



THE UNIVERSITY OF
SYDNEY

COPYRIGHT AND USE OF THIS THESIS

This thesis must be used in accordance with the provisions of the Copyright Act 1968.

Reproduction of material protected by copyright may be an infringement of copyright and copyright owners may be entitled to take legal action against persons who infringe their copyright.

Section 51 (2) of the Copyright Act permits an authorized officer of a university library or archives to provide a copy (by communication or otherwise) of an unpublished thesis kept in the library or archives, to a person who satisfies the authorized officer that he or she requires the reproduction for the purposes of research or study.

The Copyright Act grants the creator of a work a number of moral rights, specifically the right of attribution, the right against false attribution and the right of integrity.

You may infringe the author's moral rights if you:

- fail to acknowledge the author of this thesis if you quote sections from the work
- attribute this thesis to another author
- subject this thesis to derogatory treatment which may prejudice the author's reputation

For further information contact the University's Copyright Service.

sydney.edu.au/copyright

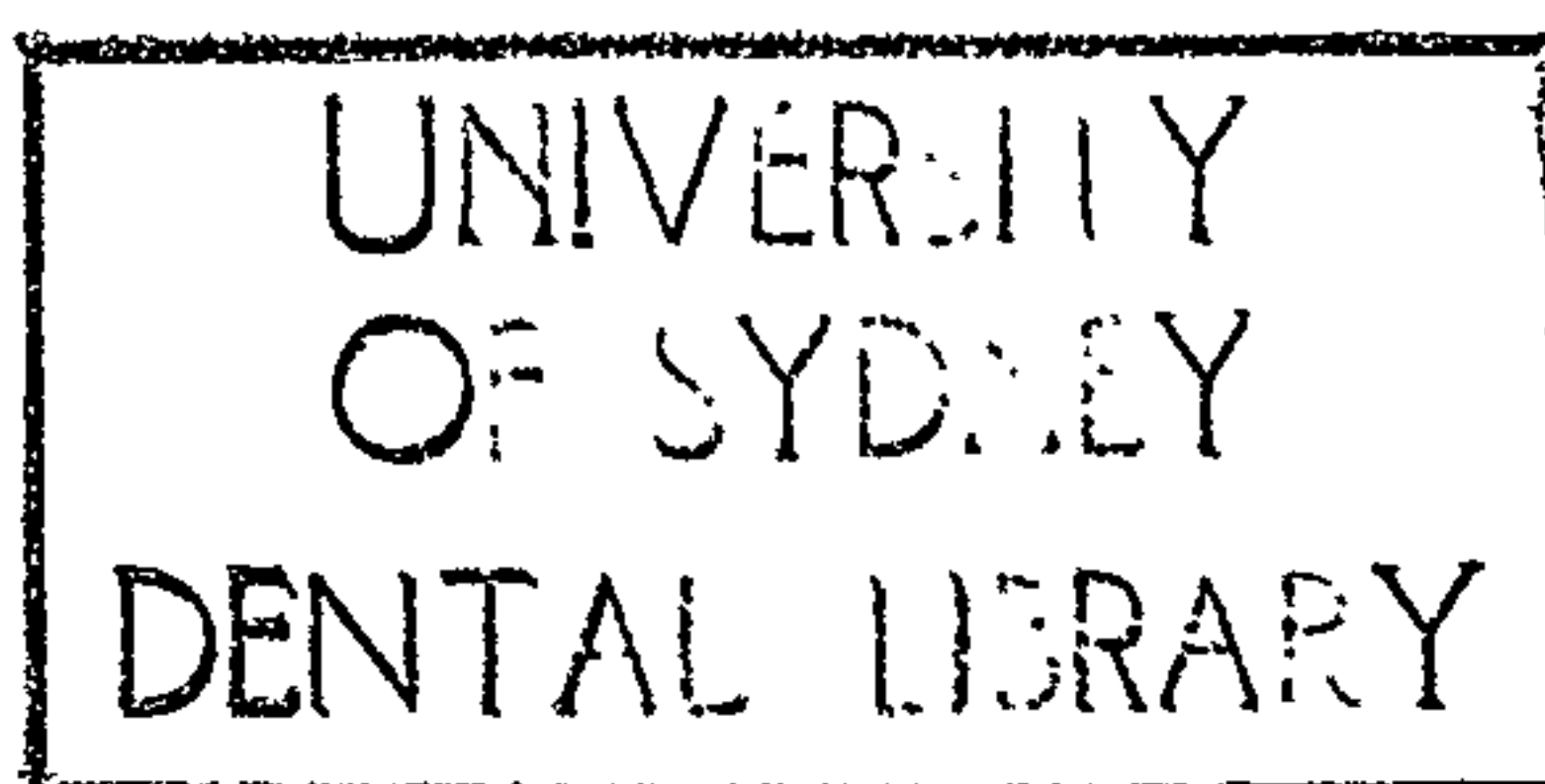
TOPICAL STANNOUS FLUORIDE (OPERATOR APPLIED)

BY

AHMAD BIN HAJI ABANG

BDS (MALAYA)

A thesis submitted in partial requirement for the
DIPLOMA IN PUBLIC HEALTH DENTISTRY



DEPARTMENT OF PREVENTIVE DENTISTRY

FACULTY OF DENTISTRY

UNIVERSITY OF SYDNEY

1984.

SUMMARY

This thesis is purely a literature review, mainly concerned with Operator Applied stannous fluoride. There is no doubt as to the effectiveness of water fluoridation in the control of dental caries. However in areas where fluoridation is not feasible other methods of supplying fluoride to the teeth have to be considered.

The introduction of this thesis deals briefly with dental caries as a public health problem. It also mentions some of the preventive measures used to control dental caries.

A detailed review of literature on the etiology of dental caries was made. The four essential components for the development of dental caries are bacterial agents, a suitable substrate, a susceptible host and sufficient time for the substrate to be converted into harmful acids by the bacteria. The bacteria that are commonly associated with dental caries are the streptococcus groups of bacteria, particularly the streptococcus mutans. The substrate that is the chief cause of dental caries is sucrose. The teeth that are particularly vulnerable are those that are just erupting, especially those with deep pits and fissures. In newly erupted teeth there are areas of hypomineralisation. These areas are not fully matured and therefore are more porous and more readily broken down by the acids that are produced as a result of bacterial metabolism.

To combat the four essential components of dental caries, four principle actions need to be considered. They

are the control of the diet that is being consumed, reducing the time of retention of the diet substrate in the mouth, reducing the number of bacteria and increasing the resistance of the host.

A very detailed literature review on the actions of stannous fluoride was made in Section 3 of this thesis. Operator applied stannous fluoride exerts its effects by acting on the bacterial plaque, the sound enamel and the demineralised enamel. Its actions on bacterial plaque result in the interference with bacterial adherence, metabolism, growth, acid production and even death of the bacteria. Its action on the enamel results in the formation of highly insoluble calcium fluoride, fluorapatite and tin phosphate. The formation of these insoluble products increases the resistance of the teeth to acid attack. In initial carious lesions stannous fluoride has been shown to arrest the development of the lesion.

Extensive literature on the clinical effectiveness and techniques of operator applied stannous fluoride was described and discussed in Section 4. On the average the success rate of operator applied stannous fluoride topical application is around 30-40% reduction in dental caries. To achieve this value certain procedures have to be followed. The recommended technique is that of multiple stannous fluoride therapy. This technique consists of a combination of a stannous fluoride prophylaxis paste (10% stannous fluoride), a topical application of a 10% stannous fluoride solution and the home use of stannous fluoride dentifrice (0.4% stannous fluoride).

Recently a new technique of topical stannous fluoride application known as the Prolonged Fluoride Application technique (PFA) was developed. This technique includes the application of a 10% stannous fluoride spot application paste to the susceptible areas. The paste is covered or held over the affected area by a stomahesive wafer. This allows the stannous fluoride paste to be in prolonged contact (at least 1 hour) with the enamel surface. This technique shows potential of reducing the dental caries in pits and fissures.

On the cost analysis basis operator applied stannous fluoride is found to be not suitable for a public health program as compared to self-applied fluoride such as tooth-paste and mouth rinsings. It is more applicable to usage in association with comprehensive dental care. This is because of the need for person to person supervision which is therefore expensive. Nevertheless it could be used in situations where fluoridation or other means of fluoride application are not possible. It is also effective in addition to fluoridation.

ACKNOWLEDGEMENTS

Thanks are due to Associate Professor Peter Bernard of the Department of Preventive Dentistry, University of Sydney, for his advice and guidance in the preparation of this thesis. His patience, encouragement and understanding have made the preparation easier to handle.

I wish to express my gratitude and appreciation to my wife Dr. Fekriah Hj. Mohd Yatim, my children Amir Adham and Awanis, and my family for their patience, support and encouragement.

Finally, I wish to thank the Government of Malaysia for sponsoring me to do this Diploma in Public Health (Dentistry) course (1984).

v

TABLE OF CONTENTS

	<u>Page</u>
Summary	i
Acknowledgements	iv
Table of Contents	v
List of Tables	vii
List of Figures	xi
<u>Section 1: INTRODUCTION</u>	1
1.1 Dental Caries Public Health Problem	3
1.2 Prevention of Dental Caries	6
1.3 Aim of Thesis	11
<u>Section 2: DENTAL CARIES</u>	13
2.1 Etiology	13
2.2 Host Factors	13
2.2.1 Tooth Morphology and Arch Form	15
2.2.2 Dental Enamel	18
2.3 Bacterial Plaque	20
2.4 Enamel Caries	33
<u>Section 3: MODE OF ACTION OF STANNOUS FLUORIDE</u>	43
3.1 Effect on Bacterial Plaque	44
3.2 Effect on Sound Enamel	56
3.3 Effect on Demineralised Enamel	60
<u>Section 4: STANNOUS FLUORIDE TOPICAL APPLICATIONS</u>	71
<u>(OPERATOR)</u>	
4.1 Development and Clinical Effectiveness	71
4.2 Technique of Application	86

	<u>Page</u>
4.2.1 Prophylaxis	88
4.2.2 Topical Application of Stannous Fluoride Solution	90
4.3 Cost-Benefit Analysis	93
4.4 Advantages and Disadvantages	100
<u>Section 5: PROLONGED FLUORIDE APPLICATION</u>	103
5.1 Development	103
5.2 Technique of Application	104
5.2.1 Indication	104
5.2.2 Material	105
5.2.3 Method	105
5.3 Clinical Effectiveness	110
5.4 Cost Analysis	112
5.5 Advantages of the PFA Technique (Craig 1975)	115
5.6 Disadvantage of the PFA Technique	116
<u>Section 6: DISCUSSION</u>	117
6.1 Introduction	117
6.2 Action of Stannous Fluoride	117
6.3 Clinical Findings	121
6.4 Cost Analysis	124
<u>Section 7: CONCLUSIONS</u>	127
<u>Section 8: REFERENCES</u>	129

LIST OF TABLES

<u>Table No.</u>		<u>Page</u>
1.	Data to show the increase in prevalence of dental caries in children aged 10-14 from selected countries. <u>Source:</u> World Health Organisation; Oral Epidemiological Data Bank. Striffler, 1983.	4
2.	Average crystallite diameters in human enamel in mm. <u>Source:</u> Arends et al., 1983.	19
3.	Ranges, percentage patterns and mean values of acids in resting plaque. <u>Source:</u> Distler and Kroncke, 1983.	30
4.	Comparison of acids in plaque before sucrose rinsing (nmol/mg wet weight). <u>Source:</u> Distler and Kroncke, 1983.	32
5.	Fluoride content of powdered enamel samples treated with SnF ₂ solution. <u>Source:</u> Chow et al., 1980.	62
6.	Fluoride concentrations (ppm) in carious and sound enamel. <u>Source:</u> Weatherell et al., 1977.	62
7.	Caries progression from age 8 to age 15 on the buccal surface of 184 maxillary first molars. <u>Source:</u> Backer-Dirks, 1966.	64
8.	Summary of caries findings. <u>Source:</u> Howell et al., 1955.	73

<u>Table No.</u>		<u>Page</u>
9.	Effect of fluorides on the number of reversals in diagnosis from carious to non-carious. <u>Source:</u> Howell et al., 1955.	73
10.	The effectiveness of one application of an 8 percent solution of SnF_2 as compared with four applications of a 2 percent NaF solution. <u>Source:</u> Gish et al., 1957.	73
11.	A comparison of the effectiveness at end of 4 years of a single application per year of an 8 percent solution of stannous fluoride to a series of four applications of sodium fluoride once every three years. <u>Source:</u> Gish et al., 1959.	75
12.	The effect of a single topical application of a 10 percent unbuffered aqueous solution of stannous fluoride on caries reduction in adults after a 1-year period. <u>Source:</u> Muhler, 1958.	75
13.	Incidence of caries following a single application of eight percent stannous fluoride solution applied annually for two years to 209 children starting at ages 12-13 as compared to a control group of 211, ages 12-13. <u>Source:</u> Jordan et al., 1959.	77
14.	Comparison of caries increments of three groups in terms of DMFT and DMFS indexes at each of four examination periods. <u>Source:</u> Muhler, 1960.	77

<u>Table No.</u>		<u>Page</u>
15.	Baseline characteristics of participants. <u>Source:</u> Beiswanger et al., 1980.	83
16.	Baseline dental caries data. <u>Source:</u> Beiswanger et al., 1980.	83
17.	Summary and analysis of dental caries increments at various examinations. <u>Source:</u> Beiswanger et al., 1980.	83
18.	Combined analysis of topical and pro- phylaxis data at various examinations. <u>Source:</u> Beiswanger et al., 1980.	83
19.	Techniques of topical application of fluoride solution (after Davies, 1973). <u>Source:</u> Fuller, 1974.	95
20.	Cost-effectiveness of topical applications of fluorides. <u>Source:</u> Davies, 1973.	95
21.	Summary of cost-effectiveness of topical fluorides. <u>Source:</u> Fuller, 1974.	97
22.	Ranking of estimated cost-effectiveness of alternative topical fluoride procedures. <u>Source:</u> Heifetz, 1978.	98
23.	Summary of cost-benefit of topical fluorides. <u>Source:</u> Davies, 1973.	99
24.	Number, mean initial DMFS and mean final DMFS scores of children in the three study groups. <u>Source:</u> Craig and Powell, 1979.	111
25.	Clinical status of occlusal surfaces of	111

Table
No.Page

permanent first molar teeth following treatment
with the PFA method.

Source: Craig and Powell, 1979.

26. Summary of results of a three year clinical trial 113
of PFA method by Craig and Powell.

Source: Enno and Craig, 1982.

27. Estimated cost of treatment per tooth. 113

Source: Enno and Craig, 1982.

LIST OF FIGURES

<u>Figure No.</u>		<u>Page</u>
1.	The four circles diagrammatically represent the essential etiological factors involved in the carious process. All four factors must be acting concurrently (overlapping of the circles) for caries to occur. <u>Source:</u> Newbrun, 1983.	14
2.	Cross-section of an occlusal fissure showing the inability of an explorer or toothbrush bristle to reach the base. <u>Source:</u> Newbrun, 1983.	14
3.	Curves showing the annual probability of caries attack of the permanent teeth of male children in Kingston, New York. Semi-logarithmic scale. <u>Source:</u> Carlos and Gittelsohn, 1965.	17
4.	Development of dental plaque on a clean enamel surface. <u>Source:</u> Marsh, 1980.	22
5.	Outline of the reactions involved in the degradation of Sucrose, Lactose and Starch, the most common of the dietary carbohydrates fermented by the bacteria in the oral cavity. <u>Source:</u> Kleinberg et al., 1981.	26
6.	Showing the Sucrose-phosphoenol pyruvate-phosphotransferase system (PTS-System). <u>Source:</u> Nicholas, 1983.	28
7.	To summarise the fate of pyruvate. <u>Source:</u> Silverstone, 1981.	28

<u>Figure No.</u>		<u>Page</u>
8.	Mean percentage pattern of acids after sucrose rinse. <u>Source:</u> Distler and Kroncke, 1983.	31
9.	Micrograph of White Spot lesion of enamel. Compare the extensive demineralization of the subsurface enamel with better mineralized surface layer (original magnification X100). <u>Source:</u> Newbrun, 1983.	35
10.	Microradiograph of an artificial lesion created on abraded enamel. Approximately 500 microns of the original enamel was ground off before the experiment. The lesion has penetrated the outer two-thirds of the remain- ing enamel and shows a deep surface zone that appears well mineralised. Striae of Retzius, prisms and cross striations can be seen in the demineralised region X100. <u>Source:</u> Silverstone, 1968.	37
11.	Schematic representation of model for sub- surface demineralization. <u>Source:</u> Moreno and Zahradnik, 1974.	37
12 to 16	SEM-photograph of initial surface changes cervical to approximal facet (AF). Details of the framed areas A, B and C are shown in Figures 13, 14, 15 and 16 (X128). Figure 13: Higher magnification of A showing deepened Tomes' process pits (TPP) and eroded focal holes, arrows (X416). Figure 14: Detailed appearance of eroded focal hole in	41

Figure
No.

Page

Fig. 13 and microfractures along the perikymata edge and the 'opening up' into the less discernible pits in the overlapping part of the perikymata. Arrow indicates stage of fissure formation (X416). Fig. 16: Detail of area C with fractured perikymata edge with marked disintegration of microsurface (X576).

