CURRENT TOPICS in review

Fluoride supply and effects in infants and young children

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Abstract

The variations of F supply to infants and small children have been mapped as far as possible; the greatest increase of F supply occurs with water-diluted powder formulas, notably when water containing >1 ppm of F is used. Earlier recommended F supplement schemes may in some cases cause temporary overdosage, particularly if combined with a powder formula feeding. In addition, considerable evidence points to a special influence on enamel formation from the plasma F peaks caused by single, rapidly absorbed F doses. Conservative principles for caries-preventive F supply to small children are suggested. Important areas for further research are pointed out.

Introduction

The dosage, distribution and effects of fluoride (F) in infants and young children deserve special attention particularly because their enamel development is sensitive to F, their skeletal mineralization is rapid and prone to high F uptake, and their metabolic rate and nutritive conditions differ from those of older children and adults.

Research in the supply, body tissue distribution, storage and excretion of F in infants and young children has been remarkably scanty during the decades since the effects of F on tooth development and resistance to dental caries were discovered. F dosage has, therefore, largely been based on early studies where estimates were made of the amount of ingestion of foods and water containing optimal F concentrations.[1, 2] It has not been determined whether the beneficial effects of fluoride are directly dependent on the total amount of F ingested daily or whether the concentration of F in drinking water and foods is more important. Also, when supplements are given, it is

uncertain whether single or divided daily doses have differing effects.

There are many explanations for the lack of knowledge in this area: analytical difficulties; uncertainties and misconceptions regarding the state and kinetics of F in human body fluids and the transfer of F through the placenta; ethical problems in sampling and experimentation using children as subjects; and the need for long-term studies before the F effects are reliably known.

The problem is accentuated by changing infant feeding patterns and the early introduction of beikost (foods other than milk or formulas) in the infants' diets.[3] The use of commercially prepared infant foods has greatly increased, and these preparations may have varying F contents due primarily to the varying F concentration in the local water used for manufacture or dilution.

The F content of baby foods, and the fluoride intake obtained with these and various programs of F supplementation have been the subject of several recent studies and reviews. This paper will therefore refer to or summarize such reviews, and add some recent data on enamel fluorosis with caries-preventive F supply.

The reader who is not familiar with Dean's clinical grading of enamel fluorosis is referred to his original article[4] or to that of Nevitt et al.[5] A recent review by Fejerskov et al.[6] describes the clinical and histologic aspects of enamel fluorosis in great detail. It should be stressed that only the two highest grades, 3 and 4, are regarded as esthetically objectionable, and that the lower grades often are not noticed by the subjects of their families. There is no public health hazard with a low community index of fluorosis, and some have suggested that the questionable category of enamel fluorosis may enhance the appearance of the teeth.[7]

However, in the implementation of large scale preventive methods, continued efforts must be made to optimize the administration and dosage so that even minor side effects such as slight enamel hypoplasia would be minimized. Areas for further research will therefore be pointed out.

The reports of notable frequencies of mild enamel fluorosis related to F supplementation programs have prompted a review in the light of recent data on F physiology.

Prenatal F supply

The newborn have a very low F content in the mineralized parts of their bones and teeth.[8] There has been discussion whether or to what extent F ingested by pregnant women passes through the placenta into the fetal circulation and is subsequently incorporated in the developing bones and teeth.[9-12] It is now known that the F concentration in the blood of the newborn is about the same as that of maternal blood which, together with the F content of fetal bones, clearly shows that there is passage of F through the placenta.[9, 10, 13, 14]

Some reports also indicate that the F content of fetal mineralized tissues is slightly higher in areas with high water F content.[9, 15] On the other hand, investigations using radioactive fluorine and animal models have shown a very limited transfer of single F doses from the mother to the fetus.[16-18] On the basis of recent studies and understanding of F kinetics, it appears that temporary F peaks in the maternal blood are largely barred by the placenta in contrast to the steady state levels of F. Since most of the caries-susceptible surfaces of both dentitions are formed postnatally, there is questionable benefit in prescribing prenatal F supplements.

Driscoll[19] reviewed clinical studies in which prenatal F was provided either by the drinking water or by F tablets. He concluded that there is insufficient evidence to indicate any caries-preventive effect in both the primary and permanent teeth from prenatal F supplementations either via drinking water or by the use of F supplement. In 1966, the U.S. Food and Drug Administration banned advertising that claims fetal caries-preventive benefits for the expected child of F ingested as a prenatal supplement.[20] This ban simply was aimed to confine the promotion of F products for prenatal use, but did not prevent the prescription by physicians and dentists of F preparations for pregnant women. The safety of the F preparations was not questioned.

F supply with human and cow's milk

It was only recently discovered[21-24] that human milk as well as cow's milk has a much lower F content than previously reported. The average F content for human milk as well as cow's milk determined by recent investigations varies somewhat because of still existing analytical difficulties, but is generally found to be far below 0.1 mg/liter. This information has an important implication for modern infant feeding because water-diluted formula preparations have now become a major dietary source of the infant's diet in many countries. These commercial preparations provide several times the amount of fluoride intake obtained from the same volume of milk.

