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Guest Editorial

Nutrition and inflammation: the missing link between periodontal disease and systemic health in the frail elderly?

Focused Perspective on Ogawa et al., J Clin Periodontol 2006; 33: 312–316.

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Irrespective of their primary focus, all health professionals involved in the care of older adults share a common concern for the health, quality of life and functional independence of their patients. General and specialty dentists who are seeing growing numbers of older patients (Shay 2004) are and must be represented in clinical and research efforts designed to improve the health of this vulnerable population. Recent years have witnessed great advances in our ability to understand the aging process and to offer health care to the elderly that is evidence-based and effective. Several lessons learned through such research efforts are of particular relevance to the report presented by Ogawa et al. in this issue (Ogawa et al. 2006).

While many people remain remarkably robust through their eighth and ninth decades, others experience significant declines in physical and cognitive function. Chronic diseases, including those involving the oral cavity, may impose significant burdens (Petersen & Yamamoto 2005). Changes may occur even in seemingly robust individuals, and are not solely associated with the frail elderly. The 80-year old body represents a highly variable culmination of genetics, lifestyle, health habits, as well as physical and physiologic insults. As such, health care for older adults must be adapted to their highly individual needs, but above all it must move away from a single disease focus to a paradigm which incorporates the multiplicity of factors affecting an individual's health status (Sheiham & Watt 2000). The complex interplay of co-morbidity and altered physiologic function of multi-organ systems must also be taken into account in research trials.

Traditionally, the concept of frailty had been used as a mere clinical descriptor of enhanced vulnerability at advanced age. More recently, this term has been more clearly defined and has even been operationalized as a syndrome of physiologic changes including unintentional weight loss, feelings of exhaustion, weakness (grip strength), slow walking speed and low physical activity (Fried et al. 2001). There is no single blood test for frailty, but changes in immune and inflammatory markers have been found to predict future disability and mortality, independently of chronic disease (Fried et al. 2005). Interestingly, elevations in inflammatory markers also possess predictive value for future disability and mortality even in older adults who appear to be robust and remain living independently in the community without apparent functional dependence (Reuben et al, 2002). No single insult can explain frailty. According to our current understanding, this geriatric syndrome most likely involves multiple physiologic systems, with a vulnerable individual entering into a ''cycle of frailty'' that causes a downward and progressive spiral of increasing physical and cognitive dysfunction (Walston 2004).

Traditional approaches to health care have emphasized the distinct or unique aspects of each profession, leading to professional ultra-specialization and the fragmentation of clinical services. With these considerations in mind, it is perhaps not surprising that oral health is typically overlooked by physicians and that the worlds of dental and geriatric research have not yet fully intersected. Poor oral health care contributes to tooth loss, edentulism, oral pain syndromes, periodontal inflammation and oral mucosal diseases. However, the impact of these conditions extends beyond the oral cavity, affecting nutrition and causing chronic systemic inflammation. Research also suggests that poor oral health is linked to other chronic illnesses such as diabetes mellitus and cardiovascular disease. As both periodontitis and many other common co-morbid conditions are associated with systemic elevations of inflammatory mediators, it has been proposed that the benefits of aggressive dental care could extend beyond the oral cavity, for example, to improved diabetic control or to cardiovascular health. Now that poor nutrition and excessive inflammation have been linked to frailty, can poor oral health be

added to the list of conditions whereby frailty, disability and the future trajectory of aging experienced by individuals could potentially be modified?

The study by Ogawa et al. (2006) ''Association between Serum Albumin and Periodontal Disease in Community – dwelling Elderly'' is of interest to clinicians as its stated purpose was ''to evaluate the relationship between periodontal disease and general health status in community-dwelling elderly using serum albumin concentration as a criterion index of the severity of an underlying disease and nutrition status.'' While highlighting exciting opportunities for future inter-disciplinary research in this area, this work also illustrates the infancy of this area of research. This was a prevalence study of periodontal disease as measured by the percentage of LA 6+ mm sites documented on oral exam in community-dwelling elders. Health histories and functional status were obtained by questionnaire, body mass index (BMI) was calculated from height and weight, while albumin, C-reactive protein (CRP), total cholesterol, and IgG were measured. Unfortunately, a number of important issues remain unanswered. For example, future studies in this area will need to provide information on other conditions which could influence albumin or CRP levels. These include information: (1) co-morbid conditions that could contribute to a chronic inflammatory state; (2) medications that could affect serum markers (e.g. lipid lowering agents) or that could interfere with oral health; (3) weight and diet history and (4) dental history, including access to oral health care and routine self-care. The subjects were all community dwelling and sufficiently able-bodied to participate in the study. This does set them apart from institutionalized or homebound individuals. However, many people with chronic illness, including heart, renal or liver disease, live at home, yet are dependent on family support and/or other services to remain living independently. Finally, as this is a prevalence study, longitudinal outcome data would be needed to explain the clinical significance of the findings.