Source: Thylstrup and Fejerskov, 1981).

17. Rapidity of the inhibitory action of fluoride upon enolase. Abscissae: time (minutes). Ordinate: absorbancy at 240 mμ. 46

Source: Cimasoni, 1970.

18. Mean plaque index scored by plaque standard deviation is indicated by the vertical lines. 53

Source: Bay and Rolla, 1981.

19. Example of plaque formation after 3 days without oral hygiene following a previous rinsing with water. 53

Source: Bay and Rolla, 1981.

20. Example of plaque formation after 3 days without oral hygiene following a previous rinsing with SnF₂. 54

Source: Bay and Rolla, 1981.

21. Example of plaque formation after 3 days without oral hygiene following a previous rinsing with NaF. 54

Source: Bay and Rolla, 1981.

<u>Figure No.</u>		<u>Page</u>
22.	Calcium phosphate deposition and dissolution after SnF ₂ application. <u>Source:</u> Purdell-Lewis, 1981.	67
23.	Microprobe analysis of SnF ₂ treated demineralised enamel. <u>Source:</u> Purdell-Lewis, 1981.	67
24.	Progress of initial lesions: Control. <u>Source:</u> Purdell-Lewis, 1981.	70
25.	Progress of initial lesions: SnF ₂ treated group. <u>Source:</u> Purdell-Lewis, 1981.	70
26.	Left - Adult size Garmers clamp for lower left quadrants. Right - Junior size Garmers clamp for lower left quadrants. <u>Source:</u> Craig and Dunn, 1971.	92
27.	Left - Position of cotton rolls in Garmers clamp for the isolation of a lower right quadrant. Right - Topical application of a stannous fluoride solution to a lower quadrant with cotton rolls and a Garmers clamp in position. <u>Source:</u> Craig and Dunn, 1971.	92
28.	Some of the material used in PFA technique.	106
29.	Guidelines for sizes of stomahesive wafers. <u>Source:</u> Pedodontic Department, University of Sydney Lecture notes.	107
30.	Showing the treatment sites where 10% SnF ₂ paste has been placed.	109

Source: Pedodontic Department, University of Sydney Lecture notes.

31. Wafers in situ.

109

Source: Pedodontic Department, University of
Sydney Lecture notes.

1. INTRODUCTION

Dentistry is concerned with the prevention and treatment of oral diseases and their sequelae. Many of the oral diseases can be prevented or controlled if proper measures are taken to minimise the known causative agents. The most widely known of these diseases is dental caries which is highly prevalent in our modern societies. It has been shown to exist even in ancient civilisation. However, there are differences between caries of the past and the present civilisation. From ancient skulls it has been shown that there was a low prevalence of carious lesions which were mostly on the cervical region of the teeth. The caries that are commonly seen today usually begin in pit and fissure surfaces and develop later on the proximal surfaces of the teeth. These differences may reflect quality or nature of the diet of ancient and present day man. Food consumed in early civilisation was coarse and there was little in the way of food preparation.

The diet has been suspected of influencing the etiology of caries since the time of the early Greek philosophers. With the advance of modern technology, food processing industries grew and man developed new habits and tastes. A majority of modern diets contain refined sugars, particularly sucrose, as one of their ingredients. Sugar is sweet and almost everyone enjoys eating sweet-tasting foods. Refined sugars, especially sucrose, have been widely used as a primary sweetening agent. Today's markets are flooded with sugar bowls, candy counters, vending machines, bakery and pastry

shops and soda fountains. Although positive proof of the diet's role in human caries has not been easily established, sugar, especially sucrose, has been indicated as "the arch criminal" of dental caries (Newbrun 1971). The relationship between diet and dental caries has been widely studied. Perhaps the best-known research project into diet and dental caries is the Vipeholm study (Gustafsson et al. 1954) which took place between 1945 and 1952. In this study 436 adults, inmates of a mental institution (Vipeholm) in Sweden, were divided into 9 groups. The control group received a sugar diet which contained a varying amount of sugar, up to 24 sticky toffees. The conclusions obtained from this study still hold up today. They are:

- "1. Sugar consumption increases caries activity.
2. The risk of increased caries activity is greater if the sugar is in sticky form.
3. The risk is greatest if the sugar is taken between meals and in a sticky form.
4. The increase in caries under uniform conditions shows great individual variation.
5. The increase in caries disappears upon withdrawal of sticky foodstuffs from the diet.
6. Caries can still occur in the absence of refined sugar, natural sugar, and total dietary carbohydrates."

(Young, W.O. 1983, p.30)

1.1 DENTAL CARIES PUBLIC HEALTH PROBLEM

Caries in Latin means decay. Thus dental caries simply means decay or rotting of the teeth. It develops as a progressive destruction of enamel, dentine and cementum initiated by microbial activity at the tooth surface (Silverstone et al. 1981). Grene and Suomi (1977) have noted that dental caries is a disease of modern man occurring world wide. A varying intensity indicates that there is a difference in the prevalence and incidence of dental caries between different countries and nations. With differences in the diet of the population, caries incidence increases with increased refined carbohydrate (sucrose) diet of highly developed countries. Third world populations, which are largely rural, almost invariably have far lower rates. Rural or native diets did not contain any sucrose other than the relatively small amounts found in fruits and vegetables. As the country develops, the diets change to include products containing sugar and caries prevalence is therefore expected to increase. In other words, with urbanisation there is deterioration in the health of the teeth. As a result the prevalence and intensity of dental caries in many developing countries today is rising at an alarming rate as shown in table 1. These data indicate that caries in many such countries had advanced from negligible proportion to a public health problem of the first degree (Striffler et al. 1983). As far back as 1948 in the U.S.A., Gruebbel stated that 'from the public health stand point caries is a serious disease' (Gruebbel 1948, p.426). That was about thirty six years ago and within this thirty six years a lot has been achieved by the develop-

Table 1. Data to Show the Increase in Prevalence of Dental Caries in Children Aged 10–14 From Selected Countries*

Country	Increase in DMF		Within Number of Years
	<i>From</i>	<i>To</i>	
Ethiopia	0.2	1.6	17
Kenya	0.1	1.7	21
Iraq	0.7	3.5	9
Thailand	0.7	4.5	15
Vietnam	2.0	6.3	11
French Polynesia	negligible	7.5	50
Greenland	1.5	10.4	20

*World Health Organization, Oral Epidemiological Data Bank.⁸¹
(Burt B.A., 1983)

ing countries. With development and exposure to culture and technology of highly developed countries, dental caries became more serious than ever.

Although dental caries are seldom life threatening, it is a discomfort to those who suffer from it. It affects the normal masticatory process and if the pulp is involved it can lead to various complications such as cellulitis and may provoke infective endocarditis in a patient with rheumatic or congenital heart disease. If the carious teeth are removed, the result may be aesthetic deterioration, impairment of speech and masticatory function and diseases of oral soft tissues and of the temporomandibular joint may supervene. To avoid this sequelae of dental caries, the affected tooth has to be restored. To restore a carious lesion needs the service of a professional such as the dentist or the dental therapist and, furthermore, the process is time consuming, expensive and may be painful or uncomfortable to the patient. Above all, in many countries today there are not enough resources of finance, manpower and dental facilities to restore every carious lesion. Therefore, the only hope is the use of preventive measures which are less expensive, not painful and not as time consuming as restorative procedures and may require fewer personnel who may not necessarily require as much training as a dentist.

The phrase 'prevention is better than cure' is well known, especially among the medical and dental profession, and it is the main objective of dental public health to prevent dental diseases and the unnecessary loss of teeth in the community.

1.2 PREVENTION OF DENTAL CARIES

Due to its highly prevalent nature and the seriousness of its complication, the control of dental caries is a concern of all the people and not merely a few. However, the fact that dental caries is not a fatal disease imposes certain limitations upon the method that may be applied in its control or prevention. "The ideal control measure should possess immediate, high and lasting effectiveness, be innocuous and reach all the population at a cost in money and facilities well within the economic capabilities of the population" (Young et al 1983, p.155).

Caries prevention is based upon attempts to:-

1. control the diet;
2. reduce the time that the substrate is in the mouth by limiting the frequency of intake;
3. lower the numbers of microorganisms in contact with the tooth (plaque control), and
4. increase the resistance of the host.

Dietary control could be achieved through limitation of sucrose consumption at meal times, replacement of sucrose by other sweeteners, and addition of caries inhibiting agents to food. Limitation of sucrose consumption needs individual initiative and many people are not willing to change their dietary habits just for the sake of avoiding dental caries which may only occur in the month or years ahead. Similarly, the addition of sugar substitutes and non-nutritive sweeteners in place of sugars will not be acceptable to most consumers and manufacturers. Furthermore,

the limitation of sugar consumption and addition of sugar substitutes and non-nutritive sweeteners in place of sugars is not in the interests of countries whose source of income comes from sugar cultivation and sugar related industries. To duplicate the flavour, texture and other characteristics of a sugar-sweetened product with a non-nutritive sweetener is virtually impossible. For example, cookies and cakes baked with non-nutritive sweeteners tend to be hard and tough. Although many naturally occurring dietary components inhibit or have been claimed to inhibit dental caries, their addition to human foods presents a problem since the individual consumption varies from person to person. Furthermore, unlike many animal tests which give positive results for many food additives in reducing caries, the results in man have been less impressive. Thus there are problems in applying the results of animal experiments to the human situation. However, research into these fields is still being conducted and it is hoped that in the near future ways of modifying human diet which could be acceptable and applicable for use by the community will be discovered and successfully marketed. One such study was the fluoridation of sugary products. Very recently Luoma (1984) reported that the incorporation of fluoride in cariogenic sugary products has lessened their cariogenicity.

The second factor in prevention is the reduction of the time that the substrate is in the mouth by limiting the frequency of intake, again depends entirely on the patient himself. The most that the public health or preventive officer or dentist could do is to give advice and motivate

the patient, the rest is up to the patient. Therefore, this technique of prevention together with the one mentioned earlier is less effective.

The next factor, that is to lower the numbers of microorganisms in contact with the tooth or plaque control, could be achieved by:-

1. using agents acting against the microflora per se,
2. using agents interfering with bacterial attachment by:
 - (a) attacking plaque matrix components, or
 - (b) altering the tooth surface, and
3. mechanical removal of plaque (Newbrun 1983).

Further mention of these measures will be made in this thesis.

There are a few ways by which the host resistance to dental caries could be increased. These include fluoride therapy, occlusal sealants and immunization. Since this thesis deals with operator applied stannous fluoride, only the role of fluoride therapy in increasing the resistance of the teeth will be expanded later in this thesis.

There are several ways by which fluoride could be used as a preventive measure against dental caries. These include community water fluoridation, systemic fluoride in the form of drops, tablets or lozenges, operator applied topical fluoride and self applied fluoride agents.

Water fluoridation is the preventive agent that has proved most potent and practical. The first fluoride introduced into the community water supply was in Grand Rapids on the 25th January, 1945, in the form of sodium fluoride (1 part per million). After 6½ years of fluoridation

the result was so impressive that the city officials in the control town of Muskegon decided to fluoridate their own water supply in July 1951. Caries reduction as a result of fluoridation ranges from 40-50% in deciduous teeth and 50-60% in permanent teeth (Murray et al 1982). Numerous other studies provide overwhelming evidence of the efficiency of fluoridation. By 1977, 38 countries in the world have been reported to have fluoridation reaching some 208 million people (Young et al. 1983). However, despite these successes, fluoridation also suffered set-backs in some countries. For example, in Holland the legality of fluoridation has been successfully challenged in the court and it has now been discontinued. In Ireland, fluoridation has successfully withstood a legal challenge. Progress in other parts of the world is slowly beginning to take shape. Fluoridation of the community water supply is strongly supported by the World Health Organisation.

Other systemic administration such as drops, tablets or lozenges can only reduce dental caries if they are taken regularly. Thus its success depends on the patient and the parents' initiative and interest. Dental health education also plays an important role in educating the public, especially through parent organisation, to understand and adopt various techniques of prevention.

Operator applied topical fluoride had been used to prevent dental caries even before the first addition of fluoride to public water supply (Knutson and Armstrong 1943). There is no doubt that fluoridation is at the moment the ideal preventive measure for dental caries. However, there are areas

where fluoridation is not possible and in these areas other means of increasing the resistance of the teeth to dental caries could be useful. These preventive measures include other systemic administration of fluoride, which has been mentioned earlier, operator applied topical fluoride and self applied fluoride.

The four main types of operator applied topical fluoride that have been widely used are neutral sodium fluoride solution (2%), stannous fluoride solution (usually 8% or 10%), acidulated phosphate fluoride (1.23% fluoride) in solution or gel form and varnishes containing fluoride. They are usually applied following a prophylaxis. Solutions are applied directly to the teeth for 4 minutes; gels are usually applied in trays. The effectiveness of these procedures vary, but when conducted semi-annually could reduce dental caries by about 40% (Newbrun 1983). Topical fluoride could produce additional preventive effect when used in the community whose water has been fluoridated. Since each patient requires individual attention by the dentist or dental therapist, the procedure is rather costly.

Self applied fluoride, in terms of application can be divided into 2 categories. Those that are applied under supervision (mouth rinsing) and non-supervised application (dentifrices). The materials most often used as mouth rinses are NaF in either 0.2 percent concentration used weekly or 0.05 percent fluoride used daily. There is not much difference in the benefits obtained between daily and weekly rinsing. Daily rinsing seems to provide only slight benefit over weekly rinsing (Heifetz et al. 1980). Thus for a school-

based program, weekly rinsing is more practical and less costly. For the individual patient, daily use is more appropriate as part of the daily oral hygiene routine. Studies have shown that the use of recommended NaF mouth rinses results in reductions in caries of the order of 35 percent (Horowitz et al. 1971, Ripa et al. 1980). Fluoride in dentifrice is known to be of benefit in the prevention of caries. In the fluoridated areas, use of a fluoride tooth paste seems to provide some added benefits. Reductions of dental caries in the range of 15 to 30 percent have been reported as a result of using dentifrice (Muhler 1962, Peterson 1979).

In this thesis only Operator Applied Topical Stannous Fluoride will be reviewed. As such, subsequent chapters will deal in detail with the usage of operator applied topical stannous fluoride as a preventive measure for dental caries.

1.3 AIM OF THESIS

Stannous fluoride is more effective than sodium fluoride. This may be due to the ability of both the stannous ion and the fluoride ion to be involved in the reaction to reduce dental caries. Recently new techniques and procedures for the use of operator applied stannous fluoride are being developed and studied. One such development is the technique of prolonged fluoride application. It is the aim of this thesis:

1. to review literature associated with operator applied stannous fluoride,
2. to review the literature on the technique of prolonged

fluoride application, and

3. to evaluate the usefulness of prolonged fluoride application as a preventive technique.

2. DENTAL CARIES

2.1 ETIOLOGY

To treat a disease successfully the cause of the disease must be known. Only when the source or factors directly or indirectly related to the cause or etiology of the disease are known then and only then can effective measures be taken to control or to treat the disease. In other words the etiology of the disease is very important where prevention and treatment are concerned.

The etiology of dental caries is very broad, it involves both local and general predisposing factors. It is a multifactorial disease, however, the three main essential components of dental caries are the host, the microflora and the substrate. Dental caries do not develop into a cavity in a short time. It takes time for initial caries to develop into clinical caries. In other words, caries is a chronic disease, as such the time taken for the substrate to be made available to the microflora or the time taken for the caries to progress must be taken into account when discussing its etiology (Newbrun 1983).

In short, for caries to take place it requires a susceptible host, a cariogenic oral flora and a suitable substrate which must be present for a sufficient length of time (Fig. 1).

