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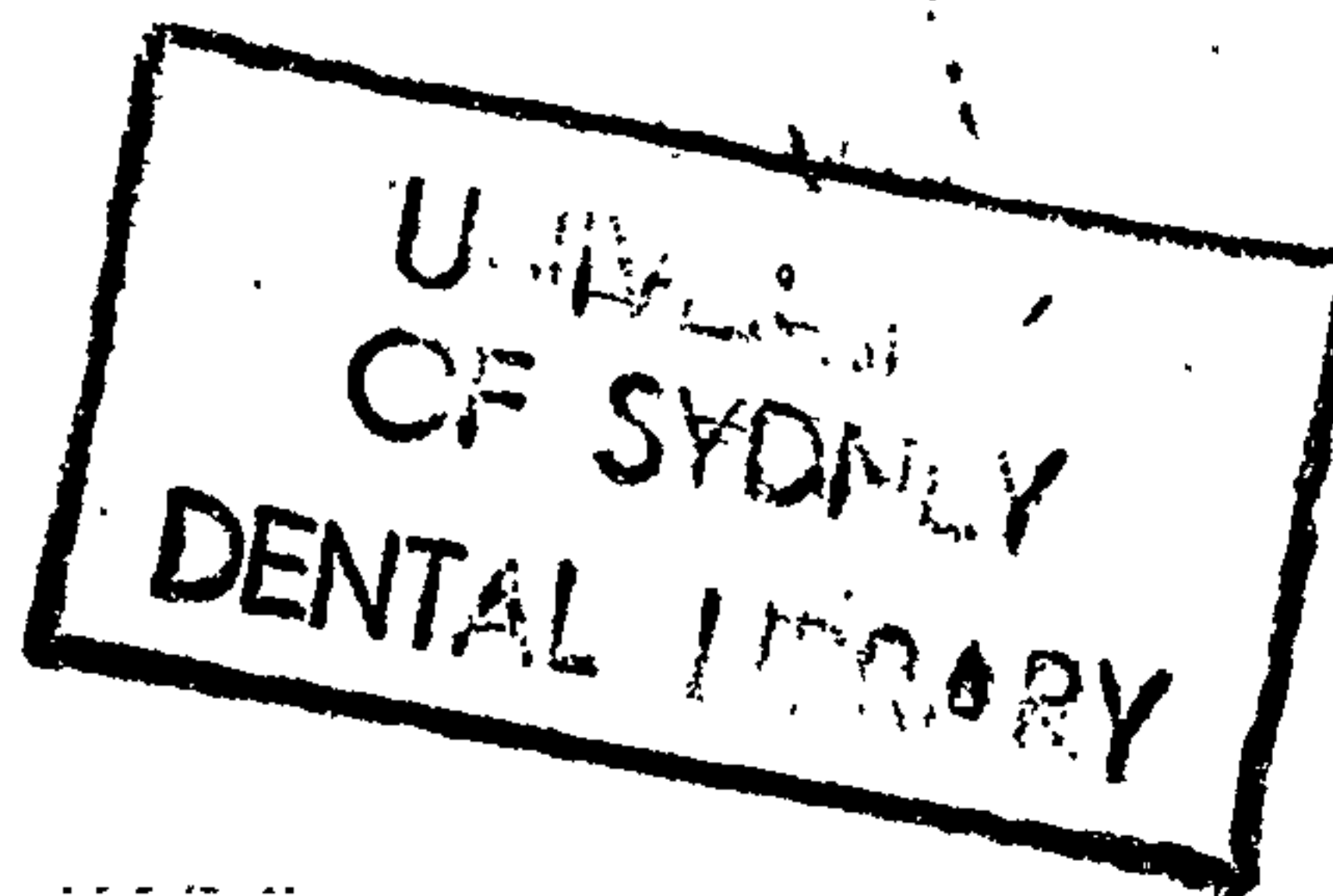
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DENTAL FLUOROSIS

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I. INTRODUCTION

1. OBJECTIVE

The use of fluorides in caries prophylaxis has given the element a special status in the field of dentistry. Adding fluorides to communal water supplies will inevitably expose large sections of the population to higher levels of the element than they have hitherto been accustomed.

Assessments must therefore be made not only of its effectiveness as a caries-preventive weapon, but one should also view the possible hazards of increased fluoride ingestion and absorption.

One of the indications of pre-eruptive exposure to 'high' levels of fluoride concentrations, which the dentist may encounter at one time or another is, dental fluorosis.

It is thus, the objective of this paper to review some of the important aspects of fluorine, i.e. chemical and physiological properties of fluorine; how it's metabolized and absorbed by the body and teeth; the biological effects which it exerts at different levels of concentration; sources of fluorine; and its availability from food and water sources for absorption.

All this information is intended to promote a better perspective of dental fluorosis, fluorine being the main causative agent.

The latter part of this paper deals with the pertinent aspects of dental fluorosis. It also attempts to correlate all the variable

factors which may influence its prevalence and severity, utilizing the information gathered from the investigations of dental fluorosis in different countries.

2. NOMENCLATURE

Dental fluorosis, is the only one out of the numerous terminologies used, which I think is most appropriate, to describe or refer to that defect manifested on human enamel caused by fluoride intoxication during the period of teeth development; or as Sognnaes put it, a low grade fluoride poisoning.

Other terms used, at one time or another, referring to this same condition are the following (Forrest, 1965)⁷⁷ :

'denti scritti'

'denti neri'

'denti di chiaie'

'dientes veteados'

'darmous'

'Colorado brown stain'

'Mottled enamel'

W.H.O., under its 'International Classification of Diseases to Dentistry and Stomatology', ICD-DA (1973)²¹³, has under the category 'Mottled Teeth', 3 subcategories:

'Endemic (fluoride) mottling of enamel' (synonymous to dental fluorosis);

'Non-endemic mottling of enamel' (synonymous to non-fluoride enamel opacities); and

'Unspecified'.

It is unfortunate that the term 'mottled enamel' has been

used to describe all grades of dental fluorosis, for although it does apply to the unsightly conditions seen in severe grades, it can't be said to describe the slight flecking and whitening of enamel in milder degrees which are associated with fluorides.

Pindborg (1970)¹⁶⁸ recommends the use of 'enamel fluorosis' or 'endemic dental fluorosis' to refer to this same condition, because it usually occurs in well-defined geographical areas.

To avoid the term 'dental fluorosis' being mistaken by terms which imply some similarity in clinical appearance yet may be due to etiologic factors other than fluoride, the terms 'idiopathic' or 'non-fluoride opacities' or 'non-endemic opacities' are used to describe those other conditions.

Fluoride, denotes the ionized, physiologically available form of the element.

Fluorine, denotes exclusively the gaseous form of the element.

By analogy with iodine, fluorine may be used to denote collectively the element in all its forms - ionized, ionizable, or non-ionizable. Where doubt exists as regards ionizability, eg. in certain foods, fluorine is actually the better, more comprehensive word (Ericsson, 1970)⁶⁸.

II. HISTORICAL BACKGROUND

The invariable occurrence of fluoride in the human body, in bones, teeth and soft tissues was noted by Gay Lussac about 160 years ago, but the fluoride content of the teeth was first investigated by Ehrhardt, a German scientist in 1847. In 1892, Sir James Crichton Browne, stressed the importance of fluoride supply during the development of teeth and the consequence of its deficiency in the production of 'inferior enamel' (Cannell, 1960)³⁷.

The brown stain associated with dental fluorosis was recognized as early as 1888, in a family emigrating from Mexico to Germany. In 1901, J.M. Eager, described a condition, which was frequently observed in inhabitants of certain villages near Naples. Teeth affected by this condition were then known as 'chiaie' teeth, after a celebrated Neapolitan professor who first described this peculiarity. Its etiology was connected with 'volcanic fumes or the emanations of subterranean fires, which fouled the atmosphere or formed a solution in drinking water' (Hardwick, 1965)⁹⁴.

It was not until 14 years later that such a condition was mentioned again in El Paso County, Colorado (Dunning, 1970)⁶². Frederic McKay of Colorado, who noticed mottling and brown staining on the teeth of many of his patients, invited another American dentist, G.V. Black (Black & McKay, 1916)²⁶, to join him in a local study. The name 'Colorado Brown Stain' eventually gave way to that of mottled enamel. The process soon became associated to communal water supplies, usually (though not

always) from deep wells (Newbrun, 1972¹⁶¹; Cannell, 1960³⁷; and Dunning, 1970⁶²), but the etiologic agent was not yet identified. A study was carried out during the same year in Britton, South Dakota, which revealed uniform mottling of enamel among children brought up in the town ever since a new well had been added to the communal water supply in 1898 (Dunning, 1970)⁶².

In 1925, it was noticed that the children of Oakley, Idaho, who were brought up on the warm-spring water supply (artesian water) had prevalent mottling compared to those brought up on a shallower water supply. At about the same time, McCollum, Bunting and others, undertook a study where rats fed a large quantity of fluoride developed staining in the incisors (Dunning, 1970)⁶².

In 1928, an exceptionally high incidence of mottling was observed in Bauxite, Arkansas which caused quite a stir. The chief chemist of the Aluminum Corporation of America (ALCOA), H.V. Churchill, initiated a spectrographic study of the water samples of the area, since ALCOA mined most of its aluminum supply from Bauxite. He also asked McKay to send samples of water from other endemic areas and the results were as follows (Dunning, 1970⁶²; Murray, 1973¹⁵⁶):

	<u>ppm fluoride in water</u>
Deep well, Bauxite, Arkansas	13.7
Colorado Springs, Colorado	2.0
Well near Kidder, S.D.	12.0
Well near Lidgerwood, N.D.	11.0
Oakley, Idaho	6.0

Round about this time, the Smiths in Arizona, tried to re-

produce mottled enamel experimentally in rats after having observed the condition on residents of St. David, where the water supply yielded a fluoride concentration of 3.8 to 7.2 ppm. Within a month of feeding concentrated St. David water, the enamel was found to be 'strikingly dull in appearance and pitted' (Smith & Smith, 1932)¹⁹⁴. In the United Kingdom, Norman Ainsworth took particular interest in the prevalence of mottling in Maldon's (an Essex town) children and gave statistical data showing caries experience in a fluoride area was lower than average (Ainsworth, 1928⁵; 1933⁶).

Thus, it was not until 1931, that fluoride was shown to be the toxic agent for mottled enamel. Churchill and three biologists named Smith, Lantz, and Smith showed independently that the characteristic common to the water in the endemic areas is the presence of fluorides in relatively high concentration. With the discovery of the etiology of mottled teeth, the main interest in the relationship of fluorides to the teeth changed to the association between fluorides and caries (Hardwick, 1965)⁹⁴.

In 1933, the head of the U.S. Public Health Service assigned Dr. H.T. Dean, to pursue full time research on mottled enamel. He continued on McKay's work to find the extent and geographical distribution of mottled enamel in the U.S. (Dean, 1933)⁴⁹.

In 1934, he examined 7,000 children in 21 cities where mottled enamel was endemic and showed clearly the prevalence and severity of mottling was directly related to the concentration of fluoride in the water (Dean, 1934)⁵⁰. Where it was as high as 5 ppm or more, the entire

population had mottled teeth and brown staining and pitting of the enamel. As the concentration of fluoride decreased, both the prevalence and the severity of mottling became progressively less until with 1.0-1.5 ppm fluoride, only a few faint white translucencies were found in not more than 10% of the children (Forrest, 1965)⁷⁷.

A standard of classification of mottling was subsequently developed in order to quantitatively record the severity of mottling within a community (Dean, 1934)⁵⁰, so that he could relate the fluoride concentration in the drinking water to the severity of mottling in a given area. His aim was to find out the 'minimal threshold' of fluorine in the level at which fluoride began to blemish teeth. In 1936, he showed conclusively that the severity of mottling increased with increasing fluoride concentration in the drinking water (Dean & Elvove, 1936⁵⁵; Dean, 1936⁵¹). Two years later, in conjunction with McKay, he summarized the knowledge of mottled enamel in a paper given to the Epidemiological Section of the American Public Health Association. This information was the 'most conclusive and direct proof that fluoride in the domestic water was the primary cause of human mottled enamel' (Dean & McKay, 1939)⁵⁸, which thus, brought to a successful conclusion McKay's search for the cause of mottled enamel which began in Colorado Springs.

III. CHEMICAL AND PHYSIOLOGICAL ASPECTS OF FLUORINE

Fluorine, symbol F, with an atomic weight of 19, is a chemical gaseous element of the halogen group. Being the most electronegative of all elements, its chemical activity make it physiologically more active than any other elemental ion. In fact, it's so reactive chemically that it's rarely or never encountered in nature as elemental fluorine (Cannell, 1960³⁸; Banks & Goldwhite, 1966¹⁵).

It has the ability to interact with other organic and inorganic body components. Combined chemically in the form of fluorides, fluorine is the 17th in the order of abundance in the earth's crust (Cannell, 1960)³⁸.

The possible mechanisms of action at physiological concentrations can be enumerated as follows (Bhussry, 1970)²³:

(1) Ionic exchange with hydroxyl of the apatite in the calcified tissues - thus, reducing its solubility. In very low doses, it reduces the number of carious lesions by well over 50%, and reduces the severity of the collective caries attack.

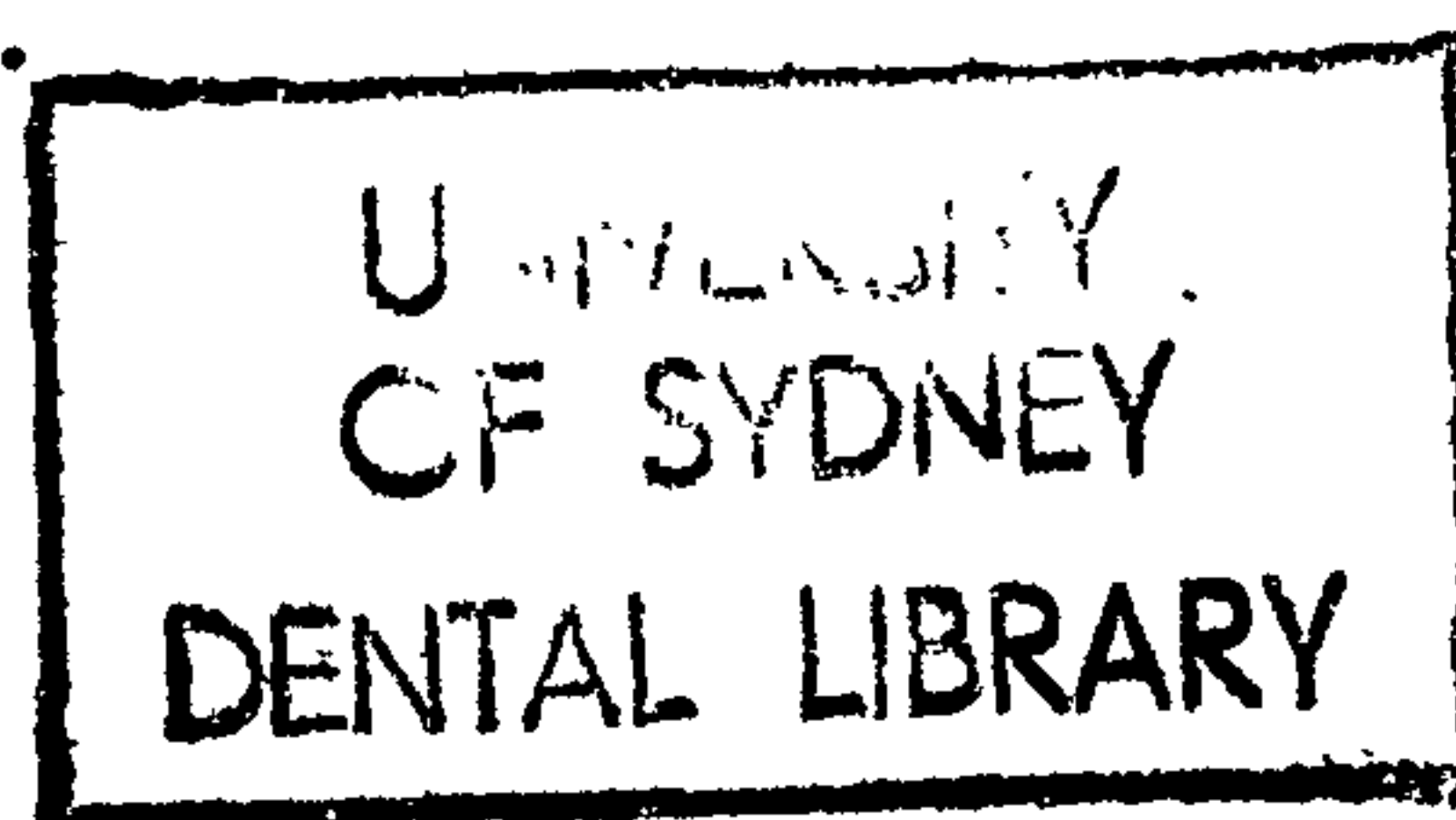
Other effects on the dental organ have been more or less established, i.e. the influence on tooth form and appearance, on eruption time and alignment in the dental arches, and on the frequency and severity of periodontal disease, which are probably secondary to the effects of fluoride in reducing caries (Jenkins, 1970)¹¹³.

Excessive fluoride intake during the period of tooth formation causes mottled enamel.

(2) Influence on the precipitation of mineral from saturated solutions of calcium phosphate - its affinity for calcium phosphate makes it the most exclusive bone-seeking element existing. Therefore, it is accumulated in every tissue showing calcification, be it physiological or pathological.

(3) Low concentration of fluoride ion inhibits and, in some cases activates or stimulates enzymatic processes.

1. METABOLISM OF FLUORIDES



It has often been expressly assumed in the past that fluoride is absorbed and metabolized mainly as the simple fluoride ion. However, a number of reports indicate the considerable importance of several complex fluoride ions, eg. calcium fluoride, magnesium fluoride, and even more complex fluorine compounds may be formed and metabolized in the body (Ericsson, 1970)⁶⁸.

In dilute solution, fluorides are almost completely ionized, and it is the fluoride ion which is rapidly absorbed from the gastrointestinal tract (Martin, 1965)¹³⁸. Wagner in 1973²⁰⁴, on p.45, states that once fluoride has been absorbed, its metabolism can't be affected by other ions ingested at a later period.

Inside the body, the fluoride is rapidly distributed through the blood and tissue fluids prior to excretion by the kidneys, sweat glands and intestines or to fixation in the skeletal system (Martin, 1965)¹³⁸.

When fluoride is administered over a short period, about half the amount absorbed from the intestines is excreted in the urine (Largent, 1973)¹²⁸. McClure and Kinser (1944)¹⁴⁶ indicated that when there is little or no fluoride in the drinking water, the amount of fluoride excreted seldom exceeds 0.4 ppm Presumably, such fluorides are derived from foods. When the urinary excretion of fluorides rises above 0.4-0.5 ppm, the increase in fluoride excretion is directly proportional to but slightly less than the amount of fluoride ingested in the drinking water.

When the fluoride intake remains constant over a prolonged period, a 'state of balance' is ultimately reached in which the average quantity excreted equals the intake (Machle, Scott & Largent, 1942)¹³⁵. This state of equilibrium which probably occurs at levels of intake of 1 mg. fluoride daily (Cannell, 1960)³⁸, is linked to the amount of fluoride stored in the skeletal system. Should the average intake of fluoride be increased, then more will be stored until ultimately a new state of balance is reached. The converse is also true, as was demonstrated when the fluoride content of the drinking water in the town of Bartlett was reduced from 8.0 to 1.0 ppm, and over a period of many months, the inhabitants were found to be excreting more fluoride than they were ingesting (Likins, McClure, & Steve, 1956)¹³¹.

The state of balance, however, is not perfect for it's subject to day-to-day variations in fluoride intake which are bound to occur in a normal diet, and it is further subject to the gradual increase in the amount of fluoride which is stored in the bones with advancing age. The total amount of fluoride in the skeleton therefore, depends on a per-

son's age and the concentration of fluoride in the drinking water (Jackson & Weidmann, 1958)¹⁰⁹. In later middle life and in the elderly, a condition of greater stability is reached when, provided the average intake remains constant, there is little further addition to the total fluoride content of the skeleton.

Singer and Armstrong (1960)¹⁹¹ described an important safety factor that lies in the mechanism by which the body regulates the amount of fluoride in the blood plasma preventing, except under abnormal circumstances, the building up of high concentrations in the blood and tissue fluids. Blood levels are within a range of 0.01-0.2 ppm and remain constant irrespective of the fluoride intake (W.H.O. report, 1958)²¹¹. In fluorosis, the calcium titre of blood is reduced, although these findings are not constant.

The increase following meals was found to be slight. Carlson, Bunting and Singer (1960)³⁹ showed that, following the administration of a measured dose of radiofluoride, inspite of its rapid absorption, not more than 10% was present in the entire body plasma at any one time. The speed of absorption was, in fact, compensated by the speed at which additional fluoride was eliminated from the plasma.

2. ABSORPTION OF FLUORIDES

However small the amounts of fluoride ingested, a good proportion, up to about half, is incorporated and retained by the hard tissues, the remainder being rapidly excreted. The extent of fluoride uptake in different parts of the skeleton and dentition depends upon the amount ingested and absorbed by the organism, the duration of fluoride exposure and the type, region, and metabolic activity of the tissue concerned (Weidmann & Weatherell, 1970)²⁰⁸. There is thus, a great disparity in fluoride levels between different individuals and between different types of mineralized structures.

The absorbability of the fluoride ion depends on several factors, including the solubility of the compound, the physical form of the ingested fluoride, the frequency of ingestion, the inorganic ion environment of the fluoride, and the organic constituents of the diet (Cremer & Buttner, 1970)⁴⁵.

Fluoride absorption is passive in nature, and no active transport mechanism is involved in the process. It can be assumed that the mechanism for the removal of fluoride from the gastrointestinal tract is one of simple diffusion (Stookey, Dellinger & Muhler, 1964)¹⁹³. Inhaled fluoride would be readily absorbed in the respiratory tract.

- A. Mechanism of Absorption of Fluorides in Teeth

Neuman and Neuman (1958)¹⁶⁰ proposed a three-stage mechanism

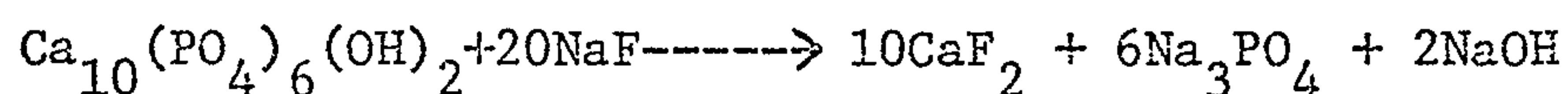
to describe the entry of fluoride ions into the apatite crystal lattice.

First stage. The crystallite was considered to be surrounded by a hydration shell and the incorporation of fluoride into the crystal lattice is prefaced by its exchange with one of the ions or polarized molecules present in this loosely integrated sheath.

Second stage. Involved the exchange of fluoride in the hydration shell with an ion or group at the surface of the apatite crystal. Such entry of fluoride into the apatite crystal surface could be accomplished not only by hetero-ionic exchange with hydroxyl or bicarbonate groups, but also by iso-ionic exchange with fluoride already present in the crystal as demonstrated by Brudevold, Hein, Bonner, Nevin, Bibby, and Hodge (1957)³².

