

Serum and Salivary Antibodies to Glucosyltransferase in Dental Caries in Man

RECENT evidence strongly suggests that dental caries is an infective disease caused predominantly by *Streptococcus mutans*¹⁻³. This organism has two major characteristics responsible for its cariogenicity: first, in the presence of fermentable carbohydrates it is capable of rapidly producing acid to below the pH required for dissolving enamel, and second, the organism produces glucosyltransferase which is a constitutive enzyme responsible for the synthesis of extracellular polysaccharides⁴. These polysaccharides are glucans which are commonly referred to in the literature as dextran; they form a major component of the bacterial plaque matrix and may be responsible for adhesion of the bacterial plaque to tooth enamel⁵.

We have investigated the immune response in man to a variety of antigens derived from *S. mutans*, to find a rational basis for immunization against caries. Estimation of immunoglobulins showed a significantly lower level of salivary IgA ($P < 0.01$) and a slightly higher level of serum IgA concentration in subjects with a high caries incidence as compared with those having a low caries experience⁶. Differential serum antibodies to cariogenic streptococci have been found in subjects with different caries experience using cell wall preparations and ultrasonicates of the bacteria^{7,8}. A correlation between serum antibodies to cell walls of cariogenic streptococci and the index of decayed, missing and filled teeth (DMF) has also been reported⁹.

In view of the importance of glucans in adhesion of dental bacterial plaque to tooth surfaces and their synthesis by glucosyltransferase, we explored the possibility that antibodies may be formed to this enzyme. Immunity to dental caries might be related to specific serum or salivary antibodies which inhibit the enzyme function. If this hypothesis were correct it would then be possible to immunize with a suitable enzyme preparation to elicit active immunity against the enzyme and this would prove to be an effective measure in preventing dental caries.

The usual method of indicating whether antibodies play a role in a disease is to establish a differential antibody level between patients and controls. In dental caries this approach is not applicable as virtually the entire population suffers or has suffered from caries, so that the level of antibodies must be related to the extent of the disease. A series of seventy-two subjects was divided into two groups: (a) a "passive" group consisting of thirty-seven subjects who were either caries free or had filled teeth not in need of any conservative treatment, and (b) an "active" group, each of whom had at least one carious lesion in addition to any treated caries. This division was intended to distinguish between the effects of past treated caries and present untreated caries on the antibody response.

Samples of serum and parotid saliva were collected from each subject and stored at -20°C for antibody assay. The enzyme was prepared from the supernatant of a culture of *S. mutans* and purified by hydroxylapatite chromatography¹⁰. Antibodies in both serum and parotid saliva were assayed by the passive haemagglutination technique. The starting dilution for serum was 1:10 and for saliva 1:2.

Serum antibodies were detected in all subjects, with titres ranging from 1:10 to 1:640. The passive group revealed a significant negative correlation between antibody titre and the DMF index ($P < 0.01$) so that as DMF increased the titre decreased, whereas a positive correlation was observed in the active group (Table 1). Different relationships were found with saliva; antibodies were present in titres of up to 1:64 and these showed a significant positive correlation in the passive group ($P < 0.05$). The salivary titres in the active group did not correlate with the DMF index and in only five of the

Table 1 Coefficients of Correlation between Antibody Titre to Glucosyltransferase and DMF Index

	Group	No. of subjects	Correlation coefficient	Significance <i>P</i>
Serum	Passive	37	-0.493	<0.01
	Active	35	+0.404	<0.02
Parotid saliva	Passive	32	+0.350	<0.05
	Active	31	-0.201	N.S.

thirty-one subjects was the titre greater than 1:4, as compared with fifteen of thirty-four in the passive group ($P < 0.02$).

The serum antibody titres in the passive group could be interpreted on the basis of a protective function in that the highest levels are found in those who have experienced least disease. A further interpretation of this relationship is that exposure to glucosyltransferase early in life leads to immunization and that, in those who respond with high antibody levels, little or no caries develops. In others the level developed may not be high enough to be protective as suggested by the subjects with a high DMF in this group. In the active group subjects with a DMF > 10 have a significantly raised titre, in comparison with those in the passive group ($P < 0.01$). It is possible that persons with a high incidence of caries have an immunological defect in that they are unable to sustain raised levels of antibody, which fall after caries is removed and the subject may again become susceptible to the disease. Detailed interpretation, however, must await the results of long term sequential immunological studies now in progress.

It has been suggested that repeated immunization is needed to achieve high levels of antibodies in secretions^{11,12}. Indeed, the positive correlation between salivary antibodies and the DMF in the passive group may reflect the cumulative caries experience, so that the titre is greatest in those who have had repeated carious attacks, and presumably repeated immunization with the enzyme. The low titres in the active group may indicate either that caries may appear when the salivary antibody level falls below a critical level, or that the titre becomes depressed following onset of caries.

In the oral cavity immunoglobulins from saliva are in direct contact with teeth, and immunoglobulins from serum are found in the crevicular fluid which surrounds the necks of the teeth¹³, so both sources of antibodies could participate in caries immunity. If antibodies to glucosyltransferase were to inhibit the enzyme activity then immunization with glucosyltransferase might prove a valuable measure in preventing dental caries.

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