2.2 HOST FACTORS

The host factors that are involved in the formation of dental caries are the saliva and the tooth itself. The

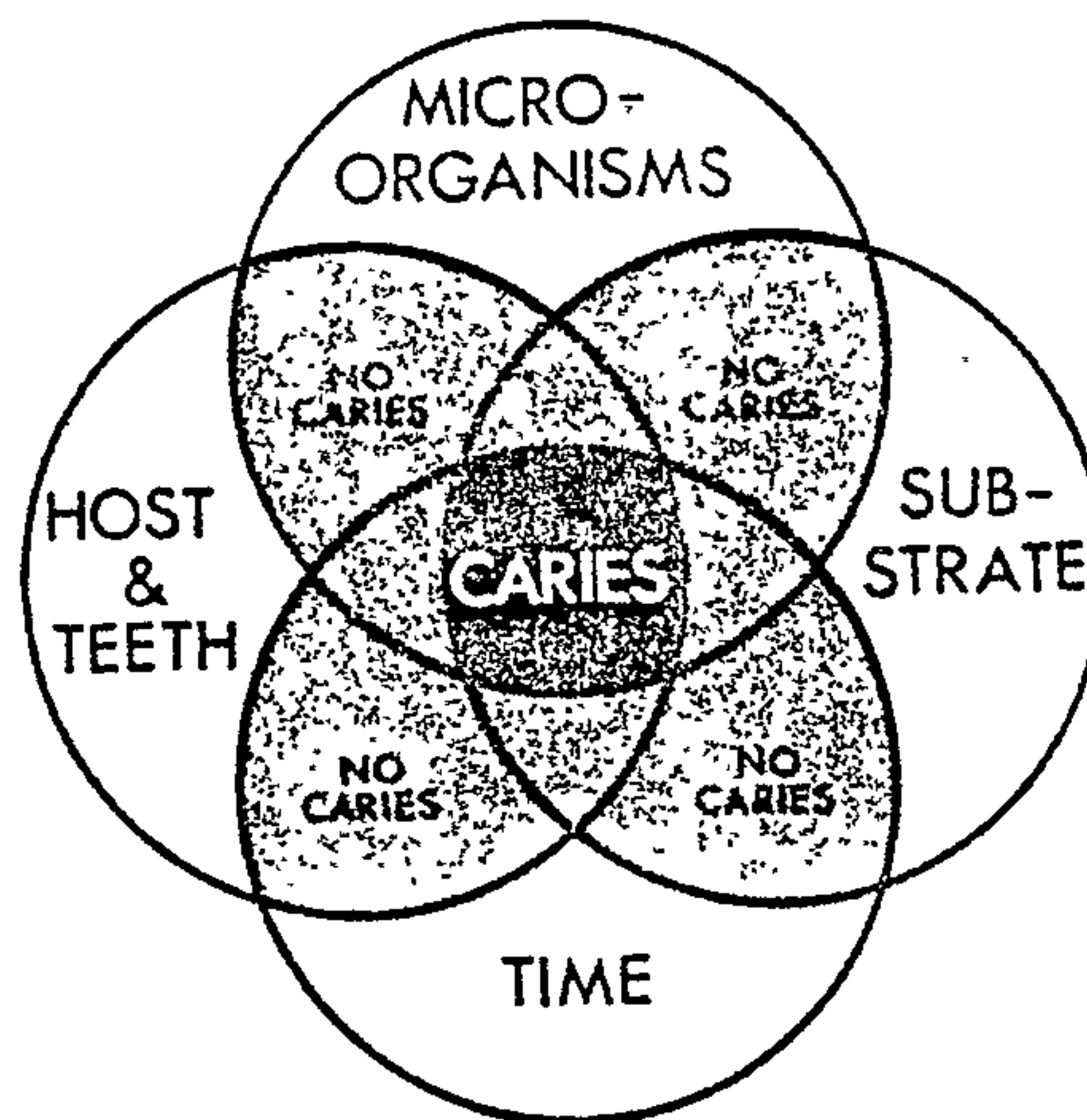


Fig. 1 The four circles diagrammatically represent the parameters involved in the carious process. All four factors must be acting concurrently (overlapping of the circles) for caries to occur.
(Newbrun, 1983.)

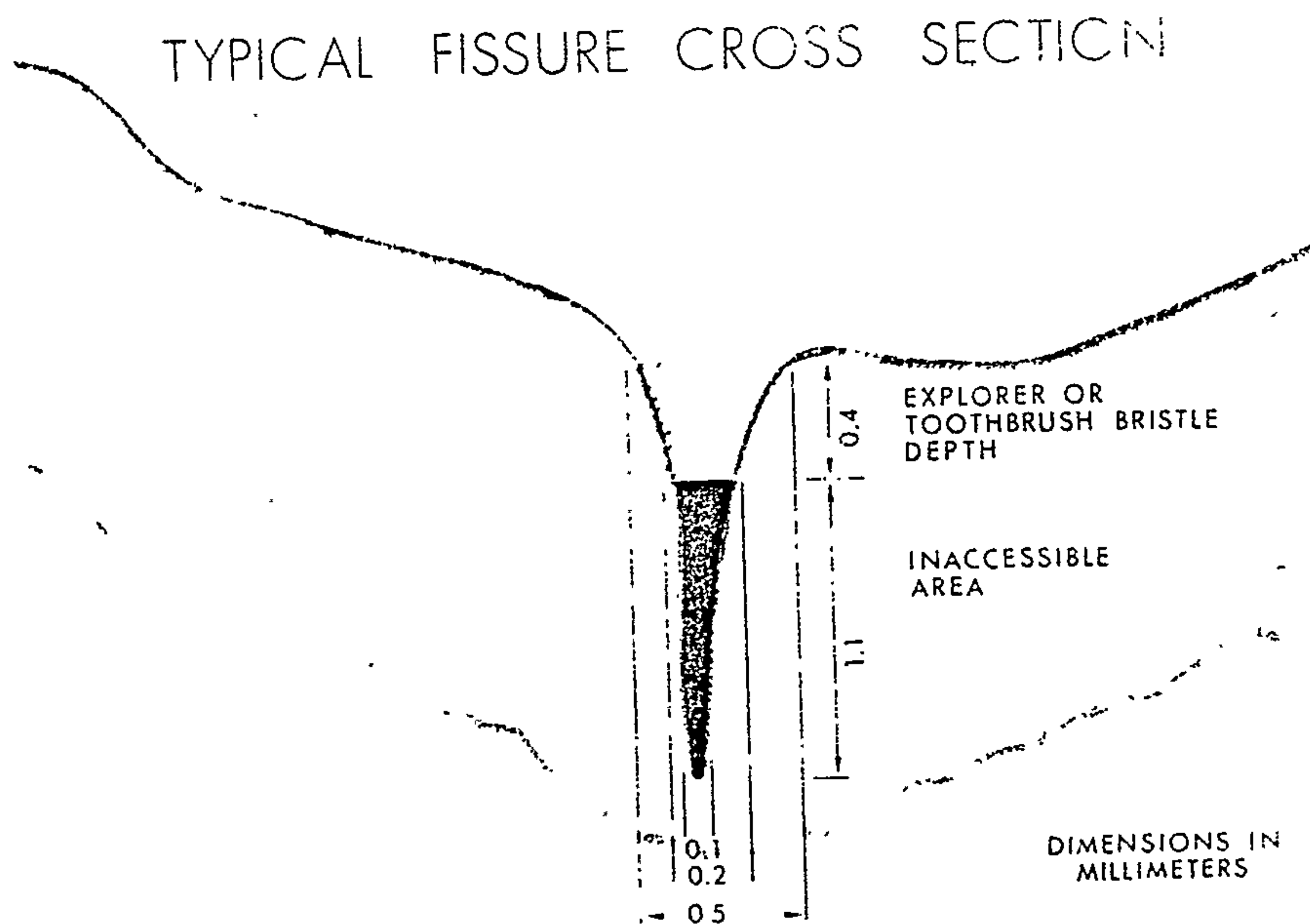


Fig. 2 . Cross-section of an occlusal fissure showing the inability of an explorer or toothbrush bristle to reach the base.
(Newbrun, 1983.)

saliva is the fluid present in the mouth and surrounding the tooth. The tooth is where the dental caries take place, without a tooth no caries formation will occur. In this presentation saliva will not be presented in detail, however, a brief mention of it will be made here. Newbrun (1983) stated that saliva is the mixture of secretions in the oral cavity. It is the oral fluid derived from the major salivary glands, minor glands of the oral mucosa and traces from the gingival exudate. In patients who suffer from such conditions as xerostomia, Sjörgren's syndrome, surgical intervention, drug therapy and obstruction of salivary duct there is a deterioration of the oral health. Rampant caries developed in patients with little or no previous caries experience and widespread cervical lesions are characteristically produced (Llory et al. 1971, Brown et al. 1975). It seems that the physical washing and irrigating effects of saliva appear to be necessary for maintaining a clean mouth. Besides these actions it is also known to act as a buffer in reducing the effect of acids produced by the microflora.

2.2.1 Tooth Morphology and Archform

The importance of tooth morphology in dental caries was demonstrated as early as 1929 in Lady Mellanby's classical studies (Konig 1965). Attempts to induce caries in dogs even with hypoplastic enamel and dentine failed because of the wide spacing and the conical shape of their teeth.

Clinically, the pit and fissure areas of the posterior teeth are highly susceptible to caries. This is so because food debris and microorganisms readily impact in the fissure.

Some of the fissures may be very deep so that tooth brushing and in some cases even probing are not possible to remove the impacted food completely (Figure 2). The relationship between caries susceptibility and the depth of the fissure has been investigated.

Certain surfaces of a tooth are more prone to dental caries than others. In the lower first molars the likelihood of decay in ascending order is lingual, distal, mesial, buccal and occlusal, whereas in the upper first molars the order is distal, buccal, palatal, mesial and occlusal. The lingual cingulum of the upper incisors are more prone to caries than the buccal surface. These differences in the site of caries attack on the tooth are due to the morphology of the tooth (Newbrun 1983).

Besides the morphology, the type of teeth and the arch form also influence their susceptibility to dental decay. The most susceptible permanent tooth is the lower first molar, followed by the upper first molars and the upper and lower second molars. The next in sequence are the second premolars, upper incisors and first premolars. The lower incisors and the cuspids are the least likely to develop lesions (Figure 3). Carlos and Gittelsohn (1965) stated that all teeth exhibited similar patterns of annual attack curves (of differential intensity) which reached a peak 2 to 4 years following eruption, and decline after that, indicating that there is a "maturation-factor" operating after this period.

The arch form also contributes to the susceptibility of the tooth to dental caries. Overcrowding and irregularities in arch form create a stagnation area which favours carious formation.

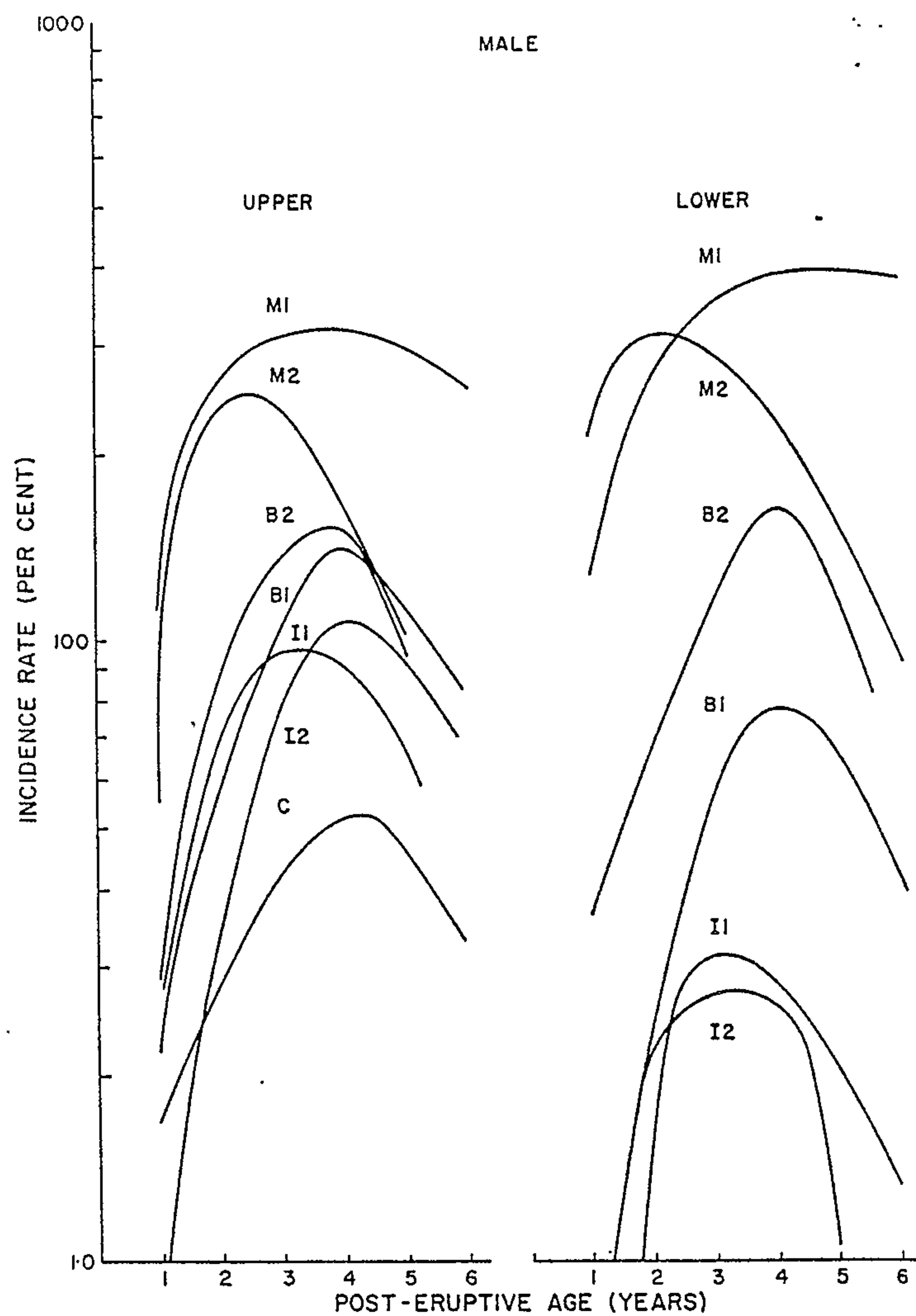


FIG. 3. Annual probability of caries attack ($100 Q_x$) of the permanent teeth, male children, Kingston, New York. Semi-logarithmic scale.

M2 = second molars, M1 = first molars.

B2 = second premolars, B1 = first premolars,

C = canines, I2 = lateral incisors, I1 = central incisors.

(Carlos and Gittelsohn, 1965.)

2.2.2 Dental Enamel

Dental enamel forms the hardest substance of the body and a highly calcified enamel is made up of about 97% by weight of mineral, 1% organic matter and 2% water (Brudevold 1962). The organic matter of enamel is made up of fractions of lipid, protein, peptides, carbohydrates, citrate and lactate. The inorganic components consist of apatite crystals $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$ whose inorganic components, calcium, phosphate and hydroxyl ions may be replaced by other ionic species.

Structurally the enamel is dominated by a wavy pattern of enamel prisms which run from the dental enamel junction to the outer enamel surface. The enamel prism is made up of tiny crystallites which form the building stones of the enamel as a whole. As mentioned earlier these crystallites made up the mineral part of the enamel and consist of non-stoichiometric impure apatite. These rod shaped crystals of apatite are packed closely together. They aligned themselves approximately along the length of the prism in an orderly arrangement. A prism in cross section contains between 500-1000 crystallites. The crystallites diameters are larger near the surface than away from it in deciduous and permanent teeth, whereas there is no difference between crystallite diameters near and far from the surface in non-erupted teeth (Arends et al. 1983). This is illustrated in table 2. From this study Arends et al. concluded that after eruption the combined effect of demineralisation and remineralisation cycle, relatively small crystallites dissolve partly or completely and form larger crystallites. This reflects the influence exerted by the oral environment on the demineralisation and remineralisation

Table 2: Average crystallite diameters ($\bar{d}$) in human enamel in nm.

	permanent (age group 35-40)	deciduous (age group 10-12)	non-erupted (age group 35-40)
2.5 μm from the surface	59	88	50
150 μm from the surface	38	46	46
ratio	≈ 1.6	≈ 1.9	≈ 1

Arends et al., 1983

process. The presence of larger crystallites near the surface than far away from it indicates the presence of a chemical gradient within the enamel which influences this type of formation. This chemical gradient relates to the distribution of the inorganic and organic matters of the enamel. The distribution is rather complex but the general pattern has been studied by Robinson et al. (1983). Calcium and phosphate distribution decrease in concentration from the surface towards the amelodentinal junction. Their concentration is also lower beneath the molar fissures, lingual pits of the anterior teeth, around the cornua and towards the cervical margin. These areas are usually coincident with low density enamel with a relatively high protein content. As for fluoride, the concentration is higher at the enamel surface falling to a plateau in the mid-enamel and then slightly increasing towards the amelodentinal junction. Conversely, carbonate and magnesium, both of which have been associated with a more soluble mineral, increase in concentration from the surface to the interior.

2.3 BACTERIAL PLAQUE

The microflora and the substrate components of dental caries etiology will be discussed together under this title. The reason being that they form the major components of the dental plaque or bacterial plaque. Dental plaque may be described as a complex aggregation of bacteria which are embedded in a matrix of polymers of bacterial and salivary origin found on the tooth surface (Silverstone 1981).

On eruption teeth are covered by organic structure

of embryonic origin. This structure is soon worn away and replaced by the acquired pellicle upon which dental plaque are formed. The development of the dental plaque could be explained as follows (Figure 4). When a tooth surface is thoroughly clean and polished and then exposed to saliva, the salivary components including glycoproteins adhere to the tooth surface forming the pellicle. The pellicle is about 0.3-1.0 μm thick and is composed of undergraded salivary glycoproteins which are made up of amino acids and sugars. Within 2 hours after cleaning Coccal bacterial are absorbed onto the pellicle coated enamel (Bowden et al. 1975). The pioneer bacteria include streptococci and Neisseria (Ritz 1970). In about 24 hours 95% of the total cultivatable flora can be made up of streptococci. In order to form a successful colony the bacteria must first adhere to or be retained at the surface of the tooth and then multiply. Bacteria adhere to the pellicle or the tooth surface through various means. For example, they can be retained in the rough, pitted or cracked surface of the enamel. There can also be a non-specific interaction base or charge or hydrophobic properties and specific interaction of bacterial surface receptors with components of pellicle. Last but not least, adhesion between bacteria, either of the same or different species may also occur (Marsh 1980). The bacteria once they adhere to the enamel surface will then multiply forming microcolonies embedded in an organic matrix of salivary glycoproteins and bacterial extracellular polysaccharides. Both gram-positive and negative cocci are present and these may be aerobic or facultative anaerobes.