Third stage. Ions present in the crystal surface might migrate slowly into vacant spaces into the crystal interior during recrystallization.

Fluoride incorporation does not appear to alter the Ca/P ratio of the mineral salt. The element does not replace phosphate groups of hydroxyapatite to any great extent. The only deviation from this general picture arises during the topical application of concentrated fluoride solutions to enamel surfaces (Brudevold, 1962)³¹. In this case, a double decomposition will occur, CaF_2 being precipitated and phosphate released according to the following equation:



This displacement of phosphate only occurs, however, when the apatite reacts with fluoride solutions at least a hundred times as concentrated as those encountered during ingestion of normal diets. Under such context, it can be said that fluoride seem to be incorporated almost exclusively by a simple substitution which involves no severe disruption of the apatite structure.

Fluoride may also enter the mineral by its incorporation during the phase of crystal growth. Substitution of fluoride for ions in crystal surface is usually termed "exchange", whereas, incorporation into the apatite lattice during crystal formation or growth is designatd as "uptake by accretion" (Weidmann & Weatherell, 1970)²⁰⁸.

Uptake by accretion will be maximal during the phase of tooth development when a large proportion of the crystallites are still forming. Once incorporated into developing teeth, it does not appear to be reabsorbed and ultimately excreted, but remains static. Exchange reactions will also be maximal at this stage, since the crystallites are then predominantly small in size, large in number and offer an extensive surface area to exchanging ions.

In addition to this, the greater hydration of young mineralized tissue ensures a high permeability which provides better access of tissue fluids to crystal surfaces. The overall uptake of fluoride in dentine and enamel is therefore, maximal during periods of formation and calcification. This could be explained by, (a) the relatively great vascularity surrounding newly forming tissues (Volker, Sognnaes, & Bibby, 1941)²⁰³, and (b) the extensive and accessible surface area offered by

many small hydrated crystallites apparently far outweighs any dissimilarity in anatomical structure (Weidmann & Weatherell, 1970)²⁰⁸. The formative activity of a tissue is therefore, the overriding factor governing the extent of fluoride uptake.

Jenkins (1955)¹¹¹ suggested that full benefit of fluoride in caries prevention depended on the fluorides being ingested during the calcification period, i.e. pre-eruptive and immediately post-eruptive phases of the tooth.

Three phases of dental fluoride uptake can be visualized:

(a) That occurring in the phase of formation - during this phase, fluoride is probably taken up uniformly throughout the tissue.

(b) That occurring during the subsequent period of mineralization - uptake of which will be largest in areas where mineralization occurs.

(c) That occurring after mineralization is complete - i.e. when the teeth have fully formed and achieved complete mineralization, uptake of fluoride will be almost entirely limited to marginal regions of both enamel and dentine.

Once enamel has been formed, cellular activity ceases and the incorporation of fluoride depends solely upon ion-exchange mechanisms. Penetration of fluoride into the interior regions of enamel is obstructed by the chemical trapping of ions in the outer region and, presumably, by the decreased permeability of this highly calcified structure (Weidmann & Weatherell, 1970)²⁰⁸.

Bearing in mind that the concentration of fluoride in teeth relates closely to the quantity ingested, it is therefore expected that

the fluoride levels of both enamel and dentine correlate well with the concentration of fluoride in the drinking water (Table 1). It clearly demonstrates a linear relationship between the level of fluoride in drinking water and the concentration of the element in the enamel surface. Although the absolute levels may rise or fall, depending on fluoride uptake, the differential between enamel and dentine is maintained throughout the life of the tooth (Jackson & Weidmann, 1959)¹¹⁰.

According to Weidmann and Weatherell in 1970²⁰⁸, on p.121, teeth tend to accumulate fluoride with age, provided that the level of ingestion does not decrease, the balance between fluoride uptake and removal is clearly in favour of uptake.

B. Distribution of Fluorides in Placenta and Foetus.

The placenta is the organ across which exchanges of gaseous, nutritive and excretory products take place between the foetal and maternal tissues, i.e. between their respective bloodstreams which histologically are in close proximity.

The limited permeability of the placenta to increased concentration of fluoride suggests that the placenta plays a role in the transfer of fluoride from mother to foetus (Gedalia, Brzezinski, Bercouici & Lazarov, 1961⁸³; Gedalia, Brzezinski, Zukerman & Mayersdorf, 1964⁸⁴).

Once fluoride enters the foetal circulation, it is incorporated into foetal bones and teeth undergoing calcification.

TABLE 1. FLUORIDE CONCENTRATION (EXPRESSED AS PPM IN ASH) IN DENTINE AND ENAMEL AT DIFFERENT LEVELS OF FLUORIDE INGESTION.

Reference	Species	Age	Dose (ppm F in water)	Duration	Enamel			Dentine whole
					sur- face	inter- rior	whole	
McClure & Likins (1951) ¹⁴⁷	Man	Adult	0.1	life-long	-	-	86	332
			7.6	life-long	-	-	658	1968
Jackson & Weidmann (1959) ¹¹⁰	Man	20 - 49 years	< 0.5	life-long	-	-	108	508
		20 - 35 years	1.2	life-long	-	-	180	922
		20 - 35 years	1.9	life-long	-	-	320	1290
Jenkins & Speirs (1953) ¹¹⁴	Man	Adult	< 0.25	life-long	590	80	-	-
			1.4	life-long	960	110	-	-
			2.0	life-long	1310	270	-	-
Brüdevold, Steadman & Smith (1960) ³⁴	Man	20 - 29 years	0.1	life-long	571	48	-	-
			1.0	life-long	889	129	-	-
			3.0	life-long	1930	152	-	-
			5.0	life-long	3370	570	-	-

3. BIOLOGICAL EFFECTS AT DIFFERENT LEVELS OF FLUORIDE CONCENTRATIONS

A number of biological effects have been ascribed to fluoride. The following tabulation shows the varying concentrations of fluoride, through different mediums, and their corresponding effects (Smith & Hodge, 1973)¹⁹².

<u>Concentration or Dose of fluoride</u>	<u>Medium</u>	<u>Effect</u>
2 ppm	Air	Injury to vegetation
1 ppm	Water	Dental caries reduction
2 ppm or more	Water	Mottled enamel
5 mg./liter or more	Wine	No osteosclerosis
8 ppm	Water	10% osteosclerosis
20-80 mg./day or more	Air	Crippling fluorosis
More than 50 ppm	Food or Water	Thyroid changes
100 ppm	Food or Water	Growth retardation
More than 125 ppm	Food or Water	Kidney changes
2.5-5 g.	Acute dose	Death

Injury to vegetation - some varieties of gladiolus and some fruit trees
(such as prune and apricot).

Dental caries reduction - greatest effect from pre-eruptive dosage.

Mottled enamel - also from pre-eruptive dosage. It cannot develop in
fully formed, mature, erupted enamel, nor can it progress in the
mature tooth with continued exposure.

Osteosclerosis - refers to the increased degree of calcification of bone, described when visible as an increased radiopacity. Usually due to inhalation of industrial dust for periods of 10 to 20 years to result in crippling fluorosis (in cryolite workers).

Thyroid changes - observed in experimental animals fed with drinking water containing more than 50 ppm. Of all organs in the body, the thyroid appears to be most sensitive to fluoride.

Growth retardation - observed in most species. In a few experiments, losses in body weight were observed (eg. in dairy cows) with concentrations as low as 50 ppm.

Kidney changes - both structural and functional.

Death - from an estimated acute lethal dose of 2.5 to 5 g. in humans.

IV. SOURCES OF FLUORINE

1. FROM WATER

A. Naturally-occurring Fluorides in Water

(a) Origins of fluoride in waters

The Seas: seawater itself contains significant quantities of fluoride, levels having been variously recorded as 0.8 to 1.4 ppm. Together with other halogens, it escapes from the sea into the atmosphere and are eventually incorporated into rain or precipitation (Bell & Ludwig, 1970)¹⁸.

The Atmosphere: originates from the dusts of fluoride-containing soils (Williamson, 1953)²¹⁶; from gaseous industrial wastes (Largent, 1961)¹²⁶; from the burning of coal fires in the populated areas (Cholak, 1959⁴¹; Largent, 1961¹²⁶); and from gases emitted in areas of volcanic activity (Emeleus, 1950)⁶³.

It has been estimated that the fluoride content of soil averages about 0.03%, although it varies depending upon the composition of the underlying strata (Cannell, 1960)³⁷.

Of the industrial activities, the ones in which rock phosphate is used probably liberate the greatest total amounts of fluoride. The highest quality phosphate may contain close to 4% of fluoride when it is mined (Largent, 1961)¹²⁶. In a super-phosphate factory with no purifying or recovery plant in the USSR, a maximum concentration of

18.4 mg., was recorded at a distance of 1000 metres from the factory (Martin, 1970)¹³⁹.

The fluoride present in coal mined in certain areas is unusually high, and most or all of this fluoride is liberated when the coal is burned (Largent, 1961)¹²⁶. In populated areas, coal smoke is regarded as one of the chief contributors to atmospheric fluoride; concentrations of from 1 to 175 ppm fluoride have been found in samples of coal from the British Commonwealth, and up to 295 ppm in Utah coals (Bell & Ludwig, 1970)¹⁸.

In volcanic fumarole gases, there are appreciable quantities of fluorine compounds (0.1 mg. per litre, for example, in a sample from the Vesuvius locality); and considerable concentrations of fluoride are likewise found in the water from hot springs and geysers of volcanic origins (Emeleus, 1950)⁶³.

The Earth's Crust: it has been estimated that fluorine in the combined state constitutes about 0.065% by weight of the earth's crust (Banks & Goldwhite, 1966)¹⁵.

These are the amounts derived from the solvent action of water on the rocks and soils of the earth's crust. In rocks and soils, fluoride may occur in a wide variety of minerals, including fluorite, apatite, the micas, hornblende and a number of pegmatites such as topaz and tourmaline (Bell & Ludwig, 1970)¹⁸.

The fluoride content of rain and precipitation will largely depend on the type and availability of atmospheric contaminants. The

fluoride content of surface and underground waters, on the other hand, will be dependent on a wide variety of factors (Bell & Ludwig, 1970)¹⁸:

(i) the availability and solubility of the parent fluoride minerals with which the waters are in contact; (ii) porosity of the rocks and soils through which the water passes and the speed with which the water flows; (iii) the temperature of the interaction between rock and water; (iv) the hydrogen ion concentration of water; and (v) the concentration of calcium ions present in water. Fluoride levels will tend to be higher in alkaline waters and in the hotter waters, such as in areas of volcanic activity.

(b) Distribution of fluoride-bearing waters

Surface waters are generally low in fluoride, the level being below 1 ppm. On the other hand, underground or subsoil waters may have a greater opportunity to contact fluoriferous material so that the waters may contain appreciable quantities of fluoride, depending on geological conditions (Bell & Ludwig, 1970)¹⁸.

Table 2, shows the distribution of fluoride-bearing waters and the range of fluoride content, in different countries (Bell & Ludwig, 1970¹⁸; F.D.I., 1973⁷⁰; Barnard, 1975¹⁶).

TABLE 2. DISTRIBUTION OF FLUORIDE-BEARING WATERS IN DIFFERENT COUNTRIES.

Country	Added		Natural		
	Number of communities (b)	Population served	Range of fluoride levels (ppm) (a)	Number of communities (b)	Population served
AFRICA					
Etiopia	?	?	0-0.9	?	?
Kenya	0	0	0-2800.0	?	?
Nigeria	0	0	0-6.2	1	15,000x
South Africa	0	0	0-53.0	?(1)	?
Tanganyika	?	?	0-95.0	?	?
THE AMERICAS					
Argentina	7	216,261	0-1.6	32	628,215
Brazil	86	4,467,000	0-0.6	41	308,900
Canada	486	7,575,000(2)	0-1.2	176	218,253
Chile	73	4,342,193(3)	0-1.5	2	70,248
Cuba	1	10,000	0-0.4	?	?
Ecuador	0	0	0-1.5	11	25,000
Peru	5	?	0-1.4	6	80,000
U.S.A.	5,200	92,000,000x	0-16.0	2,630	8,000,000
ASIA					
China	?	?	0-13.0	?	?
India	0	0	0-6.4	some	?
Iran	0	0	0-1.0	many	10,000,000
Israel	0 (4)	0	0.3-1.5	some	?
Japan	1	12,000	0-20.0	1	3,000
Korea	0	0	0.8-10.0	?	?
Taiwan	2	500,000	0-1.5	?	?
Thailand	0	0	0-1.5	30	5,000,000
AUSTRALASIA					
Australia	100 x	6,162,940(c)	0-13.5	very few	85,237x(c)
New Zealand	23	1,452,600	0-0.9	0	0
Territory of Papua & New Guinea	1	38,000 (1969)	0-0.6	?	?
EUROPE					
Austria	0	0	0.4-0.8	2	very few

(. . .contd)

TABLE 2. (contd)

Country	Added		Natural		
	Number of communities	Population served (b)	Range of fluoride levels (ppm) (a)	Number of communities (b)	Population served
Belgium	1	10,000	0-1.7	?	600,000x
Cyprus	0	0	0-3.6	0	0
Czechoslovakia	34	1,700,000	0-28.0	10	15,000
Denmark	0	0	0-3.3	24	95,000(5)
England	23	3,000,000	0-5.8	9	500,000
Finland	1	63,807	0-5.0	rural	165,000
France	0	0	0-7.0	?	?
Germany	0 (6)	0	0-4.9	?	?
*Hungary	0	0	?	6	150,000
Ireland	78	1,386,000	0-0.2	1	200-300x
*Italy and Sicily	0	0	0-7.1	?	?
Luxembourg	0 (7)	0	0-1.2	0	0
Netherlands	18	3,811,850	0-2.0	0	0
Norway	0	0	0-2.7	0	0
Poland	19	2,000,000	0-1.1	2	300,000
*Portugal	1	10,000	0-22.8	?	?
Sardinia	?	?	0-5.0	?	?
Spain	0	0	0-6.3	some	?
Sweden	0	0	0-10.0	some	500,000
Switzerland	1	200,000	0-1.4	4	20,000
U.S.S.R.	85	15% x	0-7.0	?	?
*Yugoslavia	0 (8)	0	0-4.2	812	3,000,000

Sources : (a) Bell & Ludwig, 1970. (p.24-25)¹⁸.(b) F.D.I., 1973. (Appendix III, i-vii)⁷⁰.(c) Barnard, 1975. (p.10)¹⁶.

TABLE 2. (Footnotes)

- ? Number not known or not given.
- x Estimated.
- * No updated information received, therefore as at 31st March, 1972.
- (1) The natural fluoride content varies from 0.1-0.4 ppm in surface water; over 50 ppm in subterranean waters.
- (2) As at 31st December, 1972.
- (3) At present, there is an extension to the program covering 29 cities with 607,115 inhabitants of which 288,875 are served by the water supplies.
- (4) All arrangements have now been made for the artificial fluoridation of most water sources in Israel in the near future.
- (5) 53,000 people 1-1.5 ppm fluoride;
40,000 people 1.5-2.5 ppm fluoride;
1,500 people over 2.5 ppm fluoride.
- (6) A new law 1.1.1975 permits fluoridation of drinking water in the German Federal Republic.
- (7) Fluoridation is planned for a water treatment station serving 60% of the population in Luxembourg.
- (8) In some districts of Yugoslavia wells are treated with sodium-fluoride.

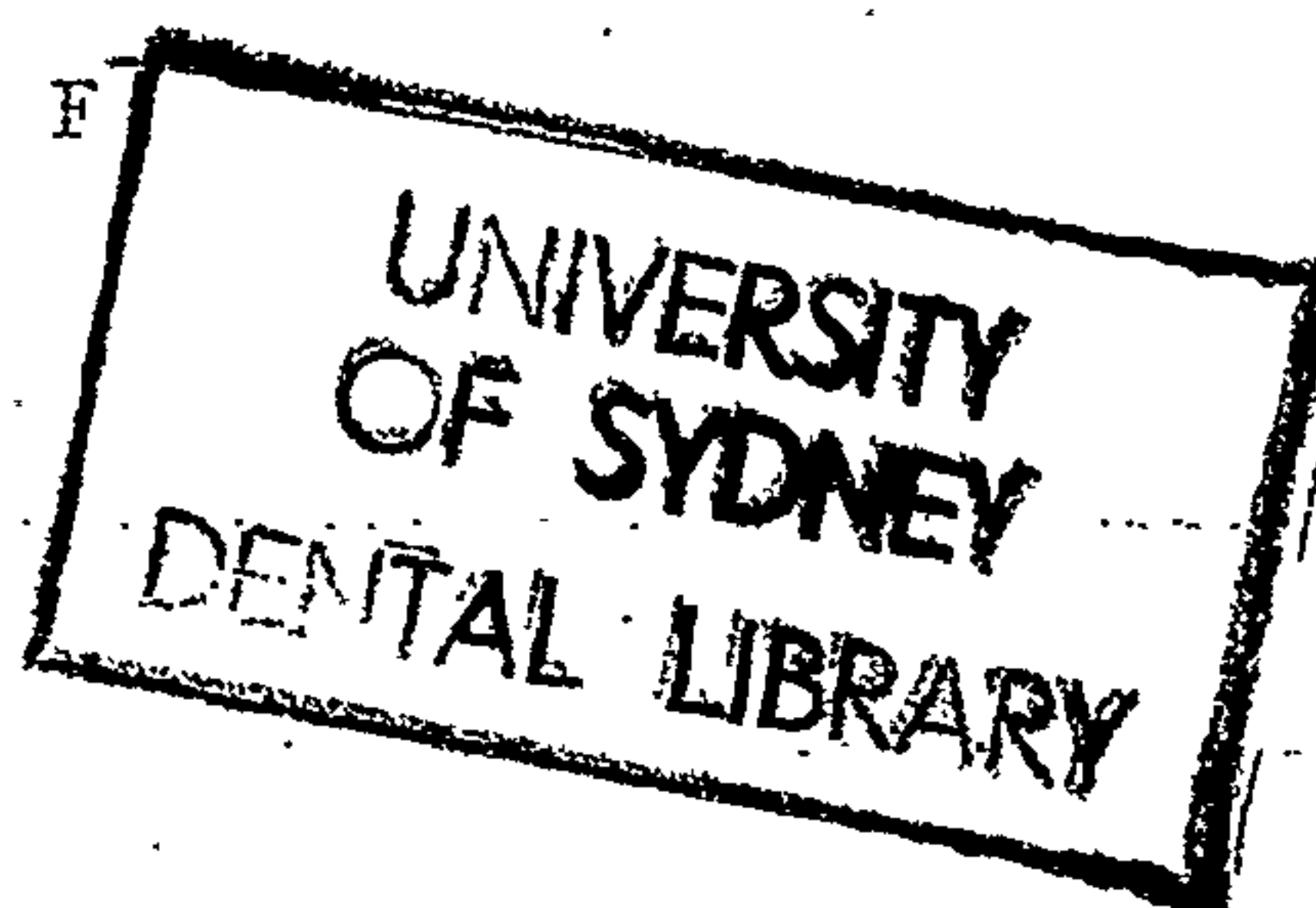
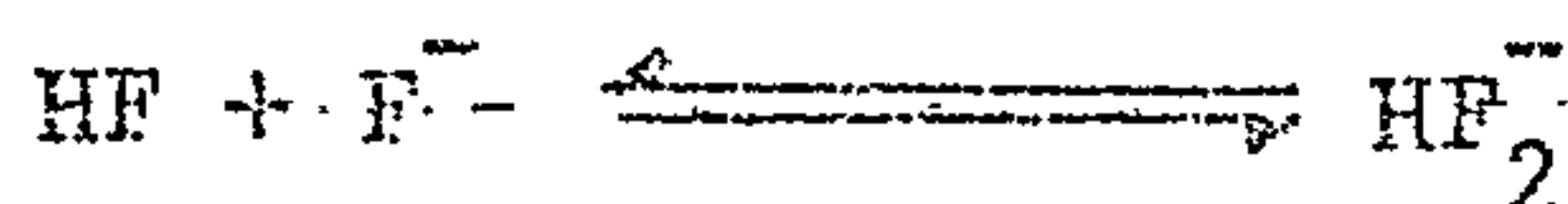
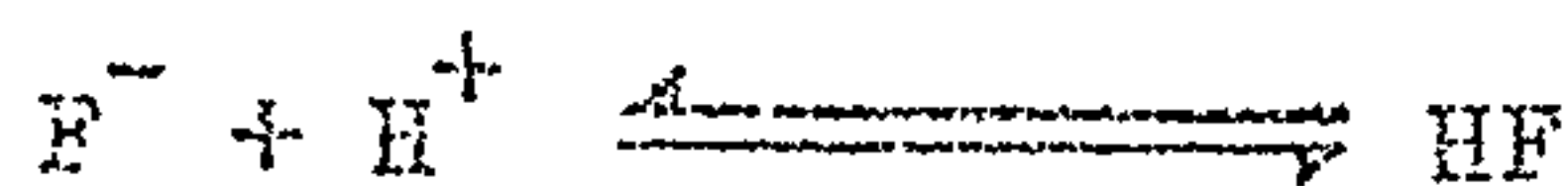
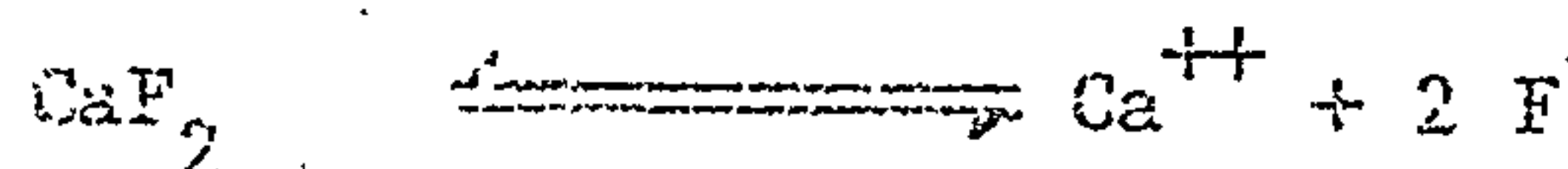
B. "Artificial" or Added Fluorides in Water

"Artificial" or added fluorides in water are actually fluoride compounds such as sodium fluoride (NaF), sodium silicofluoride (NaSiF_6), or fluosilicic acid (H_2SiF_6), that have been added to communal water supplies to obtain an optimum fluoride concentration in the drinking water. The word "artificial" is not actually appropriate here. Perhaps "fortify" would be a better word. Thus one would fortify the fluoride-deficient water supplies on the grounds that one is replacing a natural constituent of the water. Similar reasoning applies to the "fortification" of cereal grains with certain vitamin and minerals that has been lost during the milling process (Wagner, 1973)²⁰⁴.

