Salivary Gland Function and Aging: A Model for Studying the Interaction of Aging and Systemic Disease

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ABSTRACT: This review describes an approach to examining the interaction of aging and systemic disease on a key aspect of oral physiology, salivation. The approach requires several steps: defining general health, and a specific physiological function, at different ages; defining a disease of interest and the influence of the disease on the specific physiological function; and determining if the disease can affect performance of the physiological function with increased age.

KEY WORDS: geriatrics, salivation, oral health, Sjögren's syndrome.

I. INTRODUCTION

Over the past 150 years, the average human life expectancy at birth has nearly doubled (Olshansky et al., 1990). As a result, it is anticipated that by the year 2020 all industrialized countries in the developed world will have ~20% of their population age 65 or older (Brody and Miles, 1990). These trends have led to an expanded interest in the biology of aging as well as an increased concern about the health-care needs of elderly individuals (Gibbons, 1990). Oral biological and oral health research activities associated with aging have concomitantly increased, reflecting the more general situation (e.g., Baum, 1981b; Beck, 1984; Holm-Pederson and Loe, 1986; Kiyak, 1988; Baum and Ship, 1990).

For many years, our laboratory has tried to understand the structural and functional status of oral tissues in different-aged, healthy men and women (e.g., Baum, 1981a; Weiffenbach et al., 1986; Sonies et al., 1989). Although such physiological studies are important, in isolation they provide an incomplete account of the aging oral cavity. To have a more complete picture, as well as to be able to anticipate the diagnostic and management needs of the elderly, it is necessary to understand the relationship between aging and disease. According to Fozard et al. (1990), "a scientific account of the process of aging requires a systematic approach to the role of disease in the explanation." Unfortunately, there is no clear-cut, accepted method to study the influence of aging and systemic disease (or its treatment) on physiology. It is the underlying purpose of this review to describe an approach to evaluate such interactions in oral physiological studies.

To understand the interplay among health, disease, and aging (the focus of this article), we suggest following at least five steps (Table 1): (1) defining general health at different ages; (2) defining a specific physiological function at different ages; (3) defining the disease, or disease treatment, of interest; (4) describing the influence
II. DEFINITION OF GENERAL HEALTH AT DIFFERENT AGES

The first component necessary to consider is aging, or becoming old. It is particularly important to recognize exactly what is meant when defining this term. Aging has been described in various ways, which can be either complementary or conflicting. Several descriptions will be discussed here; none is perfect, but all are useful conceptually.

Several years ago, Busse (1969) described two important distinguishing features of aging: primary aging, which reflects physiological processes that are dependent only on the passage of time, and secondary aging in which observed changes are related to the environment and to disease. As we discuss later, this definition remains valuable today and is central to our thesis and work.

A second and common descriptor of aging is the term “healthy.” This is actually defined by default (i.e., by the lack of disease evidence) (Fozard et al., 1990). In our work, we have chosen to define healthy in a practical manner — someone at any age who is not being treated for a systemic disease and who is not using prescription medication for the treatment of medical problems (e.g., Baum, 1981a, b; Tylenda et al., 1988; Sonies et al., 1989; Ship and Baum, 1990). It is important to note that study of such research subjects represents an almost ideal situation. Often it is not possible for investigators to evaluate truly healthy persons, rather individuals are studied who may present with certain conditions or diseases. To such a study group, one can apply the concept of clinical cleanup (Shock et al., 1984). This is “the process of identifying and excluding subjects with (such) conditions or diseases that might influence the values of a variable under study, or of excluding certain data points . . . ” (Shock et al., 1984).

A third adjective, widely applied to aging but seldom defined precisely, is “normal.” Often normal is used synonymously with healthy. Rather than equate normal with healthy, we choose to consider normal as a statistical concept, like a normal distribution (Figure 1), with the entire elder population categorized according to their health status. Thus, there are a small number of individuals who are systemically healthy and display physiological conditions influenced mainly by the passage of time (i.e., primary aging). Most individuals experience disease that can be controlled by therapy and therefore can be considered to undergo secondary aging. A small number of people are medically debilitated and present with a functional status that is predominantly a reflection of their extremely poor health.