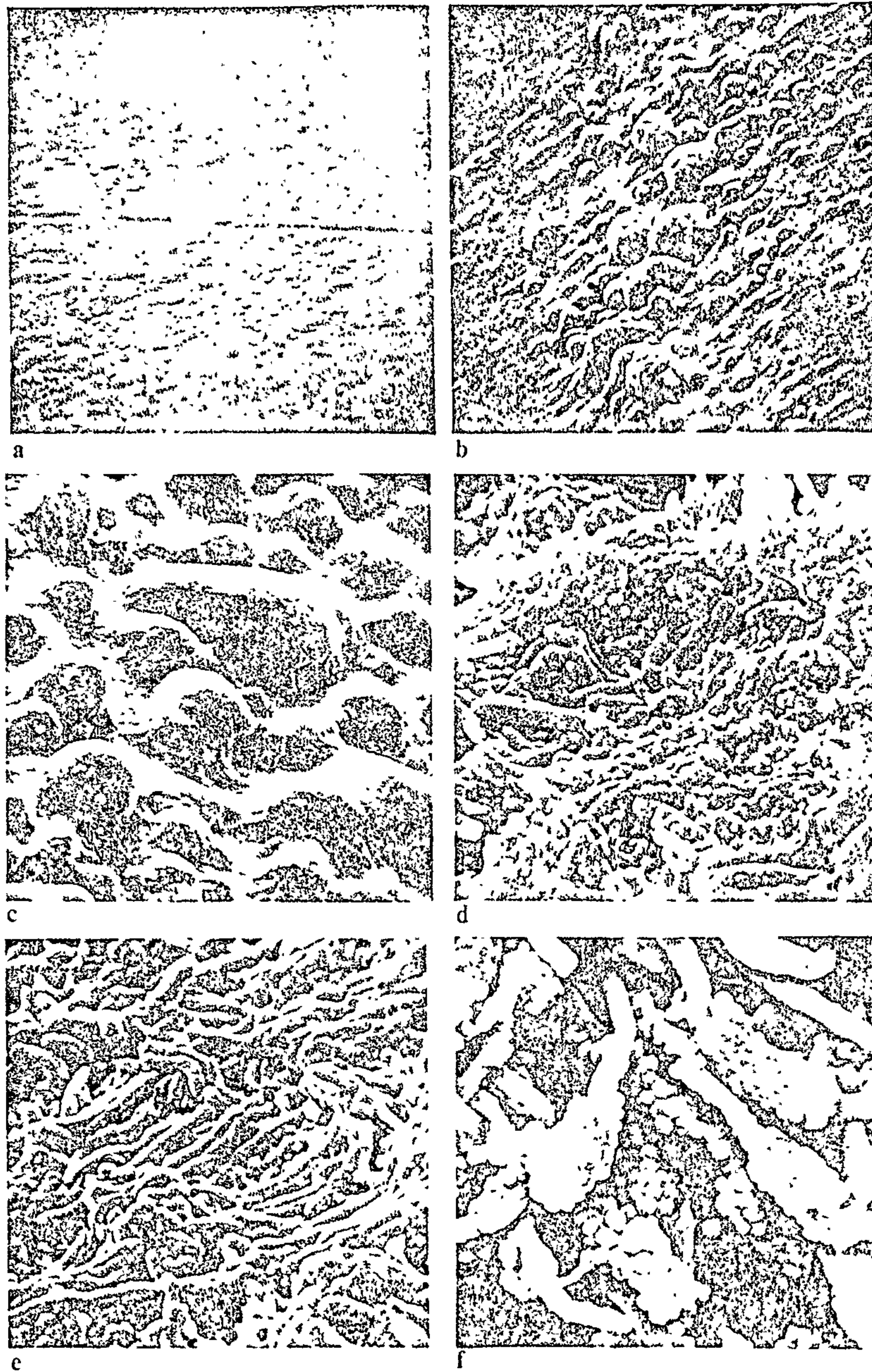


Fig. 4 Development of dental plaque on a clean enamel surface. Coccoid bacteria deposit as pioneer species (a) and multiply to form micro-colonies (b), eventually resulting in an even film of organisms embedded in a matrix of extracellular polymers of bacterial and salivary origin (c). With time the complexity of the community increases and rod and filament shaped populations appear (d and e). In the climax community many unusual associations between different populations can be seen, including 'corn cob' arrangements (f). (Magnification approx. $\times 1150$). Marsh P., 1980.

Other bacteria present at this early stage include *Actinomyces viscosus*, *S. mitis*, *Staphylococcus epidermidis*, *A. isrealii*, *Peptostreptococcus* sp. and *Veillonella alcalescens* (Socransky et al. 1977). Filamentous bacteria begin to appear on the third day and by the 7-14th days the plaque appear to be composed largely of filament. There is an increase in the anaerobic filamentous bacteria such as *Fusobacterium*, *Veillonella*, *Actinomyces* and *Bacteriodes*. However, it should be noted that while cocci, including streptococci decrease relatively, they increase in absolute terms.

The importance of bacteria to caries is shown by the following facts:-

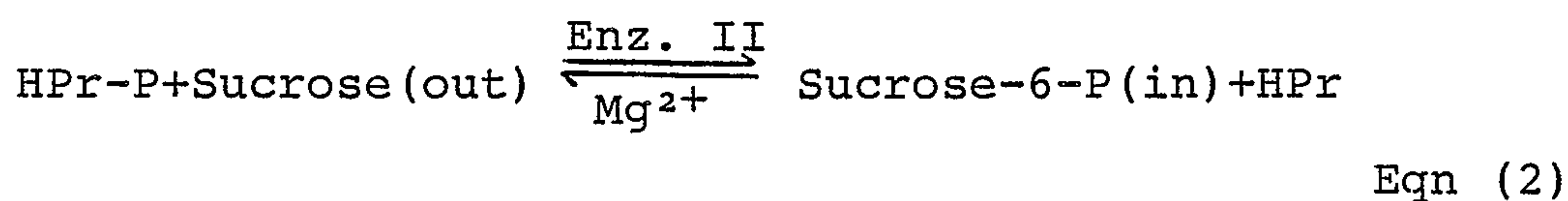
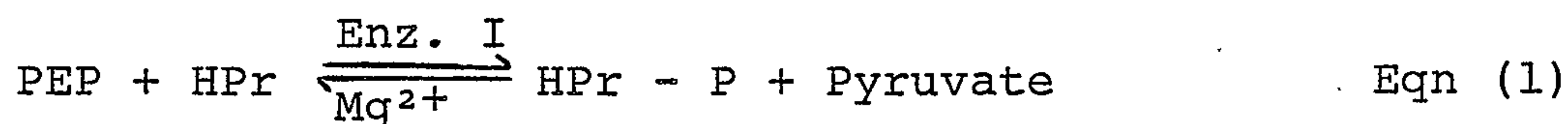
- "1. Germ-free animals do not develop caries.
2. Antibiotics fed to animals are effective in reducing the incidence and severity of caries.
3. Unerupted teeth do not develop caries, yet these same teeth when exposed to the oral environment and microflora can become carious.
4. Oral bacteria can demineralise enamel and dentine in vitro and produce caries like lesions.
5. Microorganisms have been histologically demonstrated invading carious enamel and dentine. They can be isolated and cultivated from carious lesions" (Newbrun p.50, 1983).

The absolute role of bacteria in dental caries has been firmly established by Orland and his co-workers in their study on the use of germ free animal techniques in experimental dental caries (Orland et al. 1954). And also by Fitzgerald and Keyes (1960). They showed that susceptible rodents on a highly

cariogenic diet did not develop caries under germ free conditions. Caries developed in the same animals when they are fed with the same diet after the introduction of bacteria. Keyes (1960) also proved the infectious and transmissible nature of dental caries. He mono-infected germ free animals with known strains of streptococci and showed that the organism became transferred to uninfected animals who became susceptible to dental caries.

The bacteria that are well known to be highly cariogenic are the strains of streptococcus mutans of both human and animal origin (Huxley 1976). The other oral bacteria that are able to induce caries to a certain extent are strains of *S. sanguis*, *S. salivarius*, *S. milleri*, *Lactobacillus acidophilus*, *L. casei* and *Actinomyces naeslundii* and *A. viscosus* (Silverstone 1981). Plaque bacteria obtain their energy for growth by fermenting substrates that are available in the plaque as well as in the oral environment. The substrates that are preferred are usually of carbohydrate origin. However, some oral bacteria are able to utilise amino acids as an alternative to carbohydrate while other bacteria depend entirely on amino acid. Besides these substrates bacteria in the dental plaque are continually dying and lysing, and in so doing release their components as nutrients for other bacteria to utilise. Furthermore, bacteria are also capable of using their stored glycogen when carbohydrates are not available. The results of these fermentation processes are usually the production of acids. Thus acid production is taking place all the time in the dental plaque (Silverstone 1981). This acid is enough to lower the pH of the plaque but

it is not sufficient to cause caries without the aid of dietary carbohydrates. The main fermentable carbohydrates in the diet are sucrose and starch. The main reaction involved in the degradation of dietary carbohydrates is shown in Figure 5 (Kleinberg et al. 1981). Starch is converted by salivary amylase to maltose which is further degraded by maltase to glucose. Lactose is converted to galactose and glucose. Sucrose which has been highly associated with dental caries is converted to glucose and fructose. Glucose is the central sugar in the metabolic pathways leading to the production of acid by oral bacteria. However, in the late 1970's St. Martin, E.J. and Wittenberg, C.L. in their study showed that the sucrose molecule can be actively transported across the cytoplasmic membrane into the bacterial cell (Nicholas 1983). This process is known as a sucrose-phosphoenol pyruvate-phosphotransferase system (PTS system, see Figure 6). The overall reaction is summarised by the following equation:



Where PEP = Phosphoenolpyruvate

HPr = Histidine-rich protein

Enz. I = Enzyme I

HPr-P = Phosphorylated derivative of the protein

Enz. II = Enzyme II

Mg²⁺ = Magnesium.

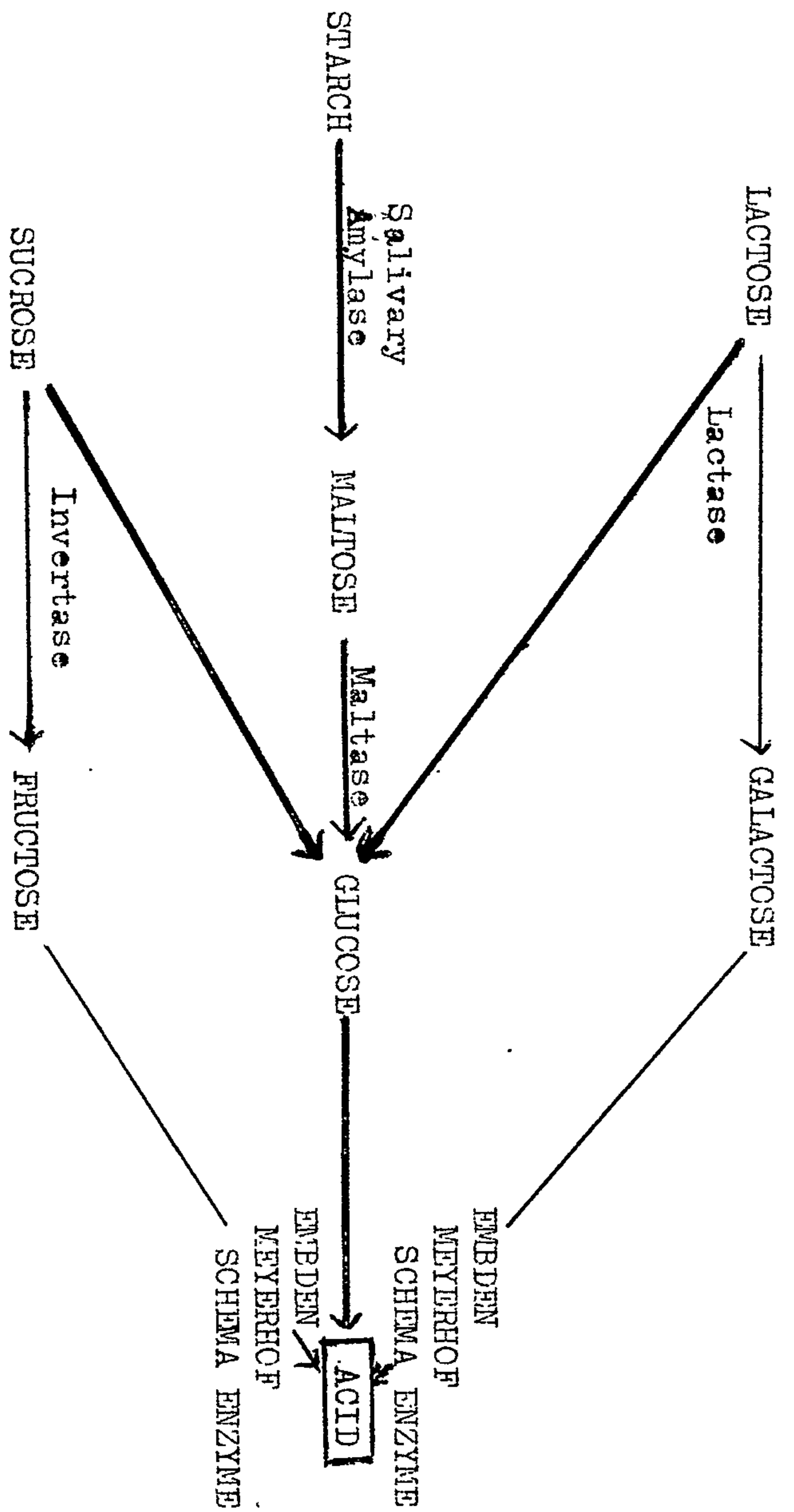


Figure.5: Outline of the reactions involved in the degradation of sucrose, lactose, and starch the most common of the dietary carbohydrates fermented by the bacteria in the oral cavity.
Kleinberg et al., 1981.

In Equation (1) pyruvate is formed from PEP (phosphoenolpyruvate) by transferring a phosphate group from PEP to the HPr giving rise to HPr-P that is the phosphorylated derivative of the protein. This reaction is catalysed by the cytoplasmic enzyme I in the presence of magnesium (Mg^{2+}).

Enzyme II which is present in the bacterial cell binds with the extracellular sucrose and the HPr-P protein. In the presence of Mg^{2+} , sucrose is actively transported across the membrane and released into the cytoplasm as sucrose-6-phosphate. This reaction is shown in Figure 6. Sucrose-6-phosphate is then metabolised to produce more PEP and subsequently lactic acid. However, under certain conditions where sucrose is limiting, formic acid, acetic acid and ethanol are produced. The process is summarised in Figure 7. This figure shows there are two alternative fates for pyruvate. If there is high concentration of carbohydrates there will be high concentration of fructose diphosphate (FDP) in the bacterial cell. This will stimulate the enzyme lactate dehydrogenase (LDH) while the enzyme pyruvate formate lyase (PFL) is simultaneously inhibited by the high concentration of glyceraldehyde-3-phosphate. This will give rise to plentiful lactic acid production (Silverstone 1981).

The acids produced as a result of bacterial activity play an important role in the initiation and progress of dental caries. Lactic acid has been associated with dental caries since the time when Miller first proposed the acidogenic theory for dental caries in 1890 (Newbrun 1983). A number of studies has indicated that many organisms present in the dental plaque are capable of producing other acids

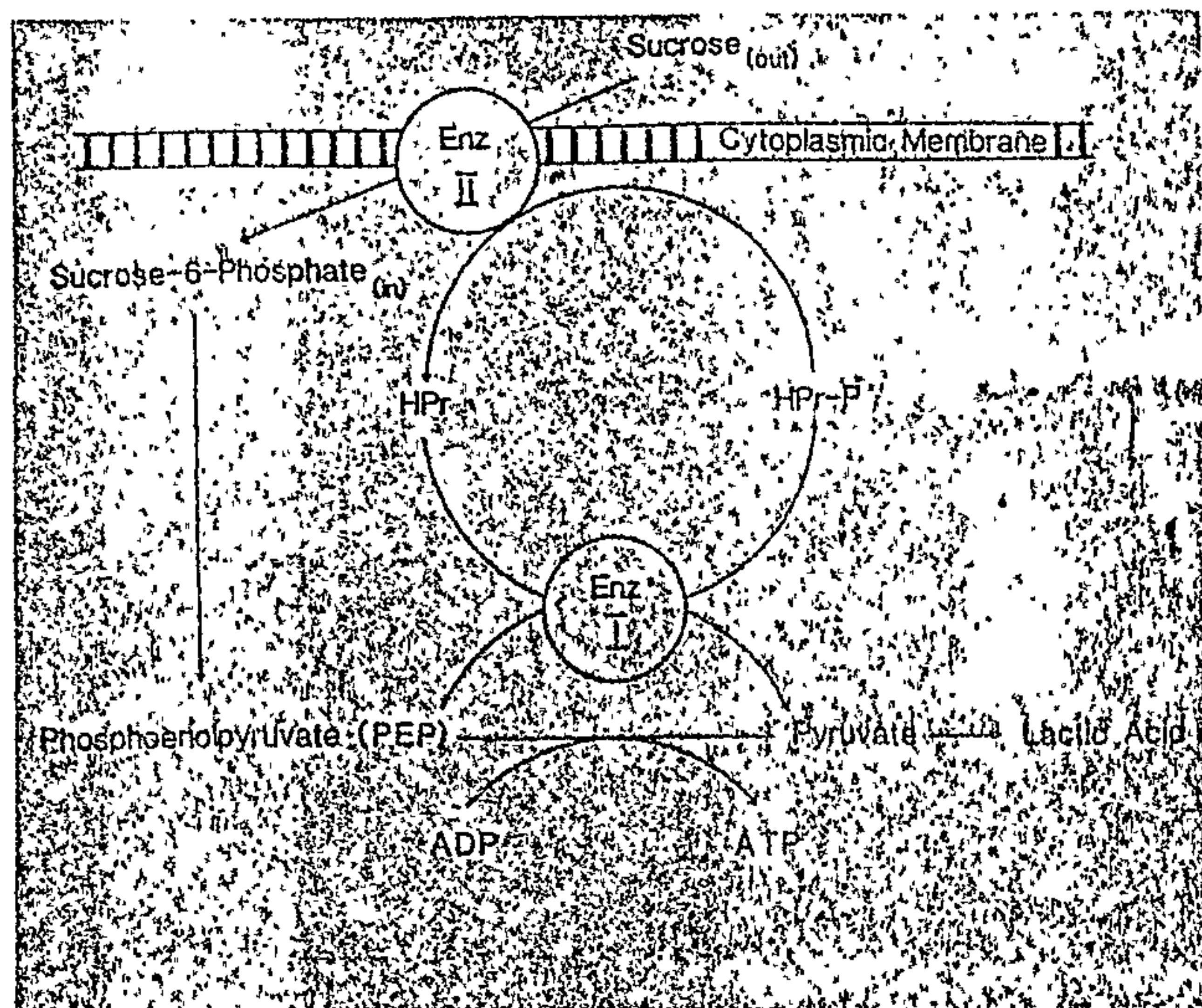


Figure.6; Showing the Sucrose - phosphoenol pyruvate - phosphotransferase System.

