic compounds in the treatment of schizophrenia (Appleton and Davis, 1980; Baldessarini, 1977; Davis, 1976, 1981). While occasionally antipsychotic medications are reported as being ineffective in the elderly psychiatric patient (Lehman, Ban, and Suxena, 1972), most well-controlled studies report equal efficacy in elderly and younger psychotics. Further, antipsychotics provide effective relief of target signs and symptoms in both types of elderly psychotic patients, i.e., the chronic schizophrenic and the behaviorally disturbed patient exhibiting excitement, or agitation secondary to a delirium or a dementing illness.

One major caution necessary when using any psychotropic drug in an elderly patient is that adverse reactions are more common. Thus, drugs whose beneficial effects are highly desirable may have to be discontinued because of adverse side effects or even toxic effects stemming from the exquisite sensitivity of elderly patients to psychoactive drugs. Further, interaction with other drugs already being taken by the elderly patient must be considered (Maletta, 1980). Also, because of the altered pharmacokinetics and pharmacodynamics, older patients respond to smaller doses of medication than usually used for younger individuals (Crooks, O'Malley, and Stevenson, 1976; Schumacker, 1980; Triggs and Nation, 1975).

Serum levels of antipsychotics are now being done regularly, although the concept of effective therapeutic range is more equivocal than with some of the previously researched antidepressant medications (Itoh, Yagi, Ohtsuka, Iwamura, and Ichikawa, 1980; Niehs, Robinson, and Friedman, 1977).

Finally, because there is no evidence that any particular antipsychotic is more efficacious than any other in treating elderly patients, the medication for a particular individual should be chosen on the basis of least troublesome side effects, which vary depending on individual patient physiologic characteristics.

THOUGHT DISORDERS OF THE ELDERLY

Thought disorders in the elderly may be divided into acute and chronic forms. The acutely impaired population experiences various types of behavioral disturbances of rapid onset, either once or recurrently. Chronically mentally ill elderly individuals may have remissions and recurrences, but remain ill for long periods, frequently throughout their entire later years (Maletta, 1982).

Schizophrenia

Schizophrenia is primarily a chronic disorder in the elderly and is considered by some to be indicative of a syndrome rather than a single disease. A large group of older individuals are diagnosed as chronic schizophrenic and have lived much of their lives in psychiatric hospitals, having been admitted long before the introduction of effective psychotropic drug treatment in the 1950s. Most older schizophrenics developed signs and symptoms in their early years which then continued into old age, with very few having the initial onset of illness late in life. Because the usual onset is in the late teens or young adult period, a 65-year-old may have a 50-year history of illness. This marks the long-standing "chronic" schizophrenic so frequently seen in the back wards of state hospitals. As in early life, although usually not as fulminant, signs and symptoms of schizophrenia in the elderly are characterized by disturbed thinking (delusional), mood (blunted or inappropriate), and behavior (grossly disorganized). Loss of reality testing such as hallucinations (usually auditory) or illusions may also be present. These observations fit into the *Diagnostic and Statistical*

Manual's (*DSM-III*) "symptomatic" criteria for schizophrenia (*Diagnostic and Statistical Manual,* 1980). The other two *DSM-III* criteria necessary for diagnosis of schizophrenia are "impairment" (deterioration from a previous level of functioning in work, social functioning, etc.) and "duration" (continuous signs of the illness for at least six months). Similar signs lasting between two weeks and six months are designated as "schizophreniform," rather than schizophrenia.

Paranoid Disorders

Although paranoid thinking is frequently seen in schizophrenia, paranoid conditions in late life may represent the initial presentation of mental illness; this has been named paraphrenia. Signs and symptoms of this psychotic illness, generally characterized by well-circumscribed delusions and/or hallucinations of a grandiose or persecutory type, may not occur until age 60 or later (Raskind, Alvarez, and Herlin, 1979).

The increase in paranoia seen in some elderly may be explained partly as a response to loss. Aging is associated with many uncontrolled losses (psychosociocultural as well as physical), including job, friends, loved ones, income, physical strength, perception, memory, and even teeth and hair. These losses are not under the control of the individual, i.e., one progressively *loses control* over self and the environment. Inability to maintain control may be a key issue in mental problems associated with elderly individuals. Psychodynamically progressive loss may lead to a search for some explanation; and using the primitive defense of projection, the problem is attributed to some outside person or force, resulting in paranoia.

Four increasing degrees of paranoid ideation may be distinguished in the elderly: (1) suspiciousness; (2) transitional paranoid reaction; (3) paraphrenia (late-onset paranoia without other evidence of schizophrenic illness); (4) paranoia associated with schizophrenia (Eisdorfer, 1980). Paranoid symptoms in the elderly frequently have a basis in reality; therefore a complete treatment plan requires a thorough and realistic examination of the psychosociocultural and family situation, rather than simply prescribing medications. Also, sensory deprivation (primarily decreased audition of high-frequency tones, decrease in visual acuity and color discrimination) must always be considered in the mental status examination of an older patient with a new "paranoia."

Affective Disorders, with Psychotic Features

The most common affective disorder in the elderly is depression, but mania must also be discussed. Each of these disorders may be acute or chronic.

The most prominent symptom of depression is a persistent dysphoric mood (sad, depressed), along with various somatic ("vegetative") and psychic signs lasting at least two weeks (anorexia, insomnia or hypersomnia, crying, fatigue). Also, anhedonia, a decrease in libido, feelings of guilt, helplessness, and hopelessness, and even suicidal ideation may be experienced. Frequently, concomitant psychotic features are seen and may include a thinking disorder (e.g., delusions), a loss or impairment of reality testing (i.e., hallucinations, illusions), or even a depressive stupor. These psychotic features may be *mood congruent,* i.e., the content is consistent with depressive themes of inadequacy, guilt, deserved punishment, death; or they may be *mood incongruent,* i.e., persecution, grandiosity, thought insertion, thought broadcasting, control.

Frequently an "atypical" depression is seen in elderly patients [similar to the "masked" depression described by Lopez-Ibor and others (Lesse, 1974), in which a patient attempts to disguise a depressive mood by assuming a lighthearted, though clearly artificial, affect]. Depression in senescense (with or without psychotic behavior) is commonly overlooked because it does not always follow the same pattern, or have the same symptoms and signs as in the younger age-group. The onset in the elderly patient is likely to be more gradual and may be directly linked to a specific environmental stress. It is likely to be primarily somatic in its manifestation (headache, backache, vague pains), thereby being easily confused with the physical illnesses which are so common in the older patient. The usual affective symptoms and signs already mentioned may be absent, and instead, a very different clinical picture may be seen. Depressed elderly patients may demonstrate a considerable impairment of memory, perception, attention, and concentration, along with a loss of initiative and prominent psychomotor retardation, with or without mood-congruent or incongruent psychotic features. These cognitive changes may be so prominent as to easily confuse a depression with a dementing illness in an elderly patient. Elderly depressed patients presenting in this manner are frequently referred to as having pseudodementia (Caine, 1981; McAllister, 1983; Wells, 1979), although as originally described, pseudodementia included any psychiatric disorder that mimicked dementia, such as chronic schizophrenia or a severe character disorder (Kiloh, 1961).

It should be emphasized that late-onset *de novo* chemical abuse in an elderly patient with no previous history frequently may be symptomatic of an underlying major depressive disorder.

Thought Disorder Secondary to an Organic Mental Disorder

Organic mental disorders are the most common psychiatric illnesses in the elderly population. Besides the obvious cognitive deficits in the areas of orientation, attention, perception, and memory, elderly patients with organic mental disorders frequently exhibit disorders of thought. These may range from a very circumscribed delusional system to a more wide-ranging disorder of thought and reality testing which mimics a schizophrenic illness. The difference between these patients and those with functional ("nonorganic") psychosis is the clear sensorium usually associated with the thinking disorder seen in those patients with functional problems. Thought disorders may be seen in elderly patients with a variety of acute (delirium) or chronic (dementia) organic brain syndromes, frequently as a result of age-related organic mental disorders, i.e., primary degenerative dementia (PDD) and multi-infarct dementia (MID) (*Diagnostic* *and Statistical Manual,* 1980). PDD, senile type, is synonymous with senile dementia, Alzheimer's type (SDAT).

The causes of delirium and dementia are many and complicate the accurate diagnosis of unusual behavior in the elderly (Cowley and Glen, 1979; Lipowski, 1980; Maletta and Pirozzolo, 1981; Seltzer and Sherwin, 1978). In particular, the following causes should be considered and carefully ruled out in an elderly patient presenting with a history of psychosis or dementia: PDD, MID, alcohol or other drug abuse, head trauma, hypoxia (acute or chronic), nutritional or metabolic disorders, and specific neurologic diseases. Dementias may have a progressively deteriorating, stable, or a remitting ("reversible") course (Cumming, Benson, and Lo Verne, 1980; Lipowski, 1980; Liptzin, 1981; Wells, 1982). Many of the patients who are demented are institutionalized, and a sizable proportion of these individuals develop secondary behavioral and social problems which may exacerbate existing psychotic or cognitive impairment. Medical, physicological, behavioral, and psychosocial problems of demented patients markedly influence not only the onset of the disease, but also the exacerbations and diminutions of signs and symptoms characteristic of its course.

INDICATIONS FOR ANTIPSYCHOTIC USE

The indications for antipsychotic use in elderly patients may be grouped into two general categories. One deals with alleviating target symptoms of the particular psychosis. The second category involves assisting in the control of severe behavioral disorders associated with those patients exhibiting organic mental disorders.

Drugs may be used as an adjunct to one of the numerous modes of therapy available, including insight-oriented and/or supportive therapy, directive therapy, environmental manipulation, behavior modification, reality therapy, reminiscence therapy, and family and cognitive therapy. This combination of pharmaco- and psychotherapy frequently provides the most effective and comprehensive treatment approach, assuming appropriate guidelines are followed when prescribing antipsychotic medication in the elderly (Hall, 1973).

Signs and symptoms of behavioral disorders exhibited by elderly patients may be grouped into distinct categories (Stotsky, 1972) (Table 7.5.).

MECHANISM OF ACTION OF ANTIPSYCHOTICS

Before discussing the selection of individual antipsychotic drugs for elderly patients, a review of classes and mechanism of action of antipsychotic medications is necessary.

Classes

Antipsychotic medications in use today are most easily grouped by chemical composition. There are presently five major chemical classes:

***1.** Phenothiazines
- (a) aliphatic (aminoalkyl)
- (b) piperidine
- (c) piperazine

2. Butyrophenones
3. Thioxanthenes
4. Dihydroindolones
5. Dibenzoxazephines

Table 7.6 lists the generic name in each of the chemical classes, gives a representative example by trade name of a frequently used drug in each group, and lists estimated equivalent dosage in milligrams, using chlorpromazine at a baseline dosage of 100.

*The phenothiazines are further classified based on the specific substituent group attached to its nuclear structure at position 10.

Table 7.5
General Patterns of Disturbed Behavior in the Elderly

1. Anxious; restless; (hand-wringing, pacing, etc.); agitated; anorectic, sometimes self-mutilating.
2. Depressed; anorectic; insomnia (particularly terminal awakening); nihilistic, guilty, and often paranoid thinking; morbid (often preoccupied with death); psychomotor retardation (including speech).
3. Withdrawn; quietly negativistic; sullen; uncooperative; frequently mute and even appearing stuporous on occasion.
4. Overelation; insomnia; psychomotor hyperactivity, with rapid and pressured speech; often disorganized thinking.
5. Boisterous; verbally hostile; aggressive; belligerent; often assaultive behavior.
6. Delusions, involving ideas of influence and reference, jealousy, paranoia, persecution, grandiosity, and/or erotic experiences.
7. Hallucination, primarily auditory and/or tactile (formication).
8. Regressed behavior, including carelessness about personal appearance and even a disregarding of lifetime moral standards; inappropriate, even silly affect (frequently with grimacing); deficits in perception, attention span, memory (both recent and remote), and orientation; poor insight and judgment.

Modified from Stotsky, 1972.

Mechanism of Action

Convincing evidence from a large number of studies in psychopharmacology indicates that antipsychotic medications alleviate symptoms and signs of schizophrenia, including disorganized thinking, by blocking dopamine receptors in certain brain areas. It is not yet clear how this blockade affects and alters the underlying pathophysiology of schizophrenia.

Many neuroscientists today think of schizophrenia as a syndrome, possibly encompassing a variety of specific etiologies, but all having in common the concept of a relative excess of neurotransmitter or transmitters, including dopamine, at synapses in key CNS areas. The mesolimbic dopaminergic pathway is considered one of these key brain areas (Cooper, Bloom, and Roth, 1982).

Table 7.6
Antipsychotic Medications

Class	*Group*	*Trade Name*	*Estimated Equivalent Dosage (mg)*
1. Phenothiazine	Aminoalkyl:		
	Chlorpromazine	Thorazine®	100
	Piperidyl:		
	Thioridazine	Mellaril®	97
	Mesoridazine	Serentil®	56
	Piperazinyl:		
	Perphenazine	Trilafon®	9
	Trifluoperazine	Stelazine®	3
	Fluphenazine	Prolixin®	1
2. Butyrophenone	Haloperidol	Haldol®	2
3. Thioxanthene	Thiothixene	Navane®	4
4. Dihydroindolone	Molindone	Moban®	6
5. Dibenzoxazepine	Loxapine	Loxitane®	7

Because the clinically effective antipsychotic drugs all have the capability, although at varying potencies, of blocking dopamine receptors, and cause a clear increase in the turnover of dopamine in the CNS, it is thought that these drugs cause some type of a negative feedback loop activation of the CNS dopaminergic neurons.

Antipsychotic medications benefit patients with other psychoses besides schizophrenia, including mania, psychotic depression, paraphrenia, psychoses secondary to delirium or dementing illnesses, and certain drug-induced psychoses (amphetamine, bromine, L-dopa). Although tempting to suggest, it is presently unclear whether blockade of dopamine receptors is the mechanism of action in psychoses other than those classified as schizophrenia. More comprehensive information concerning the dopamine theory of schizophrenia may be found elsewhere (Maletta, 1980).

The antipsychotic mechanism of these medications does not involve sedation. In fact, even though they were earlier referred to as "major tranquilizers," and some of the antipsychotics do have sedating qualities (primarily the phenothiazines), there is no relationship between the antipsychotic and sedative properties of these drugs.

It does seem that besides dopamine, alteration of other putative CNS neurotransmitters also may be related to psychosis. For example, high-dose propranolol, along with its well-known cardiovascular effects, also seems to have a salutary effect on psychosis. This theoretically would indicate some involvement of epinephrine in psychosis, since propranolol is a potent adrenergic blocking agent.

Also, acetylcholine (ACh) has been implicated in the cause and treatment of some affective disorders, including mania. Increased ACh concentrations may be directly related to drug-induced depressions, and the loss of cholinergic (ACh) ascending neuronal pathways from certain brain areas (nucleus basalis of Meynert or substantia innominata) to cerebral cortex in patients with Alzheimer's disease is now well-known (Terry and Davies, 1980).

The endorphins are another class of brain chemicals that may have psychoactive properties. These endogenous, morphinelike compounds have been reported to act as antidepressants and also to exacerbate existing psychosis (Barchas, Akil, Elliott, Holman, and Watson, 1978; Verhoeven, van Pragg, van Ree, and de Wied, 1979).