A fourth description of aging is provided by Rowe and Kahn (1987). They define two types of normal (i.e., healthy) aging: “successful” and “usual.” These authors suggest that the effects of the aging process itself can be exaggerated by environmental factors and that the modifying effects of diet, exercise, personal habits, and psychosocial factors have been underestimated (Rowe and Kahn, 1987). Within this category of normal (healthy) aging, a distinction is made between usual aging, in which extrinsic factors heighten the effects of aging alone, and successful aging, in which extrinsic factors play a neutral or positive role. Only recently have researchers attempted to distinguish between age- and disease-
related findings. However, Rowe and Kahn (1987) argue that the heterogeneity seen among older people in the nondiseased group has been neglected. Some healthy older individuals perform at a level equivalent to that seen among younger subjects, whereas others do not. They explain this heterogeneity by invoking extrinsic influences that lead to usual aging (i.e., the lower functional levels).

Our focus has been directed to subjects exhibiting primary and secondary aging, in part because many of the outcome variables that are required for analysis using the criteria established by Rowe and Kahn (1987) have not been available in our studies. Furthermore, these variables may not be appropriate for many oral functions during aging as we will discuss. In addition, we have not considered the status of severely compromised elderly people. At any given time, however, the percentage of elderly persons who are debilitated (e.g., residing in nursing homes or homebound) is small (5 to 10%). Also, at a practical level, interpreting results of studies of debilitated people is extremely difficult because their functional status is a reflection of many complex interactions. Thus, we have restricted our consideration here and in our studies to older people who exhibit primary and secondary aging.

III. DEFINITION OF A PHYSIOLOGICAL FUNCTION

A. Salivary Function

The next step is to define the physiological function of interest in general and across the human lifespan. Saliva plays a central role in maintaining oral homeostasis (Mandel, 1989). A detailed description of the function of saliva is well beyond the purpose of this review. However, a few important considerations require mention. The salivary system consists of three major pairs of salivary glands, parotid and submandibular/sublingual (referred to as submandibular in this review), and thousands of minor salivary glands distributed throughout the oral cavity. These glands secrete basally (generally considered a protective secretion) and on stimulation (to facilitate alimentation). Salivary fluid contains water, electrolytes, and exocrine proteins with specific functions in the oral cavity. Saliva plays a central role in the protection of all hard and soft oral tissues and allows proper alimentation and phonation. Among the key specific functions mediated by salivary components are dental remineralization, antimicrobial action, lubrication, mucosal repair, and buffering. Patients with sal-
ivary gland diseases or disorders provide clear examples of the necessary role that saliva plays in oral physiology. Such patients present with several problems, reflecting significant local and systemic risk. These may include rampant caries, oral infections (e.g., candidiasis), dysphagia and dysphonia, mucosal ulcerations, and considerable subjective discomfort (e.g., dryness, burning, altered taste).

B. Salivary Function at Different Ages

Once a physiological process is generally defined, it is necessary to understand if it is affected by growing old. Of particular importance is which descriptive definition of aging is used in evaluating the performance of the physiological function at different ages. Early reports indicated that there were marked reductions in salivary gland performance in elderly individuals (e.g., Meyer and Necheles, 1940; Grad, 1954). This, in conjunction with descriptive morphological studies that showed parallel “age-related” changes in salivary parenchymal tissue, created significant concern (Andrew, 1952). However, many of the early studies used infirm and medicated subjects, individuals who therefore would not currently qualify as participants in studies of healthy or primary aging according to definitions described previously.

In the discussion that immediately follows we will review “modern” data on saliva production and aging. We only consider reports on gland secretions, however, and do not discuss studies of whole saliva. Whole saliva is the mixed fluid of the mouth, and contains in addition to gland secretions, food debris, desquamated epithelial cells, serum, sputum, bacteria, and their products. It is difficult to evaluate whole saliva fluid and its components to draw conclusions about individual gland function.