Nicholas, 1983.

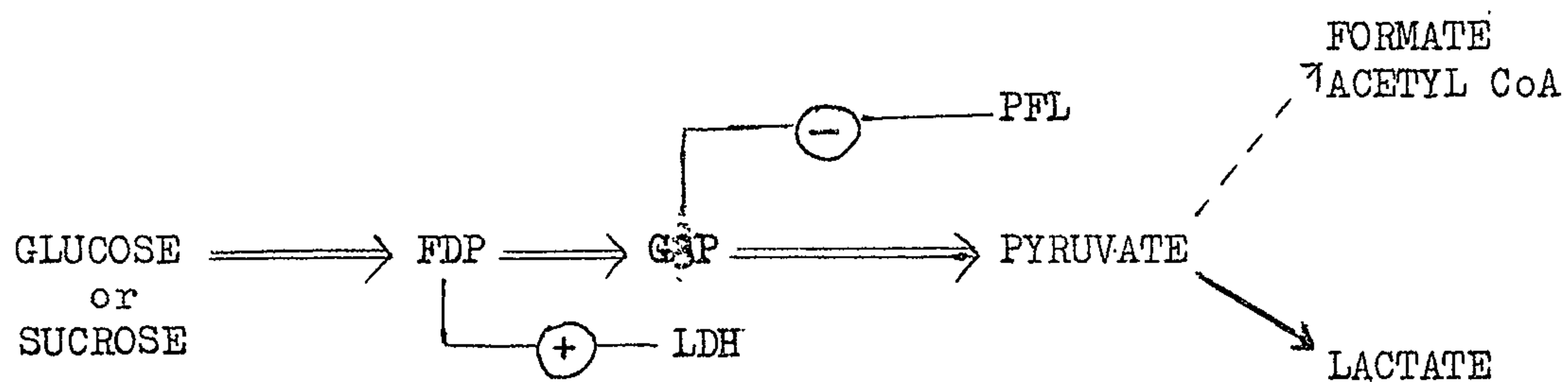


Figure.7: Summarise the fate of pyruvate.

Silverstone, 1981.

besides lactic acid as their major end products. In vitro studies of volatile acids produced after plaque metabolism had been carried out by a number of investigators such as Gilmour and Poole (1967), Geddes and Gilmour (1969). Tyler showed that volatile acids are present in dental plaque from freshly extracted teeth (Tyler 1971). In 1975 Geddes carried out a study on acids produced by human dental plaque metabolism in situ. From her experiments she concluded that both lactic acid and volatile acids are present in starved, 'resting' and rapidly metabolising plaque. After exposure to sugar under dietary conditions, high concentrations of lactic acid rapidly builds up in human dental plaque as the pH decreases (Geddes 1972 and 1975). These findings were supported by Distler and Kroncke (1983) who showed that in the resting plaque, lactic acid and acetic acid dominate and account for about 70% of total acids. Propionic and formic acid each amount to about 10% of the total measured acid. Traces of butyric, valeric and succinic acid were also detectable in low amounts. (Table 3). Following sucrose rinsing there is a steep increase in lactic acid associated with decreasing percentage of the other acids (Figure 8). This result is in good agreement with that of Geddes (1975) and Vratsanos and Mendel (1982) (Table 4). The absence of lactic acid in the resting plaque measured by Vratsanos and Mendel (1982) may be due to a different length of resting period (Distler and Kroncke 1983).

From these studies, it seems that lactic acid did play a major role in initiating caries. However, other acids are also important, but they are weaker acids when compared to

TABLE 3
RANGES, PERCENTAGE PATTERNS, AND MEAN VALUES OF ACIDS IN RESTING PLAQUE

Acid	Total Measured Acid		Mol %	
	Range ($\frac{\text{nmol}}{\text{mg ww}^*}$)	Mean ($\frac{\text{nmol}}{\text{mg ww}^*}$)	Range	Mean
Lactic Acid	3.77 - 15.32	9.24 (3.59)	23.61 - 54.97	36.09 (9.55)
Formic Acid	0.49 - 5.25	2.75 (1.56)	5.75 - 17.54	10.49 (4.21)
Acetic Acid	1.70 - 22.00	10.23 (6.23)	24.86 - 58.29	37.02 (9.97)
Propionic Acid	0.74 - 16.36	3.94 (4.31)	3.46 - 32.02	12.52 (8.28)
Butyric Acid	0.35 - 3.08	1.38 (1.08)	1.17 - 9.34	3.55 (3.28)
Total Acid	6.85 - 51.10	27.05 (13.30)		

*Wet weight calculated by ATP content.
n = 11; standard deviation given in parentheses.
(Distle and Kroncke, 1983)

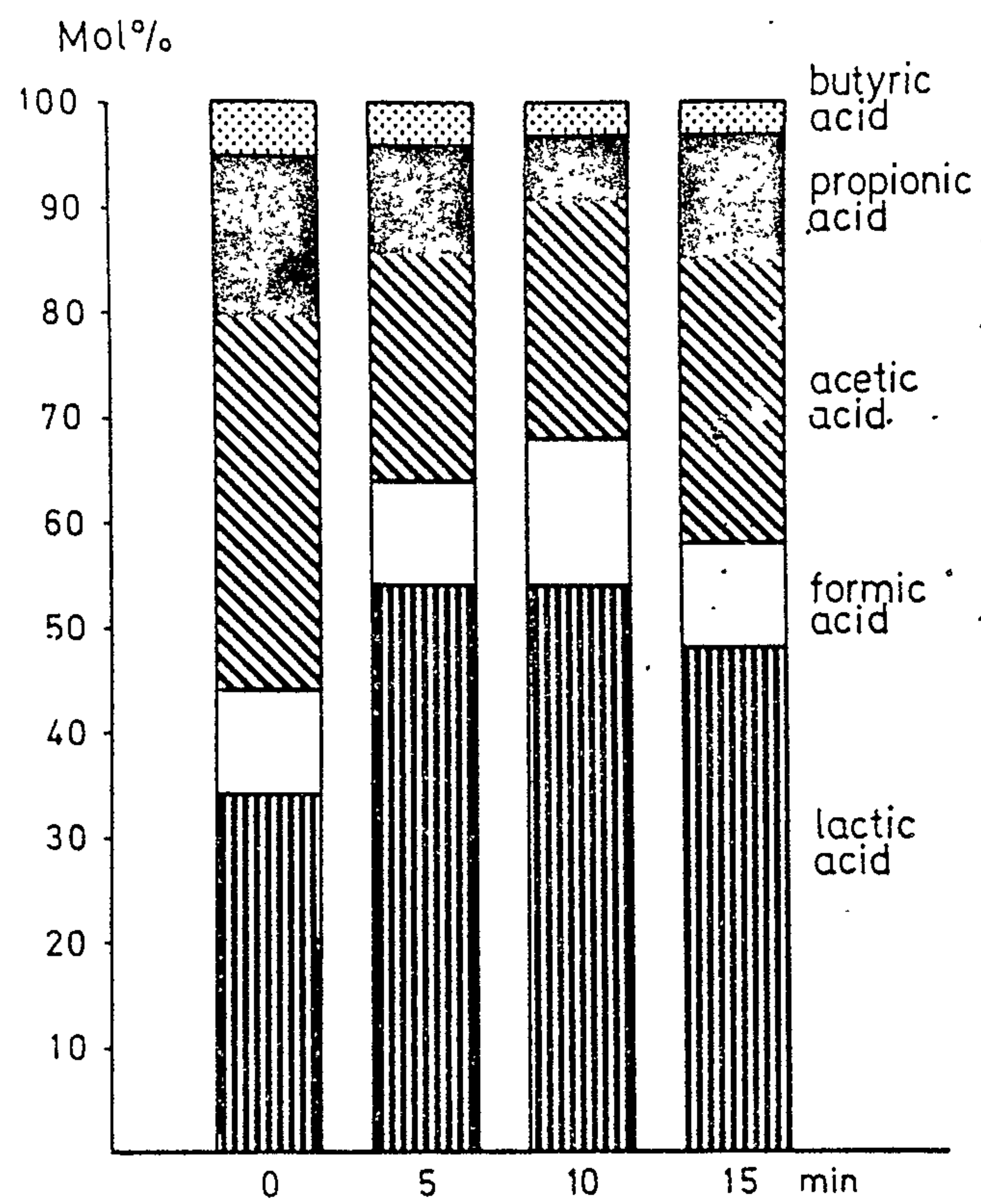


Fig. 8- Mean percentage pattern of acids after sucrose rinse.
(Distle and Kroncke, 1983)

TABLE 4
COMPARISON OF ACIDS IN PLAQUE BEFORE SUCROSE RINSING (NMOL/MG WET WEIGHT)

Acid	Geddes ⁶ Resting Plaque	Vratsanos and Mandel ¹⁴ Resting Plaque (CS)	This Study Resting Plaque
Lactic Acid	5.0	0.0	9.24
Formic Acid	.*	10.4	2.75
Acetic Acid	20.5	15.3	10.23
Propionic Acid	11.8	4.0	3.94
Butyric Acid	+†	2.2	1.38
Pyruvic Acid	.*	0.0	+†
Succinic Acid	.*	1.2	+†
Total Acid	37.3	33.1	27.05

*Not estimated.
†Only traces.

(Distle and Kroncke.1983)

lactic acid. The important factor that favours the initiation and progress of dental caries is the fact that the acid level is kept high over a prolonged period of time.

It is important to bear in mind that dental plaque helps to maintain the acid level at a higher level over a prolonged period of time. This takes place in a number of ways. The cariogenic bacteria in the dental plaque are able to produce acid rapidly from carbohydrates. They are also able to survive under acidic conditions and to proliferate upon hard tooth surface. It is also important to bear in mind that dental plaque most rapidly and extensively collects in inaccessible areas such as the interproximal areas and in pits and fissures. The organic matrix of the dental plaque has a significant effect on the ecology of the plaque and is also important in caries development. It acts as a diffusion limiting membrane or barrier, therefore potentially harmful bacterial products such as acids may be retained in high concentrations at a particular site where they can initiate caries. The same diffusion limiting effect may also render the buffering effect of saliva useless by slowing down its arrival to the site.

2.4 ENAMEL CARIES

Enamel demineralisation was demonstrated as early as 1912 by Head who studied the action of lactic acid and citric acid on human teeth. In 1914 white lesions were identified when microorganisms were seen beneath the intact surface layer (Nancollas 1983). Later subsurface demineralisation was produced by exposure of specific areas of enamel to plaque

at pH values in the range of 4.5-6.5. In contrast, surface softening in vivo as a result of contact with food and beverages, takes place at a pH of 2-4 in a relatively short time. These conditions were simulated in the work of Gray and Francis who expressed the rate of dissolution in terms of the diffusion of protons and undissociated acid molecules to the surface and also the complexation of calcium ion by the lactate buffer anion. They also showed that the rate of enamel dissolution is proportional to the acid concentration (Nancollas 1983). Thus enamel caries is essentially the result of the chemical dissolution of the enamel. The main process of dental caries is the diffusion of acids into the enamel which then demineralise the enamel. The products of this reaction then diffuse away from the reaction site.

Microradiographs of white spot lesions or initial carious lesions often reveal marked demineralisation of the subsurface enamel beneath the outermost layer of enamel (Fig. 9) (Newbrun 1959). What logical explanation could be given to explain the resistant property of the outer surface enamel to dental caries. The crystallites size and distribution described earlier contribute to the resistance of the outer enamel surface to caries. Groeneveld and Arends showed that the mineral content of the surface layer was only slightly affected by pH and demineralisation time, while the degree of demineralisation of the subsurface lesions tended to increase with lower pH and increased demineralisation time (Groeneveld and Arends 1975).

Silverstone (1968), using an acidified gel technique produced lesions on artificially abraded enamel surfaces

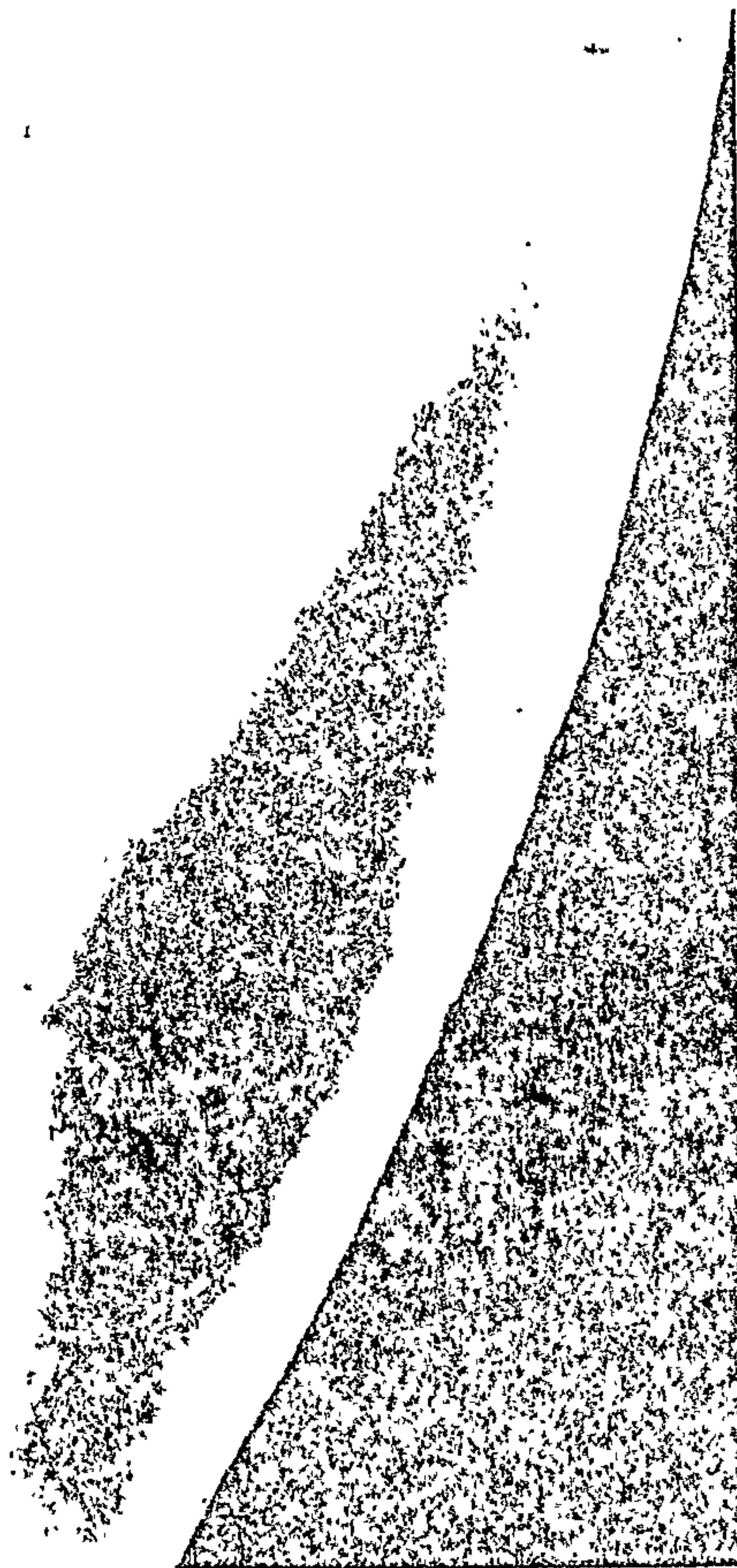


Fig. 9 Microradiograph of white spot lesion of enamel. Compare the extensive demineralization of the subsurface enamel with better mineralized surface layer (original magnification $\times 100$).