We are still in the early stages of understanding the complex interrelationship between neurochemistry and neuropharmacology and the possible etiology of psychosis.

APPROPRIATE ANTIPSYCHOTIC TREATMENT FOR AN ELDERLY PATIENT

When attempting to choose the appropriate antipsychotic medication for an elderly patient, several principles are useful, including individualization of treatment; emphasis on treatment of target signs and symptoms; duration of treatment; side effects; and drug interactions.

Individualization of Treatment

Psychological and physiologic variability among aged individuals increases compared with younger cohorts. Therefore, generalizations are dangerous and each patient must be carefully "biotitrated." "Biotitration" involves individualized treatment of elderly individuals and is necessary because of the disparity in functional physiologic capabilities among different organ systems within any one patient due to varying rates of decline, as well as differing rates of decline of the same organ system among same-aged elderly individuals. Because the prevalence of chronic disease increases from 40 percent in those under 65 to 80 percent in those 65 and over (Eckardt, 1978), it is essential to individualize choice of drug, mode and time of administration, and length of treatment for each aged patient. Generally, lower drug doses are recommended in the elderly patient. Also, introduction of an anticholinergic burden should be avoided. Both these points are discussed later.

Changes in distribution, metabolism, and excretion capabilities of an individual occur with advancing aging (Gorrod, 1974; Hayes, Langman, and Short, 1975; Richey, 1975). Thus the pharmacokinetics and pharmacodynamics of many drugs in the elderly differ from those in younger individuals, and these differences will substantially affect the action of antipsychotic medications (Azarnoff, 1975; Bender, 1974; Rischel, 1976).

The interaction of the various physiologic systems may be best appreciated by the following equation for steady-state pharmacokinetics (Solomon, 1980).

$$\overline{C}_{ss} = \frac{1.44 \times AD \times t_{1/2}}{VD \times di}$$

where

$\overline{C}_{ss}$ = average steady-state concentration of the drug in the serum
AD = absorbed dose
$t_{1/2}$ = elimination half-life
VD = volume of distribution
di = dosage interval
1.44 = constant

The components in the numerator reveal that the average concentration of a drug in the blood during steady state is directly proportional to the dose of the absorbed drug and also the length of its half-life. Assuming a constant elimination half-life, the more drug absorbed, the greater the concentration of drug in the blood. Further, the components in the denominator reveal that the average steady-state concentration is inversely proportional to the volume of distribution and the dosage interval. The larger the volume of distribution (which in the case of the lipid-soluble antipsychotics relates directly to the proportion of the fat compartment in the body), the lower the concentration of drug in the blood; also, the more frequently the drug is given (therefore the lower the dosage interval), the higher the concentration. Only two components of this equation, absorbed dose and dosage interval, are controllable by the patient or caregiver. Changes with aging in fat/muscle body composition, in free vs. protein-bound drug, in cardiovascular activity, and in liver and kidney function affect steady-state concentration and can influence the action of antipsychotic medications.

Body Composition. There is a decrease in lean body weight with a corresponding increase in body fat (except in hands, face, and forearms) with aging, especially in women. There is also a decrease in percent body water, from about 61 percent at age 25 to 53 percent by 70 (Fryer, 1962; Rossman, 1977). These changes in body compartments with aging may alter the volume of distribution of some drugs (Greenblatt, Sellars, and Shader, 1982).

Free vs. Protein-bound Drug. Electrophoretic serum protein patterns in the aged show a trivial but statistically significant hypoalbuminemia, primarily due to a decreased rate of albumin synthesis in the liver. This decrease in serum albumin causes a relative increase in free vs. protein-bound drug at the tissue level, increasing the relative amount of pharmacologically (or toxicologically) active ("free") drug available. This is especially important with antipsychotics, which are highly protein-bound. However, it should be noted that an increase in the free fraction of a drug does not guarantee an enhanced pharmacologic effect, because the same fraction is subject to biotransformation and elimination, and also may not enter certain tissue compartments (Greenblatt, 1979).

Cardiovascular Activity. Cardiac output, as well as organ perfusion, decreases with normal aging. Cardiac output decreases on the order of 30 percent between the ages of 25 and 65, and the decrease in organ perfusion involves blood flow, peripheral resistance, and substance clearance (Kohn, 1977). These alterations in the body's primary drug delivery system result in a delay of drug arrival at the site of action and also a delay in removal, and may play an important role in the observed activity of a drug in an aged patient.

Liver and Kidney Function. Antipsychotic medications are extensively biotransformed in the body, emphasizing the importance of hepatic function. The rates of biotransformation are influenced by genetic factors, i.e., rapid or slow liver acetylators, as well as by exogenous factors, e.g., alcohol, barbituates, nicotine. Although there is no overall age-dependent decrease in liver function, there are changes with aging in hepatic enzyme activity, particularly by the inducible microsomal enzyme fraction (P-450 cytochrome oxidase system) integral to the oxidation-reduction.

Creatinine clearance, effectively the same as glomerular filtration rate (GFR) and therefore a valid measure of renal function, decreases on average approximately 30 to 40 percent between ages 20 and 80, beginning about age 35 (Rowe, Andres, Tobin, Norris, and Shock, 1976). This decrease is due primarily to lowered cardiac output and narrowing of renal vessels. There is also a 45 percent decrease in nephron mass in the aged kidney. A healthy 20-year-old filters about 200 liters of plasma per day, while a 70-year-old filters about 120 liters per day. These changes in GFR lead to a prolonged elimination half-life of drugs, and therefore a longer duration of drug action.

Most antipsychotic drugs (haloperidol being an exception) have pharmacologically active metabolites, whose excretion is also prolonged by the aged kidney.

Decreases in renal function and liver metabolism, along with altered distribution volume, play key roles in the increasing drug half-lives in aged patients. A more comprehensive treatment of the effects of physiologic changes with aging on drugs has been discussed elsewhere (Maletta, 1980; Plein and Plein, 1981).

Pharmacodynamics refer to the affinity of a drug for a particular end-organ receptor, and the receptor's ability to respond to that drug. There is an increased sensitivity of certain CNS receptors to some drugs with age.

Dosage. It should be abundantly clear from the preceding information that antipsychotic (or any drug) dose should be reduced in elderly patients. Although treatment must be individualized, general guidelines for optimum choice and administration of drugs can be established. The most important point is to take a comprehensive history, including a drug history (alcohol, drugs, smoking, coffee, tea, cola, chocolate); allergies or adverse drug reactions; medication history, both past and present (including prescription, over-the-counter, street, "shared" and "social" drugs—often overlooked are nasal decongestants, eye drops, laxatives, "tonics" or special diets, vitamins and minerals) (Kurucz and Fallon, 1980). (See Table 7.7.)

Antipsychotics. Much lower doses of antipsychotic medications are generally needed in elderly psychotic patients when compared with younger ones.

When choosing initial dosage, some severe psychotic episodes require large starting doses of an antipsychotic to achieve control. These initially large doses often can be reduced after behavior is controlled. Sigmoid-shaped dose–response curves for antipsychotics also are valid in elderly patients. Administering increasing doses of a high-potency antipsychotic over a few hours to an acutely agitated psychotic patient to achieve quick improvement (Anderson and Kuehnle, 1980) is a procedure that, although not contraindicated in elderly patients, must be followed carefully because of the potential for severe side effects, such as orthostatic hypotension.

Choice of Drug

There is no evidence that any one particular antipsychotic medication is more effective than any other. All current antipsychotics are effective. However, because the antipsychotics do differ greatly from one another in type and intensity of side effects, rational drug choices can be made for elderly patients (Barnes, Vieth, Okimoto, Gumbrecht, and Raskind, 1982; Solomon, 1979).

Table 7.7
Prescribing Antipsychotics for the Elderly

1. Elucidate the cause of disease symptomatology *prior* to beginning treatment and choose the antipsychotic most effective against the particular target symptoms exhibited.
2. Know the side effect profile of the antipsychotic and relate the side effects to the particular patient and disease processes present.
3. Avoid a medication if the side effects (e.g., anticholinergic) are as disturbing to a particular patient as the disease itself.
4. Simplify dosage regimens to enhance compliance (a single daily dose at bedtime is optimum, if side effects allow).
5. When available, obtain serum levels of medication; and after achieving therapeutic steady state, administer antipsychotic long enough to evaluate.
6. Stopping an antipsychotic is frequently more beneficial than starting one; assess therapeutic response frequently and regularly and if not efficacious, discontinue.
7. Before beginning an antipsychotic in patients on other medications, be aware of potentially untoward drug–system and drug–drug (including social) interactions.
8. Use the lowest effective dose of antipsychotic for the individual. Begin at low doses and gradually (allowing time for steady-state levels) "biotitrate" upward to reach desired clinical effect.
9. Although IM therapy may circumvent GI absorption problems, there is a potential hazard in the elderly patient of postural hypotension.
10. Antiextrapyramidal agents (AEA) should be used only with an antipsychotic when necessary and then for no longer than three months continuously without discontinuation and observation.
11. Antipsychotics should be discontinued at least semiannually to ascertain their continued need, and also to observe the possible onset of signs of tardive dyskinesia that may have been masked by the medication.
12. Weekend "drug holidays" are not beneficial.

Duration of Treatment

Antipsychotic treatment duration for an elderly patient depends on the specific disorder being treated and the patient's response. Phychosis in the elderly usually has one of two origins: One is psychosis as a functional illness, usually in a patient who has had schizophrenic-like signs and symptoms for years with no sign of cognitive dysfunction. The second is in a patient where the schizophrenic-like signs and symptoms are secondary consequences of delirium or a dementing illness. Patients in the former category require treatment for many years, while those in the latter category with a secondary psychosis frequently can be treated for only days or weeks. Improvement of psychotic signs and symptoms following antipsychotic medication treatment is generally gradual, sometimes measured in months; however, considerable improvement may be seen early in the time course, frequently within the first few days of treatment.

Regardless of etiology, all elderly patients treated with antipsychotics should stop treatment periodically to assess the need for continued use, at least annually, and preferably every few months. This assessment of continued need is advisable for two reasons. First, it separates and identifies those subpopulations of psychotics who are "multiple relapsers" from those individuals who do as well without medication as they do with it. Second, the discontinuation may detect early signs of tardive dyskinesia that might have been masked by the continued medication usage.

Side Effects

Numerous side effects occur secondary to antipsychotic medications, especially in the elderly population (Peterson and Thomas, 1975; Shader and DiMascio, 1970). The number of adverse reactions to drugs in general increases with aging to approximately 25 percent of patients by age 80, with a greater prevalence in women (Fann and Wheless, 1977). These side effects must always be considered when prescribing for the elderly and should be a major factor in the choice of specific agents. Antipsychotic medications do not all exhibit the same side effect profile, and even in those that do, the intensity from individual to individual varies widely.

Generally speaking, the higher-potency antipsychotics are recommended for use in the elderly population, despite their potential for extrapyramidal side effects (EPS). EPS in an elderly patient may have a severe negative impact.

However, individualization of dose and careful monitoring of ongoing treatment substantially decrease their production. The lower-potency drugs produce postural hypotension, anticholinergic side effects—both central and peripheral—and sedation, all contraindicated in an elderly patient.

Some antipsychotics are primarily known for their sedating effects (e.g., chlorpromazine, thioridazine), others for their production of extrapyramidal motor effects (e.g., butyrophenone, piperazines). The prominent side effects among the relatively newer antipsychotics, e.g., the thioxanthenes, loxapine and molindone, are also well-known. Thiothixene, chlorprothixene, loxapine, and molindone are in the group in which extrapyramidal side effects are relatively more prominent than the sedating ones. In fact, the molindones have been promoted as "alerting agents" because of their action on the reticular activating system (RAS) of the CNS; however, few clear-cut data support this suggested feature. Chlorprothixene has soporific qualities similar in nature to its molecular analog, chlorpramazine, while thiothixene does not exhibit this side effect.

Although numerous, most side effects of antipsychotic medications are relatively mild. There are, however, those side effects that are potentially severe, even toxic, especially in the elderly, and these will be considered. A more comprehensive presentation of adverse side effects of antipsychotics in general is presented elsewhere (Maletta, 1980).

The clearest manner or organizing the multitude of side effects continues to be the modified systems approach, with separation into the following four groups: central nervous system (CNS) effects; autonomic nervous system (ANS) blockage; neuroendocrine effects; and allergic reactions.

Cental Nervous System Side Effects. Although sedation (which usually occurs in the first two to three weeks of treatment) and depression are often reported as side effects in the elderly, the most frequently seen CNS side effects are EPS which occur in 5 to 20 percent of patients treated with antipsychotics. Three short-term EPS have been described: (1) dystonia/dyskinesia; (2) akisthisia; (3) parkinsonian reactions ("pseudo parkinsonism"), including akinesia and tremor. Dystonias are manifested by exaggerated head or neck posturing, frequently painful spasms of tongue, face, or throat muscles, hypersalivation, and occasional fixed upward gaze (oculogyric crisis). They typically occur very early in treatment, usually within the first week, and sometimes even a few hours after an initial dose of antipsychotic. They are rapidly relieved by anticholinergic drugs [benztropine (Cogentin®) or trihexiphenidyl (Artane®) and in the case of oculogyric crisis, instant relief with IV diphenhydramine (Benadryl®)]. However, because elderly patients are at risk for antichlolinergic side effects, these drugs should be used cautiously and only if there is a specific indication. Dyskinesias are chronic, brief, involuntary contractions of muscle groups, frequently involving eyes (blinking), lips, tongue, or face, but also occasionally affecting shoulders, hips, or extremities. Tardive dyskinesia is a specific dyskinesia that will be discussed later.

Akisthisia is the inability to remain still, an intolerance of inactivity. It has also been used to define feelings of "nervousness" or "jitteriness." Akisthisia is very common in elderly patients, is frequently mistaken for an increase in psychotic agitation, and is inappropriately treated with more antipsychotic medication.

Parkinsonian reactions may be separated further into akinesia and tremor. The akinesia of patients with parkinsonian reactions secondary to medication are identical to that in patients with Parkinson's disease, i.e., rigidity, immobility, stiffness and slowness of voluntary movement, slow and monotonous speech, drooling, masked facies, stooped posture, and a shuffling, festinating gait. Frequently in elderly patients these side effects are not equated with medication, but are instead incorrectly attributed either to age or illness or both, and therefore go untreated. The tremor is usually the regular, rhythmic, fine oscillation of extremities, especially the hands and fingers, or described "pill-rolling" in classic parkinsonism.

Regarding extrapyramidal side effects, especially the parkinsonian signs in the elderly, there is some evidence that, besides a lower dosage limit, there appears to be a higher dosage limit as well. More specifically, at low doses of an antipsychotic (like haloperidol), no extrapyramidal side effects are seen. As the dose approaches the broad midrange, there may be an onset of parkinsonian signs. If, however, the dose (and therefore the steady-state serum level) continues to be increased, extrapyramidal side effects may disappear (Deneker, 1976). This "risk zone" may be considered as the converse to the "therapeutic window" now well known for some tricyclic antidepressants.

The mechanism of this effect is not known. One possibility is that the built-in anticholinergic (and therefore antiparkinsonian) action of high-potency antipsychotics is not prominent at low- and midtherapeutic serum levels, but may rapidly intensify as the dose is increased. Another CNS effect in the elderly of some antipsychotics is a delirium (or acute confusional syndrome) secondary to marked anticholinergic side effects of the drug. This is discussed later in the "drug–drug interaction" section.