In 1981, publications from two studies using different-aged healthy persons reported no changes in citrate-stimulated parotid flow rates (Figure 2, Baum, 1981a; Chauncy et al., 1981). Both studies involved large numbers of nondiseased subjects and were cross-sectional in design (i.e., examined different-aged persons at the same time). These findings have subsequently been reproduced by others (e.g., Gandara et al., 1985; Tylenda et al., 1988). Importantly, a recent 10-year longitudinal study (examining the same persons over a given time interval) also showed no reduction in stimulated parotid flow rate with increased age (Ship and Baum, 1990). Furthermore, two other studies have examined basal, unstimulated parotid secretion with a cross-sectional design. Both Heft and Baum (1984) and Niedermieier et al. (1989) demonstrated similar functional levels in healthy persons across the human lifespan. Thus, there is a considerable and uniform body of data to show that parotid gland fluid secretion remains stable with age.

Studies of submandibular gland secretions are less frequent in number and not as universal in agreement. For example, there are only two studies that have reported cross-sectional data on submandibular gland flow rates in different-aged persons. Pederson et al. (1985) showed markedly lower values for both unstimulated and stimulated submandibular flow rates in older, generally healthy persons. Conversely, Tylenda et al. (1988) observed no statistically significant differences in these secretions across the lifespan despite a slight trend in that direction for males. It is not clear why these two studies have yielded different results. Obviously, no firm conclusion about the functional status of submandibular glands can be presently made and must await further examination.

Finally, there have been a few studies of secretion rates from minor salivary glands. There appear to be no general age-related alterations in fluid output. Gandara et al. (1985) did demonstrate a significant reduction in labial minor salivary gland flow rates in subjects older than age 59 when compared with their younger counterparts. More recently, publications from Niedermieier and colleagues have indicated a stable level of fluid production from palatine glands across the human lifespan (Niedermieier and Huber, 1989; Niedermieier et al., 1989). It is not clear whether these results represent true differences in the types of minor glands studied (labial, palatine) or differences between the two studies as seen with submandibular glands.

Considerably less research has been conducted on the composition of saliva in older persons, and all modern reports have used parotid
secretions. The findings are consistent across studies. First, some modest differences have been reported in several electrolyte values (e.g., changes in sodium but not potassium (Baum et al., 1984; Chauncey et al., 1981). More importantly, there have been no observed changes in exocrine protein levels (e.g., Aguirre et al., 1987; Baum et al., 1982; Fox et al., 1987). Indeed, for a large number of specific, functionally relevant components (including amylase, secretory IgA, anionic proline-rich proteins, lactoferrin, and lysozyme), no reductions in salivary concentrations have been seen between different age groups.

An additional and important observation from all of these discussed salivary gland functional studies is that the measures considered (flow rates, concentrations) generally show similar levels of variability in different-aged persons. Older individuals are often considered to present with greater physiologic heterogeneity than younger persons (see previous discussion). This apparently is not true for salivary physiology (e.g., Figure 2). Although it has not been specifically examined prospectively, salivary secretions typically show considerable variability (Ship et al., 1991), but it is not increased further with age.

In summary, when considering the available literature describing major and minor salivary gland function in healthy aging, it seems reasonable to suggest that if the rates of salivary secretion decline with age, the reductions are modest and may not affect all glands equivalently (Atkinson and Fox, 1992). Clinically significant declines in flow rates and complaints of oral dryness (xerostomia) are simply not a “normal” finding in an elderly population and should not be considered a natural sequela of becoming old.

