Ciba Foundation Symposium

CARIES-RESISTANT TEETH

Edited by G. E. W. WOLSTENHOLME, O.B.E., F.R.C.P., F.I. Biol.

and

MAEVE O'CONNOR, B.A.

With 43 illustrations

1965

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CARIES-RESISTANT TEETH

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Printed in Great Britain

THE Ciba Foundation, a unique international institution, owes its inception to the generosity of CIBA Limited, Basle. However, being established under British trust law, it enjoys complete independence in practice and policy.

Under the guidance of its distinguished Trustees, the Foundation offers accommodation to scientists from all over the world at its home in Portland Place. Foremost in its activities is the organization of small conferences, the proceedings of which are published in book form in the manner of the present volume. The Foundation convenes many other informal discussions between research workers of different disciplines and different nationalities and each year invites an outstanding authority to deliver a special lecture. An exchange programme between French and British postgraduates is conducted and a library service is available. Furthermore, the Ciba Foundation attempts in every other way possible to aid scientists, whether they be Nobel Laureates or young graduates making their first original contribution to research.

The purpose of the Ciba Foundation, which is to promote international co-operation in medical and chemical research, is symbolized in the armorial bearings by five interlaced rings representing the continents, a black sacrificial cock (emblem of Aesculapius) holding a medical caduceus, and three regular hexagons for chemistry. Its domicile in London is indicated by the red sword of St. Paul and the British lion; the wyvern and the crozier, symbols associated with Basle, refer to the sponsoring firm located in this ancient Swiss town.

The Ciba Foundation

for the Promotion of International Co-operation in Medical and Chemical Research
41 PORTLAND PLACE, LONDON, W.1

Preface

IT is some six years since Professor M. A. Rushton first suggested that one of the Ciba Foundation's small international conferences might usefully provide an opportunity for thorough discussion of the problems of dental caries. At that time, however, the Foundation was already engaged in a heavy programme and the Director reluctantly decided that no such meeting could be included. Nevertheless, the idea stayed in mind and a few years later was stimulated afresh by a visit to the Foundation of Sir John Walsh of New Zealand. In the interval a considerable number of meetings on caries had been held elsewhere, and it was on the welcome advice of Professor Bertram Cohen that the particular subject of "Caries-Resistant Teeth" was chosen for discussion at the Foundation.

Professor Cohen and Professor Geoffrey Slack provided a wealth of information about research in this field, into which the Foundation was venturing for the first time, and we are greatly indebted to them both. Professor R. F. Sognnaes came from California to provide us with an outstanding example of chairmanship, invariably courteous but firm in shepherding the discussions along profitable lines, whilst his command of an elegant English was the envy of the native-born islanders present.

To these people, and to all the members of the symposium, the Ciba Foundation offers its warm appreciation. It is hoped that for them this book will revive pleasant memories and refresh and re-energize their investigations. For the far more numerous readers who could not be included in this small and comparatively informal symposium, we hope the book will provide a palatable form of encouragement to their work on this subject.

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Membership

Symposium on Caries-Resistant Teeth held 23rd–25th June, 1964

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O. Backer Dirks	Laboratory of Microbiology, University of Utrecht
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CHAIRMAN'S OPENING REMARKS

R. F. SOGNNAES

IF there is anything I have strong feelings about in academic life, it is the provision of ideal physical arrangements for sessions of education or communication such as this. The late Dr. Allen Gregg of the Rockefeller Foundation once said that if he knew the secret of the learning process, he would be willing to give up everything he had ever heard about educational systems, "including some very interesting ones". The process of communication is undoubtedly one of the biggest problems facing us today; hence it is probably inexcusable if we do not endeavour to make the physical situation as perfect as humanly possible. I salute the Ciba Foundation for having come as close to that as I have ever seen anywhere.

Further, I am sure I speak for my fellow "tooth enthusiasts" when I say how very delighted and, I might add, how proud we are, that a theme of dental science has come before this very distinguished Foundation, and we wish to thank Dr. Gordon Wolstenholme and his staff now for that opportunity.