Antipsychotics are known to lower the resting membrane potential of neurons in the CNS and therefore should be used carefully in those patients with existing or potential seizure activity. However, in practice seizures rarely occur and the use of antipsychotics in seizure-prone patients is rarely a problem. Treatment with a lower antipsychotic dose, or the addition of an anticonvulsant, will usually suffice.

Autonomic Nervous System Blockade. The antipsychotics have a variety of effects on both the sympathetic and parasympathetic components of the autonomic nervous system (ANS), involving blockade of adrenergic (alpha-receptors) as well as cholinergic receptors. Different antipsychotic molecules have differing potency for interaction with ANS receptors. ANS side effects are seen more frequently with the phenothiazines, primarily chlorpromazine and thioridazine, and rarely seen with the butyrophenones, which are primarily dopamine receptor blockers.

The most potentially hazardous side effect of ANS blockade in elderly patients is orthostatic (postural) hypotension (OH) caused by blockade of the alpha-sympathetic receptors. The most commonly accepted physiologic definition of OH is a rapid fall of systolic blood pressure of 20 mmHg or more. Like most of the ANS blockade side effects, OH usually appears during the first week or two of therapy and is frequently a transient phenomenon, with patients seeming to develop a tolerance. However, even a temporary problem of this nature in an elderly patient may be important because hypotension can cause dizziness, followed by subsequent falls and serious injury. Slowly developing subdural hematomas, sometimes over months, may be a sequela of falls secondary to OH, causing the onset of dementia. The incidence of OH in elderly patients is higher when medication is administered parenterally.

Patient education is the most appropriate and successful treatment for OH. Information concerning the necessity of elderly patients on antipsychotic medications to change gradually rather than abruptly is important. A procedure as simple as dangling the legs over the side of the bed for several seconds prior to getting out of bed in the morning can be curative.

In the rare instance when orthostatic hypotension is a major problem, the offending drug must be stopped. If treatment of hypotension is needed, epinephrine is contraindicated because it is virtually an exclusive beta-adrenergic receptor stimulator and the receptors being blocked by the antipsychotic medication are alpha-adrenergic. Epinephrine administration may cause paradoxical worsening of the hypotension. Instead L-norepinephrine (Levophed®) or metaraminol (Aramine®), which exhibit primarily alpha-adrenergic vasopressor properties, should be used.

The cholinergic receptor-blocking properties of some antipsychotics produce a multitude of varied atropine-like side effects, some potentially more serious than others, but all potentially troublesome in frail, elderly individuals. Dry mouth, constipation, urinary retention, blurred vision, aggravation of narrow-angle glaucoma, and tachycardia are all reported. A commonly overlooked side effect among older men is the inhibition of ejaculation caused by some antipsychotics, primarily thioridazine. This could have a devasting effect on an already compromised self-image in an older individual. Theoretically, a less sympatholytic drug is indicated; but difficulties in sexual performance in elderly individuals may not be a drug side effect. Instead, the therapy may unmask latent problems by a therapeutic effect of increasing sexual interest.

Although not part of ANS blockade, the effect of antipsychotics on cardiac activity will be mentioned here (Levenson, Beard, and Murphy, 1980). Based on preliminary studies, it appears that many polycyclic antipsychotic and antidepressant medications have quinidine-like properties. Elderly patients with heart block or conduction defect might have those conditions aggravated by quinidine-like drugs. Conversely (also theoretically), patients with ectopy might benefit from the antiarrythmic effect of a quinidine-like drug. Nonspecific T wave changes have been reported after use of some antipsychotics, particularly thioridazine, but these changes are presently thought to be of little physiologic significance. Also, prolonged QT intervals are seen frequently in patients on phenothiazines. Another cardiovascular effect of phenothiazines is their norepinephrine-blocking properties that cause a negative inotropic action, leading to decreased myocardial contractility and possibly congestive failure. Tachycardia, seen in some patients, occurs for two reasons: a reflex response to hypotension, and the atropine effect on heart rate secondary to cholinergic receptor blockade.

Neuroendocrine Effects. Changes in neuroendocrine physiologic parameters suggest alterations at the level of the hypothalamic-hypophyseal portal system. This system acts as a bridge, communicating between the CNS and the body systems that are hormone targets. There are two changes seen in the older patient on antipsychotic medication that can be related primarily to this system.

The first and most prominent is alteration in body temperature regulation. Hypothermia is an especially insidious problem that, if not discovered and corrected, may cause profound and life-threatening problems in an elderly patient exposed to a wide ambient temperature range. Hyperthermia may also occur in elderly patients due to the same disturbances of temperature regulation. This problem is seen primarily during use of phenothiazines.

The other problem frequently encountered in patients of all ages on antipsychotics is weight gain. The mechanism of this weight gain is unclear, but it is thought to be partly due to hypothalamically mediated increased appetite. The molindones are the only antipsychotic group that have been reported not to cause weight gain.

Increases in prolactin levels and gynecomastia may be seen in patients on antipsychotics. These changes are thought due to the antipsychotic blocking the release from hypothalamus of prolactin-inhibitory factor (PIF), which normally maintains an inhibitory regulation of this hormone from the anterior hypophysis (pituitary).

Allergic Effects. Allergy to antipsychotics involves rashes, usually on the face, trunk, and extremities. Contact dermatitis to watches, rings, chains, and other ornaments may be seen in susceptible individuals. Chlorpromazine seems to be a prime offender. Phototoxicity is another untoward side effect seen primarily with some of the phenothiazine antipsychotics, primarily chlorpromazine. Sun screens will assist in ameliorating this problem, and judicious use of antihistamines will aid in the itching of an antipsychotically induced rash. Extremely rare problems include angioneurotic edema and exfoliative dermatitis.

In a broad sense, cholestatic jaundice may be considered as an allergic reaction to the use of antipsychotics, primarily chlorpromazine, and rarely occurs with other phenothiazines. Haloperidol, thiothixene, molindone, and loxapine, all nonphenothiazines, do not cause this problem and should be considered for use in a psychotic elderly patient with liver disease. This problem generally occurs within the first few months of treatment and manifests itself by the classic prodrome of malaise, fever, nausea followed within a few days by frank jaundice, with a laboratory picture of obstructive jaundice (high alkaline phosphatase, high cholesterol), i.e., small bile duct obstruction. Eosinophils are present in serum, as well as the liver. This potentially dangerous reaction may recur in a susceptible individual following readministration of the offending antipsychotic.

A final, rare adverse reaction to antipsychotics, seen primarily in elderly women, is agranulocytosis. It is seen almost exclusively during treatment with chlorpromazine, and usually occurs within the first few weeks of treatment. Nonphenothiazine antipsychotics have not been reported to produce this side effect. Agranulocytosis should not be confused with gradually developing leukopenia, seen frequently in elderly individuals on antipsychotic therapy. Onset of a sore throat in an elderly patient during the first couple of months of treatment with chlorpromazine should alert the physician to at least consider the very remote possibility of rapidly developing agranulocytosis.

Diminished Compensatory Reflexes in the Elderly. A review of antipsychotic medications in the elderly would be incomplete without discussing the clinical observation that aged patients have difficulty in recovering rapidly from drug side effects.

Age has a substantial impact on the ability of an individual to adjust to environmental stress, whether external or internal, and maintain internal constancy. This is the cardinal physiologic concept of homeostasis, first described by Bernard (1859) and further elucidated by Cannon (1929, 1942). For example, prolonged hypotension may occur in an elderly patient as a response to a relatively low dose of a sympatholytic agent routinely used to treat hypertension. Also, while age has little effect on blood pH or electrolyte content, there is substantial slowing with aging of the *rate* at which these constituents return to resting levels following a displacement by environmental factors, including drugs.

The diminished compensatory reaction to adverse effects of antipsychotic medications is an important manifestation of the decline of the body, with aging, to combat effectively negative environmental stress ("strain"). The specific etiology for the loss of effectiveness of this crucial control mechanism remains to be elucidated. Certainly some of the changes may be explained by the pharmacokinetic and pharmacodynamic changes seen with aging. This loss has been implicated as intrinsic to the process of normal aging and must be carefully considered when choosing the appropriate class of antipsychotic, dosage, and mode of administration for an elderly patient (Finch, 1976; Timiras and Vernadakis, 1972).

Drug Interactions

Because disease prevalence and incidence increase with age, there is an increase in the number of drugs taken and an increased potential for drug–system and drug–drug interactions.

Drug–System (Drug–Disease) Interactions. This type of interaction, particularly important in elderly individuals, involves a direct or side effect of a medication exacerbating an already compromised physiologic function secondary to normal aging or disease, perhaps leading to serious negative consequences. For example, if an antipsychotic which has a tendency to cause postural hypotension is given to an elderly patient with severe arteriosclerotic heart disease, there is an increased potential risk of a serious compromise of cardiovascular function.

Drug–Drug Interactions. The large and growing group of drug–drug interactions can be organized into three distinct categories.

The first type is a direct action of one drug taken concomitantly with another, such that the action of one of the drugs is detrimentally affected. This occurs frequently in elderly patients, who usually take concurrently a large number of medications. An example is the interaction between phenothiazines and some antacids. In the presence of calcium and magnesium salts, there is a relatively decreased absorption of phenothiazine across the gut mucosa.

A second type of interaction occurs when one medication acts directly on a physiologic mechanism that results in an indirect decrease of blockade of the effective action of another, seemingly disparate, medication. An example of this type is the relationship between the phenothiazine (also the tricyclic antidepressants) and the antihypertensive guanethidine (Ismelin®). These psychotropics inhibit, to varying degrees, the neuronal re-uptake of catechol and/or indoleamines, which is the postulated mechanism of action for antidepressants. The tricyclic compounds also inhibit the neuronal re-uptake of other ring-substituted bases, including guanethdidine (whose mechanism of action occurs intraneuronally), thus preventing the exertion of its antihypertensive effect. In this situation the potential for blood pressure elevation with its serious sequelae remains, despite continued ingestion of the antihypertensive medication.

A slightly different example of this type of interaction is the well-known action of barbiturates (as well as ethanol, nicotine, and some nonbarbiturate sedatives) in stimulating the liver microsomal enzyme fraction responsible for metabolizing antipsychotic compounds and other medications (the P-450 cytochrome oxidase system). Thus, higher doses of antipsychotics are needed to achieve the same effect in a patient also ingesting alcohol or barbuturates.

The third, and perhaps most important category when considering elderly patients is the additive effect that occurs when two or more drugs exhibiting similar side effects are taken in combination. A graphic example is the anticholinergic side effects of psychotropics. All antipsychotic medications, with varying degrees of intensity (chlorpromazine and thioridazine most, haloperidol least), as well as tricyclic antidepressants and antiparkinsonian drugs, exhibit anticholinergic side effects. These side effects are seen both centrally and peripherally. "Central anticholinergic syndrome" (or atropine psychosis) is the classic example of the CNS response to an excess of anticholinergic activity. Frequently, elderly patients placed on combinations of antipsychotics, antiparkinsonians, and antidepressants (which alone might not cause problems) exhibit a toxic delirium (including impaired attention, marked disorientation, and even visual and auditory hallucinations). This drug-induced delirium secondary to addition of detrimental side effects frequently is misdiagnosed either as functional psychosis, or even as a chronic dementing illness, simply because of the age of the patient. Because of the observed decrease in cholinergic activity in some brain areas in normal aging, as well as in patients with senile dementia of the Alzheimer's type (nucleus basalis of Meynert), the elderly may be particularly vulnerable to anticholingeric effects.

This toxic delirium can be rapidly reversed with physostigmine salicylate (Antilirium®), an anticholinesterase agent that increases the relative concentration of available acetylcholine at CNS postsynaptic neuronal membrane receptors. However, overdosage with physostigmine can also cause harmful side effect, i.e., a relative overabundance of circulating acetylcholine resulting in a "cholinergic crisis" (excessive parasympathetic activity). Therefore it should be used carefully by experienced personnel and only when considered essential. The usual adult dose of physostigmine is 0.5 to 2.0 mg intramuscularly or parenterally. Because of its rapid metabolism in the body (one to two hours), it may be necessary to repeat doses of 1 to 4 mg at appropriate intervals.

Peripheral anticholinergic side effects include decreased intestinal motility, leading to constipation or rarely a paralytic ileus; urinary hesitation and retention; tachycardia; excessive mouth dryness; loss of visual accommodation and aggravation of narrow-angle glaucoma; increase in skin dryness and a decrease in sweating.

Possibly because of a decrease in "cerebral reserve" with aging (the decreasing ability of the homeostatic mechanisms of the body to respond with appropriate speed and vigor to an environmental stress), elderly individuals are particularly prone to respond with marked drowsiness, or even confusion, to the sedative properties of some antipsychotics, especially when combined with other psychotropics with sedative properties.

Thus, care must be used when giving an antipsychotic medication with marked anticholinergic and/or sedative side effects to an elderly patient, especially when another psychotropic medication with a similar side effect profile is already being administered.

MAINTENANCE USAGE

The question of how long to treat an elderly patient who has responded well to antipsychotics is an important one in view of some of the severe side effects that are known to occur with prolonged use of antipsychotics. It is now well known that a subpopulation of schizophrenics exists with a multiple-relapsing type illness. Conversely, there are those patients who, following one schizophrenic episode successfully treated, may be taken off antipsychotic medications never to relapse again.

There is little question that schizophrenic patients maintained on antipsychotic medication have fewer replapses than comparable patients on placebo (Appleton and Davis, 1980). When older psychotic patients on long-term antipsychotic treatment are removed from medication, approximately 40 percent may show no signs of symptom relapse. This phenomenon occurs as well in younger patients removed from medication, but at a lesser frequency, usually about 30 percent.

Clinical judgment as well as past history is important when deciding whether to maintain an elderly patient on antipsychotics (Solomon, 1976). Certainly, because of the potential problems with long-term side effects, stronger justification is necessary for maintaining an older patient on antipsychotics than a younger one. Since schizophrenia usually is seen initially when a patient is in his 20s, by the time he reaches his 60s or 70s, it should be possible to clinically identify those with multiple relapsing illness. Those patients should be maintained on antipsychotic medications. However, it should be emphasized that under no conditions should all elderly psychotic patients be routinely placed on prolonged antipsychotic medication without periodic reassessment.

The possibility of overdose with antipsychotic medication should be mentioned. Death from overdose of an antipsychotic alone is very rare. Sedation and perhaps extrapyramidal side effects would occur following ingestion of excessive drug. In an elderly patient, the most serious side effects would be sedative and autonomic, so that those antipsychotics with the highest potential for those side effects, i.e., thioridazine and chlorpromazine, would be the most troublesome. The risk of serious sequelae, or even death, increases markedly if antipsychotics are taken in overdose in conjunction with other drugs or alcohol. Antipsychotics are nondialyzable and therefore supportive care is the only effective treatment for an overdose with this group of drugs (Allen, Greenblatt, and Noel, 1980).

LONG-TERM EFFECTS

Long-term effects may occur following administration of antipsychotics for many years, or the effects may be produced by shorter duration of treatment with very large doses. These effects are provoked generally in a shorter time and by lower doses in elderly individuals.

Skin

Skin pigmentation has been reported following use over several years of some antipsychotics. It usually is of slate-gray, brownish, or sometimes purplish hue and occurs in areas of skin exposed to light, the face more prone to discoloration than the hands. This pigmentation occurs primarily with high-dose phenothiazines, especially chlorpromazine, and may gradually fade when the medication is stopped (Matsuo, Ozawa, Niizuma, and Ohkido, 1979).