Unlike the more modern studies of salivary gland function that dispute earlier claims of age-related decremental changes, recent studies of salivary gland structure have supported previous reports. These investigations have clearly attempted to separate aging effects on glands from disease effects by examining postmortem samples of tissue obtained from individuals without a history of salivary gland disease. Work by Waterhouse et al. (1973) and Scott and co-workers (e.g., Scott, 1977; Scott et al., 1987), using morphometric techniques has demonstrated clearly that the proportional volume of major gland tissue represented by acinar cells is reduced in a linear manner over the adult lifespan. This “lost” acinar component is replaced by fat, connective tissue and a proportional increase in ductal epithelial elements. For submandibular glands there is a 37% loss in acinar cells between ages 17 to 90, whereas for parotid glands there is a 32% loss. Studies by Scott (1980) and Drummond and

![FIGURE 2. The distribution of 2% citrate-stimulated parotid salivary flow rates in 95 healthy, different-aged men. Linear regression analysis gives r = 0.05, p >0.05. (From Baum, B. J.: J. Dent. Res. 60:1292–1296 (1981a). With permission.)](Image)
Chisholm (1984) have yielded similar observations for labial minor glands; across the human lifespan, there is approximately a 45% loss of acinar epithelial components. In aggregate, there is uniform agreement that primary aging is associated with the loss of a significant number of acinar cells from all types of human salivary glands.

These morphological observations are most important because acinar cells are the only cells within the salivary glands that are capable of fluid transport (Young and Van Lennep, 1979). Thus, there is a paradox of results because functional studies show no general age-related reductions in the fluid secretory capacity. A possible explanation for this has been suggested by Scott (1987), invoking the notion of reserve functional capacity. In this context, Scott (1987) has postulated that younger persons may actually possess an excess of acinar cells beyond that required for "normal" function. With increased age, he has suggested that this reserve is diminished and replaced by the nonsecretory components observed in morphometric studies. Thus, elders have lost their hypothesized reserve but still retain an adequate amount of acinar cell volume to maintain secretory ability (Figure 2). Although this forms a convenient explanation, there is still no unequivocal proof for the existence of a secretory reserve in salivary glands or for its diminution with increased age.

C. Age- and Disease-Related Differences between Parotid and Submandibular Flow Rates

As indicated earlier, although there is uniform agreement as to the stability of parotid gland function during aging, the same is not true for submandibular secretion. No consensus is yet possible based on data from the two published studies on this subject. In this respect, it is worth noting that submandibular gland function seems to be more vulnerable to various perturbations than is parotid gland function. For example, submandibular gland flow rates are significantly lower in patients with Sjögren's syndrome (Atkinson et al., 1990) and Alzheimer's disease (Ship et al., 1990), whereas a similar change is not seen in parotid gland secretions. Because there are multiple histologic, anatomic, neurologic, and physiologic differences between the parotid gland and the submandibular gland, the reported disease- and perhaps age-related differences may be due to many phenomena. We will now present some possible explanations of the apparently selective lability of submandibular gland function. These are based on neuroanatomical observations and neurotransmitter receptor considerations. We recognize that any explanation offered at this time, however, must be considered quite speculative. Rather, we wish only to make the reader aware of this tendency for differential gland dysfunction.

Salivary flow is regulated by the autonomic nervous system involving the interaction of the central nervous system neurotransmitters, receptors for these neurotransmitters that are located on the acinar cells, and the intracellular signal transduction process. In salivary glands, it is accepted that parasympathetic nerve stimulation leads to an increased volume of secreted saliva, whereas sympathetic nerve stimulation has greater effects on the salivary constituents, including protein content and composition (Baum, 1987). Although the parasympathetic nervous system is responsible for the bulk of salivary flow, the modulating effect of sympathetic stimulation, through signaling interactions (cross talk), has been reported for salivary glands (e.g., Horn et al., 1989; Watson et al., 1990) and may be a consideration.

There are well-documented age-related losses of neurons associated with the central nervous system, but they remain restricted to specific areas of the brain (Poirier and Finch, 1990). Although the aging central nervous system has a remarkable ability to compensate functionally for neuronal loss or atrophy with dendritic proliferation, it is possible that these localized changes may ultimately have physiological consequences (Poirier and Finch, 1990). It is well established that the parasympathetic fibers that initiate salivary secretion in the submandibular gland originate in the pons, whereas those innervating the parotid gland originate in the medulla (DeJong, 1967). Interestingly, structural abnormalities have been documented in the pons in patients with Alzheimer's disease, and nonmedicated patients with Alzheimer's show a selective submandib-
ular secretory dysfunction (Ship et al., 1990). Although the contribution of age- and disease-related autonomic and central nervous system changes to salivary secretion has not been studied directly, it seems that a relationship may exist and that a specific neuroanatomic change could conceivably cause a selective salivary gland dysfunction.