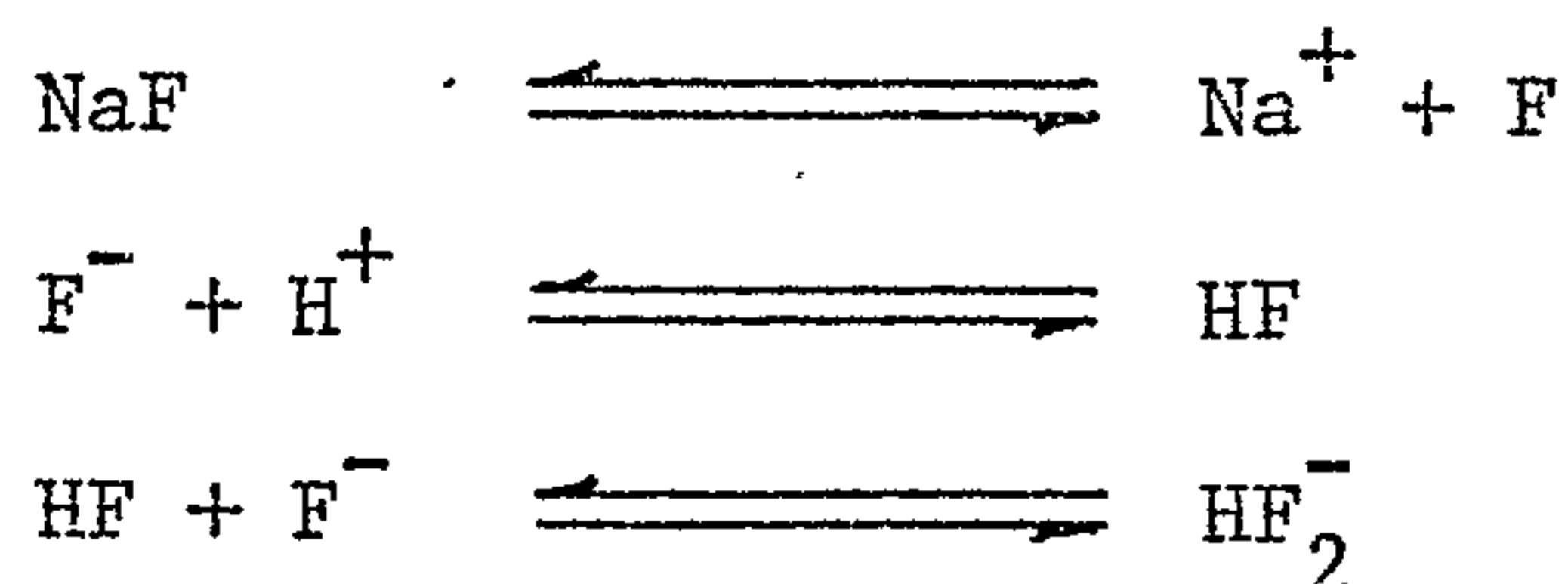
C. Natural vs "Artificial" Fluorides

Both the natural and "artificial" fluorides are inorganic, and thus, both ultimately furnish fluoride ions of physiological and hygienic importance (Smith & Hodge, 1973)¹⁹².

Assuming that CaF_2 is representative of natural fluorides dissolved in water, the following chemical reaction will take place (Borei, 1945)²⁷:



And assuming that NaF is representative of "artificial" fluorides dissolved in water, the following chemical reaction will take place (Borei, 1945)²⁷:



In both reactions, fluoride is yielded in much the same way, and these will be chemically and physiologically identical.

Nonetheless, it has been contended that there are pronounced differences in the metabolism of natural and "artificial" fluorides. It is claimed that less "available" fluorine is present in the water from areas where there is natural fluorine present than when sodium fluoride is artificially added to a natural fluoride-deficient water, with the result that there is less toxicity in naturally fluoridated waters (Wagner & Muhler, 1957)²⁰⁵. Even though recent medical studies have failed to show any significant differences in the health of people drinking artificially-fluoridated water as compared to similar people using a fluoride-deficient water supply, the objections continue to serve as deterrents for many communities which are interested in fluoridating their water supplies.

Wagner and Muhler in 1957²⁰⁵, designed a study to determine if the metabolism of fluorine in rats was significantly different if they receive identical amounts of fluorine furnished in water from a natural source, or from water obtained by adding sodium fluoride to mineral-free water. Although there was greater retention of fluoride

by the skeleton when obtained from a pure sodium fluoride solution, the differences were not significant statistically. The differences in retention, if they were real, may depend on many factors. Important among these may be differences in absorption of the fluorides from the two sources by the mucosa of the gastrointestinal tract. Since the presence of inorganic elements in the diet or water is known to decrease fluoride absorption (Weddle & Muhler, 1954)²⁰⁷, the inorganic elements present in the natural water and not in the "artificial" fluoride source may interfere with fluoride solubility and thus its availability. Since the "artificial" fluoride water was made from redistilled, mineral-free water, the increased retention of fluoride occurring from the "artificial" water should not be interpreted to mean that this would occur in a community fortifying its water supply to an optimal level with fluoride, when such water would be similar in its major inorganic composition to that of the natural water used in these studies.

2. FROM FOODS

A. Foods with Natural Fluoride Content

Table 3, indicates the fluoride content of a number of different foodstuffs (McClure, 1949)¹⁴⁵.

The average daily fluoride intake from food where the water supplies contain negligible amounts of fluoride is approximately 0.2 to 0.6 mg. The rich sources of fluoride are seafoods like fish, especially those with small bones such as sardines and salmon (McClure, 1949)¹⁴⁵. On a dry weight basis, one of the richest sources of fluoride is tea. Fluoride content of Darjeeling and Assam teas was found to be 86.7 mg. and 98.7 mg. per kg. dry weight, respectively. In five black teas, 52 to 144 ppm fluoride was found; 336 ppm in one green tea; 41 to 78% of this fluoride content could be extracted in the first infusion (Siddigui, 1970)¹⁸⁸. Cremer and Buttner (1970)⁴⁵ on the other hand, contended that approximately 90% of the fluoride in tea leaves will be extracted after infusion and the fluoride concentration of the infusion itself is around 1 ppm fluoride.

Higher figures of skeletal storage of fluoride have been reported from the adult population in England, where tea consumption is high, than from the U.S.A. (Zipkin, McClure, Leone & Lee, 1958)²²². However, Lawrentz and Mitchell (1941)¹²⁹ demonstrated that fluoride in tea is somewhat less available than fluoride in water.

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TABLE 3. FLUORINE CONTENT OF VARIOUS FOODSTUFFS.^a

Food	Fluorine content (ppm)
<i>Animal tissue:</i>	
Cow's liver, dry weight	5.20-5.80
Chicken liver, fresh weight	0.7-1.29
Calf liver, fresh weight	0.2
Cow's kidney, dry weight	6.9-10.1
Cow's heart muscle, dry weight	2.3-2.7
<i>Meats:</i>	
Chicken	1.40
Beef	2.00
Round steak	1.3
Pork	<0.2
Pork chops	1.0
Pork shoulder	1.2
Frankfurters	1.7
Lamb	1.2
Veal	0.9
Mutton	<0.2
<i>Fish:</i>	
Fish fillets	1.5
Mackerel	
boned	<0.2
with bones	3.9
fresh	26.89
dried	84.47
canned	12.10
Salmon	
canned	4.5
fresh	5.8
dried	19.3
Sardines	
canned	7.3
in olive oil	16.1
Shrimps	
canned	4.4
edible portion	0.9
Codfish	
fresh	7.0
salted	5.0
Oysters	
fresh	0.7
Crab meat, canned	2.0
Herring, smoked	3.5
Tuna fish flakes, canned	0.1
<i>Eggs:</i>	
Whole	1.2
White	1.5
Yolk	0.6
Whole milk:	0.07-0.22
Tea:	3.2-178.8
Average of ten samples	97.0
<i>Citrus fruits:</i>	
Grapefruit	
edible portion	0.36
fresh	0.36
Lemon, fresh	0.12
	0.028, 0.051, 0.174

(. . .contd)

TABLE 3. (contd)

Food	Fluorine content (ppm)	
Orange, edible portion	0.34	
Oranges, fruit, fresh	0.17-0.07	
Pomelo, fruit, fresh	0.10-0.16	
<i>Non-citrus fruits:</i>	<i>Fresh weight</i>	<i>Dry weight</i>
Apples	0.22-1.32	0.13-0.43
Apricot	0.06	0.24
Banana	0.23	0.65
Cherry	0.25	
Cherries, black	0.18	0.61
Currants	0.12	0.69
Fig	0.21	
Grapes	0.16	
Grape juice	0.093	
Gooseberries	0.11	0.72
Mango	0.18	
Pawpaw	0.15	
Pear	0.19	
Plum	0.22	0.10
Pineapple	0.14	
Pineapple, tinned	0.00	
Quince	0.06	0.37
Sweet melon	0.20	
Strawberry	0.18	
Watermelon	0.11	
<i>Cereals and cereal products:</i>	<i>Fresh weight</i>	<i>Dry weight</i>
Corn		
unspecified	0.62	0.70
canned	<0.20	
yellow	<0.10	
germ		8.0-11.0
meal, as purchased	0.22	
flakes		1.33
Ralston	0.58	
Wheat		
whole		0.53
unspecified	0.7	
bran	0.29	0.33
germ A, commercial	1.7	
germ B, commercial	4.0	
germ, pure	0.88	1.00
Cream of wheat		0.55
Flour		
wheat, white	0.35	
self-rising	0.45	
whole wheat		1.32
white	0.27	0.31
biscuit		0.0
baking	0.31	0.35
Bread, white		0.54
Rice		
unspecified	0.67	0.76
whole	<0.10	
middle	0.19	
Soybeans		4.00
Buckwheat		
unspecified		2.00
whole		1.70
bran		1.60
Oats		
unspecified		3.0
crushed	0.20	
mother's		0.92
fresh	0.25	0.29
Rye		
unspecified	0.61	0.69
black-eyed peas	0.23	

(. . . contd)

TABLE 3. (contd)

Food	Fluorine content (ppm)	
	Fresh weight	Dry weight
Rye (continued)		
cottonseed, meal	12.0	
hulls	12.0-14.0	
Spaghetti		
canned		1.15
dry		0.80
Macaroni, dry		0.82
Vegetables and tubers:	Fresh weight	Dry weight
Asparagus, canned		0.48
Beans		
string		0.64
string, canned		0.67
green	0.15	1.01
light green	0.11	0.73
lima, dry		4.51
lima, seeds		2.2
dry		1.04
dried		<0.20
navy, dry		1.70
Beets		
unspecified	0.2	
fresh		0.60
root		2.8
leaves, dry		3.80
tops		3.4
string	0.32	6.09
Cauliflower		
fresh		0.45
flower	0.12	0.86
leaves	0.08	0.83
unspecified	1.0	
Cabbage		
large		9.34
foreign		15.38
fresh		0.70
unspecified	0.13	
edible head		3.4
without leaves	0.8	9.5
Carrots		
unspecified	0.4	6.92
fresh		1.30
root		8.4
Celery		
unspecified	0.14	
edible stalks		8.5
Cress	0.24	4.38
Cucumber	0.20	
Endive	0.2	
Garlic		
green		17.72
Kale	0.16	
Lettuce		
loose, head		11.3
cabbage	0.30	4.45
prickly		5.18
fresh		0.42
Mustard		
greens	0.15	
leaves, salted, dried		3.0-4.8
Onions		
green		10.11
unspecified	0.60	
Parsley		
tops		11.3
unspecified	0.8	

(. . . contd)

TABLE 3. (contd)

Food	Fluorine content (ppm)	
	Fresh weight	Dry weight
Parsnip, roots		5.5
unspecified	0.6	
green		6.69
fresh		0.60
Potatoes		
white		0.96
unspecified	0.20	
whole	6.4	22.0
peelings	0.07	0.35
Irish, tuber		1.4
sweet, unpeeled	0.13	
sweet	<0.20	
Pumpkin	0.10	
Radish	0.8	
Rhubarb	0.4	
Rutabaga (swede)		
tops		7.0
roots		2.9
Spinach		
fresh		1.11
unspecified	1.8	
winter	0.44	3.80
Squash, fresh		0.63
Tomatoes		
unspecified	0.24	2.40
fresh		0.53
Turnips		
greens	0.10	
tops		1.7
roots		2.6
Watercress	1.0	
<i>Miscellaneous substances:</i>		
Peanuts		
unspecified		1.35
tops		1.7
kernel		1.5
Almonds	0.30	0.90
Hazelnut	0.30	0.30
Chestnut		1.45
shell		0.24
Coconut, fresh	0.00	
Cocoa	0.5, 1.0	
Plain chocolate	0.50	
Milk chocolate	0.5, 1.0	
Molasses	0.00	
Sugar	0.32	
Honey	1.00	
Gelatin	0.00	
Glucose	0.50	
Malt	1.0, 1.5	
Powdered ginger	1.00	
Baking powder		
A	220.0	
B	19.0	
C	<0.1	
Coffee	0.2-1.6	
Butter	1.50	
Cheese	1.62	
Pork and beans, canned	1.40	
<i>Wine and beer:</i>		
Chinese, Shao-sing		
best grade		0.07
second grade		0.05
Port		0.24
Beer		0.20

^a(McClure, 1949)145.

^b Containing 1 ppm fluorine.

^c Dry substance containing 0.1-1 ppm fluorine.

B. Availability of Fluoride Ion for Absorption
from Foods and/or Waters

The availability of fluoride for absorption from foods and/or waters is of importance if the ion is supplied for beneficial purposes.

It has been estimated that 86 to 97% of the soluble fluorides in drinking water will be absorbed nearly completely, regardless of the level of fluoride in the water supply (McClure, Mitchell, Hamilton & Kinser, 1945¹⁴⁸; Largent, 1960¹²⁵); whereas about 80% of the fluoride normally occurring in human diet is absorbed (Cremer & Buttner, 1970)⁴⁵. It has been demonstrated in studies on rats that the fluoride retention in bones and teeth is not significantly different from an intake of equal amounts of soluble fluoride (sodium fluoride) in drinking water or in food (McClure, 1939)¹⁴³, thus indicating that sodium fluoride is absorbed to a similar extent from food and water.

Of the inorganic elements in the water and food, calcium, magnesium and aluminum are the ions most likely to be present and interfere with fluoride absorption if present in high concentrations. In areas of magnesium or calcium-bearing rocks, one may find 1 ppm in very soft waters to as much as 100 ppm in very hard waters (Cremer & Buttner, 1970)⁴⁵.

Feldman, Morken and Hodge (1957)⁷³ pointed out that in drinking water containing 1 ppm fluoride, 0.03 to 2.8% of the fluoride will be bound to calcium, and 0.3 to 28% to magnesium, depending on

the hardness of water. Nevertheless, fluoride up to the extent of 16 ppm in any drinking water supply with a pH of 5 or higher will be available as fluoride ions for nearly complete absorption (Cremer & Buttner, 1970)⁴⁵.

If calcium (as calcium-phosphate or as calcium-carbonate) or aluminum compounds are added, the fluoride absorption is markedly reduced to about 50%. In such cases, the fluoride is bound in a less-soluble form and faecal excretion increases (Hodge & Smith, 1965)¹⁰².

In the normally composed drinking water and food, interference from the inorganic environment is rather small and can be ignored, since the normal mineral concentration will rarely be in the ranges at which the fluoride absorption may be affected significantly (Cremer & Buttner, 1970)⁴⁵.

The results of different studies by Ericsson (1966)⁶⁷, Wagner (1973)²⁰⁴, Stookey, Crane and Muhler (1962)¹⁹⁷, and Buttner (1963)³⁴, all indicated that none of the trace elements in question influenced the absorption of fluoride, since no significant changes in fluoride retention were observed.

C. Foods Fortified with Fluoride

(a) Salt fortified with fluoride

The addition of fluoride to table salt has been practised in some Swiss Cantons (Wespi, 1964)²⁰⁹, and in some countries for several years.

There is a precedent for this route of supplementation in that iodized salt has been found beneficial against goitre. The kitchen salt is sprayed with sodium fluoride to contain 200 mg. NaF/kg. Based on average salt consumption (approximately 4gm./adult/day), this represents a supplementation of only about 0.4 mg. fluoride/adult/day or about a third of the desired level (Newbrun, 1972)¹⁶¹. In spite of this low dosage, a 22% reduction in DMFT scores after 4.5 years of unsupervised use was found in 8 to 9 year-old children. This method has an inherent disadvantage in that it is difficult to accommodate to varying but suboptimal levels of natural fluoride in water supplies.

Since NaF in salt will be ingested with meals, the fluoride absorption will be slightly reduced, especially if the food is rich in calcium (Cremer & Buttner, 1970)⁴⁵. Therefore, Ericsson, Santesson and Ullberg (1961)⁶⁹ suggested that sodium monofluorophosphate ($\text{Na}_2\text{PO}_3\text{F}$) might be a more suitable compound because the fluoride absorption is more rapid and less influenced by calcium ions. This compound was found to be a more stable source of fluoride than NaF in cases where the fluoride was administered simultaneously with food containing large or varying quantities of calcium.

(b) Milk Fortified with Fluoride

Using milk as a vehicle for fluoride has certain disadvantages. Water, bread, and salt consumption increases fairly regularly with increasing age. Milk, on the other hand, is ingested in relatively large amounts during the first two years, but then consumption decreases. At the levels of administration used, it is not as great as with fluoridation of water

supplies (Hardwick, 1965)⁹⁴.

Ericsson (1958)⁶⁵, using ^{18}F , found that at concentrations of 1 and 4 ppm fluoride, the absorption of fluoride from milk was slower than that from water. However, the ultimate percentage absorbed was nearly the same whether the fluoride was supplied in milk or in water. 8 to 10 hours after administration, 17 to 19% of the fluoride in milk and 10 to 11% of the fluoride in water remained unabsorbed. It was suggested that the coagulation in milk in the stomach and incomplete diffusibility of fluoride, may be factors in retarding its absorption.

Muhler and Weddle (1955)¹⁵⁵ contended that fluoride at concentrations of 5 and 10 ppm was approximately equally available whether administered in water or in milk. They also found that when the fluoride concentration in milk reached 10 ug. (per milliliter), there is sufficient fluorine present to make the interfering effect of calcium and magnesium of little consequence.

3. FROM DRUGS

A. Drugs Used as Anticariogenic Agents

These are designed specifically for the metabolic utilization of the fluoride ion.

(a) Fluoride tablets, lozenges and troches

In general, fluoride tablets available commercially contain 0.25 to 1.00 mg. fluoride, commonly provided as sodium fluoride, an inert filler such as sodium chloride, and a small amount of disintegrant (Stookey, 1970)¹⁹⁶.

It appears that the daily ingestion of a fluoride tablet containing 1.0 mg. fluoride in children may result in a greater amount of fluoride available for metabolic utilization than that derived from fluoridated water, since children ingest less than one litre of water daily, and therefore receive a somewhat smaller total amount of the metabolically available fluoride. No objectionable dental fluorosis has been reported with the 0.5 to 1.0 mg. per day dosages, although there have been reports of mild fluorosis (Aasenden & Peebles, 1974)¹.

The fluoride in sodium fluoride-containing pills is absorbed almost completely, depending on food consumption, if ingested with meals; if ingested between meals, it is absorbed as completely as when ingested in water (Cremer & Buttner, 1970)⁴⁵.

In areas where there is some but insufficient fluoride, the following supplementation table (Table 4), can be used as guide for

communities where the recommended optimal level of fluoride is 1 ppm.

TABLE 4. RECOMMENDED DIETARY FLUORIDE SUPPLEMENTATION

Water Fluoride ppm	Adjusted Allowance	
	Sodium fluoride mg. per day	Provides fluoride ion, mg. per day
0.0	2.2	1.0
0.2	1.8	0.8
0.4	1.3	0.6
0.6	0.9	0.4

(Accepted Dental Therapeutics. Council on Dental Therapeutics of the American Dental Association, 1975)².

These allowances are for children over 3 years of age. The allowances should be reduced by one half for a child between 2 and 3 years of age.

For children under 2 years of age, generally it is recommended that water containing 1 ppm fluoride be prepared with fluoride tablets or drops, and that this water be used for the child's drinking water and for the preparation of his food and formula. The administration of 0.25 mg. of fluoride daily for the age group appears to be a satisfactory alternative.

(b) Fluoride-vitamin supplements

It has been found that persons ingesting fluoride tablets per se frequently lose interest in this form of therapy (Hennon, Stookey & Muhler, 1967¹⁰⁰; Arnold, McClure & White, 1960¹³). It has been sug-

gested that interest is maintained by the patients when supplemental fluoride is provided in a vitamin-fluoride preparation (Hennon, Stookey & Muhler, 1966)⁹⁹.

Commercially available vitamin-fluoride preparations frequently contain, in addition to NaF, vitamins A, C and D, and a few contain some members of the vitamin B complex as well. In experimental animals and in humans, the metabolism of fluoride ingested as a NaF tablet is not appreciably altered by addition of vitamins to the tablet (Hennon, Stookey & Muhler, 1964⁹⁸; Showley, Stookey, Hennon & Muhler, 1966¹⁸⁶).

(c) Fluoride-mineral Supplements

Since the systemic effect of fluorides is most important during tooth formation and calcification in utero, it has been suggested that fluoride must be provided prenatally in order to achieve maximal protection against dental caries, particularly in respect of the primary dentition. As a result, a wide variety of mineral-fluoride supplements designed for prenatal ingestion, have been made available commercially. In addition, there are now several post-natal vitamin-mineral-fluoride preparations (Stookey, 1970)¹⁹⁶.

It has also been suggested that the metabolism of fluoride ingested in the form of a vitamin-mineral supplement may be significantly different from that observed when the fluoride is ingested alone (Hennon, Burns & Muhler, unpublished data taken from Stookey, 1970)¹⁹⁶.

It is apparent that further studies along this aspect of fluoride metabolism are necessary before one can recommend the widespread

use of vitamin-mineral-fluoride supplements.

(d) Fluoride-containing Dentifrices

This is generally provided at a concentration of 1.0 mg. fluoride per gram of dentifrice (Stockey, 1970)¹⁹⁶.

Studies conducted by Schweinsberger and Muhler (1956)¹⁷⁸; 1957¹⁷⁹) and Buttner, Schulke and Soyka (1961)³⁶, indicated that in no instance was the urinary fluoride concentration significantly altered by unsupervised use of stannous-fluoride dentifrice. The amount of fluoride retained in the body following a single brushing with a dentifrice containing 100 ppm fluoride is of the order of 15 to 55 ug. (0.015 to 0.055 mg.) (Ericsson, 1961⁶⁶; Duckworth, 1964⁶¹).

Hein, Smith, Gardner, Downs, Maynard and Hodge (1951)⁹⁶, have reported that sodium monofluorophosphate is less toxic than fluoride in the form of sodium fluoride. It has been suggested that this finding is due to the presence of interfering ions, such as calcium, in the polishing agents in the toothpaste, which react with the fluoride in the gastrointestinal tract to prevent its subsequent absorption and therefore the toxicity (Shaver & Smith, 1946¹⁸⁵; Buttner, Schulke & Soyka, 1961³⁶; Hagen, 1972⁹²; Forsman & Ericsson, 1973⁷⁸). Preparations containing polishing agents like plastic particles, silicon dioxide, or bicarbonate, are inert towards the fluoride, and therefore do not exert any similar effect on the absorption (Forsman & Ericsson, 1973)⁷⁸.

(e) Fluoride-containing Chewing-gum

Clark (1962)⁴² suggests that a significant proportion of the stannous-fluoride added to chewing-gum is in some manner chemically

or physically, bound within the gum and is thereby no longer available either for reaction with the oral hard tissues or for systemic utilization from the swallowing of saliva.