Problems of the mouth, especially dental problems, have in some respects been a scientific "no-man's-land". It has been somewhat the opposite of the weather, in so far as very few talk about dental problems, at least in this kind of environment, whereas everybody sooner or later has to do something about them.

Recently, however, I think we can fairly say that problems of dental research have come before increasingly sophisticated bodies within the field of science. Firstly, I wish to draw attention to the very significant stimulation brought about here in England by the wonderfully-named organization known as the British

Bone and Tooth Society. I believe it was this very group which stimulated the first conference on the related subject of bone structure some years ago here at the Ciba Foundation (1956. *Ciba Found. Symp. Bone Structure and Metabolism.* London: Churchill). Secondly, we recognize that the British Division of the International Association for Dental Research has done a great deal to encourage this kind of research and this kind of reception. Thirdly, I think that other organizations in Europe, such as the O.R.C.A. group (Organisme Européen de Co-ordination des Recherches sur le Fluor et la Prophylaxie de la Carie Dentaire), soon to convene for its annual meeting in Norway, have also set high standards for research in this field.

On the other side of the ocean I have been personally very gratified by the fact that we have been able to bring subjects of dental research before the various general scientific organizations. Thus, the New York Academy of Science has published comprehensive monographs on such topics as metabolism of oral tissues and mineralization of bones and teeth. The annual Gordon Research Conferences on the structure and physiology of bones and teeth are now in their 12th year and many of you have attended and contributed both to the scientific and social communication. The American Association for the Advancement of Science has taken a great deal of interest in the field of dental science. Of the 75 monographs so far published on the basis of symposia organized by this multi-disciplinary organization, the Section on Dentistry has been responsible for seven. With regard to new periodicals dealing with dental and oral subjects, the *Archives of Oral Biology* has helped to set standards that undoubtedly have contributed to the Ciba Foundation's interest in our affairs.

For our specific topic, we have chosen what may seem to be a limited field within the total framework of dental science. Yet I think it will become very evident as soon as we begin our proceedings that while ours is a specialized subject, it is far from

narrow; it has broad implications, and it covers a considerable spectrum from the point of view of scientific topics and disciplines. New tools relating to ultrastructures, crystallography, microchemistry, histochemistry, and not least radiochemistry, have added greatly to our knowledge of the structure and behaviour of the highly specialized tissues of the teeth.

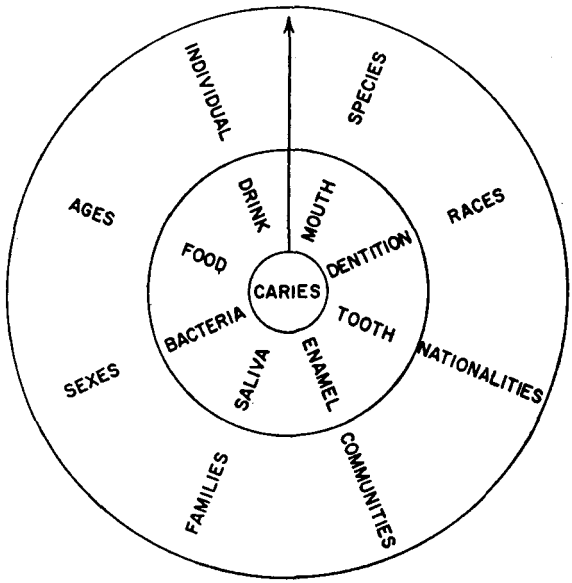

FIG. 1.

In the earlier history of biological science nearly all tools were directed to observations on cellular physiology, cellular pathology, blood circulation, nerve impulses and so forth, and dental enamel (this most highly specialized structure) was practically left out of the picture; it was less approachable by these means because enamel contains no cells, blood vessels, or nerves. But it now turns out within the new field of molecular science that enamel

is a biological substance somewhat uniquely suited for research with the tools of molecular biology. Physical chemists, biophysicists and even mathematicians are increasingly attracted to problems of biology generally. I am hopeful that with these new