Eyes

Eye changes, both acute and chronic, may occur in patients exposed to very high-dose phenothiazine treatment. The acute effects are due to pigmentary deposits in the anterior corneal layers. These acute changes are not to be confused with the rare retinitis pigmentosa described after high-dose thioridazine (greater than 1,600 mg daily for a month or more in young patients; much lower in the elderly). Retinitis pigmentosa is a very serious problem that interferes with vision and may not be reversible.

Further eye effects after chronic antipsychotic use include granular deposits on the posterior surface of the cornea and the anterior portion of the lens. These changes are asymptomatic and are discovered only by slit-lamp examination; however, because of the very low yield, it is not cost-effective for all elderly patients on long-term antipsychotics to have routine slit-lamp exams.

Tardive Dyskinesia

This complex syndrome of involuntary hyperkinesis was first described in 1957 by Schonecker. Tardive dyskinesia (TD) means "late-appearing abnormal movements" and is most often seen in chronically mentally ill older patients who have been maintained on high doses of antipsychotic medication for prolonged periods. It is occasionally seen in children, in individuals not on antipsychotics, and after short-term (weeks) or low-dose therapy.

There is a higher prevalence in older patients, perhaps because of longer treatment duration, and in women more than men, perhaps because of the increased longevity of women. Of course the possibility exists that aging itself somehow increases the susceptibility to tardive dyskinesia (Bourgeois, Bouilh, Tignol, and Yesavage, 1980; Perris, Dimitrijevic, Jacobsson, Paulson, Rapp, and Froberg, 1979).

Tardive dyskinesia is now known to be a problem with all antipsychotics, since its etiology is thought due to dopaminergic overactivity (either an increase in dopamine release or an increase in sensitivity of dopamine receptors) secondary to chronic blockade of the dopamine receptors in the nigrostriatum (basal ganglia) by antipsychotic usage. This disrupts the normal dopamine/acetylocholine (D/A) ratio, and the abnormal motor movements result. Anticholinergic agents, such as Artane® or Cogentin®, which further disrupt the D/A ratio, exacerbate the tardive dyskinesia. The abnormal motor movements usually involve the tongue, mouth, jaws, and lips, e.g., wormlike movements or protrusion of the tongue; chronic irregular chewing jaw movements; grimacing; smacking or puckering of the lips. These abnormalities may extend to neck twisting, body rocking, or rhythmic pelvic movements, as well as choreoathetotic or akisthisic movements of hands and arms and stamping or twisting of ankles, feet, or legs (Bateman, Dutta, McClelland, and Rawlins, 1979; Deveaugh-Geiss, 1979).

Tardive dyskinesia is thought to be relatively common among patients in chronic, long-term care facilities, but among the general psychiatric population the numbers range anywhere from 5 to 40 percent, with 10 to 20 percent the most widely accepted range (APA Task Force on Tardive Dyskinesia, 1980). Although some patients deny distress from tardive dyskinesia, this may be more true of some chronic inpatients than of outpatients (Dominguez, 1980).

The motor movements may disappear following the discontinuation of the antipsychotic, or may persist for months, years, or even permanently. Although increasing the dose of the offending drug may temporarily suppress the abnormal movements, they inevitably return. Drug discontinuation is the treatment of choice at this time. Recently, treatment has focused on attempting to increase the relative brain concentration of acetylcholine in patients by administration of massive doses of acetylcholine precursors, such as lecithin, with disappointing results. Oxypertine is another chemical approach to treatment with encouraging preliminary results (Freeman and Soni, 1980; Kazamatsuri, 1980).

Lithium, diazepam, and GABA (gamma aminobutyric acid) have been suggested as experimental treatments of tardive dyskinesia worth pursuing. Lithium may be of benefit by increasing the neuronal re-uptake and turnover of dopamine, or possibly by decreasing dopamine receptor sensitivity (Rosenbaum et al., 1980). Diazepam, known to block the enzyme phosphodiesterase, might therefore act by decreasing the intensity of the compensatory dopamine feedback loop, the normal physiologic reaction to receptor blockade by the antipsychotic. GABA may act by modulating extrapyramidal motor function through and interaction with dopamine (Casey, Gerlach, Magelund, and Christensen, 1980).

Given the possible irreversibility of this motor dysfunction and its greater prevalence in the elderly, the benefit of long-term maintenance medication must be carefully weighed against possible cost in an elderly patient, and unnecessary usage of antipsychotics should be avoided. For example, simple anxiety is never an indication for antipsychotic use. For a comprehensive treatment of tardive dyskinesia, the reader is referred elsewhere (Baldessarini and Tarsy, 1978; Berger and Rexroth, 1980; Smith and Baldessarini, 1980).

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CHAPTER 8

Podiatry for the Geriatric Patient

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INTRODUCTION

Podiatry can be defined broadly as that profession of the health sciences which deals with the examination, diagnosis, treatment, and prevention of diseases and malfunctions affecting the foot and its related structures by the employment of medical or surgical means. Various state statutes specify the scope of practice and service. The White House Conferences on Aging, in

1960 and 1970, acknowledged that foot problems were extremely common in elderly people—the fourth leading cause of complaint in institutionalized geriatric patients. Sometimes a foot problem may be symptomatic of a systemic disease, such as diabetes mellitus or peripheral vascular disease. The Conference pointed out the necessity for elderly patients to remain moving about and free of foot problems. For one thing, patients responded more readily to other forms of therapy if they were ambulatory. In addition, patients who were mobile and ambulatory in their own community settings retained their dignity and generally lived longer than those who were immobilized or institutionalized.

Podiatric problems for the elderly should be as comprehensive as programs provided by any other medical discipline. Podiatric programs must not only deliver a high-quality health care service but also must provide motivation and education to ensure the continuation of foot health as a major element in any geriatric care program.

INCIDENCE

Several factors emerge as central to the podiatric care of elderly patients: First, the physical environment in which the patient functions and, second, the particular lifestyle of that patient. Care may be directed at community-based elderly as well as those who are institutionalized. Both have ambulatory and nonambulatory components.

The ambulatory patient living independently in the community can receive treatment in a variety of clinical settings, but ultimately transportation becomes an important factor. Some geriatric patients find it difficult to use public conveyances; they may be physically unable to board the vehicle, comply with or comprehend time schedules, or secure private means of transportation by a relative or friend.

Once an appropriate method of transportation has been established, it is important to consider the various types of treatment centers. The podiatrist's office offers the widest range of treatment modalities and services, although the actual structure of the building often creates a problem for elderly patients who are confined to a wheelchair, have cardiac or other related systemic conditions, or are disabled by amputation of a limb. Such disabilities make it difficult or impossible for the patient to climb stairs where no elevator is provided.

Hospital clinics offer total one-stop care but evaluation and treatment are often hurried, which only serves to alienate the patients from the physician, when they might be looking for reassurance and comfort as much as medical care alone.

Senior citizen centers offer another facility for rendering podiatric care, especially since they are used as meeting places for the geriatric community and are usually easily accessible. Some patients may miss visits during a vital part of their treatment, however, because of inclement weather or other unforseen circumstances.

Geriatric patients who are able to maintain themselves in their own apartments or homes may still get into difficulty. If, for example, an elderly person — for the sake of appearance and self-image—wears shoes that are inadequate and dangerous, she is prone to falls which could lead to injuries of the foot, leg, or hip. If the shoes are short and tight, they may create lesions that are difficult to heal because of peripheral vascular insufficiency, diabetes mellitus, or other systemic problems. Finally, because of fixed incomes and the unavailability of Medicare reimbursement for routine foot care, elderly people often attempt uninformed self-care, which results in ulcerations or infections. Limited limb motion, failing eyesight, and unsteady, arthritic hands may exacerbate even a minor problem.

The nonambulatory geriatric patient who can no longer maintain himself in a home environment is institutionalized for a variety of reasons in appropriate facilities. Whether the patient is ambulatory or nonambulatory, oriented or disoriented, appropriate treatment should include regular visits by a podiatrist to render appropriate foot care. It is important to prevent localized pathology which might lead to further complications as well as to help the patient function to the best of his or her abilities.

DIAGNOSIS

There are numerous pathologic conditions which appear in the lower extremities. Many of them are local manifestations of systemic disease; others are purely external in origin and arise from biomechanical imbalance and/or improper foot gear. Let us focus our attention first on the podiatric history and physical examination.

In examining the elderly patient, the podiatrist first should determine what activities the patient is able to perform and what activities he or she can no longer perform. Attainable goals should be established.

An appropriate history should be obtained from the patient or a close relative. The initial approach is similar to the general medical history, but careful attention is paid to conditions and complaints involving the extremities. The chief complaint of the patient should be recorded in his or her own words as the reason the patient sought an evaluation and care. The patient should be questioned as to how long he has had the podiatric problem, as well as what treatment has already been rendered.

In the initial local examination of the foot, the skin should be reviewed for the presence of hyperkeratotic and other dermatological lesions. The pedal nails should be evaluated and compared with the nails of the hand. The texture of the skin, as well as its moisture, color, elasticity, and fat padding should be noted. Pigmentation and necrotic excoriations should be recorded. Any infection or neoplastic change should be identified and classified as local or general.

A peripheral vascular examination is next. Pedal pulses, dorsalis pedis and posterior tibial, as well as popliteal and femoral, should be evaluated and graded. Trophic changes, including atrophy and change in hair growth, edema, and varicosities, should be recorded. Special vascular studies, such as Doppler exam and oscillometry, should be employed where necessary, especially when pedal pulses are poor. This could easily reflect a reduction in collateral circulation due to proximal occlusive vascular disease.

The orthopedic exam should concentrate on the patient's foot type and gait patterns. X-ray should be employed to further evaluate conditions such as hallux abducto valgus, or bunion deformity, and in cases where osteoarthritic and degenerative bone diseases are suspected. Biomechanical studies should be undertaken where needed. Biomechanics refers to the forces which cause change in the foot itself. There is a mechanical basis underlying the development of hyperkeratotic lesions in the elderly patient. When a mechanical change takes place in the foot, the etiology must be determined and further alterations prevented; this in turn will prevent or lessen the development of painful lesions which could restrict activity and productivity.

A neurological examination follows, with particular attention paid to the patient's mental status and behavioral activities. Achilles, superficial plantar, and patellar reflexes should be tested. Motor function and gait should be reviewed. Vibratory sense, pain, touch, and temperature should be evaluated along with proprioceptive ability.

From this initial history and examination, a working diagnosis should be established and appropriate treatment goals may be outlined.

TREATMENT

Some of the more common problems which present to the podiatrist involve the integumentary system. As a person ages, there is a marked decrease in hydration of the skin coupled with diminished sebaceous activity. Along with metabolic and nutritional changes, these will produce dryness and scaling which in turn lead to pruritus. This should be differentiated from chronic tinea pedis and from numerous other conditions with a similar presentation. These include neurodermatitis, contact dermatitis, psoriasis, eczema, drug eruptions, and stasis. Treatment should be aimed at hydration and lubrication of the skin in the form of an emollient skin cream, preferably with a urea base. In cases of severe pruritus, a preparation of an emollient cream with a topical steroid usually provides dramatic relief.

Tinea pedis, commonly referred to as athlete's foot, can present itself in many forms. There are two basic methods for diagnosis: the direct microscopic examination for fungal elements using potassium hydroxide, and the fungal culture. A dermatophyte-testing medium has also been developed whereby a simple color change of the medium indicates fungal infection. This method is highly reliable.

Tinea infections are prone to developing on the feet because of the excessive warmth and moisture caused by occlusive foot gear and of the increased susceptibility of the distal tissues to the effects of peripheral vascular disease and aging. The acute form of tinea pedis usually presents with vesicular eruption, fissuring, loss of the epidermis, and quite often secondary bacterial infection. The chronic form of tinea pedis will present in the typical moccasin distribution, and unilateral involvement is not unusual.

Acute infections should be treated with frequent warm water and Epsom salts soaks and rest with elevation if edema is present. The use of systemic antibiotics is recommended when there is evidence of secondary bacterial infection. Chronic infections should be treated with topical antifungal preparations such as clotrimazole and miconazole nitrate. Soaking and frequent changing of socks is also advised.

The oral use of griseofulvin is often employed for tinea infections, but it does have some drawbacks. First, it is fungistatic, not fungicidal. Second, it relies on an adequate vascular tree, which is often absent in the elderly patient. Finally, there are some known side effects which might preclude its use in the elderly, debilitated patient, including skin rashes, urticaria, nausea, vomiting, dizziness, mental confusion, diarrhea, headache, and fatigue. Severe reactions might cause paresthesias of the hands and feet, and even proteinuria and leukopenia.

Warts, or verrucae, are rarely seen in the elderly. They are often confused with hyperkeratotic lesions and should be carefully diagnosed. They are viral in origin, and characteristically will produce pinpoint bleeding on debridement, as well as severe pain with lateral pressure. A variety of acidic preparations are available but should be employed with care in the elderly patient since even weekly treatments may be ineffective and can produce tissue damage.

Psoriasis commonly affects many geriatric patients. The characteristic lesion will appear on the foot, but there is also usually an increase in hyperkeratosis and fissuring. Pitting of the nails is often the diagnostic finding. In addition, subungual hyperkeratotic debris will be evident. Treatment consists of local application of steroid preparations and periodic debridement of the nails.

Hyperkeratotic lesions often are symptomatic in elderly individuals. Their feet have taken them through many years of walking on hard, flat surfaces, resulting in painful, diffuse lesions which interfere with ambulation. A tyloma, commonly referred to as a callus, is a lesion resulting from friction and pressure and is usually found on the plantar aspect of the foot. The tyloma is a protective mechanism of the body against undue stress and strain. It is a diffuse lesion which causes pain and a burning sensation. Treatment consists of localized debridement, taking care not to injure the underlying healthy tissue. Afterwards, an emollient skin cream should be applied for lubrication, and the areas should be padded to protect them from further trauma. Orthopedic shoes and/or biomechanical orthotic devices may be employed in extreme cases where conservative measures fail.

Another troublesome hyperkeratotic lesion is the heloma, or corn. These usually present on the toes where there may be a great deal of concentrated pressure. Treatment is usually the same as that for tylomata, with the addition of aperture padding around the lesion to evenly distribute pressure away from the prominence. Many digital devices can be fabricated when needed, and these usually provide adequate comfort for the patient.

Any of the hyperkeratotic lesions may at some time ulcerate as a complication. Treatment would then be aimed at avoiding pressure to the area which otherwise could lead to infection, lymphangitis, and osteomyelitis.

There are numerous nail conditions which present in elderly individuals. Unguis incarnatus, or onychocryptosis, is commonly known as an ingrown toe nail. This is most frequently caused by tight, ill-fitting shoes, although there is a hereditary tendency toward its development. In this condition, the lateral edge of the nail plate penetrates the underlying soft tissue, thereby causing localized inflammation, secondary bacterial infection, and severe pain. Often, as a result of self-treatment, a small splinter of nail is left to grow even deeper, causing the growth of granulation tissue, the so-called proud flesh.

Treatment is aimed at removing the cause, that is, resecting that portion of the nail that is ingrown. This is usually facilitated by the use of an English nail instrument which readily inserts under the nail plate. The use of a local anesthetic may be necessary, depending upon the severity of the condition. After the procedure is completed, the patient is advised to soak twice daily in warm water and Epsom salts, and apply a topical antibiotic ointment with a dry sterile dressing. A small piece of cotton may be inserted between the nail plate and the soft tissue to eliminate the direct pressure and reduce the likelihood of recurrence. Systemic antibiotic therapy should be employed when infection is severe.