It should be noted that calcium-carbonate and other calcium salts are common constituents of chewing-gums and knowing the presence of calcium significantly decreases the metabolic utilization of fluoride.

Emslie, Veall and Duckworth (1961)⁶⁴ on the other hand concluded, after a series of studies using ^{18}F , that 80 to 90% of the radioactive fluoride was released from the gum in 10 to 15 minutes, and that the uptake of the fluoride by a premolar tooth was about 20 ug. after 10 minutes' chewing of gum containing 100 ug. of ^{18}F . They also stated that the rate of release was not affected by the addition of 5% calcium-carbonate, but that the addition of 2% citric acid greatly increased the retention of fluoride by the chewing-gum. However, this increased retention within the gum was partially offset by an increased uptake of the ^{18}F by the teeth.

There are no references in the literature on the metabolic fate of fluorides incorporated in chewing-gums. However, it has been suggested that the metabolic fate is the same when the fluorine ion is supplied by chewing-gum as when it is supplied by any other vehicle, provided that the fluoride is not in some manner "deactivated" by other constituents of chewing-gums (Stookey, 1970)¹⁹⁶.

(f) Fluoride-containing Mouthwashes

Bossert and Dunning (1945)²⁸ suggested that : (i) 3 to 11% of the total fluoride content of the mouthwash after single rinses were

retained; and (ii) as much as 6% of the 0.1% sodium fluoride mouthwash may be swallowed and the fluoride thereby made available for gastrointestinal absorption. Hellstrom (1960)⁹⁷ reported that following the use of 0.1% sodium fluoride mouthwash, an average of 2 mg. of fluoride in adults and of 0.85 mg. in children were retained; and that about 30% and 19% of the fluoride in 15 ml. and 10 ml. quantities of the mouthwash was retained by adults and children, respectively.

Additional studies are needed to determine the metabolic fate of fluoride provided in a mouthwash, particularly in children under unsupervised condition.

B. Drugs Used for Purposes Other Than Anticariogenic Agents

In these drugs, fluoride is employed in a biologically inert form.

(a) Dentine obtundents

The metabolism of the fluoride provided in such treatment procedures per se has not been fully investigated. It has been suggested that only minute quantities of fluoride actually reach the pulp from such treatments. Owing to the high electronegativity of the fluoride ions and its pronounced affinity for cations, it would seem that most of the fluoride from such treatments would become chemically bound to the inorganic components of dental hard tissues. Such fluoride would then be considered metabolically detoxified. The reported failure in previous

studies of these fluoride treatments to elicit any untoward soft tissue response in the pulp provides further evidence that very little fluoride actually reaches the dental pulp and is metabolically available for deposition in the calcified skeletal structures or for excretion (Stookey, 1970)¹⁹⁶.

(b) Treatment of osteoporosis and related metabolic skeletal disorders

Use of large dosages of systemic fluoride in treatment of various skeletal disorders involving loss of the calcified component of bone. It was found that substantial amounts of fluoride are being retained by subjects taking fluoride in large dosages prescribed for treatment of such conditions (Stookey, 1970)¹⁹⁶.

There is some suggestion that with the increasing length of fluoride exposure, the amount of fluoride retained within the body decreases (Stookey, Epperson & Johnston, unpublished data in Stookey, 1970)¹⁹⁶.

Many other metabolic aspects of this use of fluoride merit further investigation.

(c) Fluorinated corticosteroids

No apparent physiological stability of the fluorine-carbon bond renders the fluorine metabolically unavailable and it is therefore not subject to the metabolic patterns observed with the free fluoride ion provided by inorganic fluorides (Stookey, 1970)¹⁹⁶.

(d) Fluorine-containing anaesthetic agents

Since the fluorine present in these compounds is again

bound to carbon and since this fluorine-carbon bond is not cleaved by biological processes, the fluoride is not metabolically available and does not enter the normal pathways of fluoride metabolism. The fluoride is therefore eliminated from the body along with the parent compound (Stookey, 1970)¹⁹⁶.

(e) Miscellaneous fluorine-containing drugs

Other additional usages of organic fluorocompounds have been suggested. Some have been suggested for use as muscle depressants, while the fluoride analogues of tyrosine and phenylalanine have been suggested as possible therapeutic agents in thyroid disorders. Other organic fluorine compounds have been tried out with some success as chemotherapeutic agents in the treatment of cancer. However, owing to the chemical nature of these compounds, i.e., the presence of the carbon-fluorine bond, the fluorine present is metabolically inert.

Another class of fluorine-containing compounds are the phosphofluoridates, where fluoride is bound to phosphorus, and within the body, this bond is easily broken by protein interaction, releasing fluoride as free fluoride ions, and thus becomes metabolically available. One example of this is diisopropyl-phosphofluoridate (DPF), which has had application as a nerve gas and as an insecticide (Stookey, 1970)¹⁹⁶.

4. INHALATION FROM DUST OR VAPOURS

A. Dusts

This refers to fluorides dispersed in air especially in areas where mineral deposits were located at or near the surface of the ground.

Dusts inhaled and later swallowed may be of importance, but its importance is difficult to appraise. Any serious hazard from dusts is likely to concern only the very readily soluble fluoride compounds such as sodium fluoride and potassium fluoride (Largent, 1970)¹²⁷.

Acute changes observed in animals and man have been caused by fluoride-containing dusts, but for the most part these changes relate more to ingestion than to inhalation of dust. Chronic changes by fluorides in dusts may include dental changes in animals, and man, both of which are related to ingestion rather than inhalation of the dust, either as a contaminant of food, or suspended in drinking water (Largent, 1970)¹²⁷.

Where water is fluoridated at 1 ppm, the additional fluoride intake of the population in areas where there is industrial pollution might create a hazard. In most circumstances such fears may easily be discounted. The average man engaged on moderately strenuous work is known to inhale about 20 cubic metres of air per day (Largent, 1970)¹²⁷. If, therefore, the fluoride pollution of the air of any place is known, it is a simple matter to calculate as an upper limit the maximum fluoride

uptake on the assumption that all fluorides inhaled are retained.

Some studies in the past have shown that the amount of fluoride absorbed from the atmosphere would be but a fraction of that contained in the diet. By contrast however, the maximum possible adult intake of atmospheric fluoride concentration near a super-phosphate plant in the U.S.S.R. was found to be from 1.9 mg. to 9.7 mg. and high levels of fluoride intake were, in fact, confirmed by the finding of dental fluorosis and a low incidence of dental caries in schoolchildren in that area (Martin, 1970)¹³⁹.

B. Gaseous Compounds or Vapours

The most widely encountered of which is HF from industrial processes. When the gas is inhaled by animals or man, severe damage to the respiratory tract may occur, and the results can be fatal if the level of HF is much above 25 to 30 ppm and if the exposure is allowed to continue for too long a time (Machle, Thamann, Kitzmiller & Cholak, 1934¹³⁶; Machle & Kitzmiller, 1935¹³⁴).

The levels of HF used, in the neighborhood of 3 ppm, are thought to be safe for repeated exposure : 8 hours daily over periods of many years (American Conference of Governmental Industrial Hygienists, 1965)¹⁰.

C. Gaseous and Particulate Fluorides Suspended Together

Such a mixture is most likely to be found in (Largent, 1970)¹²⁷: (i) the processing of fluorapatite to make phosphate fertilizers; (ii) certain phases of manufacturing iron, aluminum and fluoride chemicals generally, including HF. This applies to workmen who operate equipment for manufacturing HF and hence, their potential exposure will be both gaseous and particulate material.

In situations where the exposure to fluoride is completely overwhelming, it doesn't matter whether it is inhaled and/or ingested from this source, it still leads to the same chronic effects of exposure.

D. Particulate Fluorides Dispersed in Water

In areas where the particulate fluorides may be of no significant importance as inhaled materials, the particles may bear some significance as contaminant in the food eaten or dispersed (undissolved) in the water ingested.

Acute effects of these particulates have not been observed. However, one fatal case of inhalation of an aqueous mist (derived from NaF in high concentration dissolved in water) has been reported (Largent, 1943)¹²⁴.

Generally, there have been no effects on health of man from the inhalation of airborne inorganic fluorides within his place of residence. Any effects of any kind induced by airborne fluorides have concerned : (i) the few instances when fluoride was present in the at-

mosphere within the area where men were at work; or (ii) where the fluorides became a contaminant which was ingested with food or water or both.

Largent (1970)¹²⁷ seems to think that there hasn't been amounts of dusts released into communities adjacent to industrial operations, that are sufficient to influence the intake of fluoride by man. When the contamination of food and drinking water by dusts becomes an important health problem, it may be the result solely of the minerals deposited naturally in the soil.

V. DENTAL FLUOROSIS

1. ETIOLOGY

The earliest established fact concerning the etiology of dental fluorosis, came about when the incidence and severity of the 'mottling' of human enamel was directly related to the concentration of fluorine in the drinking water.

It is now recognized that the ingestion of fluoride-containing water, or other fluoride-containing sources for that matter, beyond the physiologically-acceptable limit*, during the period of tooth development and calcification, may result in dental fluorosis. Although the severity of which generally increases with an increasing amount of fluoride intake, there are numerous factors which may cause wide individual variations.

* This refers to the optimal fluoride concentration specific for a certain community or country, depending on the extrinsic and intrinsic factors, which will be dealt with in the latter sections, 'Factors influencing severity of dental fluorosis' and 'Optimal fluoride concentration'.

2. DENTAL FLUOROSIS CLASSIFICATION AND INDEX

The assessment of dental fluorosis is particularly important in areas where the natural fluoride content of the water supply is high. It is also important to record the prevalence of dental fluorosis both before and after the introduction of controlled water fluoridation. Such an assessment is based on a Classification of Dental Fluorosis (Table 5), which has become a standard in many epidemiological works (Dean, 1934⁵⁰; Dean, 1942⁵²).

Each tooth is examined according to the criteria set out in Table 5. The subject is then given a Dental Fluorosis Index Score according to the two teeth showing the most severe fluorosis. For example, if two teeth are graded as "moderate", and the rest of the dentition "normal", the subject is counted as having moderate fluorosis, with a score of 3.0. If one tooth is graded as "mild", another "moderate", and the rest of the dentition "normal", the subject is counted as having mild fluorosis, with a score of 2.0. If only one tooth appears to have fluorosis, the subject is graded as "normal", with a score of 0.0. It is recommended that the condition be reported in terms of percentage of persons in each category, and Dean's Community Index of Fluorosis, for the same age groupings (W.H.O., 1971)²¹².

Community Index of Dental Fluorosis (Dean, 1942)⁵².

This is a means of calculating the prevalence or degree of fluorosis in a group or community. Using Dean's Classification of Dental Fluorosis, and the W.H.O. criteria for scoring, the Community Index is

computed by averaging the weights or scores assigned to each of the individuals examined in the group : one weight figure per person. The formula becomes:

$$\text{Community Index} = \frac{\text{sum of } f \times w}{n},$$

where f = frequency, w = weight, n = number of cases examined.

One should bear in mind though, that the recording of dental fluorosis according to Dean's proposed classification is based on presumed etiology. When the "questionable" category was made, it points out that all other grades are non-questionable, and implied certainty as to fluoride as causative factor. The ideal approach of course, will be to record the condition once defined and well established, according to that definition, and not on the basis of presumed etiology.

TABLE 5. DENTAL FLUOROSIS CLASSIFICATION AND INDEX.

Grade of Fluorosis	Description of Fluorosis	Dental Fluorosis Index Score
Normal (N)	The enamel presents the usual translucent, semi-vitriform type of structure. The surface is smooth, glossy, and usually of a pale, creamy-white colour.	0.0
Questionable (Q)	The enamel discloses slight aberrations from the translucency of normal enamel, ranging from a few white flecks to occasional white spots, with a tendency to form horizontal striations. This classification is used where a definite diagnosis of the mildest form of fluorosis is not warranted but a classification of normal is not justified.	0.5
Very Mild (VM)	Small, opaque, paper-white areas scattered irregularly over the tooth but involving less than about 25% of the tooth surface. Frequently included in this classification are teeth showing no more than about 1-2 mm. of white opacity at the tip of the cusps of the premolars or second molars.	1.0
Mild (M)	The white opaque areas in the enamel of the teeth are more extensive, but still involves less than 50% of the tooth.	2.0
Moderate (Mo)	All enamel surfaces of the teeth are affected, and surfaces subject to attrition show marked wear. Brown stain is frequently a disfiguring feature.	3.0
Severe (S)	All enamel surfaces are affected and hypoplasia is so marked that the general form of the tooth may be affected. The major diagnostic sign of this classification is the discrete or confluent pitting. Brown stains are widespread and teeth often present a corroded appearance.	4.0

(Dean, 1934 50 ; Dean, 1942 52)

3. CLINICAL FEATURES

Dental fluorosis is characterized by faint white flecking of the enamel, white patches or striations or, in more severe cases, by yellow, black or brown stain and hypoplasia of varying degree (Figs. 1 to 5). On account of the roughness and porosity of the enamel surface, secondary staining from food pigments is likely to be superimposed.

In severe fluorosis, there may also be confluent pitting with the teeth appearing corroded (Fig. 5), and loss of tooth form. Sometimes, the enamel chips off easily because of its brittleness.

Staining occurs mostly in the incisors and canines, i.e. in the teeth most exposed to light, except in very severe cases where it is widespread. This stain is in the enamel structure and not on the enamel surface (Forrest, 1965)⁷⁷.

Fluoride opacities occur symmetrically and except in severe cases where all the teeth are usually affected, they are found mostly in premolars, less so in the upper incisors and second molars, and least of all in the first molars and lower incisors (Forrest, 1965)⁷⁷.

Susceptibility of mottled enamel is restricted to a sharply defined age group. The reason is that fluorine is deposited in teeth during the period of calcification of the crown of the permanent teeth. This period extends from infancy, when the central incisors may be affected, to 16 years of age, when the calcification of the crown of the third molars has been completed (Siddiqui, 1970)¹⁸⁸.

Both sexes are affected with equal frequency, although in

two investigations on the prevalence of dental fluorosis, one in Uganda (Møller, Pindborg, Gedalia & Roed-Petersen, 1970)¹⁵¹, and the other in Thailand (Leatherwood, Burnett, Chandravejjsmarn & Sirikaya, 1965)¹³⁰, the frequency was found to be higher in the males.

The condition is largely confined to permanent teeth, although in areas of marked severity, sporadic instances of deciduous teeth being affected have been observed - evidence of placental transmission of fluorine (Gedalia, 1970)⁸².

The degree of mottling depends largely on the amount of fluorine ingested during tooth development and calcification; at 6 ppm, the incidence of mottling is 100% (Siddiqui, 1970¹⁸⁸; Cannell, 1960³⁸; Bhussry, 1970²³; Adler, 1970⁴). The surfaces subjected to attrition show marked lesions.

It has been established that the fluorine content remaining the same, the incidence of dental caries varied inversely with the Dental Fluorosis Index (DFI) score of a community as shown in Fig. 6; although the tooth structure is sometimes so disorganized that the teeth appear more vulnerable to caries attack.

It is interesting to note in this context an observation by Dean, Jay, Arnold, McClure and Elvove (1939)⁵⁷, in a study at Galesburg, where there was no significant difference in the amount of caries between those children with mottled enamel and those without. The amount of dental caries in the 114 children with mottled enamel was 200 per 100 children examined; in the 129 listed as not having mottled enamel, it was 186 per 100 children. It'd appear that the factor responsible for the low a-

mount of caries in this city was operative irrespective of whether the child showed macroscopic evidence of mottled enamel.

The clinical feature of dental fluorosis and non-fluoride opacities especially in the slighter forms is rather similar in some respects. They may be difficult to diagnose and distinguish from one another.

FIG. 1. 'QUESTIONABLE' DENTAL FLUOROSIS.



FIG. 2. 'MODERATE' DENTAL FLUOROSIS.

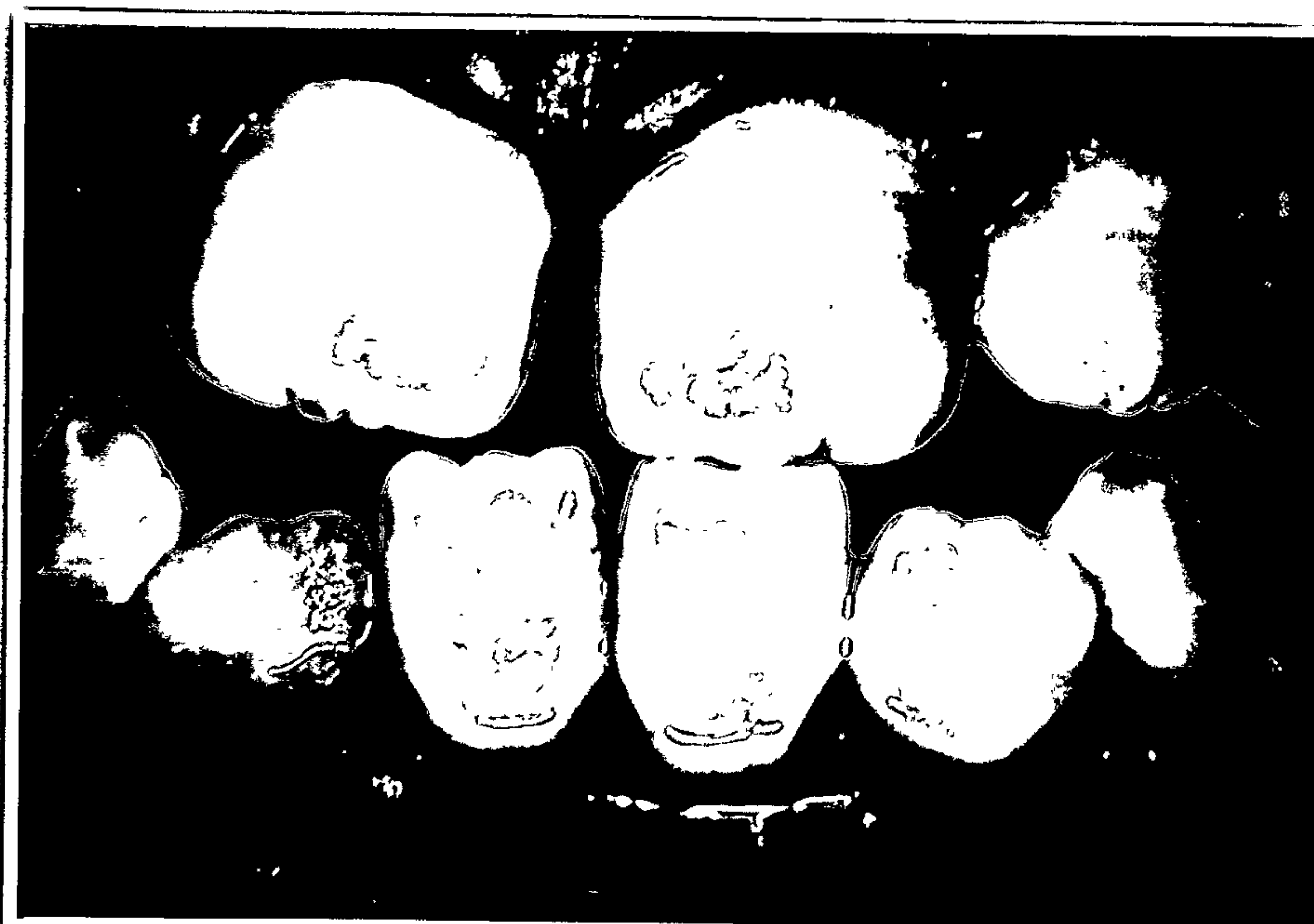


FIG. 3. 'MODERATELY-SEVERE' DENTAL FLUOROSIS.