(Newbrun, 1983.)

which had up to 500 μm of surface enamel cut away prior to the experiment. The lesions created on these surfaces still showed well mineralised surface layers (Fig. 10). This experiment indicates that the special physical and chemical properties of surface enamel relative to subsurface enamel are not entirely responsible for the presence of a well mineralised surface zone above the small carious lesions. The reason for the surface zone remaining well mineralised in this experiment could be because it is the site where calcium and phosphate ions released by sub-surface dissolution or derived from the saturated solution in the plaque become reprecipitated into the surface enamel. The high fluoride concentration of surface enamel, presumably released at the initiation of solution of outer enamel, would also favour precipitation. Hence this special property of surface enamel relative to the subsurface enamel is also responsible for maintaining its resistance to caries dissolution for a longer period.

Silverstone identified zones in artificial white lesions very similar to those naturally occurring. These zones are described as the translucent zone, the dark zone, the body of the lesion and the surface of the enamel. Each of these zones is clearly identified from the other (Silverstone, L.M. (1973)).

The translucent zone lies at the advancing front of the carious lesion and is the first observable change in structure in the tissue in the carious lesion. The zone appears translucent because of the presence of spaces or pores. These pores are located at the prism boundaries, and

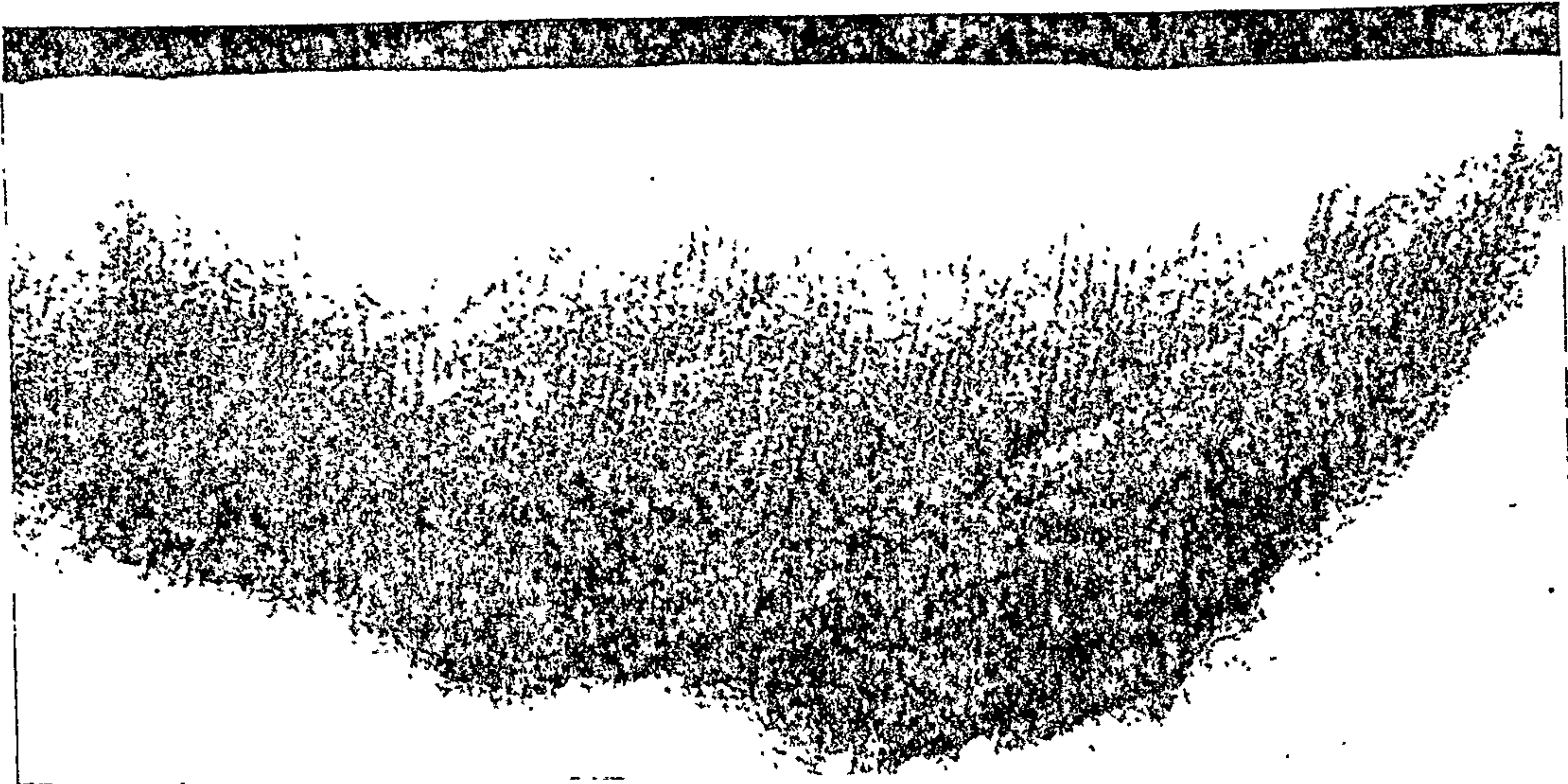


FIG. 10—Microradiograph of an artificial lesion created on abraded enamel. Approximately 500 microns of the original enamel was ground off before experiment. The lesion has penetrated the outer two-thirds of the remaining enamel and shows a deep surface zone that appears well mineralised. Striæ of Retzius, prisms and cross striations can be seen in the demineralised region. $\times 100$.

Silverstone, L.M., 1968.

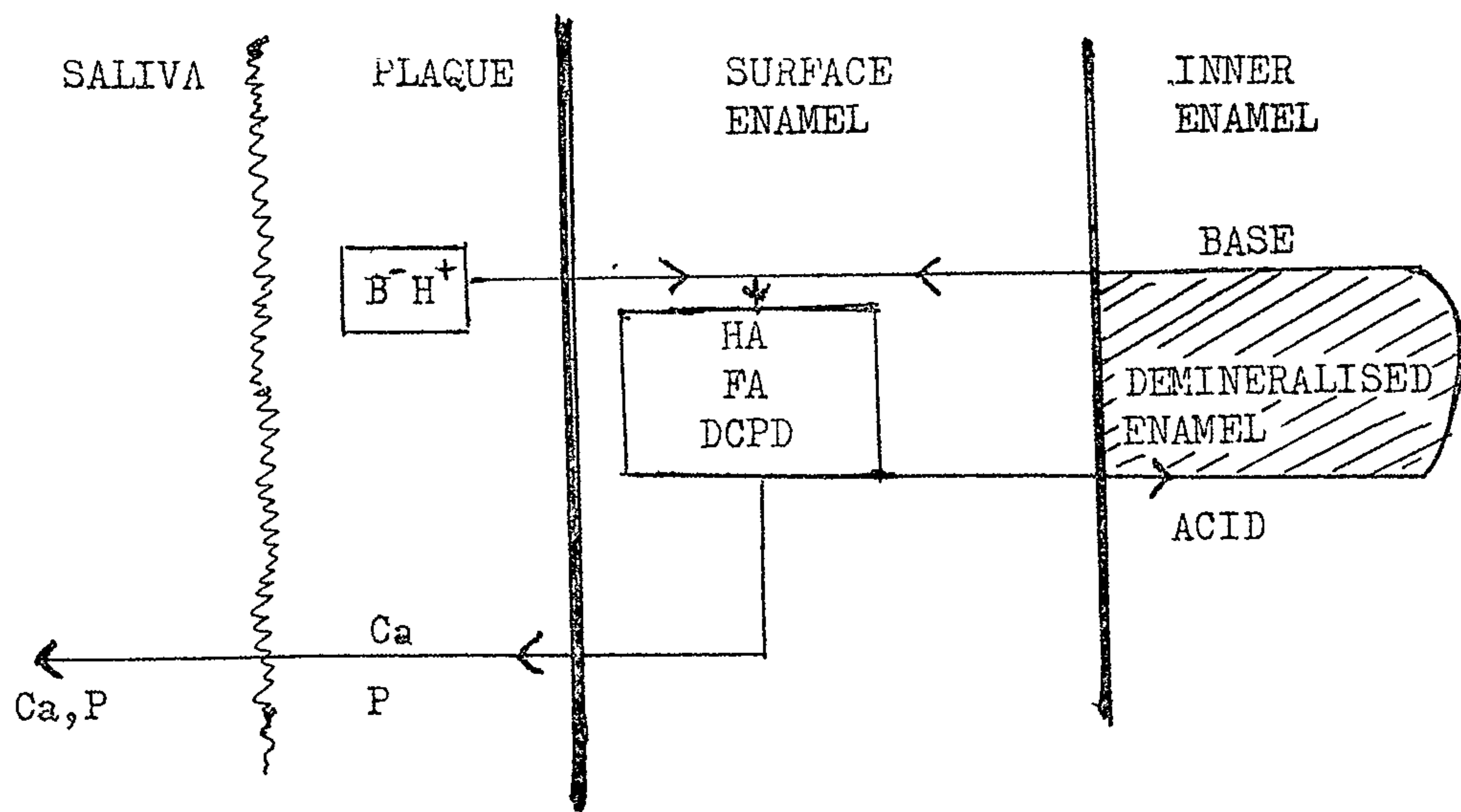


Fig.11: Schematic representation of model for subsurface demineralization.

Moreno and Zahradnik, 1974.

other junctional sites during the early carious process. It has been proposed that the spaces or pores are due to the removal of the mineral content of this zone (magnesium and carbonate rich minerals). The fluoride content of this zone is found to be relatively higher than the adjacent sound enamel (Weatherell 1971).

Superficial to the translucent zone lies the dark zone. Unlike the translucent zone the spaces or pores in this zone are relatively smaller. There are two possibilities that may govern the size of the spaces or pores in this zone. The first is that this formation of micropores could be due to the continued process of demineralisation. On the other hand experimental studies on the remineralisation of enamel caries indicate that following exposure to calcifying fluid in vitro there is a significant reduction in pore volume throughout the lesion (Silverstone and Poole 1968, Silverstone 1977). Furthermore, it has been found that lesions of "arrested" caries have a wide and well marked dark zone (Crabb 1966). Thus the presence of micropores could be interpreted as due to remineralisation. In a way this helps to explain the concept that the carious process in enamel is a dynamic process with phases of demineralisation alternating with remineralisation.

The body of the lesion lies superficial to the dark zone and deep to the relatively unaffected surface layer of the lesion. By far this zone is the largest proportion of the carious enamel in the small lesion. In this zone 20-30% of mineral is lost and this mineral is associated with calcium hydroxyapatite (Robinson 1983).

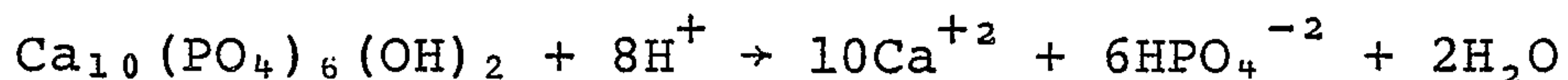
The surface zone is maintained at a relatively low level of demineralisation throughout the lesion formation and progression until a later stage.

Moreno and Zahradnik (1974) proposed a model to explain the subsurface enamel demineralisation and supported it with their in vitro experiments. The proposed model is that of a pumping mechanism whereby matter is pumped from the subsurface enamel to the surface zone and into the saliva (Figure 11). The surface enamel appears unaltered because it is continuously being regenerated. According to the model, acid produced by the activity of the microorganism in the plaque diffuse through the pellicle into the surface enamel. Under certain conditions of acid concentration and initial pH, a slight dissolution of the enamel surface occurs followed by precipitation of the solid phases; $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ [dicalcium phosphate dihydrate (DCPD)] and $\text{Ca}_5\text{F}(\text{PO}_4)_3$ [Fluoro-apatite (FA)]. The fluoride for the precipitation of FA comes from the naturally occurring fluoride in dental enamel. These solid phases in the surface layer are in quasiequilibrium with the solution in the pores of the "sound surface enamel layer". The chemical potential of both the organic and phosphoric acids is higher in this surface zone than in the subsurface enamel. Therefore, diffusion of acid constituents occurs from the surface zone into the subsurface enamel. The reverse is true for the chemical potential of calcium hydroxide. Furthermore, as the acid constituents diffuse deeper into the enamel, they are neutralised by the dissolution of the subsurface enamel mineral. Again, the chemical potential of calcium hydroxide in this neutralised solution is higher than that

in the solution of the surface zone. Therefore, basic constituents will diffuse from the subsurface region into the surface zone and finally into the saliva.

The presence of surface enamel defects in initial subsurface enamel demineralisation has been positively proven with scanning electron microscopy (Thylstrup and Fejerskov 1981). These defects take the form of eroded focal holes and tomes process pits together with the haphazard external erosion of the outer enamel surface. Figures 12-16. This changes markedly the initial stage of active carious dissolution of the subsurface enamel. This finding further strengthened the model proposed by Moreno and Zahradnik.

As mentioned earlier, enamel consists mainly of inorganic calcium and phosphate in the form of hydroxyapatite. The dissolution of dental enamel by acids occurs as a result of the reaction between the hydrogen ion (H^+) and the inorganic material of the dental enamel. The dissolution of the hydroxyapatite can simply be described as follows:-



with the form of the phosphate ion being determined by the pH of the system. This concept of dissolution is affected by the environment surrounding the enamel surface. Thus plaque, salivary pellicle, saliva and surface mineral phases may influence the overall reaction rates of enamel dissolution.

As a result of demineralisation, there is a scattered destruction of the enamel crystallites within the enamel prisms and at their borders. This destruction will, in turn, give rise to an increase in the volume of the intercrystalline

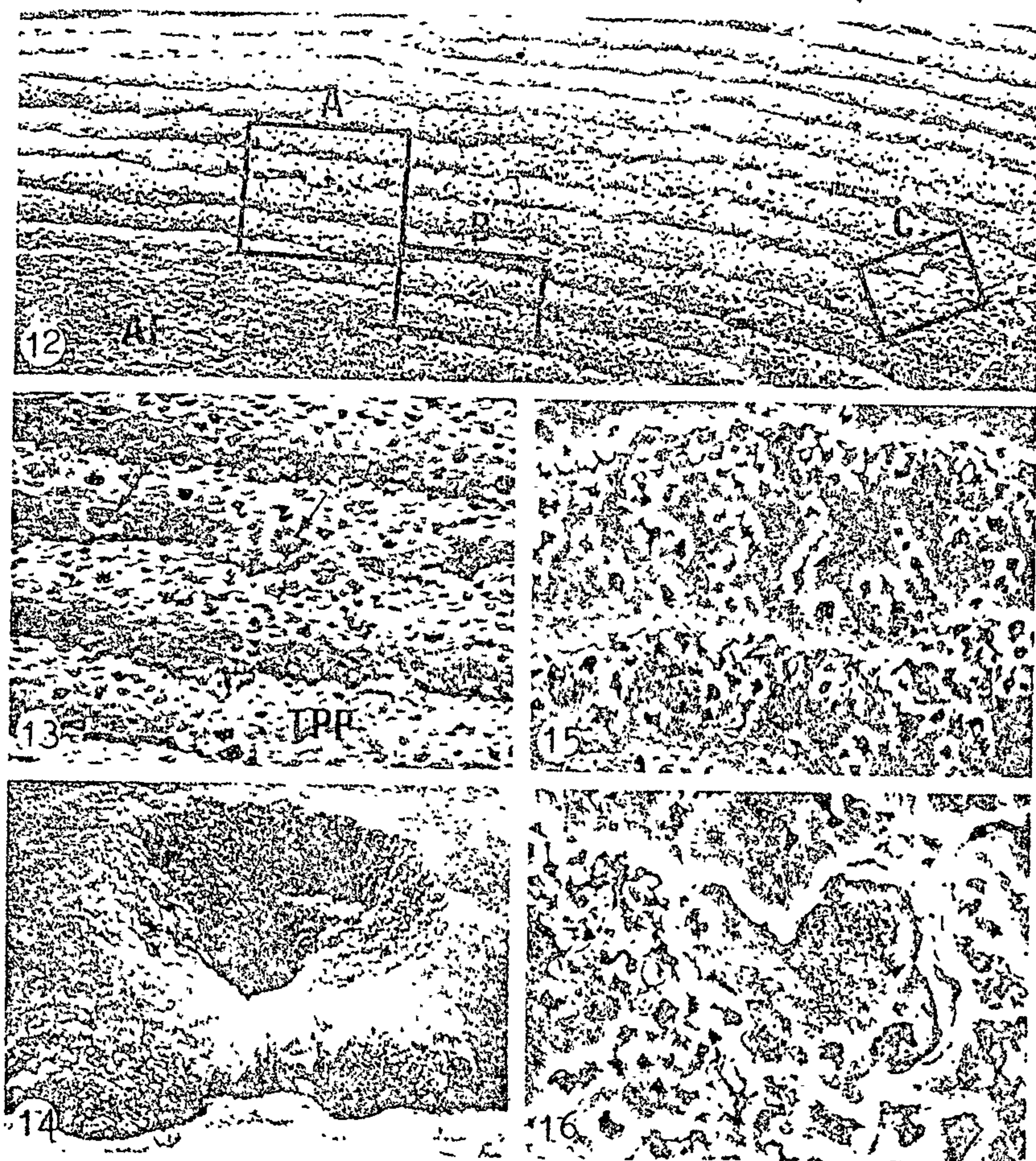


Fig. 12. SEM-photograph of initial surface changes cervical to approximal facet, (AF). Details of the framed areas A, B, and C are shown in Figs. 13-14, 15, and 16 (x 128). Fig. 13. Higher magnification of A showing deepened Tomes' process pits (TPP) and eroded focal holes, arrows (x 416). Fig. 14. Detailed appearance of eroded focal hole in Fig. 13, and microfractures along the perikymata edge (x 3690). Fig. 15. Detail of area B as observed perpendicular to the surface. Note deepened TPPs along the perikymata edge and the 'opening up' into the less discernable pits in the overlapping part of the perikymata. Arrow indicates stage of fissure formation (x 416). Fig. 16. Detail of area C with fractured perikymata edge with marked disintegration of microsurface (x 576). Thylstrup and Fejerskov 1981

spaces. These spaces are then occupied by amorphous material and some of this material gives a positive histochemical reaction for carbohydrates, which is not seen in normal enamel (Johnson 1967).