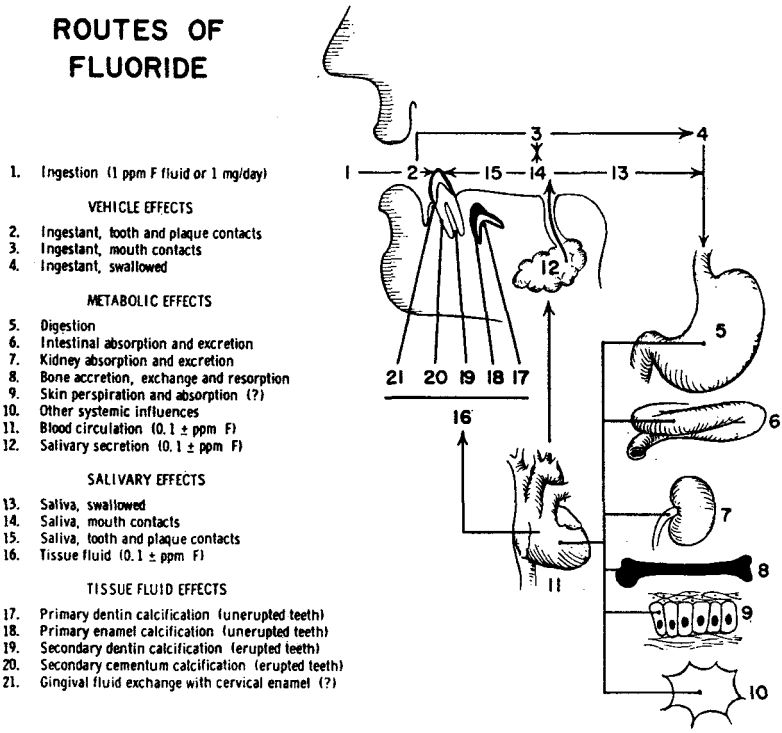

FIG. 2.

approaches we shall indeed develop a great deal of interest in our field among colleagues in other fields of science.

As I review the programme for this meeting, I congratulate those who have been principally responsible for the sequence of events, which I think is excellently planned. I am impressed by the few formal papers. This takes courage, but on the other hand

it places on all of us a responsibility to take full advantage of the ample time set aside for discussion.

For a general view of the topic I have taken the liberty of preparing two illustrations: Fig. 1 shows in the outer ring the subjects we will primarily deal with this morning, namely the caries distribution in different species, races, nationalities, communities, sexes, ages, and individuals. Within the individual (the middle ring of Fig. 1), we shall look at the mouth as a whole, at the dentition, and at the individual teeth, notably the enamel and its environment of saliva, bacteria, food and drink that enter the mouth, and directly relate to the central problem of caries.

The second point I wish to illustrate is that even if we examine a very specific element that has a bearing on the caries problem, we shall find that it is not necessarily a limited one; on the contrary there may be involved problems of general systemic, as well as of local environmental influences. Thus, in trying to follow the fate of the fluoride trace element taken into the mouth (Fig. 2), it is interesting that some 21 interactions may be involved: after fluoride in drinking water is taken into the mouth it first acts on the tooth surfaces as a sort of topical application; secondly it enters into interaction with the environment of the mouth; then, after being swallowed, its ultimate fate depends on its action in the stomach, in the intestines, certainly in the kidney, where a great deal is excreted, in the bones, where it is built in and exchanged, in the skin in terms of perspiration and possibly in terms of uptake (from the bath tub or from baby's urine). Next, when fluoride enters the general circulation, it reaches the salivary secretion, again interacting with the environment of the mouth, and serving as a milder but continuous topical application. Meanwhile, other circulating fluoride, through the tissue fluids, reaches the developing dentine and enamel by way of the dental papilla and enamel organ, and reaches the erupted tooth by way of the pulpal and periodontal blood supply. Finally (Route No. 21 in Fig. 2), I am proposing that some fluoride from connective tissue fluid may

seep out through the gingival crevice and again provide an additional topical application on the enamel that covers the gingival or cervical area of the teeth.

But let me not get ahead of our story. Besides, my 15 minutes are up. We shall now proceed with discussions ranging from human communities to the microcosmos of dental plaques, from gross morphology to crystal ultrastructure, from whole food to trace elements of nutrition.

To do so we have brought together talents representing many disciplines from many lands. Thus, I hope that we shall live up to the Ciba Foundation's purpose of promoting international co-operation in medical and chemical research.