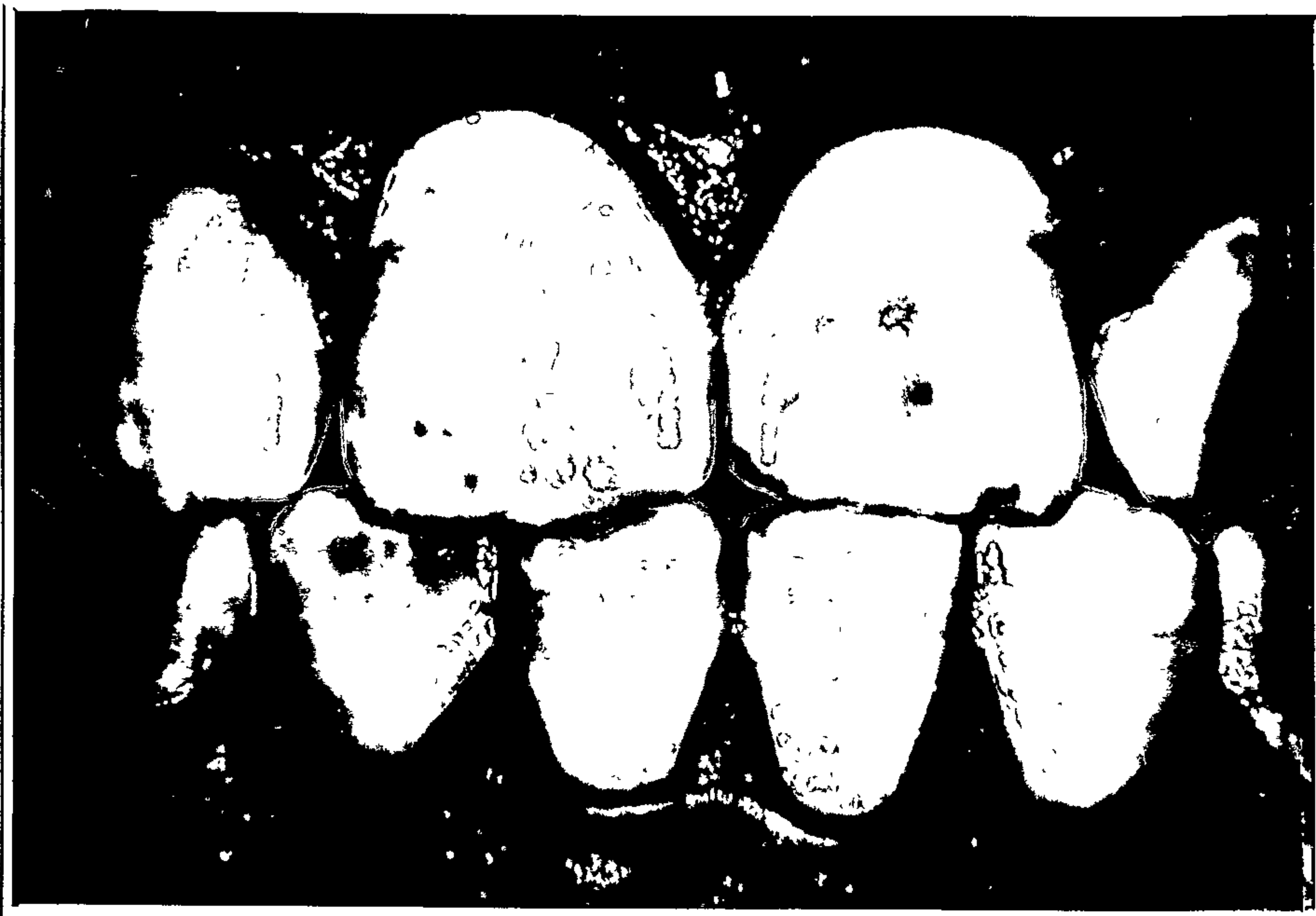


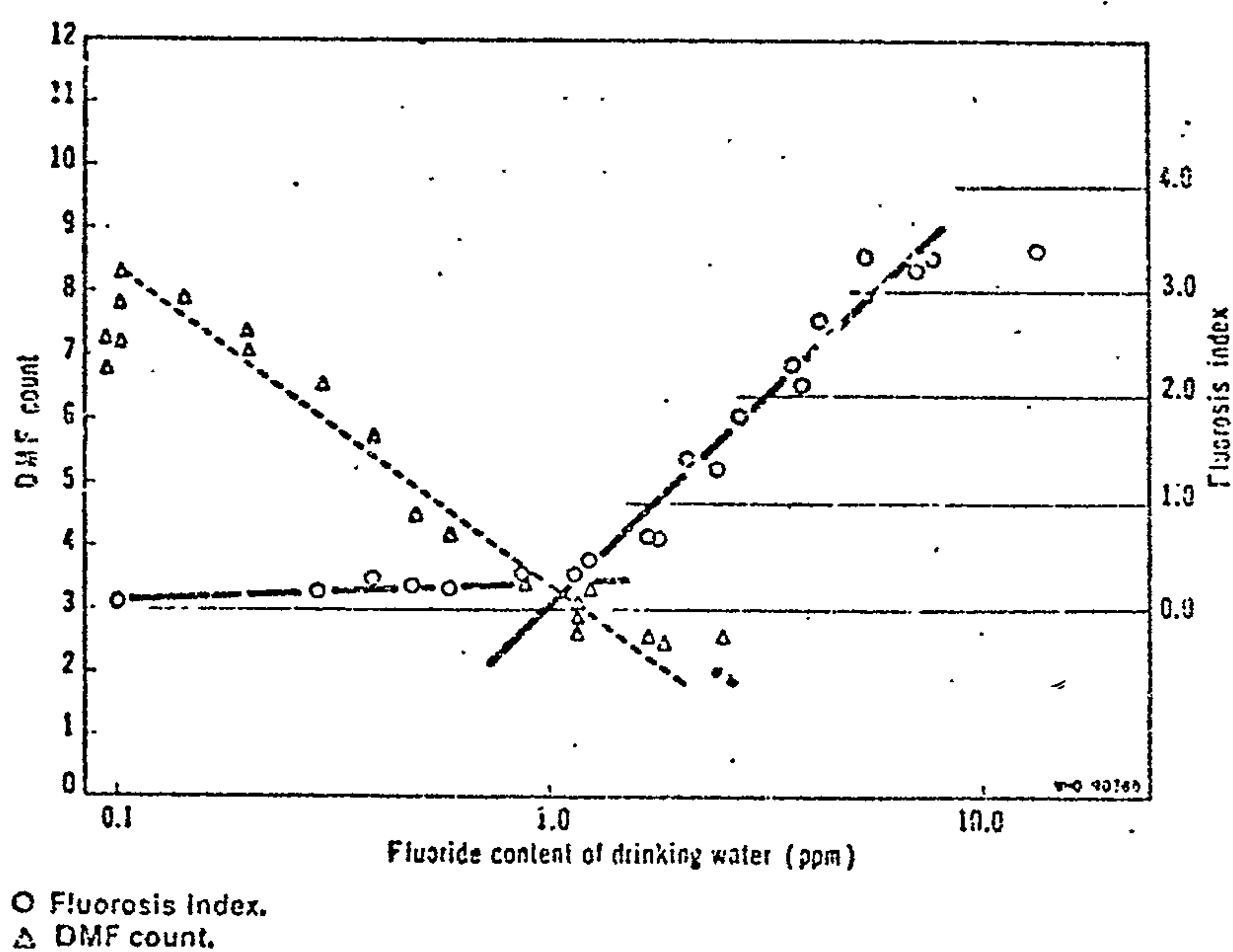
FIG. 4. 'MODERATELY-SEVERE' DENTAL FLUOROSIS.



FIG. 5. 'SEVERE' DENTAL FLUOROSIS.



FIG. 6 . RELATIONSHIP BETWEEN FLUORIDE CONTENT IN DRINKING WATER, CARIES REXPERIENCE AND DENTAL FLUOROSIS.



(Hodge, 1950)¹⁰¹.

4. PATHOGENESIS

The series of mechanisms leading to fluorosis in human enamel during its development and mineralization are as yet not well understood. Several hypotheses on how it actually develops have been cited from different investigations.

The lesion produced in dental fluorosis is developmental in origin. When the fluoride level intake is high, toxic levels may build up in the region of the tooth just prior to the final stages of maturation, and damage post-secretory ameloblasts, producing the hypomineralized or hypomaturational defects (Fejerskov, Johnson & Silverstone, 1974)⁷¹. Ameloblasts are able to lay down matrix as evidenced by the normal or regular course of the prisms even in severe cases of dental fluorosis (Fejerskov, Silverstone, Melsen & Møller, 1975)⁷².

In other words, hypomineralized regions of fluorosed enamel are produced by an arrest of maturation, possibly due to toxic damage to those ameloblasts in the absorptive or maturation phase of their life cycles (Fejerskov, Johnson & Silverstone, 1974)⁷¹.

The effect would be expected to be most marked in the outer enamel for two reasons:

- i. It is not until the full thickness of enamel is laid down that ameloblast function becomes predominantly that of controlling maturation and, according to the hypothesis, most susceptible to fluoride damage. While the outer enamel is still being secreted, some maturation of deeper enamel is likely to take place.

ii. Presence of high concentrations of fluoride in tissue fluid within the enamel organ may cause a delay in crystal formation, or sometimes a failure of nucleation sites to develop (Newbrun & Brudevold, 1960)¹⁶². If no nucleation sites are formed as the enamel increases in thickness, growth in width and thickness of individual crystals become increasingly important with increasing distance from the amelodentinal junction in order for them to fill the prisms as they widen toward the tooth surface. The gradual decrease in pore volume from the central part of the lesions towards the amelodentinal junction, and the observation by Silness and Gustavsen (1970)¹⁸⁹, that the shape of the compartments in the deeper parts of the fluorosed enamel becomes more and more irregular, indicating crystal adaptation, are consistent with this.

In normally developing enamel, it reveals partially mineralized enamel prisms delineated by arcade-like "prism-sheaths", or gaps, with no mineral content; with increased mineral deposition, this gap becomes progressively more difficult to discern (Johansen, 1964)¹¹⁵. In dental fluorosis, where there is delayed maturation, one finds periprismatic gaps instead.

Jenkins in 1966¹¹², on p. 81, suggests that the external appearance of fluorotic pigmentation is owing to defects in the rod sheaths of the enamel, with impairment of their optical refractive powers and secondary pigmentation from food substances.

This explanation fails to account for early manifestations of fluorosis in the primary dentition and in newly erupted permanent teeth. The opaque flecks of early fluorosis, for example, may persist

unchanged in colour throughout life, while secondary pigmentation from foodstuffs is extrinsic and removable. It has been demonstrated too, that the greatest accumulation of fluoride is found in uniform layers nearer the external than the internal surface of the enamel, and this location may have some common factor, to correlate the depth of penetration with degree of pigmentation. Rushton (1959)¹⁷² finds that in ground sections, the rods of fluorosed enamel may be sharply delineated by a brown substance lying between them.

If then, the pigmentation of fluorosis is to be explained in terms of refraction and food pigmentation, or in terms of oxidation changes in the chemical composition of the fluorapatite, its clinical appearance fails to give much support to either theory.

The presence of secondary dentine in fluorosed teeth tends to accentuate pigmentary changes and to complicate the clinical pattern, so that in cases of severe fluorosis, clinical distinction between enamel and dentine may be one of considerable difficulty (Cannell, 1960)³⁸.

5. DIFFERENTIAL DIAGNOSIS

A. Dental Fluorosis vs. Idiopathic Mottling

The etiology and clinical features of dental fluorosis have been clearly discussed in previous sections. It should be clearly distinguished from the common occurring types of mottling and/or opacities, which are 'non-endemic' or 'non-fluoride' (Figs. 7 & 8), and may be due to local or systemic factors as outlined below.

(a) Local Factors

i. Infection. Baeur (1946)¹⁷ has shown that abscessed primary teeth can seriously impair enamel calcification of the succeedaneous teeth, a fact previously stated by Turner (1912)²⁰¹. The instances illustrated by Baeur were hypoplastic defects associated with abscesses in primary molar and incisor teeth and, although he considered only gross defects, it is at least possible that minor defects such as 'questionable' mottling could have a similar etiology. On the other hand, Jackson (1961)¹⁰⁸ thinks that abscesses in predecessors, which could damage the developing permanent teeth or lead to premature extraction, and thus trauma, seem an unlikely cause since they are most frequent on the molar teeth and would therefore lead to a higher incidence of idiopathic mottling in their successors (the permanent premolars) which he found did not occur.

ii. Trauma. Anderson (1942)¹¹ gave the term "injury spots" to those defects of incisor enamel caused by trauma combined with infect-

FIG. 7. NON-FLUORIDE OPACITIES.

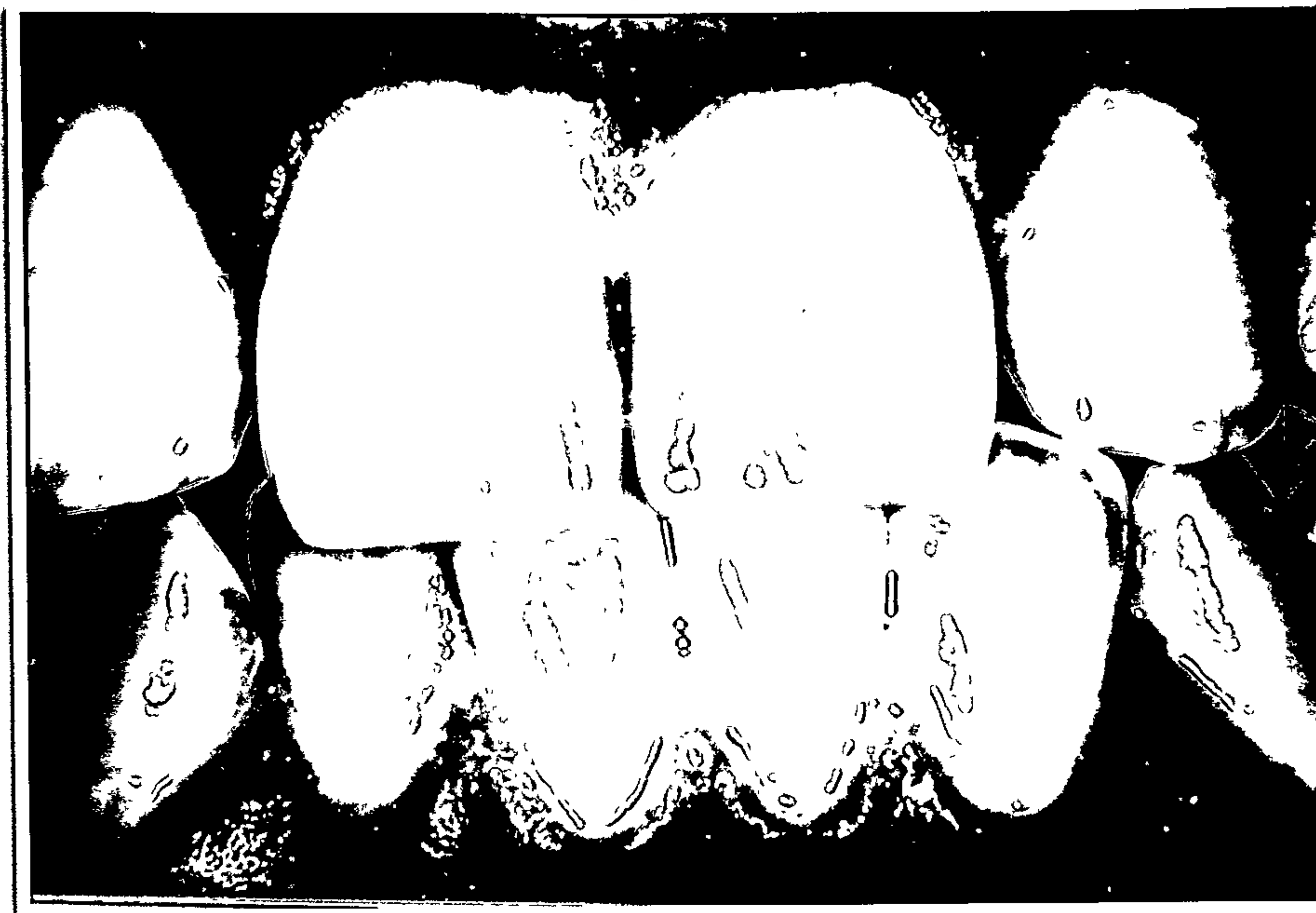


FIG. 8. NON -FLUORIDE 'MOTTLING'.



ion of the antecedent primary teeth. "Injury spots" were characterized grossly by brownish stained depressions in those portions of the enamel calcifying at the time of the injury.

"White spots" were described separately and trauma was not mentioned as an etiological factor in this type of enamel defect. Nevertheless, the degree of damage would be related to the degree of trauma and it is conceivable that minor traumatic injuries could produce minor enamel defects, particularly in the incisor teeth.

iii. Exogenous stains produced by tobacco, and pellicle which can be distinguished readily from dental fluorosis.

(b) Systemic Factors

i. Iatrogenic discolouration from tetracyclines. Many investigators have shown that both primary and permanent teeth are stained following the administration of tetracycline during tooth development (Frankel, 1970⁷⁹; Genot, Golan, Porter & Kass, 1970⁸⁵; Harcourt, 1963⁹³; Spencer, 1972¹⁹⁵; Weyman and Porteus, 1962²¹⁰; Witkop & Wolf, 1964²¹⁷; Zegarelli, Rosenstein, Kutsher, Fahn, Botwick & Silverman, 1963²²⁰).

Discolouration of the primary teeth was associated with tetracycline administration during the first 6 months after birth, and staining of permanent teeth occurred upon tetracycline administration after 11 months of age (Zadik & Eidelman, 1975)²¹⁹.

Enamel hypoplasia following tetracycline administration has also been reported (Pindborg, 1970)¹⁶⁹. It was found that the hypoplasia and staining was restricted to those teeth and portions of teeth which were undergoing mineralization at the time of tetracycline admini-

nistration. The stain is usually creamy-yellow, or yellow or brown in colour. Its distribution is classically linear but always across the full width of the tooth at the level affected, which could be the most projective cusp. The stain may extend laterally in a curvilinear distribution across several teeth. Being systemic, the distribution is otherwise bilaterally symmetrical (Pindborg, 1970¹⁶⁹; Spencer, 1972¹⁹⁵; Zegarelli, Rosenstein, Kutsher, Fahn, Botwick & Silverman, 1963²²⁰).

ii. Subclinical rickets. The ameloblast is very sensitive to disturbances of mineral metabolism, hence the high order of enamel defects in children with evidence of rickets (Jackson, 1961)¹⁰⁸.

iii. Hypothyroidism and metabolic disturbances. These are not likely factors in non-endemic mottling etiology, because of their comparative rarity relative to the high incidence of mottling in non-endemic communities (Jackson, 1961)¹⁰⁸.

iv. Exanthematous fevers, severe infections. These were stated to be a less frequent cause than generally believed.

v. Endogenous discolouration of the teeth due to:

v.i. Dentinogenesis imperfecta. This is a rare dominant hereditary defect. The colour of the teeth may range from a gray to brownish violet or yellowish brown, but they exhibit a characteristic unusual translucent or opalescent hue. The enamel at the incisal or occlusal surfaces may be lost early through fracturing away because of an abnormal amelodentinal junction (Shafer & Hine, 1974)¹⁸³.

v.ii. Erythroblastosis fetalis (Rh incompatibility).

This congenital condition may manifest in the teeth by the deposition of

blood pigment in the enamel and dentine of the developing teeth, giving them a green, brown or blue hue. The intrinsic stains do not involve teeth or portions of teeth developing after cessation of hemolysis shortly after birth (Shafer & Hine, 1974)¹⁸⁴.

The positive signs of dental fluorosis ('very mild' to 'severe') can be identified readily in epidemiological surveys. However, differentiation of questionable fluoride opacities from the non-fluoride lesions has occasionally been difficult, especially so in individuals whose history of early fluoride ingestion is unknown.

Zimmerman (1954)²²¹ pointed out certain features of enamel opacities which may facilitate (not necessarily eliminate) the differentiation of fluoride and non-fluoride white spots :

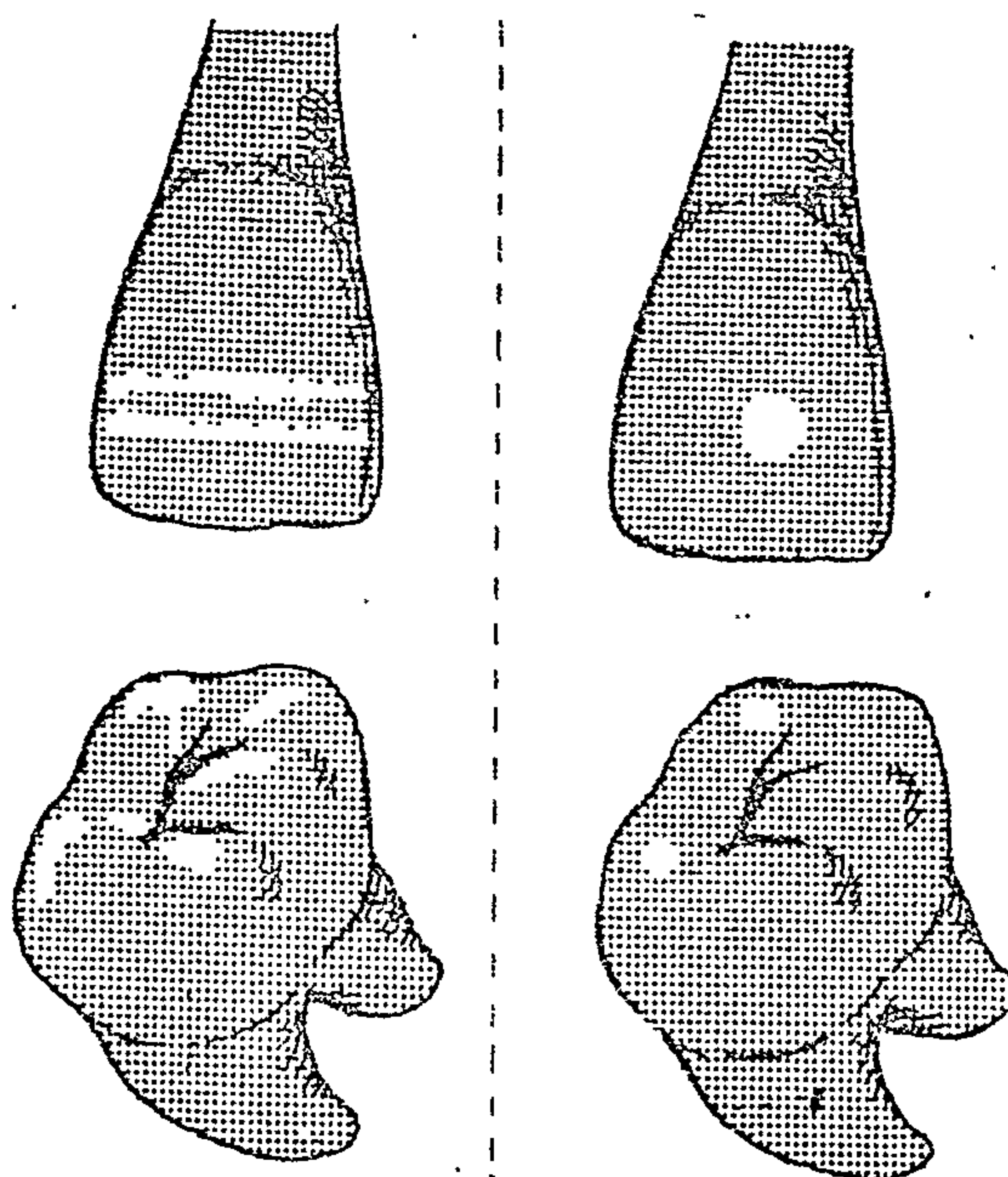
i. The physical appearance of the opacities. Idiopathic opacities are usually more oval in shape and more opaque in appearance than questionable fluorosed white spots; whereas the opacities on questionable fluorosed teeth have a tendency to form horizontal striations.

On the occlusal surfaces of the posterior teeth, the non-fluoride lesions involve cusp tips, similar to snow-capped mountain peaks; while the striae of questionable fluorosed teeth extend down cuspal ridges. These characteristics are shown in Fig. 9.

ii. The distribution pattern of the opacities. Questionable fluorosed opacities are usually distributed bilaterally in a dentition; idiopathic lesions are not ordinarily found in a definite symmetrical pattern.

Jackson (1961)¹⁰⁸ seem to think that a temporary increase in fluoride

Fig. 9 . APPEARANCE OF QUESTIONABLE FLUOROSIS LESIONS (LEFT SIDE)
AND NON-FLUORIDE OPACITIES (RIGHT SIDE).



(Zimmerman, 1954)²²¹.

intake could not be dismissed as a cause of an asymmetrical distribution of opacities on the teeth. He suggests that there may be periods of asynchronous development of homologous teeth, and if the period of high fluoride intake coincided with active growth of enamel in one tooth only, then a very limited asymmetrical defect might occur. However, the chances of these factors occurring simultaneously seem too small to account for the quite frequent occurrence of idiopathic opacities and/or mottling.

iii. The frequency of the opacities per person. The questionable fluorosed opacities usually involve several teeth per dentition; idiopathic lesions seldom affect more than one tooth. Furthermore, it was observed that non-fluoride opacities occur more frequently in the maxillary incisors, particularly centrals, three times more frequent than the other maxillary teeth (Jackson, 1961)¹⁰⁸. Zimmerman (1954)²²¹ on the other hand, reported from low fluoride area, that the second molar was most often affected in the maxilla, followed by I_1 , P_2 , M_1 , P_1 , as was the order in the Hanko and Lohja study (Haavikko & Helle, 1974)⁹¹.

Summarized in Tables 6 and 7, are the data gathered from the different investigations on the prevalence of non-fluoride or non-endemic opacities and/or mottling in different communities. From these findings, there appear to be either wide variances in the assessment of non-fluoride mottling or wide variances between communities independent of fluoride content of water supply or indeed a combination of both factors.

TABLE 6. NON-ENDEMIC OPACITIES/MOTTILING IN LOW OR NON-FLUORIDE AREAS.