Carious dissolution starts in the centre of one end of the crystal and proceeds along the crystallite long axis forming a central hole. It then extends laterally towards the external surface (Newbrun 1983). As the number of dissolved crystal increases, the previously calcified tissue becomes porous. In the region of incipient damage peripheral arcade-like clefts or channels bounded by rows of resistant crystals can be observed. These resistant crystals appear larger, more isodiametric and electron dense than elsewhere. This indicates that some recrystallisation is taking place during the carious process. Initially, these remaining crystals preserve their preferential orientation but as caries process proceed to an advanced stage, there is disorganisation of the crystal. Eventually with the diffuse destruction of the apatite crystal, numerous bacteria can be observed invading the enamel lesions.

A study by Parfitt in 1956 concluded that the average time for dental caries to progress from incipient caries to clinical caries is 18 ± 6 months in children. This study was carried out on children in institutions where there is less opportunity for between meal eating and children are presumed to follow normal oral hygiene procedure. Thus the rate of progress of dental caries must be much faster in other children who are having regular snacks between meals and also who do not follow normal oral hygiene procedures (Parfitt 1956).

3. MODE OF ACTION OF STANNOUS FLUORIDE

Fluoride has been widely used as a preventive measure against dental caries. Many studies have been conducted to determine the mechanism of action of various forms of fluoride. However, no one can be absolutely specific as to how fluoride acts. The main mechanisms of action of fluoride which have been studied by researchers can be broadly grouped as follows:

1. Antibacterial effect - can kill organism (in high concentration)
 - interfere with bacterial adherence
 - interfere with the ability of the organism to produce acid.
2. Increase enamel resistance - through the formation of fluorapatite.
3. Increase rate of enamel maturation - newly erupted enamel has hypomineralised areas which may become mineralised within a few months after eruption. The presence of fluoride in the environment surrounding the tooth helps to increase the rate of mineralisation and accelerates the rate of enamel maturation.
4. Remineralisation of incipient enamel lesions - studies have shown that incipient lesions can be arrested or actually disappear because of (redeposition of mineral within the lesion (remineralisation) if the environment is changed to allow free access to saliva (natural remineralising solution). There is much evidence to indicate that fluoride increases the rate of remineral-

isation.

5. Improve tooth morphology. This is believe to be due to the effect of systemic fluoridation. Studies on the effect of water fluoridation on tooth size and shape have suggested that fluoride tends to make the teeth slightly smaller with shallow fissures.

These mechanisms of action of fluoride cover both the action of fluoride as a systemic agent and as a topical agent. There is no clear cut as to which one is the action of systemic or topical except for the belief that the action of systemic fluoride is responsible for improving the tooth morphology (Forrest 1956). Topical application of fluoride solution to tooth surfaces has been shown to cause significant reduction in dental caries during the ensuing 2 or 3 years. It is the aim of this chapter to review the literature regarding the mode of action of fluoride with emphasis on stannous fluoride as a topical application. The action of stannous fluoride can be divided into the effect of the stannous ion and the fluoride ion on the bacterial plaque, the sound enamel and the demineralised enamel (Purdell-Lewis 1981).

3.1 EFFECT ON BACTERIAL PLAQUE

It has been well established that bacterial plaque treated with fluoride results in reduced acid production by the microorganism in the plaque. Therefore fluoride must have influence on the microorganism in the dental plaque. Many studies have been carried out on the enzyme inhibiting effect of fluoride. This antienzyme theory of fluoride action is based on the fact that fluoride is known to inhibit

many enzymes including phosphatases, catalase, peroxidase and cytochrome oxidase (Hewitt and Nicholas 1963), hexokinase (Melchoir and Melchoir 1956), phosphoglucomutase (Nejjar 1948), enolase (Cimasoni 1972) and succinate dehydrogenase (Slater and Bonner (1952)).

As far back as 1889, Tappeiner and a few other investigators found that fluoride inhibited the fermentation of sugars by yeast. Subsequently Lohmann and Meyerhof (1934) showed that the conversion of phosphoglyceric acid to phosphopyruvic acid is inhibited by fluoride. The enzyme enolase which catalyses this reaction was identified by Warburg and Christian (Warburg and Christian 1942), who showed that this inhibitory action of fluoride involved the displacement of magnesium ions from the active enolase complex by magnesium fluorophosphate, resulting in an inactive enzyme complex. The inhibition of enolase by fluoride was also shown by Cimasoni as shown in Figure 17 (Cimasoni 1970). The method used by Cimasoni involved the determination of enzymatic activity by a photometric kinetic assay whereby the increasing concentration of the products of reaction are measured with time. As shown in Figure 17, the presence of fluoride causes an immediate change in the slope measuring the enzyme activity. However, if enolase is the site of inhibition of glycolysis in the saliva or bacterial plaque, it would result in the production of phosphoglyceric acid instead of lactic acid. A number of attempts to demonstrate the presence of phosphoglyceric acid in saliva or plaque were unsuccessful. Therefore, to say that enolase is the site of action is not entirely correct. The fact that fluoride greatly reduces the pH change implies that

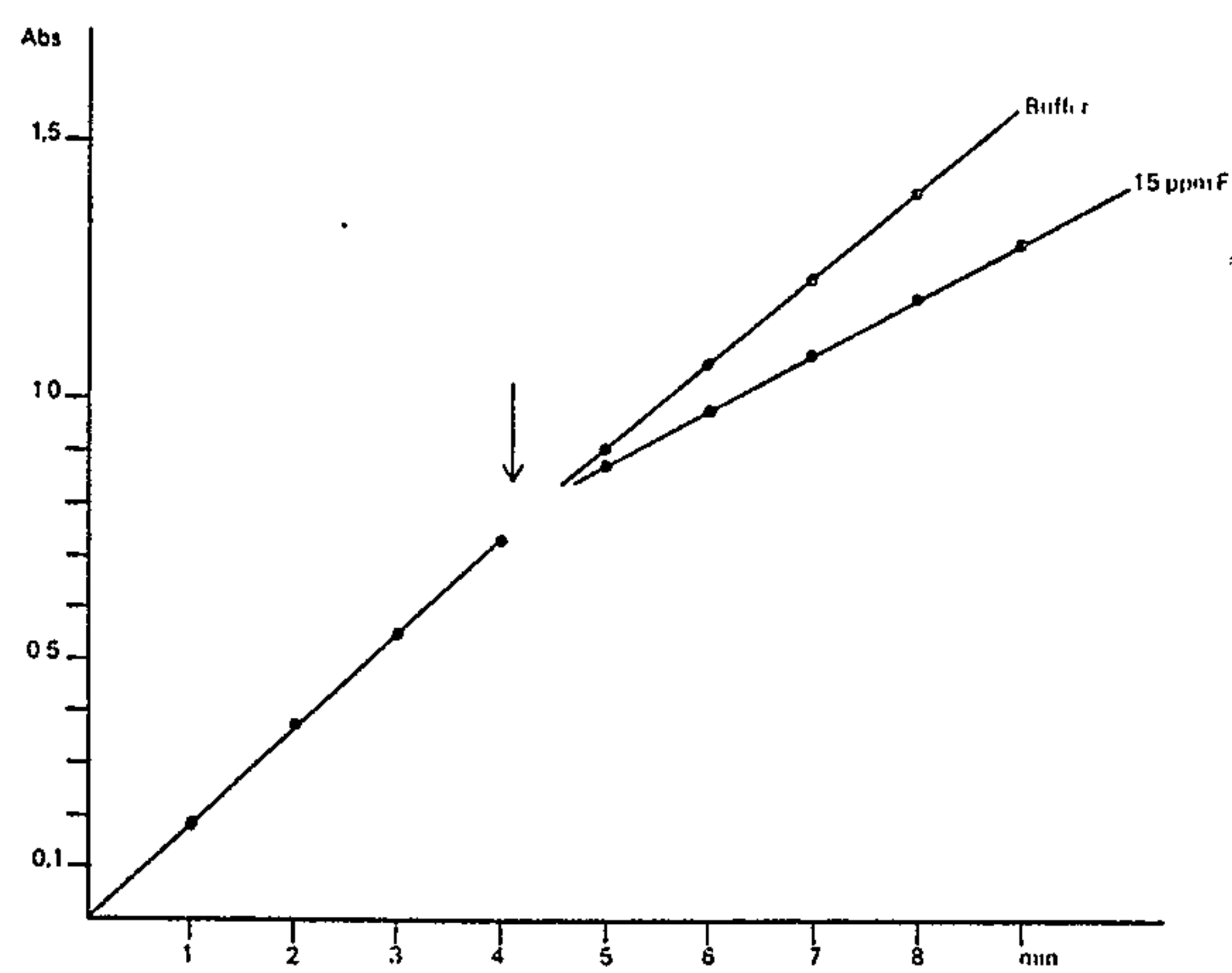


Fig. 17 Rapidity of the inhibitory action of fluoride upon enolase. Abscissa: time (minutes). Ordinate: absorbancy at 240 m μ .
Cimasoni, 1970.

it inhibits some early stage of glycolysis before that at which acid forms.

Biochemical studies on streptococcus salivarius indicated that at 9 ppm (parts per million) fluoride completely blocked the synthesis of glycogen when non-growing cells were incubated anaerobically with glucose at pH 7.0. At 1 ppm fluoride inhibition of glycogen synthesis is 15% and at 2-3 ppm inhibition is at 50%. This indicates the presence of a fluoride sensitive site in glucose absorption and phosphorylation (Hamilton, I.R. 1969).

Luoma and Tuompo in their study concluded that fluoride interacts with the cell membrane of the streptococci interfering with their ionic transport and sugar metabolism (Luoma and Tuompo 1975). In 1976, Kasket and Rodriguez (Kasket and Rodriguez 1976) showed that cells of streptococcus accumulated fluoride when incubated with sodium fluoride at pH 5.5. It was shown that fluoride binds to cytoplasmic components within the cells. Thus fluoride besides acting as an enzyme inhibitor is also capable of interfering in the transport of sugars into the bacterial cell.

Topical fluoride treatment inhibits dental caries by means of fluoride action in the outer and inner layers of the enamel. The reduction in dental caries increments as well as the increase of acquired fluoride in and on human enamel from topical treatments is well established for both in vivo and in vitro experiments (Wellock and Brudevold 1963; Englander et al. 1967; Heifetz et al. 1970; Horowitz and Doyle 1971; Arends and Schuthoff 1975; Sandham et al. 1973; Jenkins et al. 1969; Kasket and Rodriguez 1976).

Hamilton suggested that low concentration of fluoride may interfere with carbohydrate metabolism by one or more of the following mechanisms: (a) inhibition of enolase and consequently transport of glucose in cells; (b) inhibition of sugar translocation in membrane; (c) interference with cation transport and accumulation in cells and (d) inhibition of cellular phosphatases which dephosphorylate sugar phosphates resulting from transport (Hamilton 1977). According to De Jong et al. topically applied fluorides cause an alteration of the dispersion and polar surface free energy components of the enamel. These alterations will most likely disturb the adhesion of microorganisms to the enamel surface (De Jong et al. 1984).

Most of the studies mentioned above are specifically involving the fluoride ion alone and the majority of them are done in vitro. Stannous fluoride had been shown to be more effective than sodium fluoride in efficacy as well as in reducing the rate of enamel dissolution in vitro (Muhler et al. 1950; Howell et al. 1955; Gish et al, 1957), It has been shown that the number of streptococcus mutans was dramatically suppressed in groups treated with stannous fluoride whereas there is no change in the groups treated with sodium fluoride (Klock and Tinanoff 1984). The different results obtained with stannous fluoride and sodium fluoride application suggest a difference in mechanism of action between stannous fluoride and sodium fluoride (Leverett et al. 1984).

The ability of the stannous components of stannous fluoride to play a role in the inhibition of dental caries makes it more effective than sodium fluoride. Unlike the

stannous ion of stannous fluoride the sodium ion of sodium fluoride does not take part in the inhibitory reaction. According to Skjorland and his co-workers, the divalent tin cation seems to inhibit plaque formation whereas the monovalent sodium ion does not (Skjorland et al. 1978). Polyvalent cation may prevent plaque formation by interaction with negatively charged plaque components or by inhibiting some enzyme activity essential for plaque formation or interfere with the absorption mechanism for bacteria on the teeth. Oppermann stated that SnF_2 (stannous fluoride) inhibited acid production in plaque up to 6 hours after single mouth rinsing compared with ZnCl_2 (zinc chloride) effective for 4 hours, AlCl_3 (aluminium chloride) for 2 hours and the non inhibitory effect of MgCl_2 (magnesium chloride). Silver, tin and zinc in this order showed a decreasing inhibitory effect in the acid production of dental plaque (Oppermann 1981). The possible mechanism by which the stannous ion (cation) acts may be:

1. influencing the charge and thus the affinity of oral bacteria to the tooth surface (Gjeramo 1974);
2. competing with Mg^+ and calcium (which are known to be necessary for bacterial aggregation);
3. interacting with different anionic groups of protein (Gibbons et al. 1970; Gurd 1956). This interaction leads to precipitation of these proteins or as in the case of the enzyme to their inactivation either by blocking the active site or by causing configurational changes in the enzyme structure;
4. retention of the metals to anionic receptors in plaque which then react with the sulfhydryl (SH) groups present

in the bacterial enzymes. The metals which oxidise the thiol group, may inhibit the metabolism of carbohydrates by bacteria at various stages (Oppermann 1981).

Lilienthal observed that stannous fluoride markedly inhibited acid production of salivary bacteria and in fact was superior to sodium fluoride in this respect (Lilienthal 1956). The researcher carried out a study on the effect of a stannous fluoride mouthwash on acid formation in the mouth and showed that the mouth wash of stannous fluoride inhibits the oral acid forming system. This study gave further evidence of the antienzymatic action of either one of the ions of SnF_2 , or both. According to Lilienthal the mode of action of stannous fluoride on acid formation is similar to that of the Uranyl ion on the prevention of fermentation by yeast. The Uranyl ion combines firmly with the negative sites on the surface of yeast cells preventing transfer of glucose across the cell wall. In other words the stannous ion or the fluoride ion, or both, interfere with the transport of glucose into the cell. It has been shown that a single application of stannous fluoride on the teeth inhibits the acidogenicity of the bacterial plaque for several hours after application (Lilienthal 1956; Svatun and Attramadal 1978).

Tinanoff et al. used sodium fluoride and stannous fluoride at concentration of 100 ppm F^- as mouth washes to determine their effect on bacterial colonization of tooth enamel in vivo. (Tinanoff 1976). Mouth rinsing was performed either once or twice a day for up to 7 days. The enamel specimens were examined by scanning (SEM) and transmission

electron microscopy (TEM). It was shown that SnF_2 is much more effective on the microbiota in plaque than NaF. The variation in the bacterial colonisation was due to alteration of adhesion of bacteria to enamel and bacteria to bacteria as shown by both SEM and TEM. The fact that SnF_2 is more effective than NaF lends further support to the view that stannous ion plays its role in helping the fluoride ion to exert its inhibitory effect on the microbacteria. This view is supported by Svaton and Attramadal who showed that tin accumulated in dental plaque after application of solutions containing stannous fluoride (Svaton and Attramadal 1978). About 40% of this amount still retained 7 hours later. They suggested that the reduction in acid formation may be caused by stannous ions absorbing to the bacterial cell wall thus disturbing membrane transport mechanisms or through inhibition of enzyme systems essential in the fermentation of sugars.

A study by Tinanoff and Camosci further supports the antiplaque properties of SnF_2 . By using electron microscopy it was shown that streptococcus mutans specimens that have been exposed to SnF_2 indicate bacterial separation from the enamel and several other morphological alterations of the cells themselves. Both techniques of electron microscopy and atomic-absorption spectrophotometry reveal high levels of tin in plaque samples treated with SnF_2 . Thus the increased effectiveness of SnF_2 may be due to the accumulation of tin in the bacteria (Tinanoff and Camosci 1980). The transport and accumulation of fluoride in the bacterial cells is accompanied by the tin ions which enter the cell passively coupled to the fluoride ion resulting in the accumulation of tin ion in the

bacterial cell exposed to SnF_2 treatments.