Onychomycosis is a condition of the nails due to fungal invasions producing disturbances in growth and appearance. The most common causes are the dermatophytes *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum.* Monilial infections also produce onychomycosis. Clinical presentation varies from simple scaling to complete destruction of the nail plate. The nail becomes brittle, hypertrophic, and granular. There is usually progression of the disease from one nail to the next. Positive diagnosis can be made through appropriate fungal cultures or smears.

Onychomycosis in elderly patients is a serious problem. Repeated trauma to the enlarged nail plate due to shoe pressure can result in discomfort and injury. The diminished pedal blood supply of many elderly patients may interfere with the use of oral antifungal agents. Once involvement of the nail matrix, or root, has occurred, cure is rare.

Treatment consists of periodic onychial reduction and application of a topical antifungal agent. Since this is a chronic condition, such patients should be scheduled for regular onychial care.

Onychauxis, enlargement of the nail plate, and onychogryphosis, the so-called club or ram's horn nail, are also nail conditions frequently seen in elderly patients. These conditions usually become painful when pressure is applied to the area, or when the hypertrophic nail injures the toe or adjacent tissues. Treatment involves frequent debridement as well as patient education in the care of the nails.

Disorders of the sweat glands often present problems in the elderly. Hyperhidrosis represents an abnormal amount of perspiration, and bromhidrosis is a condition accompanied by a fetid odor. These are often caused by ill-fitting shoes or nutritional imbalances. Treatment involves soaking twice daily in Burow's solution (1:20) followed by the application of an absorbent powder. Systemic anticholinergic therapy has been tried to inhibit the action of acetylcholine on the sweat glands, but side effects, such as dizziness, urinary retention, blurred vision, and dryness of the mouth, preclude its use in the elderly patient.

There are many orthopedic conditions, both structural and functional, which plague the elderly patient, interfering with gait and mobility. Often elderly individuals complain of heel pain. The causes of such pain are many, and good clinical judgment will be important to render a proper diagnosis. The commonest cause is a heel spur. The etiology of this condition is varied, but it seems that the source of pain stems from the inflammation caused by the constant pulling of the plantar fascia at its origin in the calcaneus. The condition is extremely painful on weight-bearing, to the point where the patient may dread ambulating. In most cases, an excessive amount of pronation is present, and long-term treatment is aimed at controlling this imbalance. Initially, treatment consists of local injections of an anesthetic coupled with a corticosteroid, which usually provides immediate relief. The use of heel cups, plantar strappings, and physical therapy modalities have also been successfully employed. When pain subsides, the patient can then undergo a biomechanical evaluation for orthotic control.

Hallux abducto valgus deformity, or bunion, is a deviation of the first metatarsophalangeal joint (MPJ), causing the toe to drift laterally with a concomitant protuberance of the metatarsal head medially and exostosis formation. In severe cases, there may be overriding of the second toe causing a painful dorsal lesion as well as tylomata formation under the head of the second metatarsal due to pressure from the now-contracted second toe. If treatment is to be conservative, it should be aimed at reducing the painful lesions and providing adequate padding to the first MPJ to avoid excessive pressure to that area. Orthopedic shoes, custom made to the exact contours of the patient's foot, are a valuable tool in securing comfort and should be employed when affordable. Surgical intervention should be considered when there is pain and difficulty in ambulation after other means have failed.

Metatarsalgia is a condition which usually results from atrophy of the plantar fat padding supporting the metatarsal heads. There is a definite loss of shock absorption and the force of impact is borne almost entirely by the heads of the metatarsals. In treating this condition, the goal is removing the pressure or redistributing it away from the involved metatarsal head(s). This can be done by utilizing an orthotic, orthopedic shoe, or other cushioning accommodative device. In severe cases, local injections of an anesthetic agent with a corticosteroid will provide relief from pain.

The use of proper footgear plays an important role in the management of foot problems of the elderly. Patients with arthritic conditions will need a shoe that offers maximum comfort. Patients with severe arthritis of the hands will find it difficult to tie a laced shoe, and a slip-on type shoe is advised. Other geriatric patients with various structural deformities of the foot will find great relief with an orthopedic shoe which is constructed especially for them. These shoes—commonly known as "space" shoes—are made from exact casts of the patient's feet; they compensate for the numerous orthopedic problems the patient may experience. Whatever the problem may be, the patient should receive a thorough podiatric examination before it is determined what shoe type would be best suited to alleviate the condition and prevent future occurrence.

The elderly patient is often prone to falls and other traumas which result in fractures of the foot. These injuries should be treated immediately, especially since the frail elderly usually require a longer healing period than the vigorous young. Appropriate X-ray studies should be performed as soon as possible to determine the extent of the injury. Ice packs should be applied before more extensive treatment is initiated. Usually, a digital fracture can be treated effectively by splinting the injured toe to the adjacent toe. In the case of a displaced fracture, an injection of a local anesthetic agent will be necessary to realign the digit, after which the appropriate splinting may be performed. The patient must understand that a reduction in ambulation is necessary for proper healing to occur with any fracture of the foot. An elderly patient living alone may be unable to manage independently, and may require additional help. More severe fractures of the foot may require some type of casting, either rigid or semirigid (Unna Boot), thereby further restricting the patient's capacity for self-care.

PEDAL COMPLICATIONS OF SELECTED SYSTEMIC DISEASES

Often it is the podiatrist who first recognizes an undiagnosed case of diabetes mellitus based on clinical findings from examination. The diabetic's foot is prone to develop severe vascular insufficiency and neuropathy. These in turn may lead to lesions and ulcerations which progress to infection, gangrene, and amputation. An elderly patient must understand the nature of the disease and the importance of early and regular foot care. Most of these patients will have had the disease for a good part of their lives, but others who have developed a case of late-onset adult diabetes will need extra care and assurance. Complications often result when an older person, because of forgetfulness or noncompliance, neglects proper podiatric care.

The role of the podiatrist is especially important for diabetic patients. Frequent consultation and updating of treatment plans are central to good foot health. If patients experience lesions and ulcerations of the feet, weekly debridement and cleansing of necrotic tissue should be initiated. Specially designed footgear should be provided for proper balancing and dispersion of weight and pressure away from sensitive areas. Treatment for the diabetic is aimed at control of the disease and prevention of further complications.

The peripheral vascular diseases encompass numerous conditions which include vascular insufficiency, arteriosclerosis, Raynaud's disease, Buerger's disease, and causalgia. The podiatric examination should routinely include palpation of pedal and related pulses. Trophic changes originate from diminished blood supply and changes in pressure. Calluses, abnormal nail growth, ulcers, and gangrene may be considered trophic changes in the presence of a poor vascular tree. These should be noted and differentiated from fungal infiltration, malnutrition, faulty footwear, and poor hygiene. Such changes may arise from trauma and are often evident before the development of gangrene. In pregangrene the part is usually cold, may be tender, and will not blanch. This can be differentiated from Raynaud's disease where there is intermittent blanching confined to the area distal to the knuckle line; and the palms and wrists are not usually involved. In Raynaud's phenomenon there are transient episodes of vasoconstriction manifesting first as pallor, then erythema due to reflex vasodilatation, and finally, cyanosis. This is often symmetrical and bilateral, intermittent and transient, and is usually secondary to temperature change. Treatment of vascular insufficiency is directed toward improving blood supply and controlling local pathology. Appropriate referral to a peripheral vascular disease specialist is advised in extreme cases.

Most elderly patients experience some form of arthritis and find themselves incapacitated because of the associated pain and restricted limb motion. Many of these patients can be helped with the wide variety of antiinflammatory drugs currently available. Orthopedic shoes and specially constructed braces are often employed with more extreme cases, as are the various physical modalities, including ultrasound and heat.

In all cases of systemic disease, it is essential that the podiatrist work closely with the medical and allied health personnel involved to provide the total care that is necessary to maximize the geriatric patient's comfort and future productivity.

GOALS

The goals of an adequate foot health program for the elderly include the following: (1) reduction of pain; (2) restoration of maximum function; (3) retention of the maximum level achieved in function and in ambulation; (4) increase of personal comfort;

and (5) decrease of likelihood of hospitalization due to a foot problem that is the result of a related disease process. The delivery of a comprehensive foot health program will reduce stress and strain associated with foot discomfort, fatigue, and the limitation of ambulation. Fostering foot health can reduce institutionalization or maintain ambulation in an institutionalized person. For community-dwelling elderly, the ability to walk is crucial in maintaining independence. An institutionalized individual who is able to ambulate will be less socially segregated within the institution. It would seem, then, that foot health is important for independence in either case. The current focus of podiatry for most patients is on relief of pain rather than cure. This is the result of a lifetime of neglect or bad foot health habits. Foot health education for the elderly should be a part of a total educational program for the geriatric population. The average elederly individual has less education and is more dependent than members of the general population. Thus the development of an educational program in relation to foot health for the elderly must be specifically designed. Community foot health education and screening programs should be undertaken for diagnostic and referral purposes.

Our educational emphasis must be preventive: we must protect what we cannot replace. An excellent publication, developed by the United States Public Health Service, is entitled "Feet First," and is available from the U.S. Government Printing Office. It provides an adequate base of understanding for the elderly, the diabetic, and those patients with vascular impairment. Substantial information on foot health and aging is also readily available from the American Podiatry Association which instructs patients in proper foot health and how to prevent foot problems as we age.

In addition to establishing community health education programs, community physicians and allied health practitioners should understand the nature and scope of podiatric medicine and its role on the health care team. Podiatry is a unique medical specialty that contributes to the total health of the patient, not only medically, but also psychologically and socially.

The delivery of foot care to the aged population can keep the elderly walking and independent in a community setting.

The ability to remain ambulatory, even among institutionalized individuals, provides major social and psychological benefit to those with chronic impairment. Proper foot care provides mobility and freedom from pain, and is an essential component of adequate care of the elderly.

READINGS

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SECTION III

Behavioral Sciences

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CHAPTER 9

Psychomotor Performance

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Studies of most aspects of psychomotor performance in relation to age during the last ten years or so have been few. Such developments of research as there have been, however, and studies in the general field of human performance not specifically concerned with aging, have made it possible to look at what has been done earlier in a clearer light, to refine interpretations, and to focus more sharply on the points where further work is needed. It is with these developments that this review will be concerned under three main headings: first, changes in the basic mechanisms concerned with motor performance; second, the effects of physical exercise on psychomotor performance; and third, effects of practice and problems of learning motor skills.

BASIC PROCESSES

Psychomotor performance depends on the functioning not only of motor units and their immediate neural control, but of central mechanisms which select and guide action, and these depend in turn on sensory and memory systems which provide immediate and stored data, respectively, on which selection and guidance is based. The whole chain of processes is thus involved from sensory reception through perception, translation from perception to response, and the phasing of muscles to produce action, to actual execution. Performance is often regarded as depending upon the sum total of the efficiencies of all these mechanisms. However, although this may be so in a statistical sense, performance by any one person at any one task in any particular situation is likely to be limited by only one member of the chain. The limitation can be represented as in Figure 9.1, which shows a relationship between three factors: first on the abscissa is *demand* made by the task, second on the ordinate is the *capacity* of the performer, and third, as a vector, is the technique, method, or *strategy* used to deploy capacity to meet demand. It can be seen that with a given strategy and capacity, performance is adequate up to a certain level of demand but will fall short thereafter. When the demand is small, a moderate lowering of capacity, such as might occur with age, will have little effect on performance, but if the demand is greater the effect may be much more substantial. Thus it is understandable that easy tasks may be done as well, or almost as well, by older people as by younger, while there may be substantial differences with age for more difficult tasks. Performance can nevertheless sometimes be improved by adoption of a more efficient strategy. The effect of doing so would be represented in Figure 9.1 by a lowering of the slope of the vector, indicating that a greater demand can be met with a given capacity. Older people have been found to adopt more efficient strategies in some cases, and when they do so the effectiveness of their performance changes less than would be expected from a study of their capacity alone.

The relationships of Figure 9.1 apply to each of the links in the chain from sensory input to motor output, and the source of limitation in performance will depend on which of the links or stages is loaded by the demands of the task to an extent that the capacity of the stage is stretched to its limit. Whether an age change occurs, and if so what form it takes, may, therefore, depend upon precise, and sometimes far from obvious, details of the task being performed and upon individual differences of the capacities of various stages among performers.

Let us consider the main capacities in turn, starting with those at the two ends of the chain of processes from sensory input to motor output.

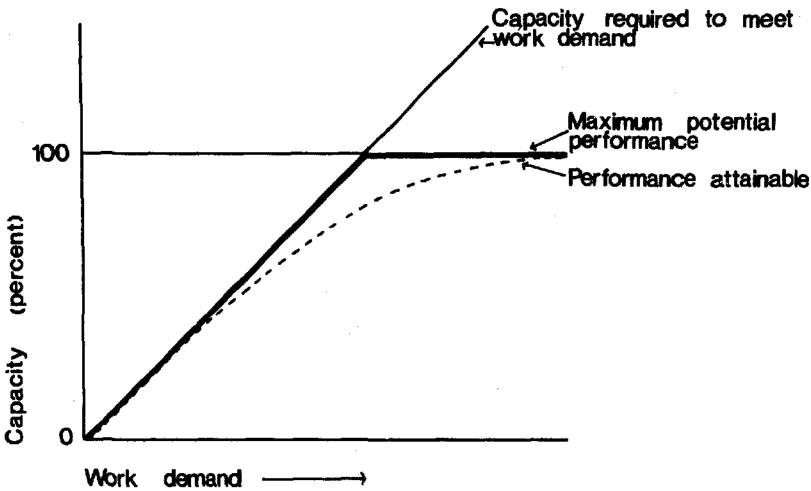

Figure 9.1 Relationship between performance, capacity, and demand. Owing to minor variations of capacity and demand in different cycles of a repeated task, the performance achieved is likely to follow the dotted line rather than show the sharp inflection of the double line.

Physical Capacities

A major recent contribution in this area is the symposium *The Aging Motor System,* edited by Mortimer, Pirozzolo, and Maletta (1982). The chapters cover muscular, biomechanical, neural, and functional changes with age in the motor system, and deal not only with general principles but include examinations of some special areas such as postural reflexes and Parkinson's and Alzheimer's diseases. Especially relevant in our present context is the chapter by Larsson (1982), which summarizes research showing loss with age of muscle units, especially fast-twitch fibers, changes in the metabolism of those that remain, and higher thresholds for neural excitation of muscle. It also considers possible causes of changes with age and methodological problems of studying them and summarizes recent research on functional changes. These latter fill out the picture sketched by pioneers from the 1920s onward which shows declines of from about 10 to 45 percent between the 20s and 60s in the maximum instantaneous force that can be exerted by a wide range of muscle groups, and declines also of maintained force and speed of movement. The relative decline may, however, depend on the way the tests are made. For example, Clarkson, Kroll, and Melchionda (1981) found that the maximum force that subjects exerted declined less with age when they were required to build up to it rapidly than when they did so more slowly. For our present purpose it should also be noted in passing that, while the maximum forces exerted by the older subjects were substantially less than by the younger, the rate at which tension built up to maximum, and thus the time taken to reach any given percentage of maximum, did not differ with age. It is important also to recognize that the performance of the organism as a whole, or of a large muscle group, may not be as great as would be predicted from the performances of component muscles or smaller groups in isolation. For instance, Yokomizo (1982) reported a study of muscular performance in which the age difference diminished progressively from tasks in which the whole arm was involved to those in which only the forearm, hand, or finger were used. This finding can, perhaps, be taken in conjunction with one by Ohtsuki (1981) that the maximum voluntary isometric strength of finger flexion was greater when the finger was working alone than when it was doing so as part of the whole hand. In other words, the capacity of the whole appears to be less than the sum of the capacities of its parts, implying some overall as well as local limitations, as well as that the former tends to be more severe than the latter for older people.