Ogawa et al. (2006) found that lower serum albumin levels correlated with lower levels of total protein, calcium, and total cholesterol and with higher levels of CRP . In other studies, hypoalbuminemia, hypolipidemia, and elevated levels of CRP have been described to be correlated with increased mortality in longitudinal studies of community dwelling older adults (Volpato et al. 2001, Don & Kaysen 2004). Hypoalbuminemia is a biological marker associated with poor nutritional status and chronic inflammation (Don & Kaysen 2004). Along with other indices of chronic inflammation (e.g. CRP, interleukin-6 (IL-6)), hypoalbuminemia has been a marker of frailty in older people (Volpato et al. 2001, Hazzard 2001, Reuben et al. 2002). The definition of hypoalbuminemia varies between studies. Some studies have used levels of <3.8 g/l (Volpato et al. 2001; Reuben et al. 2002), whereas another study chose a higher level of 4.3 g/l to define hypoalbuminemia (Schalk et al. 2004). Interestingly, studies with lower set levels found stronger correlation with frailty. The failure of the authors to establish significant levels of serum markers prior to the onset of the study weakens the final conclusions, as does a failure to control for the presence of many other co-morbid conditions also known to be associated with low albumin.

Care must be taken in drawing conclusions about relationships between periodontitis and inflammatory markers without adjusting for other co-morbid conditions known to be associated with such changes. For example, in a recent study Bretz et al. (2005) discovered that IL-6 levels were higher in individuals with more significant periodontal disease, yet this relationship no longer existed when the investigators controlled for smoking, diabetes mellitus and BMI. A positive relationship remained between periodontal disease and elevated TNF-α levels and between periodontal infection and raised CRP concentrations even when controlling for relevant co-morbid conditions (Bretz et al. 2005). In contrast, Loos et al. (2000) found that after controlling for smoking, BMI, hypertension, and cholesterol levels, periodontitis was still positively associated with IL-6 levels. Moreover, periodontal treatment has been shown to result in sustained decreases in peripheral IL-6 levels (D'Aiuto et al. 2004).

Elevations in inflammatory markers and declines in albumin predict declining function and mortality even among higher functioning, community-dwelling elderly adults(Corti et al. 1994, Reuben et al. 2002). For example, Reuben et al. showed the predictive value of serum markers of inflammation on 3 and 7 year mortality rates (Reuben et al. 2002). The authors noted that aside from known conditions associated with expression of inflammatory markers, ''it is quite possible that other unmeasured stimuli (e.g. chronic low-grade dental or periodontal infections) were also contributors''(Reuben et al. 2002). Future studies will need to examine the possibility that oral disease(s) unrecognized by non-dental health professionals represent an unappreciated contributor to elevations in peripheral inflammatory markers observed in many individuals in old age. An even greater challenge will be to define a possible role for inflammatory mediators derived from the oral cavity in the pathogenesis of frailty which might then justify potential frailty-intervention trials. These questions are crucial in developing a robust research agenda in frailty. The association between elevated inflammatory markers and frailty described in a number of population studies is clear and reproducible. Nevertheless, the nature of this relationship in terms of cause-and-effect, the specific mechanisms involved or even the direction of a possible relationship all remain to be defined.

Geriatric physicians must become more aware of the chronic burden imposed by poor oral health and periodontal disease in particular, while dentists and other related oral health professionals involved in the care of older individuals must consider the potentially beneficial, as well as adverse effects of their intervention on the global health of their patients. In order to better serve the frail elderly and those at risk of becoming frail, physicians and dentists must share knowledge and develop clinical research trials to study more closely the link of oral health and systemic health. From there, intervention programs, devised at the individual and public health level, can improve quality of life for the aging individual. Few other areas of health care will pose as great challenges as the development of comprehensive, coordinated and affordable health care for growing numbers of frail older individuals. In the United States, a major obstacle to the successful inclusion of the dental professions in this effort is the fact that Medicare provides nearly no coverage for dental care. Nevertheless, this scenario also provides the research community with unique opportunities for defining

the relationship between oral health, chronic disease burden, frailty, and mortality in old age. While traditional organ system-based approaches to health care and research have served us well in the past, new models of interdisciplinary collaborative partnerships will need to be developed if we are to succeed.

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