Review Of Investigations Into The Biology Of Dental Caries Immunity

Gordon E. Green
DENTAL CARIES is a disease that afflicts the majority of human beings in this and many other countries. It is one of the costliest diseases, in money and impairment of health. In humans, it is assumed to have a bacterial origin, based partly on germ-free animal studies by Orland, Fitzgerald and Keyes, who showed that specific bacteria could produce caries in previously germ-free small animals. It is clearly impossible at this time to perform such studies in humans, and designation of cariogenic bacteria in humans is by implication. The human mouth contains very large numbers of bacteria of many species, which increases the difficulties in studying the oral activities of any species. Lactobacilli and streptococci have been most frequently incriminated, by reason of their metabolic capabilities and occasional association with the active disease.

The causative mechanisms of dental caries originate outside the body, and the site of the disease (tooth enamel) is the most inert and least susceptible to internal physiology of all the body tissues. The current theory of caries is that certain bacteria located in sheltered areas adjacent to tooth enamel metabolize food in the mouth (principally sugars) and produce acid by-products which dissolve the inorganic material in enamel. The causative bacteria do not invade body tissues, the clinical effects of the disease are caused simply by contact of the tissues with by-products of bacterial metabolism.

Thus dental caries is a peculiar bacterial disease, not susceptible to many of the body's defense mechanisms, and complicated by the varying bacterial population and varying foods available for their nutrition.

It is well known that the incidence of caries attack may be reduced in individuals by water fluoridation, good oral hygiene, and restriction of sugar consumption. Unfortunately, these measures do not absolutely prevent caries in most people, they only reduce the incidence to various extents. There are some adult humans who do not get tooth decay during most of their lives, without receiving any of the above treatments. These persons, about one per cent of the adults in the U. S., apparently

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have an inherent means of resistance, and are termed "caries-immune". This term seems applicable, despite the fact that the site of the disease is not available to circulating serum antibodies, which are usually associated with immunity to other bacterial diseases. These immune persons are able to withstand our civilized high-sugar diet, seldom see a dentist, often have sketchy oral hygiene habits, and yet display no evidence of dental caries whatever. Since none of the recognized external caries-reductive effects are responsible for their condition, it seems reasonable to assume the existence of some inherent physiologic anti-caries mechanisms. The investigations of the author are based simply on this assumption.

A number of studies have been made by other workers on differences between caries-immune and caries-susceptible humans. Immunes have been reported to have: lower salivary lactobacillus counts, higher salivary calcium levels, greater salivary carbon dioxide capacity, more of a proteolytic enzyme, higher salivary ammonia content, higher amounts of salivary protein, and more of a salivary chemical inhibitory to lactobacilli.

Since dental caries is a bacterial disease, the assumption at the commencement of this work was that an anti-caries mechanism in immunes was probably directed in part against some oral bacteria. A quantitative survey of oral bacteria in the saliva of caries-immune and susceptible humans was made. It was found that immune salivas only rarely contained any lactobacilli, and that this was the only significant difference in oral flora. Examining the effects of saliva on lactobacilli in vitro, it was found that immune saliva induced a peculiar dissociation in lactobacilli, was more inhibitory to acid production than susceptible saliva, and was capable of lysing lactobacillus cells in an unusual manner. These results directed attention to the chemistry and antibacterial effects of saliva.

A tangential investigation resulted from the observation that certain amounts of tryptophane in media could induce a rough to smooth dissociation of lactobacilli similar to that seen with immune saliva. A report by Turner and Crowell indicating an association of salivary tryptophane with the caries-free condition stimulated further interest. A chemical analysis for salivary tryptophane was developed, and it was found that immunes had significantly more salivary tryptophane than a similar group of caries-susceptible persons. The results were published. Salivary tryptophane is associated with caries immunity, but its true relationship to the condition is not yet known.

Another study was related to the effect of sodium fluoride on lactobacilli. The beneficial effect of sodium fluoride is attributed mostly to its effect on the acid-solubility of dental enamel. Whether fluoride has any effect on organisms in the mouth to reduce their cariogenic potential is yet debated. In the author's work, it was shown that cultures of lactobacilli, originally susceptible to sodium fluoride in the range of 3 to 7,000 ppm, could, during a year's time, develop resistance to concentrations in the range of 17 to 22,000 ppm. This indicated that the ability of lactobacilli to produce acid in the presence of fluoride could be increased by long-term
contact, and that water fluoridation probably had little effect on these members of the oral flora.