THE SIGNIFICANCE OF EPIDEMIOLOGICAL STUDIES IN RELATION TO CARIES RESISTANCE

G. N. DAVIES

University of Queensland Dental College, Brisbane, Australia

THE F.D.I. Special Commission on Oral and Dental Statistics defines *Caries Resistance* as "the term used to describe the inherent or acquired capacity of the hard tooth structure to remain unaffected by dental caries" (Baume, 1962). This definition is unsatisfactory for several reasons. Since it specifies hard tooth structure it is in effect a definition of caries-resistant teeth. But resistance to caries depends not only on intrinsic factors affecting the teeth themselves; it depends also on extrinsic factors in the immediate external environment of the teeth. Furthermore, the process of dental caries is very slow, whereas many factors which affect the resistance of a person to caries vary in intensity from day to day and even at different times of the same day.

A person can be regarded as resistant to caries if he has had no caries experience. He can also be regarded as resistant if he has less caries experience, or develops fewer new carious lesions in a stated interval of time, than his peers of the same race, age and sex. The epidemiologist measures the presence or absence of dental caries in groups of people and looks for factors pertaining to the teeth and their environment which might account for differences in prevalence or incidence between groups of people. From his results he may infer that certain *people* are resistant to caries and certain people are susceptible to caries. But he does not actually measure resistance or susceptibility of the teeth themselves. Present methods make it impossible for him to do this in any

absolute sense. People whose teeth have a low resistance to caries may have no caries experience because the environmental attacking agents are of low intensity or because protective factors in the immediate external environment of the teeth are stronger than the agent factors.

Another difficulty in relating epidemiological data to the resistance of teeth is that present methods of clinical diagnosis make it impossible to detect caries reliably until the process has reached a relatively advanced stage.

A further difficulty in interpretation of epidemiological data arises from the fact that many of the host and environmental factors which may affect resistance to caries are closely related (Fig. 1). Some of these factors influence resistance to caries by affecting the teeth, others by affecting the environment of the teeth. It is also possible that many of the other known variables are related to a single determining factor which has not been recognized as yet.

HOST FACTORS IN RESISTANCE TO CARIES

Cross-sectional epidemiological studies have shown that the prevalence of caries increases with *age* but the rate of increase, which varies from one *ethnic group* to another, tends to slow down in adult life, especially between 25 and 35 years of age (Hollander and Dunning, 1939). However, in some countries where the prevalence of caries is low there is a negligible increase after the initial lesions are established (Barretto *et al.*, 1953; Afonsky, 1951). These data have been interpreted as indicating that resistance to caries increases with age.

This hypothesis may be true but data of this type do not confirm it. Better data can be obtained from longitudinal studies in which the same individuals are followed over an extended period of time. Studies of this type in children (Boyd and Cheyne, 1946; Moore, 1936) have shown that there is a wide variation in the