In line with the model of Figure 9.1, when intensive muscular work is performed over a period of time, decline with age in the various phases of energy metabolism results in either a reduction in the amount of work done—subjects reduce the demand they attempt to meet—or in more rapid exhaustion, although at submaximal rates of exertion age differences may be small (Åstrand, 1960; Ermini, 1976). As a corollary of this, Åstrand (1967) found that the levels of work-load spontaneously chosen by building workers tended to be about 40 percent of the maximum capacities of the individuals concerned. Also Cunningham, Rechnitzer, Pearce, and Donner (1982) found self-selected walking pace to be correlated with maximum oxygen uptake capacity. When maximum capacity is held constant, there is little or no association between such performances and age.

Changes of both aerobic power and maximum heart rate have been found to be small up to the age of about 50, but greater thereafter in both cross-sectional and longitudinal studies (Drinkwater, Horvath, and Wells, 1975; Plowman, Drinkwater, and Horvath, 1979).

Sensory Capacities

Research on sensory and perceptual capacities up to the mid-1970s has been reviewed, for vision by Fozard, Wolf, Bell, McFarland, and Podolsky (1977), for hearing by Corso (1977), and for somaesthesis by Kenshalo (1977). Recent studies have again filled out the picture. In particular, as regards vision, the well-known decline of visual acuity with age in terms of the finest angular resolution possible is paralleled by a decline of dynamic acuity in the sense of the least perceptible movement (Hills 1975; Hills and Burg, 1977). Also the decline in stereopsis, resulting in a progressive loss after the 40s of ability to make fine judgments of distance within a range of a few feet from the eyes, is paralleled by a fall in the ability to locate sounds binaurally (Herman, Warren, and Wagener, 1977; Warren, Wagener, and Herman, 1978). In each sensory mode older people seem less able to integrate the slightly disparate signals from the paired sense organs into a unified perception of locality.

As regards other senses, Kleinman and Brodzinsky (1978) have confirmed earlier findings of difficulty among older subjects in identifying patterns by touch; and Kokman, Bossemeyer, and Williams (1978) have confirmed the lack of change with age for proprioceptive sensitivity.

Reaction Times as Indicators of Central Capacity

Physical and sensory capacities undoubtedly limit performance and determine changes with age in some tasks, but in most work and everyday activities the critical limitations are in the central processes of integrating sensory data with memory and in translating from perception to appropriate response. A powerful tool for studying these processes that has been increasingly used in recent years is the measurement of reaction times, which since the mid-1970s have provided some important new data and raised some challenging new problems for the understanding of aging.

Reaction times are normally measured from the onset of a signal until the initiation of a responding movement, so that they include the time taken by the sense organ to convert the signal to neural impulses, for these to travel to the brain, for the brain to recognize the signal and select the appropriate response, and for the neural impulses from the brain to initiate muscular action. It was recognized well before the mid-1970s that most of the reaction time was taken up with the central processes rather than the peripheral, and that it was to the central processes that one has to look when considering changes of reaction time with age (Welford, 1977a).

For simple reaction times when one simple action such as pressing or releasing a Morse key has to be made in response to one clear signal such as a light or sound, the changes with age are relatively small—the average increase from the 20s to the 60s reported in 11 studies was about 16 percent. Gottsdanker (1982) found changes of much less than 16 percent, but his subjects, like those of Galton (1899), who also found only small changes with age, were self-selected volunteers the older of whom were unlikely to have been a representative sample of their age-groups. Increase with age was greater—30 percent or more—if a larger or more powerful movement, which presumably loaded the motor side more heavily, had to be made, and the same was found when the signals were rendered unclear and therefore more difficult to discriminate (Simon and Pouraghabagher, 1978). The 18 percent increase appears therefore to be due to older subjects taking longer to effect the translation required from signal to response. This view is supported by the fact that the increase is greater when any of several kinds of complication are introduced into this translation.

The most thoroughly studied of these complications is that of choice reactions where two or more possible signals occur in irregular order, each to be responded to with its own corresponding response—for example, when there are several Morse keys in a row, each corresponding to one of a row of signal lights. All studies which have compared simple and choice reaction times have found the latter longer than the former and, with two exceptions, the difference has been found to be greater among older subjects. The exceptions are studies by Stern, Oster, and Newport (1980) and by Corpolongo and Salmon (1981), who found that the increase from the 20s to the 60s was equal for simple and two- or three-choice reaction times. Their results can be questioned, however, because the simple task was always given before the choice, so that differences between them were confounded with possible practice effects. The discrepancy between their results and previous ones does, nevertheless, deserve further investigation.

The essential difference between the simple and choice reaction tasks lies not only in the need to distinguish between signals and choose responses in the latter, but in the fact that when only one signal and response are involved, reaction can be prepared in advance more completely than when, right up to the moment the signal arrives, it is uncertain which it will be and which response will be required. The fact that reaction times in both simple and choice tasks rise with age implies that the decisions involved take longer for old people than for younger, but the greater rise with choice tasks may in part be due to older people being less able to prepare their reactions in advance. There is some evidence that this is so (Welford, 1977a, p. 473).

Times taken for both discrimination of signals and choice of response appear to increase with age, although which shows the greater change is in some doubt: Naylor (1973) found changes to be proportionately about equal in both, while Simon and Pouraghabagher (1978) found the former to change more than the latter. The amounts of the changes are likely to depend on precise details of the experimental tasks, and there seems to be room for considerably more research on the question of just what factors are important.

With clear signals, as in most reaction time experiments, the main difference with age in choice reactions seems to be in the translation from signals to responses. There is, however, conflicting evidence about the form of the increase. Most studies of choice reaction have been found to be expressible in terms of the equation

$$\text{Choice Reaction Time} = a + b \log N \qquad (1)$$

where N is the number of equiprobable choices and is equal to the number of alternative signal-response pairs (n) or to $n + 1$ according to details of the experimental arrangements (Welford, 1980a). With increasing n, the effect of age has sometimes been in b, indicating a proportionate increase of reaction time as the degree of choice became greater, but more often it has been in a, implying that the increase is by a constant amount regardless of degree of choice. Much of the data are covered by the generalization that the rise with age is mainly in a when the signals are exposed only briefly, but that substantial rises of b occur when exposures last until response begins. However, some cases have been reported in which the longer exposures were associated with a rise of a but little or none of b (Welford, 1977a, b; Larish and Stelmach 1982). Also Deupree and Simon (1963) and Tolin and Simon (1968) found no interaction between signal duration and age. A common feature of all of these apparently anomalous cases has been either that the task has been such that, when a signal appeared, subjects had at once to shift their attention to a target to which the response was to be directed, or that they have been observed often to look away from the signal toward their responding member. In such cases, although the signal remained until the response began, actual inspection of it was likely to have been brief. A similar explanation might apply to the finding by Rabbitt (1980) of cases in which a rise of b early in practice disappeared later and gave way to a rise of a only: after extensive practice it is likely that the time for which signals are inspected becomes shorter—a quick glance—even when they are available until response begins.

A possible explanation of how the observed age effects arise comes from a model of choice reaction times proposed by Smith (1980). The model takes account of the fact that the brain is spontaneously active so that signals from outside and from one part of the brain to another have to be detected against a background of random neural activity (neural "noise") and their effectiveness depends on the ratio of signal strength to noise level (Welford, 1977a, p. 453). Well-known changes in the sense organs and brain mean that signal strengths tend to decline with age, and there is some evidence that noise increases. Signal-to-noise ratio therefore tends to become lower with age. Smith's model proposes that

$$\text{Choice Reaction Time} = k \log \left(\mathrm{n} \frac{C}{E} + 1\right) \tag{2}$$

where E is the signal-to-noise ratio of the perceived signal which is mapped onto the responding mechanism, and C is the signal-to-noise ratio that has to be built up by E over time in the responding mechanism for a response to be triggered. One possible reason for an increase with the age of a rather than b in equation (1) can be seen by rewriting equation (2) as

$$\text{Choice Reaction Time} = \mathrm{K}(\log C - \log E) + \mathrm{K} \log\left(n + \frac{E}{C}\right) \tag{3}$$

$K(\log C - \log E)$ is constant for all degrees of choice and corresponds to a in equation (1), while $K \log[n + (E/C)]$ corresponds to $b \log N$ and rises with degree of choice. The effect of lowering E (or raising C as some authors have suggested happens) with age would be to increase $\log C - \log E$, and thus the intercept a, while the corresponding reduction of E/C would have only a small effect on the slope.

This does not in itself explain why rises of a tend to occur with brief exposures and of b with longer ones. However, it can be suggested that, with brief exposures, E cannot build up activation of response over time and so, if a response is to be triggered, C must be lowered. Doing so will result in an increase of errors. If E falls with age, the lowering of C must be correspondingly greater, leading to a greater increase of errors among older than among younger subjects, as observed by Vickers et al. (1972).

If this explanation is correct, it can account for the finding that complications of the relationships between signals and responses tend to increase b at all ages, but more among older people than among younger. Complications, by elaborating the mediating processes required to relate signals to responses, are likely to increase K, so that the effects of such complications and age would be multiplicative. Conversely, the reduction of mediating processes required as relationships became "built in" in the course of practice could account for Rabbitt's (1980) result already mentioned.

The model outlined implies that a powerful signal, even if brief, would trigger a response which was relatively little slowed with age. If so, it could perhaps provide an alternative explanation of the lack of interaction between signal duration and age found by Deupree and Simon (1963) and Tolin and Simon (1968). They dimmed the room lights during their experiments, and doing this would have made the signals relatively stronger than they would otherwise have been.

Relationships Between Signals and Responses. What are the complications of relationship between signals and responses which cause rises of b in equation (1)? Studies made in the 1950s pointed to two main types: first, spatial transpositions as when signal lights are at a distance from response keys, or are mirror-image reversed or rotated; and second, cases where a symbolic recoding is needed, as when signals are digits spoken or shown visually and responses are made by pressing the corresponding one of a row of keys (Welford, 1977a, pp. 478–485). Recently, however, Stern, Oster, and Newport (1980) have suggested that slowing in cases where a signal on the left has to be responded to with the right hand and vice versa is due to the fact that the signal comes to one hemisphere of the brain while the response is made from the other. This seems at best a very partial explanation. Studies not concerned with age have shown that the time to cross from one hemisphere to the other is short—a few milliseconds only—and far less than the effects they noted. Furthermore, several studies have been made with the hands crossed so that a signal on the left is responded to by pressing a key on the right but with the left hand, and vice versa. In these cases both signal and response are handled by the same hemisphere, yet the slowing is *greater* than if the hands are uncrossed and different hemispheres are therefore used (Welford, 1980a, p. 97). Again, mirror effects which reverse far and near rather than left and right impair performance especially among old people (Welford, 1958, pp. 129–135). Also, reversals within displays of signals on the same side and responded to with the same hand have a slowing effect (Welford, 1971). The interaction of the hemispheres in older people needs further exploration, but the evidence so far points to the importance of disturbance in the spatial relationships between signals and responses rather than to interhemispheric effects.

As regards symbolic recoding, studies by Corpolongo and Salmon (1981) and by Jordan and Rabbitt (1977) confirm and supplement the rather sparse previous data. Corpolongo and Salmon used a row of three response keys and compared: (a) signal lights corresponding in position to the keys, (b) signals consisting of digits 1, 2, or 3 all shown in the same position and responded to with the left, middle, and right keys, respectively, and (c) with 1, 2, or 3 of a row of signal lights instead of the digits. Jordan and Rabbitt used signal lights which could take six possible forms—the symbols + or − combined with either a green, amber, or red background. Three conditions were compared: (a) with two response keys, one for + and the other for − regardless of background color, (b) again with two keys one for green + or − and amber +, the other for red + or − and amber −, and (c) with six response keys each corresponding to one of the possible signals. The results of both studies are shown in Table 9.1 together with the most nearly comparable data from previous studies. Two points should be noted: first that complication of the relationships between signals and responses increased the difference between older and younger subjects disproportionately; second that with simpler relationships the older tend to be more accurate, but with the more complex less so, than the younger. A third and especially interesting result is shown in the last row of the table. Jordan and Rabbitt noted in their condition (b) that the older subjects became more accurate than the younger and that the difference between the age-groups in time taken was less during

Table 9.1
Effects on Reaction Times of Increasing Complexity of Relationship Between Signals and Responses. All Times in Milliseconds. Probability of Error per Response Shown in Brackets.

	Young	*Old*	*% Diff.*
Kay (see Welford, 1977a)			
Age-groups 25–35 and 65–72.			
a. Ten lights in row, ten keys in corresponding row above.	797 (0)	897 (0)	13 (0)
b. As (a), but keys 3 ft. away.	1,257 (0.140)	1,583 (0.080)	26 (−43)
c. As (b), but corresponding key had to be found by number on card above keys. Numbers in random order.	2,710 (0.065)	4,235 (0.155)	56 (138)
Birren, Reigel, & Morrison (1962)[a]			
Age-groups 18–33 and 60–80.			
a. Ten lights in row, ten keys in corresponding row above.	610	770	26
b. As (a), but lights and keys coded. Keys in random order.	1,530	2,431	59
Corpolongo & Salmon (1981)[a]			
Age-groups 20–30 and 60–70.			
For description of tasks see text.			
a. Least complex	570	740	30
b. More complex	40	840	31
c. Most complex	690	970	41
Jordan & Rabbitt (1977)			
Age-group means 20 and 69.			
For description of tasks see text.			
a. Least complex	531 (0.006)	582 (0.004)	10 (−33)
b. More complex	695 (0.006)	775 (0.024)	12 (300)
c. Most complex			
First 500 reactions	977 (0.007)	1,294 (0.013)	32 (86)
Last 500 of 2000 reactions	896 (0.005)	1,015 (0.03)	18 (−40)

[a]No data on errors provided.

the latter part of a run of 500 reactions. In their condition (c) they therefore took 2,000 readings and compared the first and last 500. It can be seen that the trends they noted in condition (b) emerged clearly. The question is, Would still further practice have made the difference of time between young and old proportionate or even absolute as found by Rabbitt (1980) for more straightforward choice reactions?

Effects of memory. Why do complex translations from signal to response make performance disproportionately slower and less accurate in older subjects? Rabbitt (1980) has pointed out that it cannot be due to slowing with age in a long chain of neurons between signal and response. Indeed Craik (1948) emphasized that reaction times cannot be regarded in this way but involve some kind of computation to arrive at a *decision.* It has often been suggested that such computations involve an element of memory and that this is an important and perhaps a sufficient cause of many age effects. Several different types of memory factor have been suggested, all of which may operate in different cases. We shall consider four briefly:

1. Complex translations are usually made according to some rule, and older people may have difficult in retaining the rule or applying it quickly and accurately. Perhaps in line with this are results by Plude and Hoyer (1981) using a card-sorting task in which cards bearing certain letters among others had to be separated from those which did not. They found that the difference with age in speed of sorting was greater when the target letters varied from pack to pack than when they were always the same and could presumably be learned thoroughly. It is only fair to comment, however, that the variation might be confusing quite apart from any memory factor and also that some rules, such as that of Jordan and Rabbitt's task (b) in Table 9.1, introduce conflicts of criteria between different features of the signals. The relationships between memory and confusion in such tasks deserve further investigation.