Salivary gland acinar cells have many types of cell surface neurotransmitters receptors, including those for substance P, adenosine, vasoactive intestinal polypeptide (VIP), as well as the more often studied alpha and beta adrenergic receptors and muscarinic receptors (e.g., Baum, 1987). A change in the number of receptors, or in the binding characteristics of the receptor, could result in an altered secretory response (Baum, 1987). Only muscarinic receptors are discussed here.

There are now considered to be five major genetic subtypes of muscarinic receptors, m1 through m5 (e.g., Bonner, 1989). These genes are expressed in a tissue-specific fashion and can mediate different cellular signaling events. In 1986 and 1987, Batra et al. reported that a single class of muscarinic acetylcholine binding sites (receptors) exists in the human parotid gland at a density (B\text{max}) of 507 and 456 fmol/mg protein with a dissociation constant (Kd) of 33 and 34 pM, respectively. Recently, Vanderheyden et al. (1990) reported the muscarinic acetylcholine receptor density of the human submandibular gland at 913 fmol/mg protein with a Kd of 118 pM. From these limited data, it appears that muscarinic receptors occur in roughly similar (i.e., <twofold differences) quantities in both the human parotid and submandibular glands. However, there is a three- to fourfold difference in the reported Kd values for the receptors between the two glands. The Kd is an important indicator of binding affinity, or strength of binding of a ligand (an agonist or antagonist), to a receptor. Therefore, despite rough similarities in the muscarinic receptor numbers found on the membranes from the two glands, there appear to be substantial differences in tissue-specific ligand-binding characteristics that conceivably could differentially affect fluid secretion.

A final point to mention concerns the distribution of muscarinic receptor subtypes in the two glands. Although the impression exists that both human glands exhibit only one subtype (m3), this has not been established unequivocally. Clearly, studies of animal salivary glands show that different distributions are possible. For example, Maeda et al. (1988) showed that the porcine submandibular gland expressed both m1 and m3 receptors. Recently, Dorje et al. (1991) showed that the rabbit submandibular gland contained a roughly equal number of immunologically recognized m1 and m3 gene products. Conversely, Dai et al. (1991) found evidence that the rat parotid gland expressed only the product of the m3 gene. Furthermore, these receptors were coupled to two second-messenger systems. They suggested that possible variations in the coupling of a receptor to a second-messenger system could result in tissue-specific characteristics. There are no specific data yet available on human salivary glands and their signal coupling processes.

In summary, there are some disease- and perhaps age-related discrepancies between parotid and submandibular gland flow rates. To date, there are no known explanations for these observations. We have presented some evidence to suggest that there may be specific mechanistic differences between functional components mediating secretion in the parotid and the submandibular glands. It is possible, although speculative, that differences such as those presented, in the presence of external influences (disease, medications, etc.) or the aging process, could be exaggerated and result in a selective dysfunction of the submandibular gland. Similarly, a selective dysfunction would result if the postulated secretory reserve capacity (as mentioned earlier) was different between parotid and submandibular glands (i.e., less for the submandibular).