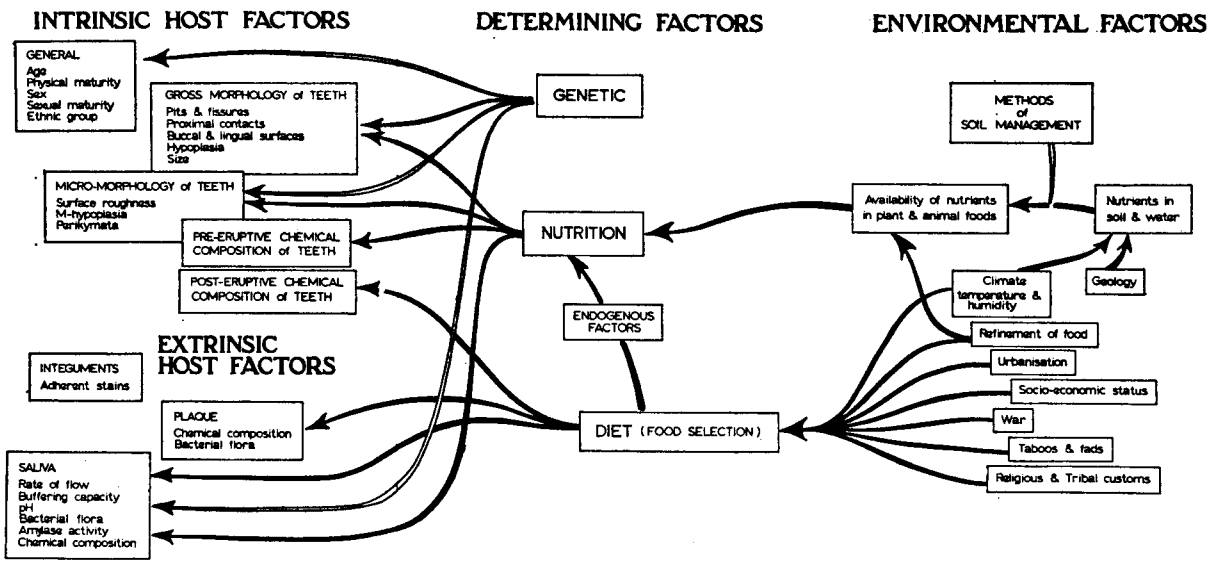

FIG.. 1. Interrelationship of major factors in resistance to caries.

incidence of caries not only between individuals but also between different observation periods. However, Parfitt and Parfitt (1954) found that in 21 out of 60 patients there was an unvaried incidence of new cavities from eruption to ages ranging from 20 to 46 years. Comparatively few patients showed a decreased incidence with age. In his longitudinal study of 50 boys and 50 girls between the ages of nine and 15 years, Backer Dirks (1961) showed that when the incidence of dental caries is determined for specific types of tooth surfaces there is a marked variation with age. When allowance is made for the post-eruptive age of teeth there is little difference between the incidence of pit and fissure lesions in first and second permanent molars. Premolars, however, have a much lower incidence of pit and fissure lesions even when allowance is made for post-eruptive age. For proximal lesions Backer Dirks' data demonstrate that adjacent proximal surfaces show greater similarity in caries incidence than do the two proximal surfaces of the same tooth. This is most marked in first premolars. The disparity between mesial and distal surfaces was greater in lower first premolars than in upper first premolars and this applied both to the prevalence of cavities at any specific age and to the incidence of new lesions between any two ages.

Similar observations in deciduous teeth have been made by Walsh and Smart (1948). At each of the ages five to 11 years, the prevalence of dental caries in first deciduous molars was much higher on distal surfaces than on mesial surfaces, and the disparity between mesial and distal surfaces was greater in lower teeth than in upper teeth. It has been customary to explain such facts in relation to agent factors alone: the larger the contact area the larger the area of stagnation where micro-organisms can produce harmful products within a dental plaque and the slower the rate of outward diffusion of acid and inward diffusion of salivary buffers. Another possibility is that the mesial surfaces of these teeth have a greater resistance to caries than the distal surfaces and that this difference in resistance may result in part from an increased

uptake of fluoride and other protective ions from saliva, water and food, with the greater uptake of ions by mesial surfaces resulting from the greater access of saliva, water and food to these surfaces than to distal surfaces. If this hypothesis were true one would expect to find that the smooth surfaces of teeth which were most accessible to saliva, food and water would have the greatest resistance and thus the lowest prevalence of caries. In addition, buccal and lingual surfaces should have a higher resistance than proximal surfaces and incisors should have a higher resistance than molars. Surfaces which contain pits and fissures are in a separate category since the localization of the agent factors in contact with enamel is determined by the size, shape and depth of the pits and fissures. It is also possible, of course, that both hypotheses are true and that the lower prevalence of caries on the mesial surface of first permanent premolars and first deciduous molars results from the combined effect of smaller stagnation areas and a more rapid uptake of protective ions.

The following epidemiological data are of special interest in this connexion:

(1) Gedalia and Kalderon (1964) found that the mean fluoride content of the outer layers of the buccal sufaces (545 p.p.m.) of 17 teeth was significantly higher than that of the mesial (490 p.p.m.) and distal (489 p.p.m.) surfaces. Although the fluoride content of mesial surfaces was higher than that of the distal surfaces the difference was not significant. This is not surprising since the investigators found that "age plays a determining rôle in the accumulation of fluoride in the surface-enamel layer" and that the teeth analysed were of unknown age.

