Letters to the Editor

Response to Per Brandtzaeg's comments

We would like to comment on the criticism presented by Dr. *Per Brandtzaeg* in a letter to the Editor of Acta Odontologica Scandinavica (1974) regarding our study entitled: »Salivary IgA in Periodontal Disease» (*Lindström & Folke*, 1973). Dr. Brandtzaeg makes several remarks which are relevantly related to the validity of his own work as well as the work of others. An objective reply would therefore seem appropriate.

Firstly, it should be pointed out that our experimental work on the relationship between salivary IgA and periodontal disease was initiated in 1967 (*Lindström & Folke*, 1968). Consequently, we decided to express salivary IgA concentrations in mg/100 ml saliva which seemed to be in conformity with concurrent and subsequent investigations (*Mancini et al.*, 1965; *Lehner et al.*, 1967; *Claman*, 1967; *South*, 1968; *Lehner*, 1969; *LoGrippo et al.*, 1969; *Oon et al.*, 1973) including the work of *Brandtzaeg et al.* (1970). In retrospect, it admittedly seems desirable to quantitate IgA as μg secreted per minute. However, the interpretation of such data remains debatable as the rate of IgA secretion varies greatly between the left and the right parotid glands as well as from day to day while the concentrations (mg/100 ml) were fairly similar in simultaneously collected fluids from the right and the left glands (*Brandtzaeg et al.* 1970). *Salvaggio et al.* (1973) have subsequently reported variable salivary IgA levels in individual subjects on repeated samplings from the Stenson's duct. It should further be pointed out that there is no method available to accurately determine flow rates of whole saliva. The ideal way of quantitating salivary IgA remains, therefore, uncertain.

In addition, there are other factors which may influence the quantitation of salivary IgA. The selection of standards is particularly important. Salivary IgA molecules are heterogenous with respect to molecular size and antigenic determinants. For example, the radial diffusion technique of *Mancini et al.* (1965), which has been generally used for titration of salivary IgA, gives different results when different standards are used. Similarly, 11S salivary IgA, with its many antigenic determinants, requires a standardized antiserum for quantitative analysis.

Concentration of saliva and centrifugation for clearing whole saliva have been standard procedures for years and have also been adopted by *Brandtzaeg et al.* (1970). Nevertheless, the potential loss of immunoglobulins during these procedures should certainly not be ignored when determining the actual levels of salivary IgA. IgA adsorbtion to oral microorganisms should similarly be considered. So far, we are not aware of any investigation reporting on this very potential source of error for determining IgA levels in whole saliva.

Whether to analyze stimulated or unstimulated whole saliva can be debated *ad infinitum*. We arbitrarily chose to determine the relative saliva content of immunoglobulins during mastication. The use of wax (*Shillitoe & Lehner*, 1972; *Lindström & Folke*, 1973) and chewing gum (*Savilahti*, 1973) for secretory stimulation will admittedly adsorb organic materials (*Berg & Tiell*, 1969). Its relative influence on the outcome of the studies referred to above has not been determined. However, factors such as smoking may play a far more important role when studying salivary IgA responses as it has recently been demonstrated that smokers have significantly higher titers of salivary IgA than non-smokers (*Mandel et al.*, 1973).

Our data indicate increased levels of IgA in whole saliva obtained from subjects with advanced periodontal disease. *Brandtzaeg et al.* (1970) reported a similar elevation of IgA levels in unstimulated whole saliva from patients with periodontitis. However, in the discussion of their results, they invalidated their findings based on improper selection of subjects and unreliable estimation of flow rates. Yet, in Dr. *Brandtzaeg's* »Letter to the Editor», he refers to the same investigation and states that *Brandtzaeg et al.* (1970) found a significantly increased level of 11S IgA in whole saliva from patients with periodontitis.

When considering the insignificant differences between IgA levels in parotid saliva derived from normal and periodontally diseased patients, we believe it to be correct to propose the working hypothesis that the elevated levels of IgA in whole saliva from periodontally disease subjects is due to extraglandular secretion via deepened periodontal pockets. The absence or low levels of IgG in parotid saliva (*Tomasi & Zigelbaum*, 1963: *Claman et al.*, 1967; *Lindström & Folke*, 1973) and the elevated levels of IgG in whole saliva from patients with periodontal disease supports the contentions of increased extraglandular leakage of immunoglobulins in periodontally diseased patients.

Based on this information and available data referred to in our discussion (*Lindström & Folke*, 1973) and until the secretion of IgA by the submaxillary glands is clearly established, we support the supposition that locally produced IgA (gingival immunocytes) or serum derived IgA contributes to the increased IgA levels of whole saliva from individuals with advanced periodontal disease.

In conclusion, it should be explicitly stated that the secretion and biological significance of glandular and extraglandular IgA remain uncertain in reference to the initiation and progression of periodontal diseases.

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Folke D. Lindström
Medicinska Kliniken
Regionssjukhuset
Linköping
Sweden

Lars E. A. Folke
Division of Periodontology
School of Dentistry
University of Minnesota
Minneapolis, Minnesota