IV. DEFINITION OF A SPECIFIC DISEASE

A. Disease Definitions

The next step in the process is to define the disease of interest, which also has inherent complications. As indicated earlier, the way in which disease is defined affects the definition of physiological aging; that is, healthy aging is defined be default. Of particular importance is the de-
cision of how many pathological symptoms must be present before a situation represents disease (Fozard et al., 1990). In Table 2, three distinct criteria for defining disease in salivary glands are listed. Vastly different disease prevalences can emerge, depending on the criterion chosen. Choosing a definition as broad as the presence of any pathological conditions is impractical and unhelpful. For example, considering the presence of a few lymphocytes in a salivary gland biopsy as indicative of early-stage Sjögren's syndrome would be inappropriate. If a cutoff point or a preset amount of pathological symptoms is selected, the information conveyed is more valuable. However, there is still a risk that either false-positive or false-negative impressions of disease can result. For instance, there are some healthy individuals who secrete saliva at a very low flow rate (e.g., <0.1 ml/5 min, Table 2) who have no evidence of impaired oral health (Ship et al., 1991). Their dental status, periodontal health, and mucosal integrity are equivalent to subjects with an order of magnitude higher salivary gland flow rates. Accordingly, they cannot be characterized as suffering from salivary gland disease. The final criterion, the development of clinical signs and symptoms, yields a practical outcome requiring therapeutic intervention. This criterion also offers some difficulty, because the elderly frequently present with signs and symptoms different from those of their younger counterparts (Gilbert and Minaker, 1990).

A further difficulty in defining a disease is that the definition can (and should) change with time because of the advance of knowledge. Therefore, the status of a function with respect to aging can also change. A classic example can be found by comparing the studies of cardiac output and age by Brandfonbrener et al. (1955) with those of Rodeheffer et al. (1984). A revised definition of what constituted heart disease between the first and second studies resulted in a different conclusion about the relationship of age with cardiac output. In 1955, Brandfonbrener et al. (1955) concluded that cardiac output decreased with increased age, whereas 29 years later, Rodeheffer et al. (1984) concluded that cardiac output was maintained in healthy elderly subjects.

### TABLE 2

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Outcomes</th>
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<tr>
<td>Presence of any pathological conditions</td>
<td>Lymphocytes in a salivary gland indicate early Sjögren's syndrome</td>
</tr>
<tr>
<td>Preset amount of pathological conditions</td>
<td>Flow rate &lt;0.1 ml/5 min indicates salivary hypofunction</td>
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<tr>
<td>Development of clinical signs and symptoms</td>
<td>Presence of xerostomia and rampant caries indicates salivary dysfunction</td>
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### B. Sjögren's Syndrome

There is no general way to define disease. An individual disease definition must be strict and specific, and investigators should recognize that its sensitivity may change. An excellent example of a systemic disease affecting oral health, and specifically salivary gland function, is primary Sjögren's syndrome. Primary Sjögren's syndrome is an autoimmune exocrinopathy affecting both salivary and lacrimal glands. The exact prevalence of the disease is unknown, but it has been estimated to affect up to 1 million individuals in the U.S., the majority of whom appear to be postmenopausal women. The etiology of primary Sjögren's syndrome is still unclear. It has been recognized for many years that a characteristic of the disease is the invasion of salivary and lacrimal parenchyma by lymphocytes. This phenomenon results in the destruction of acinar tissue (the sole site of fluid transport by the glands) by as yet unclear mechanisms. A useful definition of primary Sjögren's syndrome has evolved (Table 3). Studies on such well-defined patients, who have no other systemic disease and are free from medication use, are ideal to conduct because they provide as direct a description of disease effects as can be currently
TABLE 3
Criteria Used for Defining Primary Sjögren’s Syndrome*

Absence of connective tissue disease
Schirmer’s tear test <10-mm wetness/5 min in both eyes
>1 Focal lymphocytic infiltrate/4 mm² on minor salivary gland biopsy
At least 1 serological abnormality (e.g., antinuclear antibody, rheumatoid factor, anti-SSA)


obtained. In practice, however, they are difficult to achieve. It is highly unusual, particularly among middle-aged and elderly people, to find a sizeable cohort presenting with a single disease and not using medications. Indeed, there exist few well-controlled human studies of single-disease effects on oral functions.