(2) Gedalia and Kalderon (1964) found that the fluoride content of the outer enamel of incisors from 11 patients (639·2 p.p.m.) was significantly higher than that of molars (447·4 p.p.m.) and premolars (503·3 p.p.m.). These differences were significant at the level of 0·006 and 0·04 respectively. Although the mean post-eruptive tooth age of the teeth concerned was 44·1 years in the

incisors, 39·2 years in the premolars and 36·6 years in the molars, it would seem unlikely that age alone could account for the major differences detected.

(3) In a study of the prevalence of caries in relation to soil types, Ludwig (1963) described "an enhanced resistance" to caries in children resident on saline, recent marine soils at Napier, New Zealand. His tentative conclusion was that the protective factor is related to an increased intake of molybdenum and possibly other microelements from vegetables grown in market and home gardens. He found that the greatest effect was manifested in incisor teeth and on buccal-lingual (gingival) surfaces.

(4) Ludwig and Pearce (1963) found that after eight and a half years' fluoridation at Hastings, New Zealand, the caries experience of children aged six to 16 years was reduced to the greatest extent on buccal-lingual (gingival) surfaces, to an intermediate extent on proximal surfaces and least on pit and fissure surfaces. The same observations were made in Holland by Backer Dirks, Houwink and Kwant (1961).

(5) Marthaler and Schenardi (1962) found that the reduction in caries which followed the administration of fluoridated salt was greater on smooth surfaces than on pit and fissure surfaces and greater on the smooth surfaces of incisors than on the smooth surfaces of molars.

(6) In a study of caries in relation to the maternal ingestion of fluoride, Carlos, Gittelsohn and Haddon (1962) found that the percentage of six-year-old children having no caries varied in accordance with the specific type of teeth in the following order, from highest to lowest: canines, incisors, first molars, second molars.

(7) In a study of more than 12,000 children in New Zealand, Hewat and Eastcott (1956) found that:

(a) Europeans of either sex have more caries experience than Maoris. In the age group six to 16 years the prevalence of caries was higher in Europeans by 83 per cent in males and 72 per cent in

females. The differences between the races were greatest for buccal-lingual surfaces, intermediate for occlusal surfaces and least for proximal surfaces. The overall yearly caries attack rate in Europeans was about double that of Maoris but the attack rate on buccal-lingual surfaces was about seven times higher in Europeans than in Maoris. This led the authors to suggest that "these surfaces are more sensitive than are other surfaces to influences which have a racial origin".

(b) European and Maori children in urban areas have a higher prevalence of caries than children in rural areas and, in the authors' words, "the greater liability of urban residents to caries is due mainly to the higher susceptibility of the buccal-lingual surfaces". The significant percentage differences between urban and rural children with respect to specific types of surfaces affected were as follows:

Europeans	%
All tooth surfaces	2
Occlusal surfaces	3·5
Buccal-lingual surfaces	12
Maoris	
All tooth surfaces	16·3
Occlusal surfaces	15·9
Proximal surfaces	15·3
Buccal-lingual surfaces	65·5

(c) European children who maintain a good standard of oral hygiene have significantly less caries than those whose oral hygiene is poor. The buccal-lingual tooth surfaces are most affected by a deterioration in oral hygiene.

(d) In European children the presence of superficial stains on teeth was significantly related to the prevalence of caries. Buccal-lingual surfaces with brown stain have a low prevalence of caries

whereas buccal-lingual surfaces with green stain have a significantly high prevalence of caries.

(8) In an investigation of dental conditions among the Polynesians of the remote Pacific atoll of Pukapuka, I found (1956*a*):

(a) An inverse relationship between caries of individual permanent teeth and their proximity to the ducts of the major salivary glands. I suggested that the degree of protection afforded by saliva is dependent upon its access to individual teeth and to areas of stagnation where bacteria and food debris are retained in contact with enamel.

(b) A significantly higher prevalence of caries of proximal surfaces between first and second deciduous molars than between first deciduous molars and canines. Caries was detected on the mesial and/or distal boundaries of 19 per cent of the DE spaces (between first and second deciduous molars) compared with only 11 per cent of the CD spaces (between first deciduous molars and canines).

