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EDITORIAL

Cytokines and Oral Disease

Studies on oral diseases and on oral secretions (e.g. saliva and gingival crevicular fluid) have not only contributed to rapid progress in our basic understanding of the oral mucosa but have also constituted the cornerstone for our general understanding of the mucosal immune system. Over 30 years ago, our group at the University of Alabama[1] and a group at Columbia University[2] reported on the presence of gamma globulin in human saliva. At this time, immunologists had just learned about the existence of IgA, a new class of immunoglobulin in the serum, and little was known of it in secretions or of its unique characteristics there.[3] Our hypothesis then was that the prevalence and severity of dental caries and periodontal diseases were regulated in part by antibodies in saliva.[1] Although we could not demonstrate such a relationship, we nevertheless stirred up interest in the immunology of oral health and diseases for the first time. Our original ideas seem rather naive in view of what we know about the complexity of the mucosal immune system, confirmed by repeated experiments of others including the most recent report by Hocini and associates.[4] Investigations on the mucosal immune system have expanded at an exponential pace ever since the pioneer work of Kraus and his group at the University of Alabama School of Dentistry. Mestecky and his group at the same institution are carrying on with this excellent work. Other active groups, particularly with respect to the oral biology, are those of Genco at the University of Buffalo and Lehner at Guy's Hospital in London, to name just two. Progress in understanding the mucosal immune system has been so rapid that a large portion of the immunology literature currently consists of reports on mucosal immunity and the mucosal immune response. International conferences such as the upcoming 8th International Congress of Mucosal Immunology to be held in San Diego, California in 1995 are being organized at frequent intervals.

The topic that has received the most attention in recent years is the role of lymphokines in oral diseases. The review paper in this issue by Sosroseno and associates at Gadjah Maha University in Indonesia entitled "The Interleukin Network in the Immunopathogenesis of Oral Diseases", is timely and gives a good overview of this fast growing area. The review is most interesting and the vast amount of literature cited verifies how extensively this area of research is being persued by clinicians and oral biologists. The review shows that investigations on the pathogenesis of periodontal diseases, in particular, have received considerable attention. There is no doubt now that cytokines are involved in these chronic inflammatory diseases of the gingival tissues, diseases that affect a significant proportion of the population in this part of the world. A large number of investigators have attempted to use the levels of various lymphokines, particularly in the gingival crevicular fluid (GCF), as markers or predictors of the severity and progression of active diseases or as indicators for the recurrence of disease after successful therapy. However, results should be interpreted with caution because lymphokines are generally present only in trace amounts and many cell types possess high affinity receptors for them. For example, I would question the relevance of elevated levels of free, unbound IL-1 in

GCF in periodontal disease. This does not mean that quantitation of free unbound lymphokines is of no value. I wish only to caution those who prematurely attribute too much significance to this phenomenon. Much more investigation is needed before a definitive conclusion can be reached on the issue. However, if sufficient data are eventually obtained which are consistent with the idea that imbalanced regulation of lymphokine production plays a role in the pathogenesis of periodontal diseases, then a regimen to correct the defect or the use of lymphokine antagonists may provide a novel approach to the treatment of these important oral diseases.

Lastly, I would like to mention that, just as studies of salivary antibodies have contributed to progress in understanding of the biology and function of the mucosal immune system, studies of $\gamma\delta$T cells in the gingival epithelium may also help to elucidate their undefined role in mucosal immunity. The recent paper by Swedish and Russian investigators on the presence of activated $\gamma\delta$T cells in inflamed gingiva suggests that this T cell phenotype may provide protection against bacterial infection through cytotoxicity directed at altered epithelial cells or through control of epithelial cell growth by secretion of regulatory lymphokines.[5] Results from such investigations could have broad implications. For example, defining the role of $\gamma\delta$T cells in localized oral disease may help elucidating the role of intraepithelial lymphocytes in the gastrointestinal tract and other organs.

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