Reference	Place of Investigation	Age Group	Mouth Prevalence	Fluoride ppm
Weaver (1944) 206	North Shields	children	27%	< 0.25
Forrest (1956) 76	Saffron Walden	12 - 14	63%	0.1 - 0.2
	West Surrey	"	60%	
Slack & Lawton (personal communications with Jackson, 1961) 108	Liverpool	11	43.8%	0.09
		12	55.7%	
Jackson (1961) 108	Leeds	12	34%	< 0.5 (average 0.06)
Hurme (1949) 107	U.S.A. : New England	13 - 30	83.5%	< 0.5
Dean, Jay, Arnold, McClure & Elvove (1942) 54	U.S.A. communities	9 - 12	2.5 - 43%	< 0.5
Zimmerman (1954) 221	U.S.A. : 2 Maryland counties	12 - 14	36%	< 0.2
Sellman, Syrrist & Gustafson (1957) 181	Sweden : Malmo	12 - 14	22%	0.5

(contd)

TABLE 6. (contd)

Reference	Place of Investigation	Age Group	Mouth Prevalence	Fluoride ppm
Al-Alousi, Jackson, Crompton & Jenkins (1975) ⁷	Leeds	12 - 15	52%	0.1
Young (1975) ²¹⁸	Essex & Norfolk, England	10 - 15	28%	< 0.2
Harris (1954) ⁹⁵	Sydney, United Dental Hospital	children	36.5%	0.0
Dean & Elvove (1937) ⁵⁶	Junction City, Kansas	children	2.1%	0.7
Haavikko & Helle (1974) ⁹¹	Finland: Espoo Hanko Lohja	children	41.2% 74.1% 66.7%	0.11 0.41 0.05
Scheinin, Kalijarvi, Harjola & Heikkinen (1964) ¹⁷⁴	Finland	children	46%	0.1 - 0.39
Barnard (1967) ¹⁶	Australia: New South Wales	12 5	40 - 64% 42%	< 0.1
Goward (1976) ⁸⁸	Liverpool, England	13 - 14	42.5%	0.12

TABLE 7. NON-ENDEMIC OPACITIES/MOTTILING IN AREAS WITH NEAR OPTIMAL OR HIGHER FLUORIDE CONCENTRATIONS.

Reference	Place of Investigation	Age Group	Mouth Prevalence	Fluoride ppm
Al-Alousi, Jackson, Crompton, & Jenkins (1975) ⁷	Anglesey	13 - 16	39%	0.9
Forrest (1956) ⁷⁶	England : West Marsea Burnham on Crouch Harwick Slough	12 - 14	96% 92% 66% 19%	5.8 3.5 2.0 0.9
Young (1973) ²¹⁸	England : Essez & Norfolk	10 - 15	37% 63%	0.2 - 1.4 > 1.4
Clarke & Mann (1960) ⁴³	England : St. James area of Kestenen	8	71%	2.0-4.5
Russell ¹¹ (1962) ¹⁷³	Grand Rapids	12 - 14	36%	1.0
Dean & Elvove (1937) ⁵⁶	Webster City, Iowa East Moline, Illinois	9 - 11	34% 25%	1.6 1.5
Haavokko & Helle (1974) ⁹¹	Finland : Elimaki	children	98.2%	1.08
Zimmerman (1954) ²²¹	Illinois, U.S.A.	children	53%	1.2
Scheinin, Kalijarvi, Harjola & Heikkinen (1964) ¹⁷⁴	Finland	children	65% 48%	1.0 - 1.59 0.4 - 0.99

B. Chemical Analysis of Mottled vs. Sound Enamel

(a) Chemical analysis of the organic material

Bowes and Murray (1936)³⁰ demonstrated a higher protein content in fluorosed enamel than in sound enamel. This finding was confirmed by Bhussry (1959)²⁰, who reported a higher nitrogen content in mottled enamel than in sound enamel. He could not, however, detect any significant differences in density determinations (Table 8).

(b) Chemical analysis of the inorganic content

Several studies failed to show any significant differences (ash basis) in the calcium, magnesium, and carbonate content of mottled and non-mottled teeth (Bowes & Murray, 1936³⁰; Montelius, McIntosh & Ma, 1933¹⁵³; Smith & Lantz, 1932¹⁹³; Ockerse, 1943¹⁶³). This may partially explain the lack of density determinations of these teeth (Bhussry, 1959)²⁰.

In a chemical analysis of the teeth of rats, McCann and Bullock (1957)¹⁴² have shown that the incorporation of fluoride slightly alters the chemical composition of tooth mineral. The carbonate and citrate contents are lowered and the magnesium level increased; the Ca/P ratio, however, remains unchanged (Table 9).

Schour and Smith (1934)¹⁷⁶ on the other hand, found a slightly increased Ca/P ratio in fluorotic teeth of rats that they took to indicate CaF_2 deposition as a result of precipitation reaction.

It would be interesting to note that the outermost layer of shark's teeth contains more than a thousand times the fluoride content of human mottled enamel, yet there are no signs of disturbance in its

mineralization (Bhussry, 1970)²³.

Using biophysical and chemical methods (Glas, 1962)⁸⁷, it was demonstrated that the size and orientation of the apatite crystallites in the shark 'enamel' and its degree of mineralization was the same as in human enamel. In contrast to hydroxyapatite occurring in human enamel, the inorganic phase of shark's 'enamel' consists of an almost pure fluorapatite, which is formed during normal mineralization (Buttner, 1966)³⁵.

Unlike human enamel, which is of epithelial origin, the 'enamel' of shark develops from mesodermal tissues and has been referred to as "duro-dentin" and "petrodentin" (Bhussry, 1970)²³. This suggests that the epithelial enamel organ of human teeth demonstrates specific sensitivity to fluorides.

TABLE 8. COMPARISON OF MOTTLED ENAMEL AND SOUND ENAMEL.

	Density (g/cm ³)		N ₂ content (mg/g)		N ₂ content (mg/cm ³)	
	No. of teeth	Mean $\pm$ SE ^a	No. of teeth	Mean $\pm$ SE ^a	No. of teeth	Mean $\pm$ SE ^a
Mottled Enamel	161	2.88 $\pm$ 0.02	105	0.75 $\pm$ 0.05	105	2.17 $\pm$ 0.15
Sound Enamel	261	2.81 $\pm$ 0.02	282	0.56 $\pm$ 0.02	243	1.59 $\pm$ 0.06

^a The standard error is based on the within-group standard deviations (pooled estimate), which are : density, 0.29; nitrogen (mg/g), 0.57; nitrogen (mg/cm³), 1.54. (Blussry, 1959)²⁰.

TABLE 9. EFFECT OF FLUORIDE ON THE CHEMICAL COMPOSITION OF TEETH^a.

Species	Tissue	F (ppm in ash)	Ca/P	Ca/CO ₂	Ca/Mg	Ca/citrate
Rat.	Incisor dentine	500	1.74	14.0	18	-
		6400	1.81	14.2	14	-
	Incisor enamel	21	1.99	-	139	-
		2030	1.97	-	50	-

^a P, CO₂, Mg, and citrate percentages are related to Ca.
(McCann & Bullock, 1957)¹⁴².

6. MICROSCOPIC APPEARANCE OF DENTAL FLUOROSIS IN HUMAN TEETH

Investigations into the ultrastructure of fluorosed human enamel started almost as early as when the relation of dental fluorosis and its possible etiology was being queried.

As early as 1916, McKay and Black reported varying degrees of discolouration of the enamel surface in ground sections of fluorosed teeth. They stated that in the area of mottling, there is lack of inter-prismatic substance of the outer third of the enamel, together with the presence of brown pigmentation (Black & McKay, 1916)²⁶.

It was found that areas of fluorosed enamel are more easily permeable to dyes and silver nitrate than normal enamel, possibly owing to the developmentally defective nature of the outer enamel, a manifestation of altered function of the ameloblast during enamel formation (Williams, 1923)²¹⁴.

Ainsworth (1933)⁶ found that while sound enamel normally fluoresces bright blue under ultraviolet light, the brown stain in the mottled enamel did not fluoresce. He suggested that the lack of inter-prismatic substance of enamel may provide a pathway for the stains which may be of extrenuous origin. Contradiction arose when Bhussry (1959)²⁰ demonstrated high intensity fluorescence emitted from pigment areas in the outer third of the fluorosed enamel when examined under ultraviolet light.

Applebaum (1936)¹² using soft X-rays to examine sections of mottled enamel observed a low X-ray density in the outer region of fluor-

osed enamel, and the X-ray radiolucency was directly related to the severity of mottling in teeth.

Darling and Brooks (1959)⁴⁶ confirmed previous findings that the lesion is an area of diffuse hypocalcification lying beneath a narrow well calcified surface layer. In severe lesions, the hypocalcified area extends toward the amelodentinal junction, but there is always a well-calcified band of enamel at and parallel to the junction. It is possible that fluoride ions no longer interfere in the metabolic process once they are incorporated into the apatite crystals, but the presence of high concentrations of fluoride in the fluid of enamel organ may cause a delay in crystal formation. Accordingly, the outer layer may be better calcified than the subsurface layer because it is in direct contact with the tissue fluid for a considerable length of time after the matrix formation has been completed (Newbrun & Brudevold, 1960)¹⁶².

Although the hypocalcification of the interprismatic substance was again confirmed, it wasn't possible to tell whether the prism cortex as part of the better calcified or poorly calcified enamel. Nevertheless, Fejerskov, Johnson and Silverstone (1974)⁷¹ was able to show a dissolution pattern, commencing with the central portions or cores of individual crystals.

Gustafson (1961)⁹⁰ surveyed fluorosed enamel using polarized light and microradiographic techniques and found that mottled areas are actually areas of hypomineralization from the variations in the radiodensity and birefringence in irregular hypomineralized areas of fluorosed enamel. It was more pronounced along the striae of Retzius. The arcade-

shaped junction between enamel and dentine was found to be much more pronounced, which may just be an exaggeration of the "normal" enamel, and may be due to an effect on the enamel epithelium or on dental papilla. An increased number of denticles were observed in fluorosed teeth which may be due to the fluoride affecting the connective tissue in some way. The latter two observations were however not duplicated in the study by Fejerskov, Silverstone, Melsen and Møller (1975)⁷². The fact that the protein matrix is different from that in normal enamel, such a difference impedes mineral salts from being seeded in the normal way (Gustafson, 1961)⁹⁰.

Gerould (1945)⁸⁶ using the electron microscope, demonstrated that sections of mottled enamel etched with hydrochloric acid exhibited much finer detail of background structure than similarly treated normal enamel. He suggested that structural changes may be due to reduced acid solubility of the fluorapatite of mottled enamel as compared to the hydroxyapatite of normal enamel.

Awazawa (1962)¹⁴ reported that mottled enamel was relatively rich in organic material while there was deficiency of inter-rod substance. The enamel rods were poorly mineralized with abnormal crystal size. An apparent thickening of the organic matrix as calcification becomes poorer, was noted by Darling and Brooks (1959)⁴⁶, when they examined the core of the prisms in decalcified sections. In the interprismatic substance, there is an apparent thickening of the organic matrix in the less severe parts of the lesion, but in areas of poorest calcification, the organic matrix seems to be absent.

Fejerskov, Johnson and Silverstone (1974)⁷¹ described fluorosed enamel examined under the electron microscope as characterized by periprismatic gaps or channels almost entirely lacking of enamel crystals, which explains previous observations of extensive pores located mainly in the interprismatic regions as revealed by polarizing microscope, and the interprismatic hypomineralization seen in microradiographs of fluorosed teeth (Darling & Brooks, 1959⁴⁶; Newbrun & Brudevold, 1960¹⁶²).

The individual crystals usually are regular hexagons in cross-sectional profile, often with large intercrystalline spaces, especially at the prism periphery and in the tail region. The size and gross organization of prisms does not appear to differ from that of normal adult human enamel (Fejerskov, Johnson & Silverstone, 1974)⁷¹. It was also stressed that in hypomineralized as well as in normal enamel, no variation in mineral content was evident between the rods and their inter-rod extensions - the tail regions - the only difference being a gradual change in orientation of the crystals.

When sections of carious lesions are examined in quinoline, a characteristic dark zone appears as a positively birefringent zone over the advancing front of the enamel lesion (Silverstone, 1967)¹⁹⁰. The study by Fejerskov, Silverstone, Melsen and Møller (1975)⁷², demonstrated this zone which used to be regarded as 'typical' of carious lesions, in fluorosed enamel. The presence of a dark zone has originally been interpreted as a stage of enamel breakdown caused by demineralization (Poole, Mortimer, Darling & Oldis, 1961¹⁷⁰; Darling, Mortimer &

Poole, 1961⁴⁷). It has further been suggested that the dark zone is a manifestation of reprecipitation in the lesion following an initial dissolution phase, but the dark zone may well be an expression of reprecipitation with established porous regions.

However, in these developmental, as opposed to carious lesions, the precipitation is moving in a direction from the amelodentinal junction to the centre of the lesion. This may partly explain why the outer part of the enamel is most severely affected although the damage might have been of the same degree throughout the period of amelogenesis and enamel mineralization. Once again, it was shown that the interprismatic area and the cross-striations, are the regions of low mineral content, relative to the prism core, in fluorosed enamel (Fejerskov, Silverstone, Melsen & Møller, 1975)⁷².

7. PREVENTION AND TREATMENT OF DENTAL FLUOROSIS

Since fluoride has been singled out to be the causative agent of dental fluorosis, it is likely to assume that by elimination of the cause, the effect will be prevented from occurring.

Fluoride availability from the different sources have been clearly detailed in the section 'Availability of fluoride ion for absorption from foods and/or waters'. The combined ingestion of the different sources of fluoride may be either a useful or a harmful nutritional practice. Therefore, it follows in the same context, that a reduction of fluoride intake and maintaining it to an optimal level at which beneficial effects, i.e. caries reduction, can still be derived, is most logical in preventing the occurrence of dental fluorosis. Care needs to be exercised in avoiding the constant use of high fluoride foods from sources not proved important to dental health.

In other words, prevention of dental fluorosis may involve a change of dietary patterns for people known to take foods of high fluoride content, as well as regulating fluoridated communal water supplies to the desired optimal level of concentration.

One of the earlier known studies regarding the change from a water supply containing a high fluoride content to one practically free of fluorides was recorded by Dean and McKay (1939)⁵⁸, where the production of chronic endemic dental fluorosis was halted at Oakley, Idaho; Bauxite, Arkansas; and Andover, South Dakota.

In water supplies where the natural fluoride content is

high, a process of lowering the fluoride level to the desired concentration may be necessary. Such is the process of defluoridation of communal water supplies, usually through chemical means.

Three methods have proven effective and practical for the chemical removal of excessive amounts of fluorides from water. Two of these methods involve the use of activated alumina and bone char, insoluble mediums which remove fluorides as the water percolates through them. As these mediums become progressively saturated with fluoride, they become less efficient. Therefore, they must be periodically regenerated to remove the accumulated fluorides. The third method involves the use of magnesium compounds, which remove fluorides by absorption. The magnesium and the absorbed fluorides are subsequently removed by sedimentation and filtration and are discarded (Horowitz, Maeir & Law, 1967)¹⁰⁵.

Defluoridation was actually employed in a small town in Bartlett, Texas in 1952, where the drinking water contained 8.0 ppm fluoride (Horowitz, Maeir & Thompson, 1964¹⁰⁶; Horowitz & Heifetz, 1972¹⁰⁴). This method effectively reduced the original fluoride concentration to an average of 1.0 ppm. A preliminary survey was conducted in 1952, and a more extensive one was carried out two years later to establish baseline data for this study.

The percentage distribution of children examined in 1954 and 1969 according to fluorosis classification are shown in Table 10. Nearly all children (96%) had some degree of fluorosis in 1954. This percentage had decreased dramatically to 18% in 1969 (Horowitz & Heifetz, 1972)¹⁰⁴.

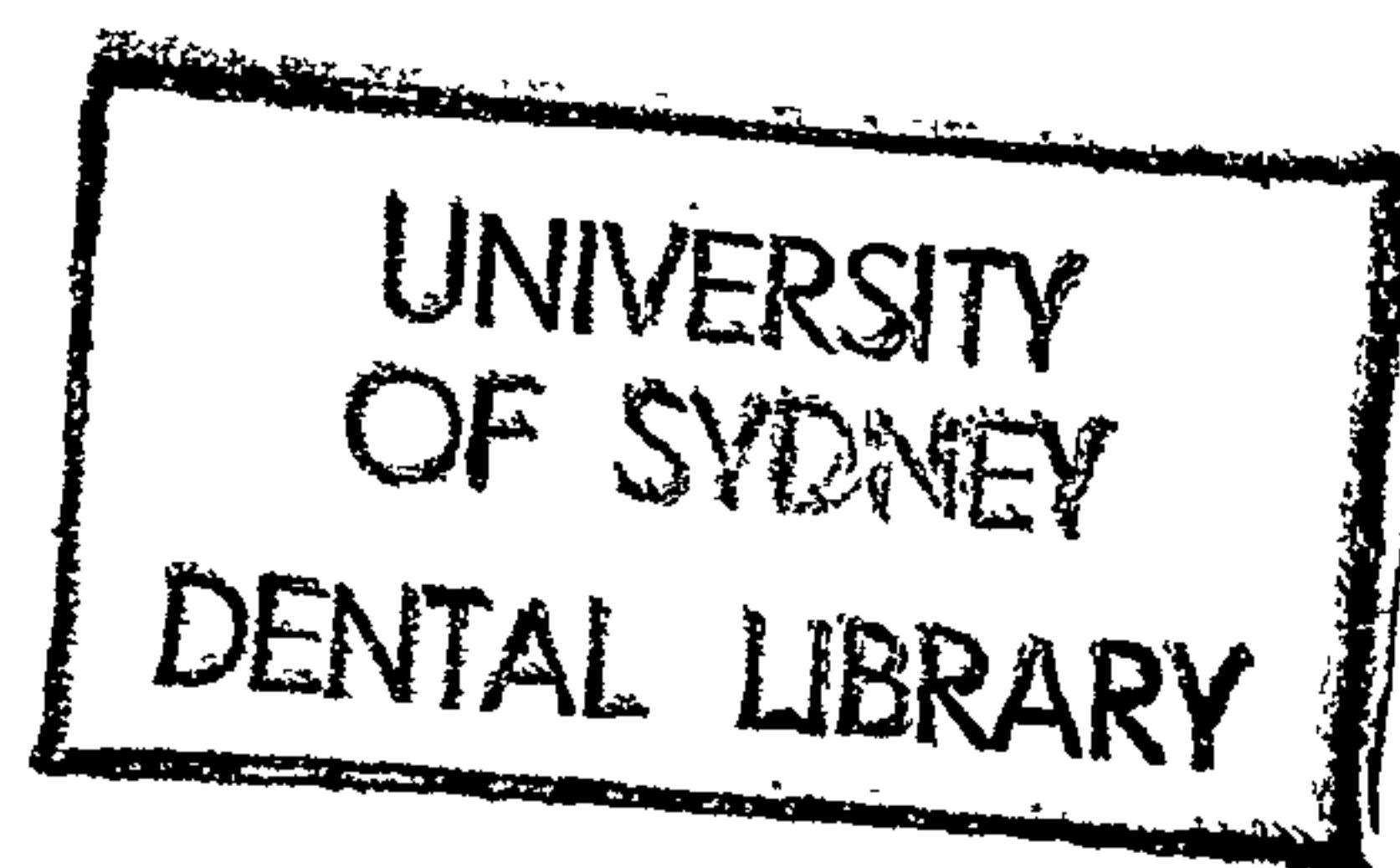
TABLE 10. PERCENTAGE DISTRIBUTION OF CHILDREN IN BARTLETT
BY FLUOROSIS CLASSIFICATION, 1954 and 1969.

Year	Fluorosis absent			Fluorosis present				
	Normal	Question- able	Total	Very Mild	Mild	Moderate	Severe	Total
1954 (N=132)	2.3	1.5	3.8	3.0	43.9	34.9	14.4	96.2
1969 (N=157)	49.0	32.5	81.5	12.1	5.7	0.6	0.0	18.4

(Horowitz & Heifetz, 1972)¹⁰⁴.

The characteristic feature of dental fluorosis varies with its severity, and can be as disfiguring as a facial scar or a birth defect. Several methods have been advocated for the treatment of fluorosis-stained teeth. One method involves the use of various chemicals, principally hydrogen peroxide, alone or in combination, with the principle of bleaching the teeth to remove the stains (Colon, 1973⁴⁴; Dua, Riar & Mohan, 1973⁶⁰; Bouschor & Dorman, 1973²⁹). Sometimes, heat is used to accelerate the chemical reaction, but it may cause minute fractures of the enamel (Colon, 1973)⁴⁴. After active bleaching, another chemical, principally, sodium hypochloride, is used to neutralize the bleaching-etching (if low concentrations of hydrochloric acid is added to hydrogen peroxide) solution, to prevent the accumulation of the solution in the pits, which may result in possible damage to the pulp (Colon, 1973)⁴⁴. This bleaching procedure is carried out periodically, since the teeth continue to stain.

Another method is employed whereby operative procedures, such as sandpaper-disking (Chandra & Chawla, 1975)⁴⁰, or sometimes procedures requiring excessive removal of tooth structure (usually employed in severe types of dental fluorosis), are carried out, after which an appropriate restoration in the form of crowns may have to be placed, in order to restore tooth shape and form, and possibly, function.



VI. EXPERIMENTAL FLUOROSIS

Investigations using experimental animals have demonstrated that the influence of fluoride on teeth always appears to be identical, regardless of the mode of administration of fluoride (Bhussry, 1970)²³, i.e. in drinking water, in the diet or by injection. Hoffman, Schuck and Furata (1942)¹⁰³ observed otherwise. According to their study, the animals receiving fluoride in water were most severely affected by gross changes in dental structure, in milk next, and in dry diet the least.

Fluorosis in the white rat is manifested as a pronounced alteration in the development and appearance of the incisor teeth.

To date, numerous studies have been done along this light as early as 1925 (McCollum, Simmonds, Becker & Bunting, 1925)¹⁴⁹. Bethke, Kick, Hill and Chase (1933)¹⁹ demonstrated hypoplasia of tooth enamel in rats receiving fluorine in the diet. Sebrell (1933)¹⁸⁰ observed changes in the teeth of the rats given concentrated drinking water from an endemic mottled enamel area. The incisor teeth lost their natural orange colour and appeared chalky white and brittle. Dean, Sebrell, Breaux and Elvove (1934)⁵⁹ demonstrated minute striations on the incisor teeth of rats receiving 25 ppm NaF in drinking water daily for 23 days. The severity of alterations in teeth of experimental animals was proportional to the concentration of fluoride in the drinking water received. The initial appearance of minute striations was followed by formation of irregular brown patches and, finally, the enamel became white and brittle.

Schour and Smith (1935)¹⁷⁷ reported that developing enamel and

enamel-forming cells were the first to respond to intraperitoneal injections of NaF. The disturbances of the ameloblastic layer were reflected in the newly formed enamel matrix, which was poorly mineralized, while the rate of apposition was not affected (Schour & Poncher, 1937)¹⁷⁵. When the cumulative action of fluorine was reached, a further toxic effect on the ameloblast, and a disturbance of both appositional growth and mineralization of the enamel matrix which resulted in hypoplastic defects of enamel was observed.

Alterations of cell structure of the ameloblasts have been demonstrated in animal experiments and with in-vitro tooth cultures following prolonged administration of fluorides. Some of the changes observed were the following (Fleming, 1953⁷⁴; Grinstein, 1941⁸⁹): (i) appearance of vacuoles in cytoplasm; (ii) thickening of cell walls; (iii) loss of polarity of nuclei; and (iv) disappearance of golgi apparatus.

Muhler in 1954¹⁵⁴ demonstrated that pigmentation of the incisors of rodents decreases as the level of concentration of ingested fluoride rises. Such observation have been attributed to the loss of pigment due to the interference by fluoride on the action of enzymes in blood pigment formation, or possibly on haematin itself, and that the depigmentation is in effect, a form of anemia. Such a supposition can not be disregarded, but is not particularly convincing.