(c) A much higher involvement of gingival surfaces compared with that observed among Europeans. For example, although the mean numbers of deciduous occlusal and proximal surfaces affected were similar in Pukapuka and New Zealand, there was a 12 times higher involvement of buccal-lingual surfaces in Pukapuka than in New Zealand.

All this evidence is consistent with the hypothesis that the resistance of teeth can be modified post-eruptively by exposure to saliva, food and water and that the most sensitive epidemiological index of resistance is the prevalence or incidence of caries on the smooth buccal and lingual surfaces. Estimates of resistance to caries based upon DMF (decayed, missing and filled) teeth or DMF surfaces are difficult and can be misleading since the prevalence and incidence of caries show marked variations between different types of teeth and between different surfaces of the same type of teeth. Furthermore, the predisposing factors influencing caries on pit and fissure surfaces and proximal surfaces are more

complex than those influencing caries on buccal and lingual smooth surfaces. If DMF teeth data are to be used, sophisticated methods of statistical analysis are necessary in order that the relative importance of known variables can be determined. It is only recently that the importance of this principle has been recognized. A good example of the value of this is to be found in the report of Mansbridge (1958) on the prevalence of dental caries in relation to maturity. He used the technique of multiple regression analysis in which the dependent variate was DMF teeth and the independent variates were height, weight, age, number of teeth erupted and sexual maturity. From the results of this analysis he was able to show that for boys sexual maturity and dental caries are associated and that this association is related to adolescence but not to pubescence. The difference attributable to maturity alone, in DMF teeth, between adolescent and pubescent boys of the same chronological age, was 1·8 teeth. Mansbridge recognized that individual variations in the prevalence of DMF teeth are large, so that any difference in DMF rates between groups of people must be large to be statistically significant.

This type of analysis using modern computer techniques should be undertaken in the future to determine the relative importance of measurable host factors to both the prevalence and incidence of caries on specific surfaces of specific teeth.

Complex statistical techniques are also necessary in order to determine the influence of genetics and race or ethnic group on resistance to caries. An ethnic group represents one of a number of human populations which maintain their individual physical differences by means of isolating mechanisms such as geographical or social barriers. No population should be described as a race unless there is good evidence that there is a genetic basis upon which a racial distinction is being erected (Ashley Montagu, 1950). It is a fact that differences in the prevalence of caries exist between different racial or ethnic groups. If Ashley Montagu's view is accepted then by definition these differences must be partly genetic

in origin. But, as Osborne (1963) points out, what can be inherited is not an excess or absence of dental caries but genetic material which sets the limits of an individual's capacity to react to his environment. The presence or absence of dental caries is the consequence of an interaction between genetic material and the environment. There are several methods of evaluating the genetic and environmental causes of variance. Studies of monozygotic and dizygotic twins by Horowitz, Osborne and De George (1958), Ludwig (1957), Mansbridge (1959), Goldberg (1930), Goodman and co-workers (1959), and Finn and Caldwell (1963) have established that genetic factors do affect the aetiology of caries, but they do not provide information concerning the genetic mechanisms involved. Further studies are required to determine the specific genetic and environmental factors, and Osborne (1963) recommends the co-twin control method for this purpose. But such a study should be longitudinal in type rather than cross-sectional since the hereditary factors may affect the saliva, the teeth or both. As Horowitz (1963) points out, "A contemporary sample of saliva may bear little relation to the composition of the saliva or microflora of the mouth that existed at the time when the carious lesions were being initiated". Here again DMF teeth and DMF surface scoring systems are not sufficiently sensitive for studies of this type which use limited numbers of subjects.

Sib and family methods were used by Böök and Grahnén (1953) and they concluded that genetic factors which are probably polygenic play an important part in determining resistance against dental caries.

In 1950 I made a study of genetic and environmental factors in relation to dental caries on the isolated Pacific atoll of Pukapuka. These results confirmed those of Böök and Grahnén and demonstrated that in a community where the environmental factors promoting caries are of relatively low intensity, genetic factors play an important rôle in determining resistance to the disease. The additional finding of a significant association between the