2. Rabbitt (1979a) has suggested that difficulty may sometimes lie in rapid recovery of data from long-term memory. Both he and Fozard (1981) have described series of experiments showing that recovery of items from memory is slower in older than in younger subjects. As regards primary memory, the slowing is slight. It is much greater for secondary memory probably, in part at least, because data have been less well recorded there. Recovery is, however, slower even from very long-term memory of thoroughly well-learned material. In the present context, one of Rabbitt's experiments will serve to illustrate his suggestion. Subjects were required to respond as quickly as possible when either of two target letters (e.g., A or B) appeared in a display of eight letters on a cathode ray screen. The letters might be in upper- or lower-case. The appearance of the display was preceded by a warning which might be either of the critical letters or an asterisk. Reactions were quicker by both young and old subjects when the warning letter and the target letter were identical, but only by young subjects if the warning letter was uppercase and the target letter lowercase or vice versa. Rabbitt argued that effecting the translation from one case to the other involved the additional task of recovering the alternative form from long-term memory, and that the longer time taken to do this was the reason for the slower reactions by the older subjects.

3. Many complex translations involve holding data briefly while other data are obtained: for instance, a single digit on a display while seeking the same digit on a keyboard differently arranged. There is considerable evidence (see Welford, 1958) that in such cases subjects, especially older ones, tend to forget the earlier data while seeking the later: it seems as if switching attention is liable to delete memory of what was attended to immediately before. A recent study by Wright (1981) using a mental arithmetic task in which two-digit and three-digit numbers had to be added, and also a task in which problems had to be solved while retaining strings of digits, found that while young as well as old were affected as the tasks became more demanding, the speed or accuracy or both of older subjects suffered more. She suggests that performance depends upon the extent to which the tasks load working memory and that the capacity of working memory declines with age.

4. When in a series of signals one occurs substantially more often than others, reactions to the frequent signal tend to be faster than to the infrequent: the subjects appear to bias their attention and readiness so as to respond quickly to the frequent signal (Welford, 1980a). Griew (1962), using a task in which one signal appeared in 75 percent of the trials and the other in 25 percent, found, as is usual in such tasks, that reactions to the more frequent signal became faster, and to the less frequent slower, over a series of trials, and that the changes were greater for older than for younger subjects, so that age differences were larger for the less frequent signals. Biasing one's attention to the more frequent source is an efficient strategy in the sense that it minimizes average reaction time, and it seemed as if the older subjects were either better at detecting the relative frequencies of the signals or, perhaps more likely, readier to adopt the more efficient strategy. However, Rabbitt and Vyas (1980), in an experiment in which one of four signals appeared in 52 percent of trials and each of the others in 16 percent, found the opposite result—the difference with age was larger for the more frequent signals. The difference between these two results is probably due to the fact that in Griew's experiment the signals followed each other at random so that the more frequent could be identified by a greater number of repetitions, whereas in Rabbitt and Vyas' experiment no signal was ever repeated immediately and, in order to detect bias, subjects would have had to remember more than one back in the series. Older subjects find it extremely difficult to do this (Kirchner, 1958) probably because, as in (3), the shift of attention to each new signal tends to delete memory of those that have gone before. Somewhat similar results, indicating that older subjects are less influenced by events further back in a chain, have been found by Maule and Sanford (1980) using a simulated industrial plant monitoring task, and confirm earlier work by them. Explanation in terms of failure to detect bias can, however, be questioned because in both Rabbitt and Vyas' and in Maule and Sanford's experiments the older subjects were afterwards able to report that they were aware of the fact that some signals were more frequent than others. Their problem seems to have been in using this knowledge to guide their moment-to-moment responding. The problem could, however, still perhaps be due to failure to take account of items more than one back in the series: it would mean that older subjects, despite their recognition of unequal frequencies, were unduly dependent on what had gone on immediately before, because that was all they could remember in detail.

Two further points about reaction time and age will be considered briefly.

Serial Effects. A considerable number of experiments not concerned with age have shown that, in a series, reaction times to repeated signals differ from those to others. The evidence is somewhat conflicting, but in most tasks where there are two simple signals and two simple corresponding responses, and where each signal is well separated in time from the previous response, different (or as they are termed "alternate") signals are reacted to faster than repeated signals. As the number of signals increases or the interval between a signal and the previous response becomes shorter, or if the signals or the translation between them and responses are complex, or after extensive practice, the advantage to alternate signals gives way to an advantage to repeated ones—the so-called repetition effect. Kirby (1980), who has reviewed these effects, has shown that no one factor can account for them all, but that some of the repetition effect must be attributed to an after-effect of a signal and response, "priming" the system in such a way as to facilitate reaction to a similar signal immediately following.

With relatively long intervals—say 1.5 sec or more—between signals, any facilitating after-effects would be likely to have dissipated and, indeed, it has been found that for both young and older subjects reaction times are commonly shorter to alternate than to repeated signals. These "alternation effects" are presumably due to expectations and can be manipulated by instructions or by biasing the frequencies of repetitions and alternations in a series. They appear not to differ with age (Fozard, Thomas, and Waugh 1976). They tend, however, to give way to repetition effects when the intervals between signals are short so that facilitating after-effects could still be operating when the next signal arrives.

Since neural after-effects tend to lengthen with age (see Welford, 1965), it has seemed a reasonable hypothesis that such facilitating effects might be specially favorable to older people so that repetition effects would be greater in older subjects. Results from two sets of experiments given in Table 9.2 show that this increase was not found. When the interval from the end of one response to the onset of the next signal (response-signal interval or RSI) was 2 sec, the percentage rise of reaction time with age was about equal for repetitions and alternations. When it was short (0 or 40 msec) the percentage rise was greater for repetitions than for alternations.

The present author (Welford, 1977b) found evidence which suggested that the repeated signals were somewhat less "insis-

Table 9.2
Examples of Repetition and Alternation Effects. All Times in Milliseconds.

	Response-Stimulus Interval	*Reaction Times*		
		Young	*Old*	*% Diff.*
Welford (1977b)				
Age-groups 17–26 and 67–87				
a. Two lights each with corresponding key				
Repetitions	2,000	332	416	25
Alternations		276	349	26
Repetitions	0	353	524	48
Alternations		361	466	29
b. Eight lights with corresponding keys				
Repetitions	0	573	749	31
Alternations		662	830	25
Jordan & Rabbitt (1977)				
Tasks and subjects as in Table 9.1				
a. Repetitions	40	478	544	14
Alternations		577	617	7
b. Repetitions	40	565	659	17
Alternations		745	819	10
c. First 500 reactions				
Repetitions	40	609	836	37
Alternations		1,051	1,386	32
Last 500 of 2,000 reactions				
Repetitions	40	582	709	22
Alternations		914	1,076	18

tent" and so were perceived a little more slowly than alternate ones and that this resulted in attention during a brief period—perhaps 100 to 150 msec—after the end of a response being captured by monitoring the completion of the response. During such time, the new signal could not be dealt with. The slowing appeared to be a little greater among older subjects so that their attention was more frequently captured by monitoring and their dealing with the next signal consequently more often slowed. It is consistent with this general picture that Rabbitt and Vyas (1980) found that with extensive practice—4,000 reactions as opposed to 200 to 500—older subjects come to show greater repetition effects than younger: the percentage rise with age for repetitions became *less* than for alternations. It is known that the time taken up by the monitoring of responses tends to diminish with practice (Welford, 1980b). Well-practiced older subjects might, therefore, not monitor their responses any more frequently than young subjects. If so, an increased facilitating effect with age when a previous response is repeated would have the opportunity to show. An alternative possibility, not mutually exclusive with the foregoing, is that older subjects' improvement with practice is for some reason greater for repetitions than for alternations.

Errors. Until recently, errors made in reaction time tasks were seldom reported. Interest in errors has arisen because of the finding that speed and accuracy are often compensatory in the sense that as speed increases errors become more frequent, and vice versa. The form of the relationship has been discussed by Salthouse (1979), who has shown that although older people tend to move in the direction of accuracy rather than speed, this is not the sole explanation of their slowness. What the compensatory relationship does mean is that no valid assessments of the meaning of reaction times, or comparisons between groups such as younger and older, can be made without taking errors into account, and that for this reason most previous research is inadequate and needs to be repeated.

Meanwhile, as we have seen in Table 9.1, there are characteristic variations with age in numbers of errors made and in the types of task and circumstance in which they increase or decrease. The study of errors in relation to age is as yet far from adequately developed. However, a significant attempt to define landmarks has been made by Rabbitt (1979b), who gathered the results of several experiments to show that older subjects were often able to detect and correct errors as readily and quickly as younger. He suggests, however, that older people do not adjust their speed as accurately as younger so as to avoid errors without becoming unnecessarily slow. We might add that when memory factors are operating, speed and accuracy are likely to cease to be compensatory because any slowing increases the load on memory and thus increases the chance of error due to failure of memory. What are probably examples of this have already been noted in discussion of Table 9.1.

Graded Movement

Several principles similar to those which apply to reaction times apply also to the execution of movement. Thus the time taken to make movements reflects the degree of control required rather than the time taken for muscles to contract, and limitations with age are normally in the speed of control. This has been expressed in a number of formulas, of which the best fitting appears to be

$$\text{Movement time} = K \log \left(\frac{A + \frac{1}{2}W}{W}\right)$$

where A is the distance from the starting point to the center of the scatter of repeated shots in a target, and W is a measure of the scatter—approximately four standard deviations (Welford, 1968; Welford, Norris, and Shock, 1969). The increase of time with age is slight for very simple movements, and greater for complex ones, and there is again a compensatory relationship between speed and accuracy. Little research in this area seems to have been done in relation to age during the 1970s. A study by Kochar (1979), however, is significant as attempting to relate the approach of equation (4) to industrial problems of older workers.

The early work on movement was limited by lack of apparatus for detailed recording, and the more sophisticated apparatus now available which enables the precise end points and times taken by individual movements in a series to be recorded suggests that the time is ripe for a fresh round of research. Studies which appear to be especially needed are:

1. Older people appear to have difficulty in overlapping the execution of movements with the making of decisions about subsequent movements. How far is this due to the tendency we have already seen for them to have their attention captured by monitoring of movement, and how far is such monitoring needed to ensure accuracy?

2. What are the effects of long practice on the speed and accuracy of movements by people of different ages? Studies of writing—a well-practiced task—have shown that speed declines with age among those in clerical grades (La Riviere & Simonson, 1965). Does this finding imply an effect of greater practice?

3. Movement tends to be initiated in phase with tremor (Travis, 1929). Is there a tie-up between tremor and the speed and accuracy of movement with age?

4. Of more practical interest is a question which arises from the fact that movements are not made to particular extents but to points in space defined in terms of a schema of the body, of limbs in relation to the body, and of both in relation to surrounding space. It is obvious that many factors contribute to this schema, such as sensory data which form the basis of distance perception, motor factors, and proprioceptive data concerned with the control of movement, and memory functions which enable data to be integrated over time. A pioneering study by Szafran (see Welford, 1958, p. 185) found that time taken to locate targets at different points around the body, especially when blindfolded, rose progressively from the 30s to the 50s, indicating some impairment of the body–space schema at later ages. A similar implication is contained in results by Jordan (1978), who compared the accuracy of groups of subjects with average ages of 20.6 and 70.2 years when attempting to reproduce the extent of a given movement or, more correctly, to locate a point in space judged to be an equivalent distance from a given starting point. He found that accuracy was markedly lower for older subjects when they could see what they were doing, but there was no significant difference between the age-groups when blindfolded, although both were less accurate. If the above two studies are taken together, it appears that older subjects rely less on vision than younger, and that when deprived of vision, the body–space image is as accurate as that of younger subjects, although the older take longer to use the body–space image to guide movement. All this is in line with findings noted earlier that vision becomes poorer in several ways while proprioception seems little impaired with age. These studies are of interest in relation to what appear to be minor clumsinesses which seem commonly to afflict older people, causing them to hit against objects or to damage things they are handling by knocking them against others. Just what are the

factors involved in such clumsiness, and how might it be avoided?

Causes of Slowing with Age

Possible reasons for slowing of performance with age have been surveyed recently by Birren, Woods, and Williams (1979, 1980). They note that slowness is one of the most widespread and characteristic changes in old age and affects many cognitive and memory processes as well as psychomotor performance. It is clear that slowing is plausibly regarded as affecting all the stages from sensory input to motor output (Salthouse and Somberg, 1982a). Its doing so must, however, be subject to the provisos discussed in connection with Figure 9.1. In other words, although any stage may cause slowing in certain circumstances, limitation of performance at any particular task is usually due to one stage only which is fully loaded, while other stages, working well within their capacities, contribute little or nothing to limitation.

Birren, Woods, and Williams consider slowing with age in relation to physical factors including circulatory capacity and other factors affecting the supply of oxygen to the brain, neurologic factors such as brain damage and degeneration, disease conditions such as parkinsonism, depression, and psychoses, the possible role played by physical fitness in preventing or minimizing slowing, and psychological factors such as caution. The present author (Welford, 1977c) has suggested that all of these factors can be understood in terms of reduced signal-to-noise ratios in older people in that all tend either to reduce signal levels—for instance, circulatory deficiency in the brain; or to increase neural noise levels—as seems to occur in psychoses; or, like caution, to be compensatory by allowing time for signals to be accumulated.

There is need for a great deal of further thought and research to test ideas formulated in these terms. Such work seems the more worthwhile since it appears possible in principle to distinguish between reductions of signal and increases of noise. Gregory (1974) pointed out that a person whose internal neural noise level was high should be *less* affected by external sources of noise. By contrast they should be more affected by any diminution or degeneration of signals.

EFFECTS OF EXERCISE

The effects on the motor system of physical fitness and exercise in relation to age have been surveyed by Spirduso (1982) with regard to both man and laboratory animals, and to muscular, circulatory, and neural mechanisms.

The fact that physical exercise can increase muscular strength, cardiovascular effectiveness, and vital capacity has suggested to many that declines in these respects and consequent limitations on motor performance that may come with age could be postponed or prevented by programs of physical exercise for the elderly. Such programs might not only improve performance but prevent the vicious circle whereby an older person ceases to be as active as formerly, then because of this, muscles atrophy and exercise becomes painful, leading to further decrease of activity and perhaps eventually to becoming housebound or bedridden, with the consequent lack of stimulation, resulting in mental deterioration.

Many studies made of people in their 60s and beyond have shown that regimens of exercise severe enough to increase fitness can improve their physical condition. For example, Liemohn (1975) found that 15 minutes of exercise 3 days per week for 6 weeks increased muscular strength, and Stamford (1972) and Niinimas and Shepard (1978a, b) found that exercise rising from 6 to 20 minutes per day for 5 days per week over 12 weeks improved cardiovascular function. Both Suominen, Heikkinen, and Parkatti (1977) and Sidney and Shephard (1977a, b) found that following a severe regimen, older subjects showed increased aerobic capacity and activity, and the latter found indications that this carried over to produce a more active lifestyle, although, surprisingly, the subject rating of the effort required for any given level of physical work was not reduced. Studies using less vigorous or shorter regimens have shown little effect, although subjects' attitudes may have been improved and they have said they feel fitter (Clark, Wade, Massey, and Van Dyke 1975; Gutman, Herbert, and Brown, 1977).