Bhussry (1959²¹; 1960²²) investigated the histochemistry and microradiographic aspects of influence of various concentrations of NaF on the developing teeth of rats. All experimental animals demonstrated abnormalities of amelogenesis, the degree of severity depending

upon the amount of fluoride received. There was a wide zone of pre-enamel matrix, suggesting a delay in homogenization of the Tomes processes of ameloblasts. The apposition and mineralization of enamel matrix was retarded and calcification disturbed. Large patches of incalcified enamel matrix were evident and accentuated incremental lines in enamel were occasionally present (Hoffman, Schuck & Furata, 1942)¹⁰³. There was a distinct reduction in the mucopolysaccharides and glycoprotein-staining components of enamel matrix.

Using microradiographic techniques, Parikh (1960¹⁶⁶; 1961¹⁶⁷) investigated the calcification pattern in the developing teeth of newborn animals receiving toxic doses of NaF. He reported a disorganization of the ameloblastic layer and the presence of large radiolucent areas in the enamel microradiographs indicating a disturbance in the pattern of enamel mineralization.

Fleming and Greenfield (1954)⁷⁵ conducted a histological study to observe changes in the teeth and jaws of mice following administration of very large doses of sodium and calcium fluoride (60 to 100 ug. daily) to the female parent during gestation. Structural alteration of the ameloblasts layer resulted in the retardation of enamel matrix formation and its mineralization. Calcium fluoride seemed to be more toxic to the foetus than sodium fluoride.

Allan (1963)⁹ observed narrow hypermineralized striae of Retzius preceded by a hypomineralized zone in the forming enamel matrix of 3-day old pups injected with 2% NaF in doses of 10 mg./kg. to 50 mg./kg. body weight. However, when NaF was given to pups during the period of

enamel mineralization, diffuse hypomineralization of the mature tissue was noted.

Mottling doses of fluoride produces distentions of the granular endoplasmic reticulum of ameloblasts (Kruger, 1968¹¹⁸; 1970¹²⁰), and a reduction in their uptake of tritiated proline (Kruger, 1970)¹¹⁹. Doses of borderline mottling toxicity did not produce any detectable ultrastructural changes nor did they significantly alter the uptake of tritiated proline (Kruger, 1970¹²⁰; 1970¹¹⁹).

Interference with mineralization of enamel when the heavy mottling doses of fluoride are administered was further confirmed by Suga, Katagiri and Musachi (1964)¹⁹⁹, Toda and Van Huysen (1966)²⁰⁰, and Kruger (1970)¹²¹. Under similar conditions, Adkins and Kruger (1966)³ observed the production of thinner layers of enamel.

A graded series of mottling doses of fluoride has been shown to produce a graded series of ultrastructural changes in the ameloblasts with a parallel response in the uptake of tritiated proline.

Kruger (1972)¹²² investigated the effect of submottling doses of fluoride on the uptake of another tritiated amino acid, (³H)-serine, by ameloblasts, and on its incorporation into enamel matrix. His findings can be added to the fairly large amount of published evidence that large doses of fluoride impair the ability of various cells to synthesize protein.

In-vitro experiments suggest that sodium fluoride in large doses alters the concentration of magnesium necessary to stabilize the amino-acryl-t-RNA complex by which amino acids are bound to ribosomes,

and that fluoride is also able to cause nascent peptide chains to separate from ribosomes (Matthews, 1970¹⁴¹; Kruger, 1972¹²²).

A clear distinction must be made between acute toxic effects, which result from a single massive dose, and the chronic toxic effects of large doses spread over a number of years. The latter may be confined to a minor physiological alteration or may produce a major crippling disorder. Experimental fluorosis are usually produced with massive dosages of different forms of fluoride; whereas in chronic endemic fluorosis, the effect is due to doses taken over a span of time.

VII. INVESTIGATIONS OF DENTAL FLUOROSIS IN DIFFERENT COUNTRIES

The prevalence and severity of dental fluorosis as related to the fluoride content (ppm) in the drinking water from the different countries under investigations have been tabulated in Table 11.

The overall mouth prevalence, expressed in percentage, of the frank manifestations of dental fluorosis have been summed up accordingly, i.e. the overall figure in bracket includes the 'questionable' category, while the overall figure without the bracket excludes the 'questionable' category.

TABLE 11. INVESTIGATIONS OF DENTAL FLUOROSIS IN DIFFERENT COUNTRIES.

Reference	Place of Investigation	Age Group	Percentage Affected (Mouth Prevalence)								F/ppm In Water
			Q	VM	M	Mo	Mo-S	S	Overall*		
Kunzel & Padron (1976) ¹²³	<u>CUBA</u> Oriente, Sur, Holguin	7 - 12	8.9	-	-	-	-	-	0 ⁰ (8.9)	0.10	
			9.2	4.5	1.5	-	-	-	6 ⁶ (15.2)	0.6 - 0.8	
			27	3.8	3.8	-	-	-	7.6 (34.6)	1.1 - 1.6	
			21.6	18.9	5.4	29.7	-	5.4	59.4 (81)	2.3 - 3.6	
Binder (1973) ²⁴	<u>AUSTRIA</u> A. Mallnitz B. Silz, Umhausen C. Seefeld	7 - 14	-	-	18	-	-	-	18 48	1.0 1.5 - 1.8	
			-	-	43	5	-	-	-	3.0	
Møller & Poulsen (1975) ¹⁵²	<u>MOROCCO</u> Khouribga	7 - 14	5.9	19.5	29.3	29	-	12.9	90.7 (96.6)	0.25-0.54	
Møller, Pindborg, Gedalia & Roed-Petersen (1970) ¹⁵¹	<u>UGANDA</u> A. Acholi B. Bugisi Africans Asians	5 - 19	20.7	7.5	4.4	4.4	-	1.3	17.6 (38.3)	0.11-0.57	
			31.4	5.7	-	2.9	-	-	8.6 (40)		
			32	1.8	1	-	-	-	2.9 (34.9)	0.19-0.30	
			19.2	7.7	-	-	-	-	7.7 (26.9)		
			16.1	11.1	21.4	9.2	-	-	41.7 (57.8)		
	C. Toro Africans Asians		16.1	11.1	21.4	9.2	-	-	41.7 (57.8)	0.66-2.0	
	D. Kigesi Africans Asians		44	7.3	4.9	-	-	-	12.2 (56.2)		
			1.4	1	0.7	0.3	-	-	2 (3.4)	0.17-0.30	
Nanda, Zipkin, Doyle & Horowitz (1974) ¹⁵⁹	<u>INDIA</u> Lucknow	6 - 17	50	11	1	-	-	-	12 (62)	0.0 - 0.40	
			38	18	5	1	-	-	24 (62)	0.41-0.80	
			35	18	16	7	-	-	41 (76)	0.81-1.20	
			16	26	17	23	-	-	66 (82)	1.21 & >	
Senewiratne,	<u>CEYLON</u>		-	41.7	18.6	10.1	3.6	3.5	77.5	0.34-3.75	

Hettiarachchi & Senewiratne (1974) 182	B. Polonnaruwa C. Kandy	7 - 20	-	31.8	12.9	5.2	1.7	1	56.2	0.26-4.55
Bischoff, van Der Merwe, Retief, et al (1976) 25	SOUTH AFRICA Saulspoort	14 - 23	-	-	14.8	27.2	-	40.9	83	0.40-6.0
Venkateswarlu, Rao & Rao (1952) 202	INDIA A. Madhavadhara		-	-	-	-	-	-	0	0.3
	B. Peddnarava		-	-	12	-	-	-	12	0.5
	C. Waltair Uplands		-	-	38	-	-	-	38	0.5
	D. Isakathota		-	-	57	12	-	4	73	0.5 - 0.8
	E. Peddhawaltair		-	-	25	-	-	-	25	0.9
	F. Gopalapahnam	3 - 14	-	-	5	-	-	-	5	0.9
	G. Marrepalem		-	-	26	19	-	-	45	0.9
	H. Chintanippula-graharam		-	-	24	-	-	-	24	0.9
	I. Naravakota		-	-	14	-	-	-	14	1.0
	J. Chenulagraharam		-	-	37	12	-	3	52	1.3
	K. Kothapalem		-	-	25	31	-	-	56	1.4
Lyth (1946) 132	CHINA Kweichow	school-children	-	-	29.1	-	43.3	-	72.4	5.9 - 6.3
Messler & Schour (1952) 140	ITALY Campagnano di A. Rome B. Quarto	12 - 14	-	5.2	37.7	53.2	3.9	0	100	3.5
			-	22.9	16.6	10.4	8.3	2.1	60.3	1.3
Williamson & Barrett (1972) 215	AUSTRALIA Yuendumu, Northern Territory	4 - 24	3	40	26	27	-	1	94 (97)	1.5
Katlis & Silva (1967) 116	AUSTRALIA Carnarvon, Western Australia	6 - 16 (Caucasian)	3.4	18.6	19.2	4.2	-	-	42 (45.4)	1.5
Katlis & Silva (1970) 117	AUSTRALIA Carnarvon, Western Australia	6 - 16 (Aborigines)	3.5	25	32.6	17.4	5.8	-	80.8 (84.3)	1.5
	U.S.A. A. Zanesville, Ohio		13.1	1.5	-	-	-	-	1.5 (14.6) 6.1	0.2

Dean, Arnold & Elvove (1942) ⁵⁵	C. Kewanee, Illinois D. Joliet, Illinois E. Colorado Springs, Colorado F. Lubbock, Texas G. Bauxite, Arkansas	12 - 14	35	10.6	1.6	-	-	-	12.2 (47.2)	0.9
		9 - 12	1.1	12.2	21.7	46	-	-	25.3 (59.5)	1.3
		14 - 19	-	3.9	3.9	38.5	-	-	73.8 (93.6)	2.6
									97.8 (98.9)	4.4
									100	14.1
Leatherwood, Burnett, Chandravej- ismarn & Si- rikaya (1965) ¹³⁰	<u>THAILAND</u> 9 regions	All age groups (majority 20 - 24)	35.25	-	-	0.33	-	0.06	0.39 (35.64)	0.0 - 0.8
	<u>TAIWAN</u> A. Formosa a. Neiwei b. Yuchang c. Hoping Pu & Lillienthal (1961) ¹⁷¹		-	11.2	4.5	-	-	-	15.7	0.0
			-	21.1	7.5	0.7	-	-	29.3	0.2 - 0.4
			-	35.2	9.1	-	-	-	44.3	0.2 - 0.4
		6 - 11	-	40.1	14.3	4.8	-	-	59.2	0.6 - 0.9
			-	36.1	37.7	9	-	-	82.8	0.85
			-	21.1	36.8	24	2.5	-	84.4	1.6
	B. Pescadores a. Hushi b. Pasha		-	33.2	33.6	18.8	-	-	85.6	0.5
			-	35.3	21.6	5	0.7	-	62.5	0.5

*Overall = Q (Questionable) + VM (Very Mild) + M(Mild) + Mo (Moderate) + Mo-S (Moderately-Severe)
+ S (Severe).

Overall figure without brackets = Q excluded,

Overall figure in brackets = Q included,

1. FACTORS WHICH INFLUENCE THE PREVALENCE AND SEVERITY OF DENTAL FLUOROSIS

Comparison of the findings among the different countries will be drawn under the following headings:

A. Fluoride Intake

(a) From drinking water

The severity and prevalence of dental fluorosis has a definite relation to the concentration of fluoride in water, and to the length of time of ingestion.

Referring back to Table 11, the following countries have very high fluoride content in drinking water, with a correspondingly high prevalence of dental fluorosis.

<u>Country</u>	<u>F/ppm</u>	<u>Prevalence</u>
Bauxite, Arkansas, U.S.A.	14.1	100% (53.8% - severe)
Lubbock, Texas, U.S.A.	4.4	97.8% (17.9% - severe)
Colorado, U.S.A.	2.6	73.8% (1.5% - severe)
Campagnano di Roma, Italy	3.5	100% (0% - severe)
Kweichow, China	5.9 - 6.3	72.4% (0%-severe)
Seefeld, Austria	3.0	52% (6% - severe)
Holguin, Cuba	2.3 - 3.6	59.4% (5.4% - severe)

In many areas where there is less than 1 ppm fluoride in drinking water, the prevalence as well as the degree of fluorosis is higher than would be expected (Table 11). Such highly varying manifest-

ations of dental fluorosis in different parts of the world, lead to the inference that there are other factors, peculiar or characteristic to each community or country which influences the effect of fluorine on teeth, or the total fluoride ingestion other than that from water.

(b) Fluoride content from foods

There are times when the amount of fluoride in water can not account for the relatively high prevalence of dental fluorosis. Other possible sources of fluoride consumption have to be looked into, like the dietary patterns and habits of a community.

Referring back to Table 11, it can be seen in Pescadores, Taiwan (Pu & Lilienthal, 1961)¹⁷¹, where the fluoride in water amounts to only 0.5 ppm, the prevalence particularly in Hushi was 85.6%, as compared to Neiwei, Formosa, where the fluoride in water is 0.6 to 0.9 ppm, yet the prevalence is lower, i.e. 59.2%.

The villagers from the Pescadores were found to be dependent on fish and sweet potatoes as basic diet. The children had as much as 1 lb. or more of fish of smaller varieties, where the skeleton is also consumed. In this situation, the water was neither the sole nor the major source of fluoride intake, which led to a consideration of the contribution which sea-food, especially fish, could make to the fluoride intake. As shown in Table 12, it is obvious that at least as much fluoride daily could be taken with food as with water.

TABLE 12. POSSIBLE FLUORIDE CONTRIBUTION FROM DIET AND WATER IN THE PESCADORES.

Fluoride from 1 lb. fish at		Fluoride from water (0.5 ppm)	
10 ppm	15 ppm	1.1	1.5
0.91 mg.	1.37 mg.	0.5 mg.	0.75 mg.

(Pu & Lilienthal, 1961¹⁷¹).

Another source of fluoride most commonly consumed is tea. It was found that in Ceylon (Senewiratne, Thambipillai, Hettiarachhi & Senewiratne, 1974)¹⁸², the children consume about 5 cups of tea per day. Infusion contained 0.3 to 1.23 ppm fluoride more than the water in which it was prepared.

Aside from the food itself, the inorganic component of the diet, specifically calcium and phosphorus, have to be accounted for as well. There has been a general agreement that calcium deficiency increases the severity of the manifestations of fluoride intoxication. In fact, fluoride metabolism of calcium and phosphorus are closely inter-related.

It was found in Lucknow, India (Nanda, Zipkin, Doyle & Horowitz, 1974)¹⁵⁹, that the consumption of calcium and phosphorus, is low compared with the Recommended Dietary Allowance for American diets. This factor may have exerted some enhancing effect on fluoride availability. This could partly explain the difference in prevalence of dental fluorosis between Lucknow, India, with 0.41 to 0.80 ppm and 0.0

to 0.40 ppm, resulting in 24% and 12% prevalence, respectively; as opposed to 0.9 ppm and 0.4 ppm, resulting in 12.2% and 6.1% prevalence in Kewanee, Illinois, and Marion, Ohio, respectively.

The way the food is prepared has to be taken into account too. Children in the Arizona group of Spanish descent, usually eat beans prepared by boiling for rather long periods of time. Since boiling in fluoride-bearing water results in a concentration of the fluoride ion in many cooked vegetables, there may have been an increase in dietary fluoride intake of this group to a greater degree than would be observed for a group of children on a more varied diet (Galagan & Lamson, 1953)⁸⁰.

(c) Sources of water, with special reference to the sediments of drinking water

In Lucknow, India (Nanda, Zipkin, Doyle & Horowitz, 1974)¹⁵⁹, and the Hyderabad-Deccan (Siddiqui, 1955)¹⁸⁷, it was found that all children were using subsoil waters from wells, which were stored in earthen or metal pitchers. Nanda and Kapoor (1972)¹⁵⁸ showed that water with suspended impurities had more fluoride than decanted water.

In Ceylon (Senewiratne, Thambipillai, Hettiarachhi & Senewiratne, 1974)¹⁸², it was established that the children especially in rural areas, drank water from unpurified wells and streams, ingesting too certain amounts of sediments, which may contain fluoride.

Siddiqui (1955)¹⁸⁷ reported high levels of fluorine, 0.09%, 0.11%, and 0.15%, respectively, in sediments and mud samples obtained from wells in areas of endemic fluorosis in India.

(d) Fluoride from industrial dusts

The exemplifying situation that can be cited, referring back to Table 11, is the case in Khouribga, Morocco (Møller & Poulsen, 1975)¹⁵². The fluoride content in water at the time of investigation was found to be 0.25 to 0.54 ppm, but the community studied had a dental fluorosis prevalence of 90.7%, as contrasted to a community in Cuba, with 0.6 to 0.8 ppm fluoride in water, and having only 6.0% prevalence of dental fluorosis (Kunzel & Padron, 1976)¹²³.

Obviously, the prevalence and severity of dental fluorosis was really much higher than could be ascribed to the fluoride concentration in water. Air-borne fluoride-containing phosphate dusts emitted from a phosphate-mining industry located around Khouribga, was found to be the most important etiological factor in this situation.

B. Climatological Variables

(a) Temperature

About two-thirds of man's total fluid intake is water, the remainder, other fluid substances. Except for temporary circumstances of an emotional nature, the amount of fluid ingested is determined by water deficiency. Every bit of body water lost must be replaced and the replacement amounts are obligatory. In growing children, fluid intake may be slightly greater than water loss since some additional water is needed to build new tissues; but generally speaking, water intake and water loss will be equal over a 24-hour period (Galagan & Lamson, 1953)⁸⁰.

Excessive temperature causes bodily demand for fluid over and above that usually required for normal physiological processes. When environmental temperature rises above skin temperature, the only method by which the body can cool itself is vaporization. Heat loss can no longer be affected by radiation or conduction. The water output of the body is therefore increased in proportion to the need for increased vaporization. It follows that there will be an increase in the amount of water ingested in order to maintain body water balance (Galagan & Lamson, 1953)⁸⁰.

(b) Radiant heat gain

This aspect also plays a part in the amount of fluid ingested to maintain water balance.

Individuals exposed to the same air temperature and different amounts of direct sunlight are subject to varying influences of water loss. It has been demonstrated that there is an increase in sweating rate of about 20 gms/hour for each degree increase in air temperature (Galagan & Lamson, 1953)⁸⁰.

Direct sunlight causes an elevation in the sweating rate equivalent to that resulting from a 10°F increase in air temperature. Therefore, exposure to direct sunlight increases water loss by increasing radiant heat gain (Galagan & Lamson, 1953)⁸⁰.

(c) Relative humidity

It was suggested that a lower relative humidity tends to increase water loss, temperature being equal.

On the other hand, it was also pointed out that since moist-

ure is decreased in humid air, more skin surface has to be wetted (and more sweat produced) to achieve the equivalent of cooling experienced in dry, absorbent air of comparable temperature (Galagan & Lamson, 1953)⁸⁰.

Therefore, a humid atmosphere would tend to increase water loss merely by making the body secrete more sweat in order to gain the same amount of evaporate cooling accomplished in arid areas with less water loss.

The effect of humidity upon water loss is not clearly understood as a whole. Notwithstanding the fact that the influence of relative humidity upon the water intake of infants and children is difficult to assess.

Referring back to Table 11, the following examples demonstrate the effect of climatological influences, particularly air temperature, which in turn influences fluid intake, on the prevalence and severity of dental fluorosis.

<u>Country</u>	<u>Mean Maximum Temperature</u>	<u>F/ppm</u>	<u>Prevalence</u>
India, Isakathota	89°F	0.5 - 0.8	73% (4% - severe)
South Africa, Saulspoort	77.5°F	0.4 - 0.6	83% (40.9% - severe)
U.S.A.	67.2 - 72.2°F	0.9	12.2% (0% - severe)
	67.2 - 72.2°F	1.3	25.3% (0% - severe)
	67.2 - 72.2°F	2.6	73.8% (1.5% - severe)

The climatological variables are taken as extrinsic factors which influences the drinking habits between geographical localities. Although the precise determination of water intake, thus giving an approximate of the fluoride intake from this source, seem difficult to ascertain, McClure in 1943¹⁴⁴, estimated the fluid intake of children aged 1 to 12 years from water containing 1 ppm fluoride (Table 13).

Galagan and Lamson (1953)⁸⁰, also considered this aspect extensively, and they pointed out that intrinsically, the amount of water required is influenced too by body size and weight, kind of food eaten, habit patterns and physical activity.

TABLE 13. ESTIMATED DAILY INTAKE OF FLUORINE FROM DRINKING WATER CONTAINING 1 PPM FLUORINE.

Age (years)	1 to 3	4 to 6	7 to 9	10 to 12
Energy allowance (calories)	1200	1600	2000	2500
Water requirement (ml)	1200	1600	2000	2500
Drinking-water consumption:				
(1) When water drunk is equal to 25% of the total daily water requirement and (a) 10% and (b) 20% of the total water content of the food is of drinking-water origin, the total daily consumption of drinking water would equal:				
(a)	390 ml	520 ml	650 ml	812 ml
(b)	480 ml	640 ml	800 ml	1000 ml
(2) When water drunk is equal to 33% of the total daily water requirement and (c) 10% and (d) 20% of the total water content of the food is of drinking-water origin, the total daily consumption of drinking water would equal:				
(c)	480 ml	640 ml	800 ml	1000 ml
(d)	560 ml	746 ml	933 ml	1166 ml
Total daily fluorine ingested from drinking water containing 1 ppm fluorine under the preceding conditions of water ingestion would equal:				
In water intake (a) . . .	0.390 mg	0.520 mg	0.650 mg	0.810 mg
In water intake (b) & (c)	0.480 mg	0.640 mg	0.800 mg	1.000 mg
In water intake (d) . . .	0.560 mg	0.745 mg	0.930 mg	1.165 mg

(McClure, 1943)¹⁴⁴.

C. Individual Variables

(a) General health status particularly the nutritional status

Dental fluorosis prevalence and severity was much more noticeable in the 2 Italian communities, than in some American cities, with equal amounts of fluoride in their water supplies. This statement was borne by the following findings (Table 11):

<u>Communities</u>	<u>F/ppm</u>	<u>Prevalence</u>
Quarto, Italy	1.3	60.3% (2.1% - severe)
Joliet, U.S.A.	1.3	25.3% (0% - severe)

On the average, the water intake of Italian children was much lower than the American children. The only discernable reason for an increased prevalence and severity in Quarto compared to Joliet, was the fact that malnutrition was much more severe in the Quarto children and the adults than those in Joliet.

Furthermore, the prevalence of the moderately-severe and severe types of dental fluorosis was higher in Quarto (8.3% and 2.1%, respectively), than in Campagnano di Roma (3.9% and 0%, respectively), inspite of the fact that the fluoride content in water of Quarto, i.e. 1.3 ppm, was much lower than that in Campagnano di Roma, i.e. 3.5 ppm. Comparing the nutritional status of the subjects between these 2 communities, Quarto was categorized as having 'very poor' and Campagnano di Roma, 'fair' nutritional status (Massler & Schour, 1952)¹⁴⁰.