V. DISEASE INTERACTION WITH A PHYSIOLOGICAL FUNCTION

Next, one should know how the function of interest is performed in people with the specific disease (in this example, primary Sjögren’s syndrome). Studies of Sjögren’s syndrome patients (median age, 57 years) who meet the rigorous criteria described earlier, reveal significant alterations in salivary gland function (Atkinson et al., 1990). Marked reductions in both unstimulated and stimulated parotid and submandibular salivary flow rates are observed. Even with such strict disease definition, however, substantial salivary functional heterogeneity can be seen. Different individuals may present with a complete absence of saliva or may secrete saliva at rates “generally considered” to fall within acceptable physiological levels. Furthermore, there are differences in specific gland effects. Thus Atkinson et al. (1990), as noted, have reported that both unstimulated and stimulated submandibular secretions are more dramatically impaired than those from the parotid gland. Also, tissue destruction does not appear limited to acinar cells because compositional changes, which suggest alterations in duct electrolyte resorption, occur as well (Atkinson et al., 1990).

Similar difficulties in assessing functional sequelae arise in clinical studies if the effects of treatments for a systemic disease are examined. There are some clear examples of iatrogenic effects on oral functions in any age group, for example, ionizing radiation on salivary secretion or cytotoxic chemotherapy on mucosal integrity. However, the effects of many treatment regimens are not as clear and are particularly difficult to study in the elderly. Older people frequently use more than one medication, and there are many treatments available for most diseases. Furthermore, drug metabolism is often altered in elderly people. All of this makes sorting out a possible disease effect from a therapy effect difficult.

VI. DISEASE INTERACTION WITH A PHYSIOLOGICAL FUNCTION AT DIFFERENT AGES

The essential and extremely difficult question that forms the central theme for this review is if aging and a defined disease (or treatment) process can interact to affect a specific function. For the example of salivary secretion, the answer is probably yes. As outlined previously, there are no general, significant age-related alterations in salivary acinar cell functional measures (flow rate, exocrine protein release) despite reduced acinar cell volume across the human lifespan. Although not unequivocally supported through experimental data, the possible explanation for these paradoxical findings suggested by Scott (1987) of the existence of a secretory reserve is helpful.

Conceptually, this can be visualized, as shown in Figure 3. The cylinder depicted indicates the level of acinar tissue required for physiological levels of saliva output. The region beyond the borders of the cylinder represents the reserve of salivary gland secretory capacity. As indicated, young adults contain a substantial excess of such tissue (the amount shown is speculative). With age, acinar cells are lost and replaced by fat and connective tissues, which are incapable of secreting fluid. Thus, older people deplete their secretory reserve. Despite these changes throughout the adult lifespan, adequate or young-adult
levels of secretory function could still be achieved as long as no further stress is placed on the system (an older person remains generally healthy). Most older adults, however, are not free from disease and are likely to be at increased risk from many nonphysiological or exogenous conditions (e.g., common pharmaceuticals, antineoplastic therapies, autoimmune disease) that could further reduce or compromise the gland's limited reserve capacity. Salivary glands of older people may be viewed as having an endogenously adequate functional capacity, but being vulnerable to external insults. Based on this hypothesis, one can postulate that any condition that could negatively affect salivary function would probably lead to a greater impairment in an older compared with a younger person. The lack of a secretory reserve in elderly people combined with negative exogenous influences (such as antidepressant drugs or X radiation) could render the gland unable to function satisfactorily, resulting in disastrous consequences. Therefore, such an interplay between aging and disease or treatment processes on this single oral function (salivation) can result in pleiotropic effects (rampant caries, dysphagia, sensory problems, infections, and so forth).

VII. CONCLUSIONS

The major purpose of clinical studies that describe oral physiology during aging, or describe the oral sequelae of a disease or its treatment, is to predict potential clinical problems. Hopefully, this information will lead to the development of early preventive or corrective therapies. The aging process presents multiple problems for the biomedical scientist (Gibbons, 1990). Tissues and their functions do not "age" at uniform rates and the effects of disease or therapy are often heterogeneous. To understand the interaction of aging and disease/treatment with oral functions, more data must be obtained. Although there is presently no well-established way to use such data to account for this interaction, we have attempted in this review to describe an approach that we find useful. We emphasize the focus on a single oral function and define, based on substantial research information, the performance of this function during health and during a specific disease or therapy. We believe that only by following such detailed and specific evaluations can an aggregate understanding of the process of growing old, which accounts for disease, be
achieved and practical benefits be realized in the care of the elderly.

REFERENCES