With few exceptions, studies in this area have lacked young control groups so that it is not possible to say that the exercise brings older subjects to equality with younger: indeed it is obvious that in most cases it does not. Subjects have also often been atypical of their age-group, being either inmates of a hospital or institution where they are unusually inactive, or self-selected persons who are unusually active. It is possible that those who exercise voluntarily at later ages differ from those who do not in ways other than physical fitness. For example, Hartung and Farge (1977) found that middle-aged joggers and runners were, on average, more intelligent, imaginative, reserved, self-sufficient, sober, shy, and forthright than the general population. It is an open question as to how far these characteristics are the result or the cause of their exercising. Three further observations fill out the picture. First, Durnin and Passmore (1967) noted that activity at later ages is correlated with activity in youth. Second, Webb, Urner, and McDaniels (1977), who studied a champion runner aged 77, found that, despite his continued activity, he showed some losses of physical capacity typical of older persons. Third, Goodrick (1974) found that mice who were exercised in an exercise wheel lived a little, but not very much, longer than those who were not. Exercise appears, therefore, to be of benefit in keeping older people in a sounder condition than they might otherwise be, but can only mitigate and not completely counter declines of physical capacity with age.

Physical Exercise and Mental Functioning

While physical fitness may remove some physical limitations on psychomotor performance, of more interest in the context of this review is the claim made in several studies that physical exercise can improve cognitive, decisional, and memory functions (e.g., Powell, 1974, 1975). Especially has exercise been associated with shortening of reaction time. For example, Spirduso (1975) compared subjects who were and were not active in sports in two age-groups, 20 to 30 and 50 to 70, using a reaction time apparatus which required subjects, when a signal light appeared, to lift the hand from a microswitch and move it to another corresponding to the light. She compared simple and three-choice times, separating in each case the time taken to release the first microswitch from the time taken to move from this to the indicated switch. The results are set out in Table 9.3, from which it can be seen that the release times of the active subjects were shorter than those of the inactive, especially among the older, while the movement times of both active groups were shorter than those of either inactive. The older active group was not, however, as fast as the younger active in the simple reactions, or as either younger group in the choice reactions. These results were confirmed by Spirduso and Clifford (1978).

In a further study by Clarkson and Kroll (1978), the results of which are also shown in Table 9.3, older active and inactive groups with ages from 55 to 79 were compared with younger ranging from 18 to 28. When a signal light appeared, subjects had to raise their heel from the ground and kick a corresponding target. Simple and three-choice reactions were again tested. For

Table 9.3
Relationships Between Activity and Reaction Times. All Times in Milliseconds.

	Active			*Inactive*		
	Young	*Old*	*% Diff.*	*Young*	*Old*	*% Diff.*
Spirduso (1975)						
Age ranges	20–30	50–70		20–30	50–70	
Simple reactions						
Release times	243	263	8.2	264	327	23.8
Movement times	137	149	8.8	181	250	38.1
Three-choice reactions						
Release times	287	317	10.5	303	355	17.2
Movement times	159	172	8.2	196	271	38.3
Clarkson & Kroll (1978)						
Mean ages	22.2	65.7		21.9	63.1	
Simple reactions						
Release times	211	247	17.1	222	273	23.0
Movement times	113	136	20.4	134	189	41.0
Three-choice reactions						
Release times	240	291	21.3	255	323	26.7
Movement times	117	146	24.8	142	193	35.9

both simple and choice reaction and movement times, the order was the same, with the old inactive slowest, followed by the old active, the young inactive, and the young active. The reaction times were further subdivided into premotor times before EMG indications of incipient muscle activity, and motor times required for the muscles to contract. The same pattern of results applied to both times.

Clearly in none of these studies did activity bring the older subjects to equality with the younger, although in all measures it brought them closer together both absolutely and proportionately.

Spirduso (1980) has provided an excellent review of her own and other studies and gives a valuable list of references. She recognizes that there are severe methodological shortcomings in most work done so far, because of the sampling problems already noted and also because in "before and after" studies of the effects of physical training, the "after" results are confounded with practice effects. These can be substantial even in such seemingly simple and straightforward tasks as reaction times (Welford, 1980a). We could add that studies have also failed to control adequately for errors, so that a shortening of reaction time associated with exercise might imply no more than a shift in the speed–accuracy balance. The need for such controls is the greater because of the finding that patellar reflexes show no change of either latency or motor time with age (Clarkson, 1978).

Why physical exercise should shorten reaction times and improve central functioning generally is not at present clear. One obvious possibility is that exercise, by increasing cardiovascular effectiveness, increases cerebral blood flow which in turn improves brain function. Some support for this view as regards age comes from the similarity of some age effects to those of lack of oxygen (McFarland, 1963). Another obvious possibility is that the neural activity accompanying exercise has an arousing effect. This seems likely as a short-term result: whether it has any long-term result is not certain, but it might perhaps encourage the more active lifestyle already mentioned as noted by Sidney and Shephard (1977a). If so, the relationship between exercise and the effectiveness of central functioning could be one in which moderate exercise leads to improvement, but severe, prolonged exercise leads to overarousal and thus to deterioration of performance. Such deterioration has already been shown for the effects of exercise over periods of up to 10 minutes (Cooper, 1973; Davey, 1973). Overarousal tends to speed performance but also to reduce accuracy. Since studies of reaction time in relation to exercise have failed to record errors, there is at present no way of knowing whether the overall effect in terms of both speed and accuracy has been an improvement or not.

Spirduso (1980, 1982) notes that "muscles have a trophic influence on the nerves that innervate them and upon other immediate central connections" and that this raises the possibility that muscular activity might have a direct trophic effect on central nervous system structures. Some evidence in favor of this view is perhaps contained in Nebes' (1978) finding that the difference of reaction time between groups of subjects aged 67.7 and 20.4 years was less for vocal than for manual reactions despite the fact that, since vocal reactions are normally slower than manual at all ages, their difference with age would have been expected to be greater. He argued that the vocal muscles have more continued use into old age than those concerned with moving the hand.

Batkin (1981) has gone further and assembled evidence that activity of brain cells tends to maintain their condition and extend their dendritic connections. Such trophic effects raise, of course, the important possibility that mental activity can itself help to maintain mental effectiveness as age advances. It was found many years ago that those who go in for stimulating mental pursuits at later ages tend to show better mental performance (Sorenson, 1930), but whether this was the cause or result of mental activity is not clear.

Experiments on giving extensive practice at a mental task—the Wechsler digit–symbol substitution task—have so far been disappointing in that, while both younger and older subjects have improved with practice, their performances have not come closer together (Beres and Baron, 1981; Erber, 1976; Grant, Storandt, and Botwinick, 1978). However, Batkin's thesis does not necessarily imply that practice would produce equality.

What it would seem to imply is that improvement should be generalized rather than confined to specific tasks. In this respect Beres and Baron found that training on the digit–symbol task did not generalize to digit span or to a matching task, but only to other digit–symbol codes, suggesting that the training effect was mainly due to improved strategies. It is perhaps inevitable that the most noticeable effects of any mental training should be on specific strategies, and that refined studies on a substantial scale would be needed to sort out these from generalized trophic effects.

LEARNING AND TRAINING

Practice effects have been noted by several of the authors whose work has already been discussed. In some studies, such as that of Jordan and Rabbitt (1977), older subjects' performance has improved with practice more than that of younger; in others, such as that of Wiegand and Ramella (1983), the reverse has been found. In several cases the relative effects of practice with age depend on the measures taken. For instance Anshel (1978), whose subjects moved an arm through an arc of 80° while blindfolded, found that a group with a mean age of 74.2 years made an average error of 24.0° in the first two trials, which fell to 4.92° in the nineteenth and twentieth. The corresponding errors for a group with a mean age of 23.4 years were 17.38° and 2.80°. The absolute decrease of error was thus greater for the older subjects. However, the final errors were 20.5 percent and 16.1 percent, respectively, of the initial errors, so that the proportionate improvement was greater for the younger subjects.

A further example comes from a mirror writing experiment by Szafran (see Welford 1958, 1980c, 1981). The absolute change of time taken from each trial to the next was about equal for younger and older subjects, but the older took longer for each trial so that, in terms of time, their improvement was slower, as shown in Figure 9.2. The plotting of time per trial against the square root of the total time taken in previous trials links learning to concepts of signal-to-noise ratio. The signal detection parameter *d′*, which is a measure of signal-to-noise

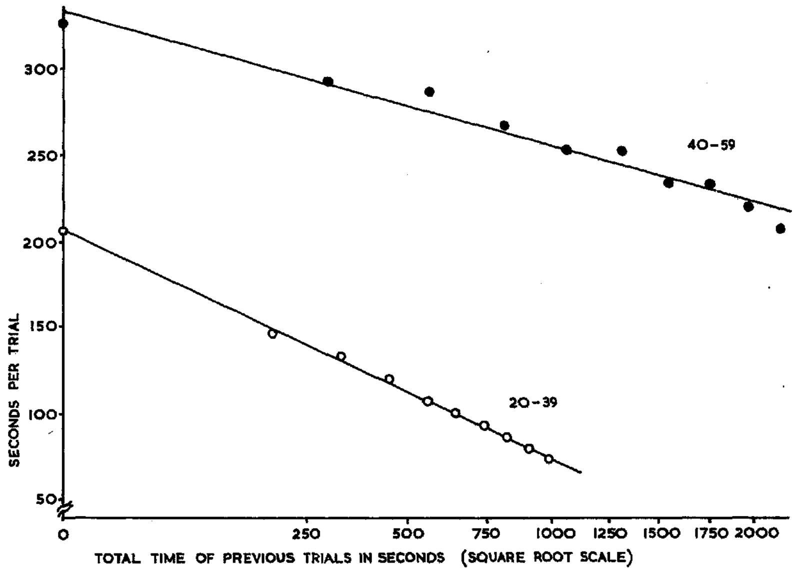

Figure 9.2 Times taken by two age-groups to write the digits 1–9 and X so that they appear normal when seen in a mirror. The subjects' hands were hidden from direct vision and could only be seen in the mirror.

ratio, has been found to increase linearly with the square root of the number of trials and probably with the time spent on any one trial. It is assumed that signal strength has to be accumulated until a critical level is reached when a response is triggered, and that this accumulation comes both from the time spent on any one trial and from what has been stored in memory from previous trials.

The conflicts regarding age effects in the evidence now available appear to make further research desirable. Little is likely to emerge, however, from simple measures of overall achievement: more detailed studies are needed along at least two lines. The first is to examine, in relation to age, some of the variables which have been shown to affect learning of psychomotor performance in general. An example of this is an experiment by Surburg (1976), who compared the effects of practice on a pursuit-rotor of groups aged 65 to 79 and 80 to 100, under conditions in which practice consisted of either actual performance, or half this and half "mental" practice, in which subjects thought about the task without performing it overtly. He found that the two conditions of practice were equally effective in both age-groups, and for both developing skill and retention as shown by a retest eight weeks later. Another example is an experiment by Weigand and Ramella (1983), who studied the effects of different conditions of giving information about accuracy of performance ("knowledge of results") between each trial and the next of a pursuit-reaction task, in which a key had to be pressed to coincide with the time at which a moving display reached a particular point. They found that delaying knowledge of results from 5 to 60 seconds after each trial did not affect the performance of groups with mean ages of 23.5 and 66.2, but that the older were more adversely affected than the younger by shortening the time from 3 to 0.5 seconds between giving knowledge of results and the signal for the next trial.

The second line of study needed stems from the fact that remarkably little is known about just what is learned during practice at psychomotor tasks (Welford, 1981). There is a need to discover what changes occur and whether they vary with age. An attempt by Salthouse and Somberg (1982b) to do this used a task consisting of a series of component operations which, in turn, involved signal detection, memory scanning, visual discrimination, and a pursuit reaction. They found that, for subjects aged 18 to 24 and 64 to 81, all these functions improved with practice, and that there was no evidence that older people performed the task differently from young. This is not surprising, as the components of the task gave little scope for variation of method and, since they were all independent of each other, there was no scope for difference in any overall strategy of performance such as that found by Brown (see Welford, 1958, p. 68) to occur with age.

It is difficult to maintain enthusiasm for long practice in the laboratory, and its effects are perhaps better studied in industry, especially in performance with machine tools where use of the various controls can be recorded, and the records can be supplemented by direct observation. Griew and Tucker (1958), in studies of this type, found differences in strategies of performance associated with age. There seems to be great potential in such studies for determining how strategies develop in the course of experience, and in relation to the age of trainees. As regards training in psychomotor skills, little appears to have been done in relation to age since the work of the Belbins in the 1950s and 1960s (Belbin, 1965, 1969). They have, however, published a further book which, although subjective in content, sets out a wealth of experience as a guide to future research workers (Belbin and Belbin, 1972).

THE PRESENT SITUATION

Pioneering research on aging up to the 1950s, especially in Britain, was to a very substantial extent on psychomotor performance with a view to eventual application in industry. Since that time the focus of interest seems to have swung rather to cognition and verbal or visual learning. The last few years, however, have seen a renewed interest in psychomotor performances, especially in reaction times and the effects of exercise. Both owe much to developments in research not specifically concerned with aging. Interest in exercise is understandable following the great expansion of research on performance in sport and athletics. Reaction times have come to be regarded as one of the most powerful psychophysical methods presently available. The one regret is that recent developments, especially in this latter field, have been almost entirely in pure research and that potential applications have not been exploited. The time seems ripe for more applied studies, not only for the practical usefulness they may have, but also because application is a valuable means of sorting out priorities and preventing pure research from becoming excessively concerned with minutiae.

Of the areas in which practical application might be made, perhaps the most obvious still is industry. The knowledge we already have about sensory-motor performance is obviously relevant to certain types of industrial task. Many tasks which at present cause difficulty for older people and lead to their moving to other jobs in their fifties could be sustained to later ages if certain modifications were made, either to machinery used or to working conditions, so as to remove key sources of difficulty. Such modifications would be likely to benefit young as well as old, but especially the latter. Their urgency is the greater with the introduction of legislation raising mandatory retirement ages. Suggestions about what could be done were made many years ago (Griew, 1964), but have, as yet, hardly been implemented.

Better recognized are the potentialities of physical exercise for preventing physical deterioration, and possibly improving mental condition, in old age. Principles are becoming clear, and application of them under controlled conditions seems likely to yield valuable further insight into means of preserving mobility and activity in older people. The possibility that, by analogous principles, mental exercise might prevent mental deterioration is an exciting prospect which needs to be explored much more than it has been so far.

Perhaps, however, the greatest potentiality for applied psychological research in gerontology at present lies in the field of training. In view of the interest of psychologists ever since the turn of the century in learning and memory, research on training in relation to age is sadly lacking. The reason is not far to seek. Present studies of learning and memory are a classic example of research which has become overconcerned with details. A sustained attempt to extend the work of the Belbins, which was mentioned earlier, and to formulate effective methods of training older people not only could lead to a major advance in gerontology with important geriatric implications but could be a valuable corrective and guide to general psychological studies of learning and memory.

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