An investigation of salivary streptococci in immunes and susceptibles was begun, to examine theories proposed by Belding and Belding,\(^{21}\) that *Streptococcus salivarius* was associated with caries susceptibility. Quantitative examination of salivary streptococci in groups of immunes and susceptibles revealed no significant difference between the two groups. It was discovered that oral streptococci elaborated an extra-cellular by-product that inhibited the growth of oral lactobacilli in vitro. Also, this inhibitory process was favored to a greater extent by the presence of immune saliva than by susceptible saliva.\(^{22}\) This indicates the possibility of an indirect mechanism by which the numbers of lactobacilli could be reduced in immune mouths.

Dental caries is actually initiated by bacteria in plaques, which are aggregations of bacterial cells, living and dead, precipitated salivary components, and food material derived from the host's intake. Plaques may form on all surfaces of all teeth, adherent to dental enamel, are most conspicuous in areas protected from mechanical dislodgement, and are coherent masses. It is considered that the vital processes of sugar conversion to acid and consequent decalcification of enamel occur only in and under a developed plaque. Since, according to this concept, the bacteria responsible for dental caries must be present in plaques, and any antibacterial effect of immune saliva must be reflected in plaque development and composition, a comparison was made of plaque flora in immune and susceptible persons. This included mature plaques, and plaque accumulation on previously cleansed enamel surfaces. It was found that mature plaques in immunes had fewer of possible cariogenic bacteria, and that the process of plaque development showed that immune saliva had a depressing effect on accumulation of plaque flora when compared to developing susceptible plaques.\(^{23}\) These results are in agreement with those previously reported by Hemmens et al\(^{24}\) with respect to cariogenic plaques.

The claim that salivary lactobacilli are associated with the carious process has been mentioned, which seemed more interesting in view of the usual absence of these organisms in caries-immune saliva. The association of lactobacilli with dental caries has been discussed in many papers, some for,\(^{3,5,25-32}\) and some against.\(^{33,34}\) In the course of this investigation, the association of salivary lactobacilli and dental caries activity was examined in two age groups, children and young adults.\(^{25,26}\) In both groups it was found that quantitative estimates of salivary lactobacilli were not associated with caries activity during the following year. A corollary of the former of these,\(^{35}\) was the discovery that dental restoration of existing carious lesions reduced caries activity during the following year by 50 per cent. This indicates that restorative dentistry is as good a caries-preventive agent as anything acceptable today, and poses the suggestion that open, untreated carious lesions are conducive to development of other new lesions.

A description of the clinical and bacteriological aspects of caries immunity was published.\(^{37}\) The relative absence of lactobacilli in caries-immune persons is a pheno-
menon not clearly related to the role of salivary lactobacilli in caries-susceptible persons. However, the rarity of lactobacilli in saliva of caries immunes is certainly associated in some way with the immune state.

Detailed study of the lactobacillus-lytic material (termed immune factor) in caries-immune saliva continued. It was found that the protein was less soluble in salt solutions than serum gamma globulin, possessed an electrophoretic mobility on the order of serum beta globulin, and could be separated from whole saliva in a homogeneous fraction. It is heat-labile, and its properties resemble those of described human normal antibodies. It appeared that possibly the caries-immune human is really different from susceptible persons, in possessing an antibacterial salivary factor conferred by genetic background.

At the present time, most of the studies in this laboratory are related to salivary protein, salivary gland function, and further characterization of the biology of caries immunity. These studies are listed briefly as follows:

1. Study of technics of fractionation of saliva by chromatography, gel filtration and electrophoresis.
3. Study of blood types in immunes, and their ability to secrete blood antigens and antibodies in saliva.
4. Investigation of the relation of serum proteins to salivary proteins, by studying persons who are normal in comparison to patients with clinical agammaglobulinemia and hypergammaglobulinemia.
5. Study of familial relationships for the presence of caries immunity. This involves examination of available blood relations of several immune persons for dental condition, blood type and salivary composition. It is hoped this will yield information on the type of genetic transfer of caries immunity.
6. Continued study of the mechanisms by which the immune factor exerts its antibacterial effects.

Since caries-immune humans exhibit complete inherent resistance to a disease in which there is no similarly effective means of designed control, the major purpose of these investigations is to determine how the immune system works, and attempt to apply such information to development of an equally effective means of disease control for those persons who do not have it inherently.

REFERENCES