This observation confirms similar findings in the literature (Day, 1948⁴⁸; Pandit & Roa, 1940¹⁶⁵; Murray & Wilson, 1948¹⁵⁷).

(b) Physiological variation as regards fluoride metabolism between population groups

This factor can't be totally ignored considering the disparities in the manifestations of dental fluorosis between different communities with the same amount of fluoride in the drinking water, and with all other extrinsic variables remaining constant.

<u>Communities</u>	<u>F/ppm</u>	<u>Prevalence</u>
India:		
Peddhawaltair	0.9	25%
Gopalapatnam	0.9	5%
Marrepalem	0.9	45%
Chintanippulagraharam	0.9	24%
Formosa, Taiwan:		
Yuchang	0.2 - 0.4	29.3%
Hoping	0.2 - 0.4	44.3%
Australia:		
Yuendumu	1.5	94%
Carnarvon	1.5	80.8%

(c) Genetic differences of susceptibility, with reference to

(i) Ethnic differences

In Uganda (Møller, Pindborg, Gedalia & Roed-Petersen)¹⁵¹,

it was found that the prevalence of dental fluorosis was higher among Africans than among Asians, with all other factors remaining constant. Asians in high fluoride areas have less severe dental fluorosis than Africans, whereas, no differences in severity between Africans and Asians could be detected in areas with low fluoride concentration in water.

Whether this finding is related to racial differences per se or indirectly to differences in certain characteristic habits and practices among ethnic groups, like eating or drinking habits, could not be determined.

Ockerse (1953)¹⁶⁴ on the other hand, found that dental fluorosis was more prevalent among Asians than among African children in Kenya, East Africa. This was probably due to the fact that during the 1945 and 1946 water shortage, the town supply in Eastleigh, Nairobi changed; the Asian schoolchildren derived their water supply from boreholes, which contained a relatively high fluoride content than previous water supply.

In Australia, it was found that the Aborigines in Carnarvon, Western Australia (Kailis & Silva, 1970)¹¹⁷, and those in Yuen-dumu, Northern Territory (Williamson & Barrett, 1972)²¹⁵, exhibited higher prevalence and severity of dental fluorosis, than the Caucasians in Carnarvon (Kailis & Silva, 1967)¹¹⁶.

	<u>Prévalence</u>	<u>Moderate</u>	<u>Moderately-severe</u>	<u>Severe</u>
Yuendumu's Aborigines	94%	27%	-	1%
Carnarvon's Aborigines	80.8%	17.4%	5.8	-
Carnarvon's Caucasians	42%	4.2%	-	-

The fluoride content of drinking water were all the same, i.e. 1.5 ppm.

One has to consider the fact that the Caucasians were exposed to a known water-borne fluoride concentration, whereas, the Aborigines' sample, especially the migrants, originated from distant areas and were thus exposed to varying water-borne fluoride concentrations, which in turn were influenced by climatological environment. Other factors that were considered, were the Aborigines' mode of life, primitiveness (or conversely detribalization) and his migratory habits. They are also known to have forced ingestion of water as a result of environmental survival which prevents dehydration when travelling long distances between water sources

MacFarlane (1969)¹³³ showed that desert Aboriginal males had a 24-hour water turnover considerably higher than that of Europeans.

(ii) Sex differences

Møller, Pindborg, Gedalia and Roed-Petersen (1970)¹⁵¹ found that the prevalence of dental fluorosis was higher in males than in females. This observation might not be real because of the small number in the groups examined to draw final conclusions.

Furthermore, there's no reason to believe that distri-

bution of dental fluorosis differs between the sexes unless specific sex taboos concerning food consumption exist in early childhood. Inquiries revealed that food taboos still exist in certain areas in Uganda. These food taboos, mainly observed by females, prohibits the consumption of fish, eggs, and chicken (Møller, Pindborg, Gedalia, & Roed-Petersen, 1970)¹⁵¹.

A similar sex difference in the severity of dental fluorosis has also been reported by Leatherwood, Burnett, Chandravejjamarn and Sirikaya (1965)¹³⁰ in a study in Thailand.

(iii) It has also been suggested that certain genetic faults could occur in small groups of ameloblasts and that these faults may be manifested in an exaggerated manner in dental fluorosis (Al-Alousi, 1975)⁸.

Unless the distribution of mottling could be firmly established as being systematic from one population to another, the hypothesis that genetic component accentuates the prevalence and severity of dental fluorosis, can not be upheld.

2. MINIMAL THRESHOLD VALUE OF FLUORINE IN DENTAL FLUOROSIS

A. Optimum Fluoride Concentration

Having looked at the various extrinsic and intrinsic factors which influence the prevalence and severity of dental fluorosis, it can be said that there is no single optimum level of fluoride concentration which is valid at all times and for all places.

The conventional optimal level of 1 ppm, which is considered optimum in temperate zones, providing maximum protection for dental caries without causing harmful effects, doesn't apply to places with tropical or subtropical climate. It was also observed in areas having similar fluoride concentration in water, dental fluorosis occurred where the mean maximum temperature was higher.

Several factors must be taken into consideration in order to establish the desirable or optimum fluoride concentration for a particular country.

It depends on the annual average of maximum daily air temperatures, which in turn influences the ingestion of fluoride through water intake. Therefore, the fluid intake provides a basis for determining the optimum fluoride concentration in water supply in relation to environmental temperature.

Galagan and Vermillon (1957)⁸¹ showed that under normal living conditions, the water intake increased directly with temperature increases. They estimated that for every degree increase in maximum daily temperature

between 50 to 100°F, water intake increased, on the average, by 0.062 ounces per pound body weight.

The relationship was described by the estimation equation, "ounces of water per pound body weight = - 0.038 + 0.0062 t". Therefore, the formula for calculating the optimum fluoride concentration was written as follows:

$$\text{Optimum ppm fluoride} = \frac{0.34}{E},$$

where E is the estimated daily water intake for children through 10 years of age, in ounces per pound body weight; t, is the annual mean of daily maximum temperatures in °F, which should be the average of 5 consecutive years.

From this formula, a table showing the relationship of optimal level of fluoride to temperature was derived by Galagan and Vermillion (1957)⁸¹, as shown in Table 14.

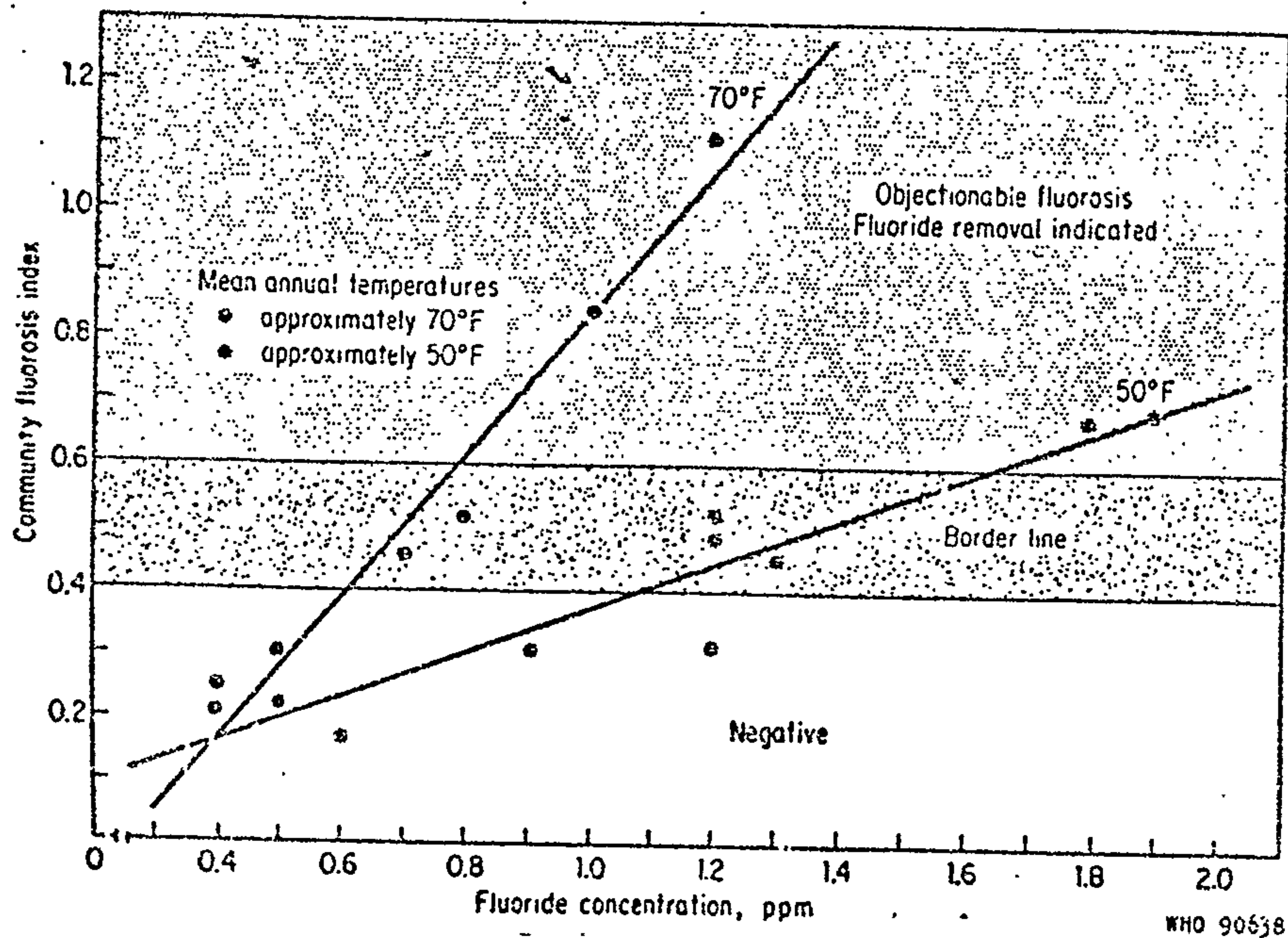
TABLE 14. RELATIONSHIP OF OPTIMAL LEVEL OF FLUORIDE TO TEMPERATURE.

Annual Average of Maximum Daily Air Temperature		Recommended Control Limits Fluoride(mg. / liter)		
<u>°C</u>	<u>°F</u>	<u>Lower</u>	<u>Optimum</u>	<u>Upper</u>
10.1 - 12.1	50.0 - 53.7	0.9	1.2	1.7
12.2 - 14.6	53.8 - 58.3	0.8	1.1	1.5
14.7 - 17.7	58.4 - 63.8	0.8	1.0	1.3
17.8 - 21.4	63.9 - 70.6	0.7	0.9	1.2
21.5 - 26.2	70.7 - 79.2	0.7	0.8	1.0
26.3 - 32.5	79.3 - 90.5	0.6	0.7	0.8

(Galagan & Lamson, 1957)⁸¹.

Using the graph shown in Fig.10 , which demonstrated the community dental fluorosis index (CFI), at different concentrations of fluoride in drinking water according to different mean annual temperatures of two areas in the United States (Maeir, 1963)¹³⁷ as reference, Minoguchi (1970)¹⁵⁰ formulated another equation for determining optimum fluoride concentration. This equation expresses the differences in water consumption as related to seasonal temperature, and differences in water consumption due to differences in temperature, between various geographical areas.

FIG.10 . COMMUNITY FLUOROSIS INDEX AS A FUNCTION OF WATER-FLUORIDE CONCENTRATION AND MEAN ANNUAL TEMPERATURE.



(Maeir, 1963)¹³⁷. The mean annual temperatures are based on the averages of the lowest and the highest temperature recorded in each 24-hour period.

The formula was calculated under the hypothesis that all the regression lines of the various annual mean temperature ($^{\circ}\text{F}$) that can be drawn between the 50°F and 70°F annual mean temperature lines, pass through the point $x = 0.4$ and $y = 0.162$, which is the crossing point of the 50°F and 70°F regression lines. The angle of regression line expressed in $t^{\circ}\text{F}$, and $y = 0.021 + 0.353x$ is in proportion to the increase in annual mean temperature. This hypothesis may be considered to be established in this narrow space of 50°F and 70°F . As a result, he obtained the following formula:

$$\text{ppm fluoride} = \frac{\text{CFI} - 0.162}{\tan (1.45585t - 53.3950)} + 0.4 ,$$

where t is the mean annual temperature in $^{\circ}\text{F}$.

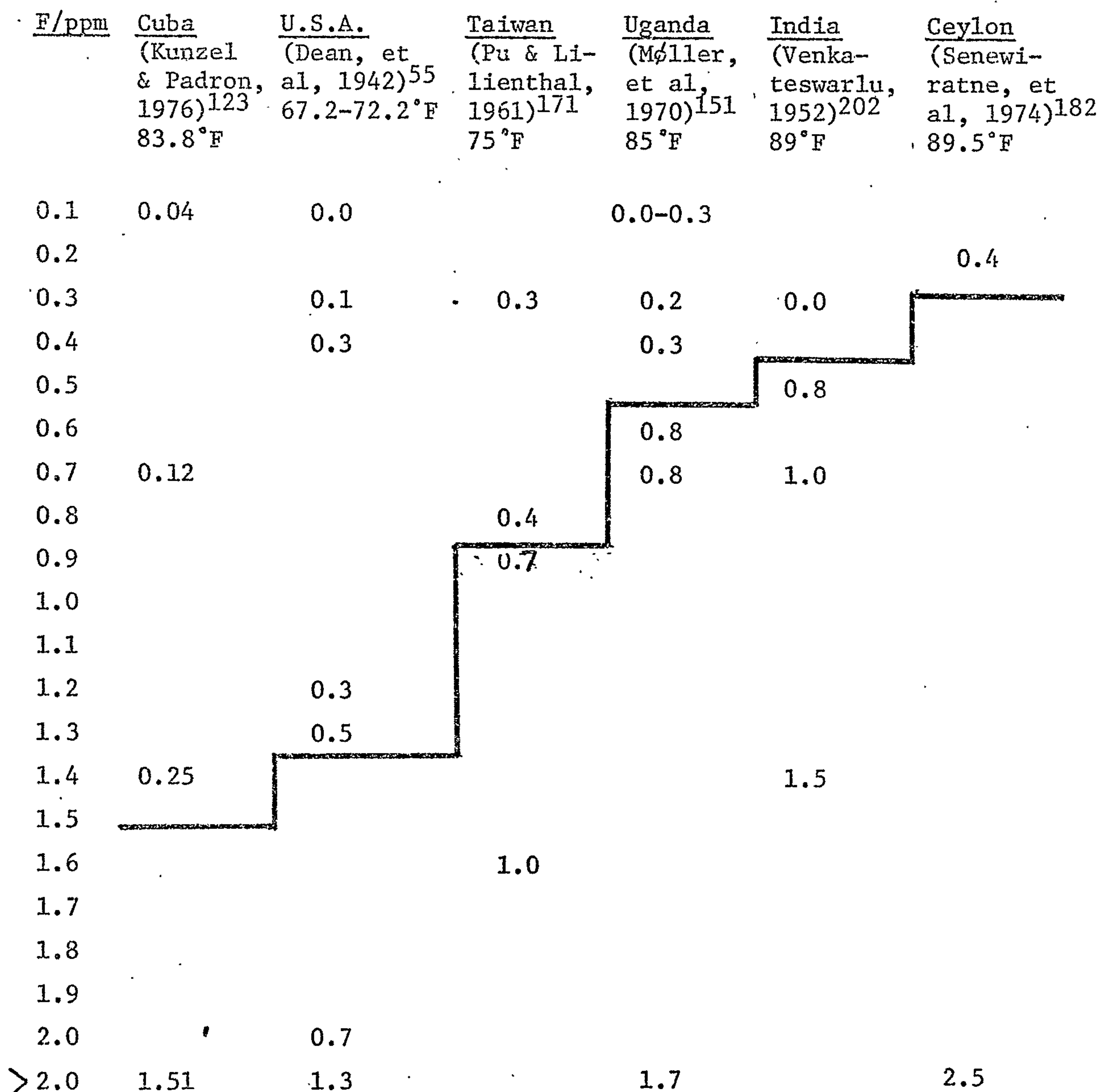
B. Objectionable Dental Fluorosis as Related to CFI and
Fluoride Concentration

Dean (1946)⁵³ stated that a CFI below 0.4 is of little or no public health concern, while indices between 0.4 to 0.6 would be of borderline significance. Above 0.6, the removal of excess fluoride is indicated. Thus, a CFI of 0.6 gives the limit of fluoride concentration.

With climatological variables playing an important part in the final assessment of the fluoride intake, it can be seen from Fig.11 , the borderline of objectionable fluorosis in different countries investigated, under the varying average maximum temperature as related to the optimum concentration allowable to ensure maximum caries reduction without producing objectionable fluorosis.

It's not surprising to find in a community where a particular fluoride concentration in ppm is used as a mass caries control measure, in another country under different environmental situations, the same concentration of fluoride may be associated with a high prevalence or even high severity of dental fluorosis. Therefore, the universal acceptance of 1 ppm of fluoride in drinking water as an optimal level for mass caries control becomes difficult.

FIG. 11 . COMMUNITY INDEX OF DENTAL FLUOROSIS IN RELATION TO
VARIOUS AVERAGE MAXIMUM TEMPERATURES IN VARIOUS
COUNTRIES.



(Line indicates the borderline of objectionable fluorosis.)

VIII. SUMMARY

The continued acceptance of fluoridating communal water supplies in the field of preventive dentistry, will require not only the constant assessment of its effectiveness as a caries-preventive weapon, but also the assessment and consideration of the possible hazards of excessive fluoride intake.

It is clearly established that systemic exposure of developing and calcifying teeth to high levels of fluoride, is the main causative factor in the development of dental fluorosis.

Having a background knowledge on the chemical and physiological aspects of fluorine, as well as the sources and availability of fluorine from these various sources, promotes a better understanding of this pathological entity.

At present, there isn't one classification of dental fluorosis that can be described as wholly satisfactory. Nevertheless, the ideal approach will be to record the condition once defined and well established, according to that definition, and not on the basis of presumed etiology.

The clinical appearance of dental fluorosis relates closely on its severity. It varies from faint white flecks, patches or striations to a discoloured and corroded appearance. Microscopically, fluorosed human enamel is characterized basically by areas of diffuse hypomineralization or porosity, particularly of the outer one-half to two-thirds of the enamel, positioned deep to a relatively well mineralized surface.

Light microscopic studies show that pores occur mainly in interprismatic regions. Chemical investigations of mottled enamel suggest an increase in the organic material, but no significant differences in the Ca/P ratio of mottled and sound enamel.

It was proposed that hypomineralized regions of fluorosed enamel are produced by an arrest of maturation, possibly due to toxic damage to those ameloblasts in the maturation phase of their life cycles.

In most cases, definite diagnosis of dental fluorosis may be derived from history of early fluoride ingestion, but when such a history is unknown, the positive signs of dental fluorosis must be clearly differentiated from opacities/mottling of idiopathic origin, which may be due to local or systemic causes.

Although there appears to be a relationship between the amount of fluoride ingested and the clinical manifestation of dental fluorosis, there are numerous factors which may cause wide individual variations. This can best be summarized in a diagram shown in Fig. 12.

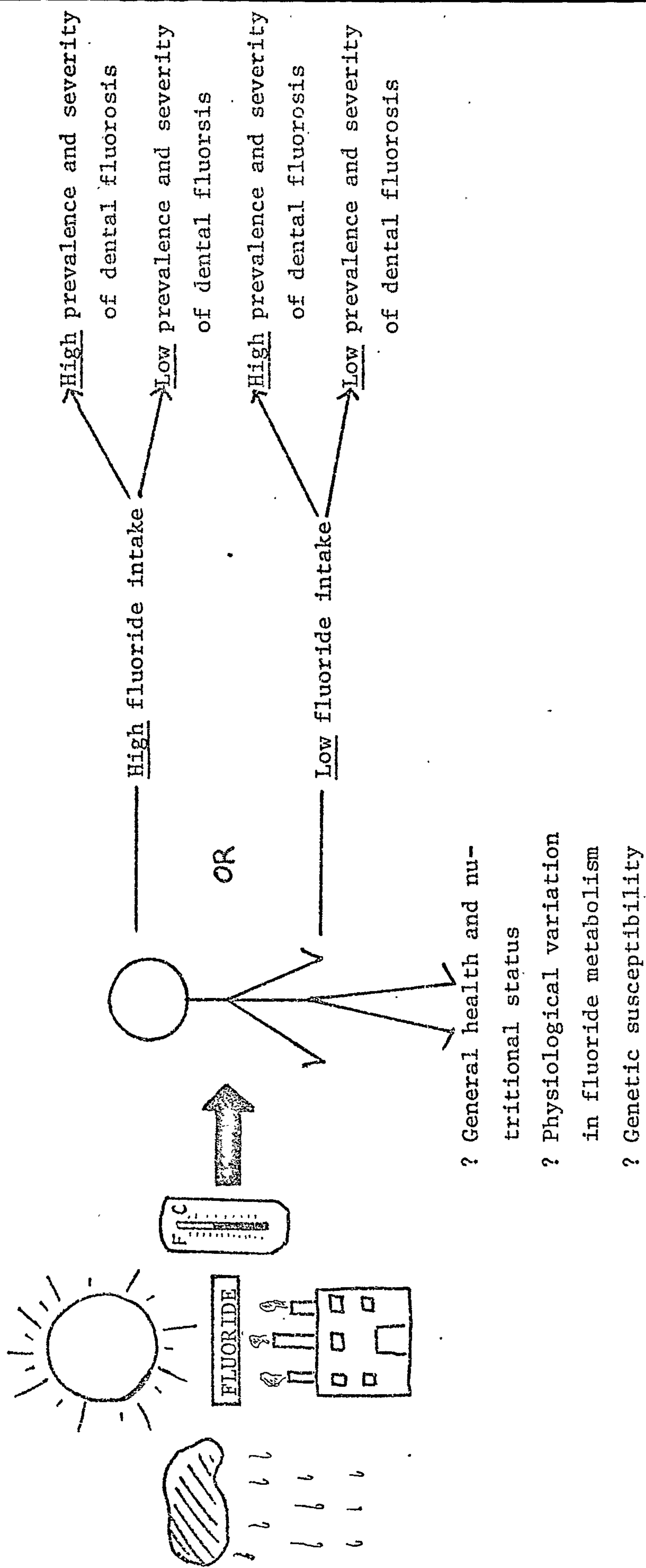
With climatological variables playing an important part in the final assessment of the total fluoride intake, the universal acceptance of 1 ppm of fluoride in the drinking water as an optimal level for mass caries control becomes difficult. Therefore, the determination of an optimal fluoride level for beneficial purposes, must be made primarily on the basis of climatological characteristic of that specific community.

Prevention of the unnecessary occurrence of dental fluorosis may involve the regulation of the fluoridated communal water supply to the desired optimum fluoride concentration, reduction of high fluoride

level in natural fluoride-bearing waters through the process of defluoridation, or even a change in dietary patterns of people known to take high fluoride-containing foods.

The removal of fluorosis-stained teeth involves mainly the bleaching of the stains with chemicals, principally hydrogen peroxide, alone or in combination. In the more severe cases, employment of more extensive operative procedures may be necessary.

FIG. 12. INTERRELATIONSHIPS OF DIFFERENT FACTORS IN DETERMINING THE PREVALENCE AND SEVERITY OF DENTAL FLUOROSIS.



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