Bay and Rolla carried out a study on the morphology of plaque formation and growth after NaF and SnF_2 rinses (Bay and Rolla 1981). Their findings are briefly described here. This double blind crossover study was carried out on 14 persons at the age of 14-22 years, all having normal dental conditions. The teeth were cleaned and polished before the start of each experiment. The test persons in each experiment rinsed their mouths with a solution of either water, 0.2% sodium fluoride or 0.3% stannous fluoride for 1 minute. The registration of plaque was performed after 3 days without brushing, and coloured photographs were taken.

From the results as shown in Figure 18 that the mean value for PlI (Silness and Loe 1964) was 1.2 ± 0.5 after water rinsing, 1.1 ± 0.5 after rinsing with NaF and 0.6 ± 0.4 after rinsing with SnF_2 . When disclosing solution was used the Plq (Quigley and Hein 1962) index 3.2 ± 0.9 for water, 2.8 ± 0.8 for NaF and 1.1 ± 0.5 for SnF_2 . When a students t-test was applied on the mean of the differences between the paired results from each individual, it was found that there were no differences between water and NaF plaque formation whereas the difference between water and SnF_2 was significant at a 0.1% level.

The coloured slides that have been taken were then projected to a wall and the plaque formation recorded onto prepared sheets with the tooth contours as shown in Figures 19, 20 and 21. The SnF_2 plaque was thin, homogeneous and nearly structureless, the sucrose and NaF plaque showed shiny colonies and were bulkier.

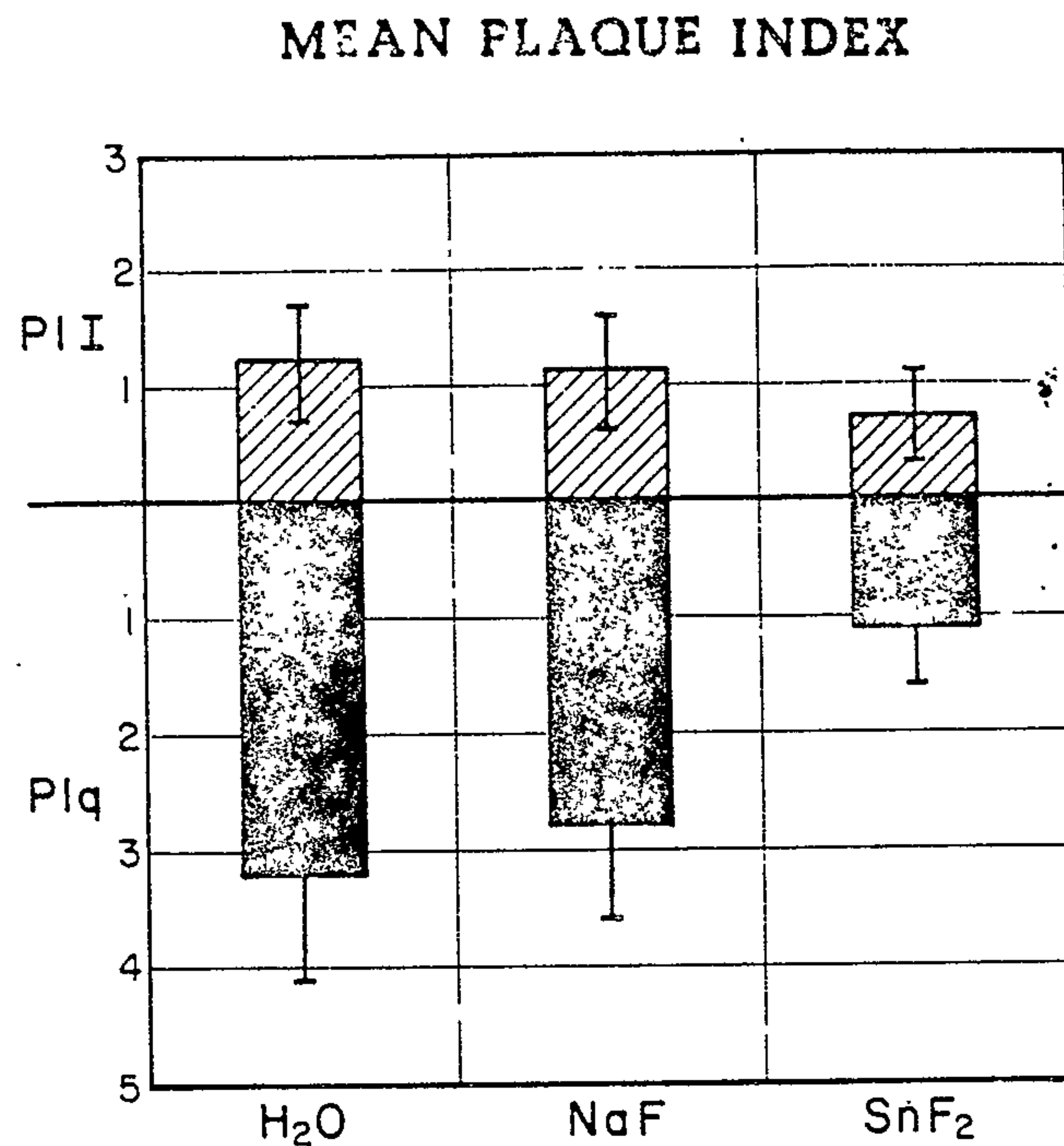


Fig. 18 Mean plaque index scored by PII and Plq.
Standard deviation is indicated by the vertical lines.
(Bay and Rolla, 1981.)

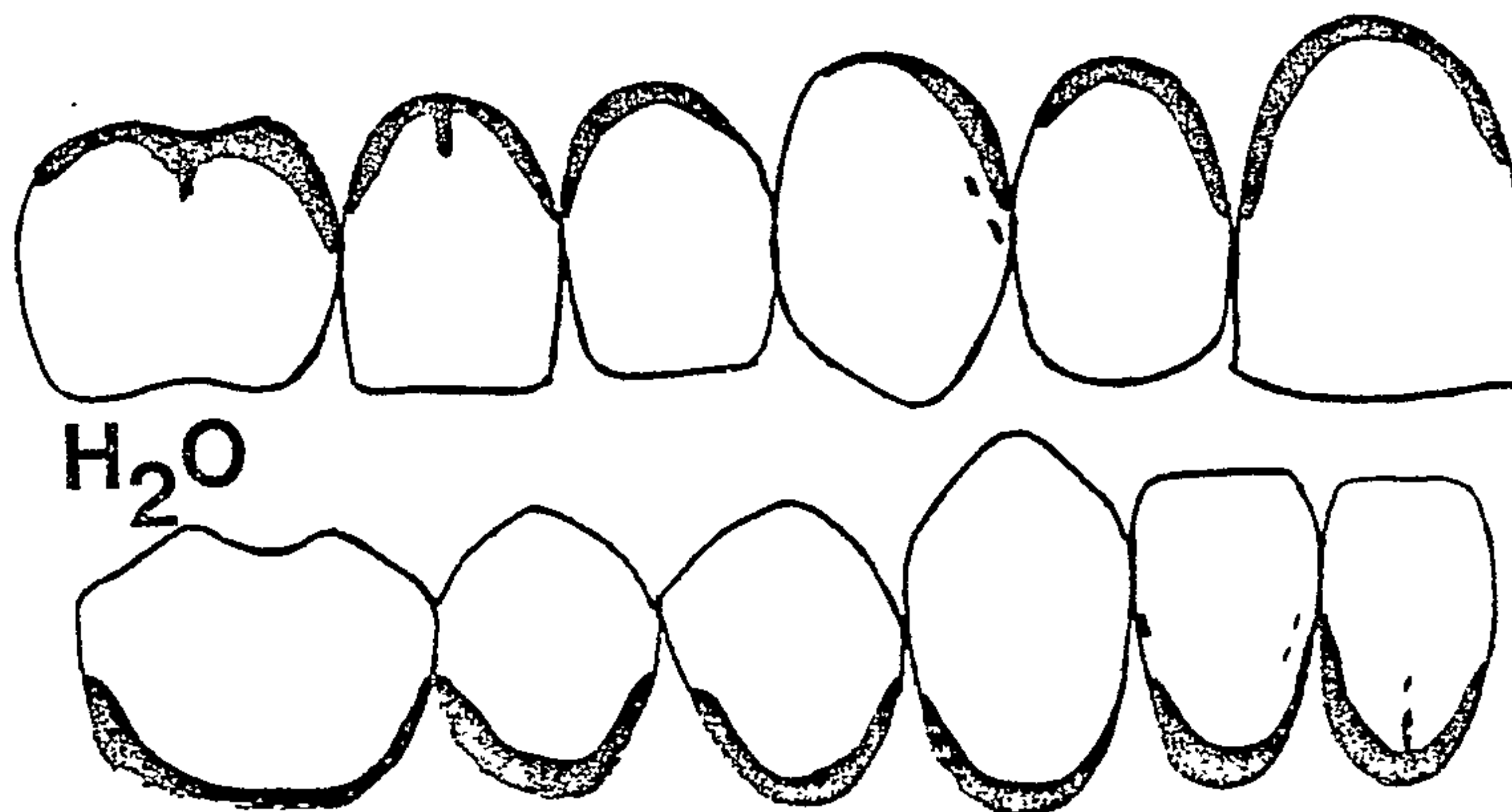


Fig. 19 Example of plaque formation after 3 days without oral hygiene following a previous rinsing with water. (Bay and Rolla, 1981.)

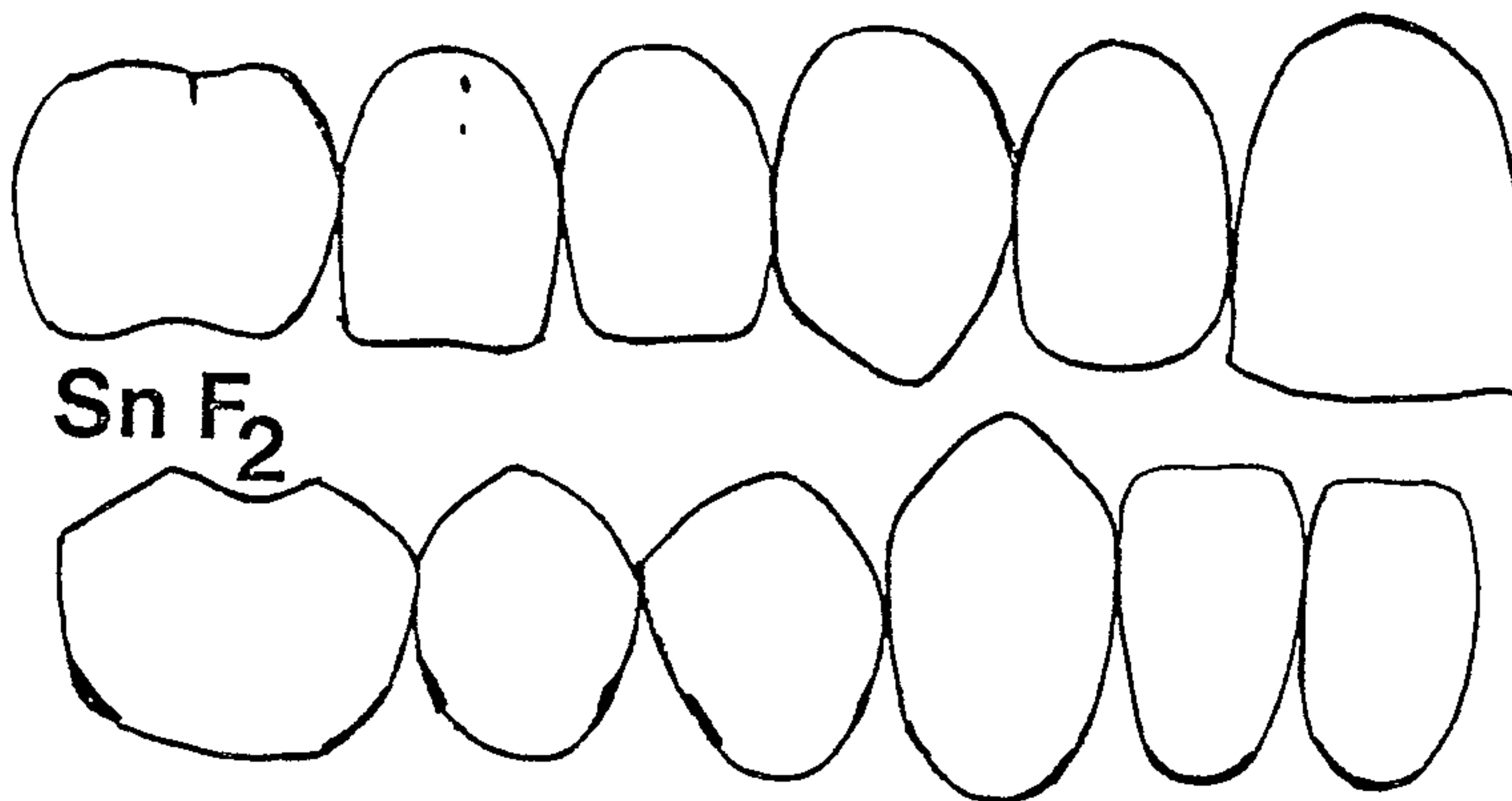


Fig.20 Example of plaque formation after 3 days without oral hygiene following a previous rinsing with SnF_2 . (Bay and Rolla, 1981.)

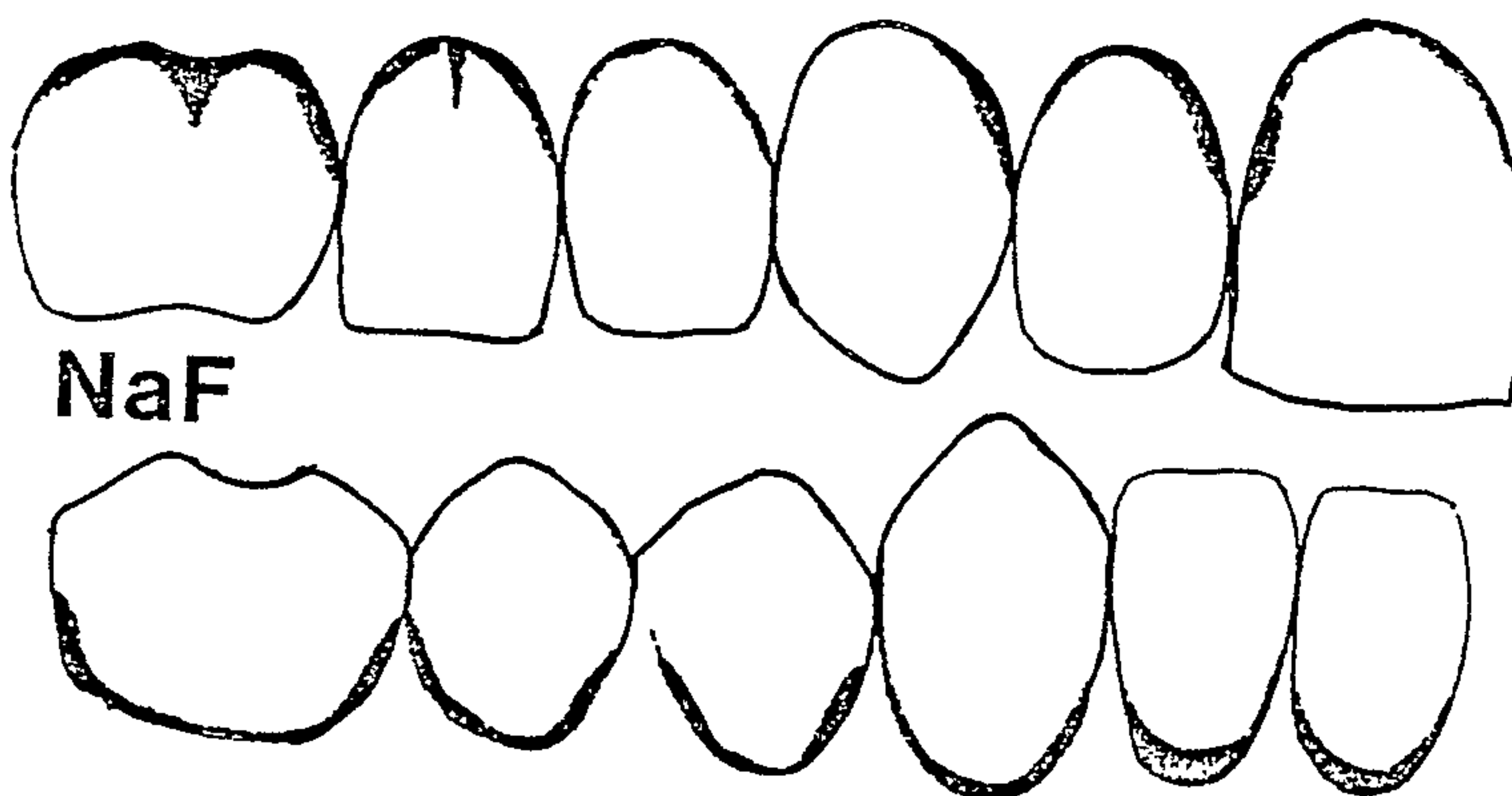


Fig.21 Example of plaque formation after 3 days without oral hygiene following a previous rinsing with NaF. (Bay and Rolla, 1981.)