F supply from infant formulas and beverages

The dietary supplies of F from ready-to-feed formulas, liquid and powder concentrates, and commercially prepared infant foods have been analyzed recently by a number of investigators. On the basis of market research data, published reports and personal communications from physicians and nutritionists, Fomon[3] has estimated the percentage of U.S. infants receiving various types of feedings. Breast feeding is usually of short duration and the introduction of beikost most often occurs by the age of six weeks. In fact, nearly three-quarters of the formulas given to infants in the U.S. are commercially prepared. As the infant grows older, the use of commercial formulas decreases with an increasing use of cow's milk. The F content of cow's milk is usually far below 0.1 mg/liter.[22-26]

Farkas and Farkas[27] reported that fresh whole milk contained about 0.5 mg of F per liter, which was much higher than the amount found by other investigators. This might possibly have been due to methodologic problems. When considering the supply of F from cow's milk, it may be of some importance to note that the absorption of F from milk is slower and less complete than absorption of F from water.[28, 29] The bioavailability of fluoride may be decreased by as much as 30% when a 3 mg F tablet is ingested with milk and by 40% when consumed with a calcium-rich breakfast.[30, 31]

Wiatrowski et al.[32] estimated the dietary F intake of infants ranging in age from 1 week to 6 months who obtained "nursery drinking water free of F." According to their measurements of F content in various baby foods, an infant aged 1-4 weeks might receive 0.32 mg of F per day, which increased to 1.23 mg of F per day for the 4-6 month old children. The calculated F intake for the newborn was 0.07 mg/kg of body weight, which doubled for the 6-month-old infant.

However, there appear to be slight discrepancies in some of their calculations, and there is some question about the validity and accuracy of the methodology used; for example, the analytical figures for several foods are notably high compared to those found by other authors. Hellström and Ericsson[33] calculated the

daily F supply by water-diluted dry-milk formulas, which are extensively used in Sweden and several other European countries. Recalculation from their data for the ages of 2–12 months gives 0.11–0.14 mg of F per day per kg of body weight when water F content = 1 ppm, and about 0.03 mg of F per day per kg when water F = 0.2 ppm. However, a wide individual variation is evident.

Adair and Wei[34] analyzed the F content of milk-based and soy-based formulas in the U.S. and found a large variability of the F concentrations in these products as well.

Stamm and Kuo[24] analyzed the F concentrations in both a variety of bottled strained foods for infants and formulas produced in Canada by two major manufacturers, both of which were located in nonfluoridated communities. Stamm and Kuo reported that most of these foods, when processed with low F water, contain less than 0.1 mg of F per liter of material. Further, although the cow's milk F levels were found to be very low, concentrated infant milk formulas could contain F concentrations up to 0.3–0.7 mg/liter. Lastly, they concluded that infants being raised on one of the higher F-containing canned-milk formulas should not be given F supplements even though the drinking water may be deficient in F.

Singer and Ophaug[36] reported the most extensive number of analyses of infant foods. They concluded that the fluoride content of the drinking water used for the manufacture of formulas and baby foods is a significant factor in the final fluoride content of such foods and beverages.

The variability of the F concentrations in fruit juices, other beverages, and concentrated milk and soy formulas is due to a number of factors, including:

a. the natural F content of fruits,
b. the nature of the ingredients as to whether liquid concentrate or dry powder was used to manufacture the product,
c. the F content of the water used in the manufacturing process, and
d. the F content of the water used to reconstitute concentrates or powders at home.

Of these factors, the F content of water used for dilution of powdered formulas has by far the greatest effect.[37]

Infants may receive as much as 0.10–0.17 mg of F per kg of body weight daily if they are fed powdered formulas reconstituted with water containing 1 ppm of F.[24, 33] This high F intake coincides with the period of early enamel formation when the ameloblasts appear to be particularly sensitive to increased levels of F ingestion.[38] The intake is proportionately lower if there is less F in the drinking water or if liquid concentrates or ready-to-feed formulas with low F content are used.

F supply with drinking water and beverages

The F supply with drinking water has been the object of comparatively more intense study. Infante,[39] summarizing the data of four groups of investigators, found that a 1-month bottlefed infant could be calculated to ingest 0.077 mg of F per kg per day, while children 6 months through 5 years would ingest 0.015 to 0.040 mg of F per kg per day—all with water containing 1 ppm F and assuming equal volumes of milk or formulas and tap water were used.

The calculated increases of F ingestion by babies given water-diluted powder formulas or water-diluted cow's milk are given in Table 1.

There is also a probability, and indeed there are some indications, that widespread water fluoridation slowly increases the total F supply of the population via different foodstuffs that are produced with the use of the fluoridated water. For example, Schulz et al.[40] found that most soft drinks in the Maryland area contain an average F concentration of between 0.8 to 0.9 ppm of F. Changing food habits, e.g., a partial replacement of milk with other beverages, may have similar effects. Only thorough, long-term studies can determine if and when this phenomenon may require revisions of the optimal F levels.

A special form of water fluoridation tried out and practiced in some American schools has been the introduction of F ranging from 4.5–6.3 ppm into the water supply of the school.[41] This can be expected to cause some elevated values of plasma F in the children according to the data presented in a subsequent section on enamel fluorosis. If this F level should produce enamel fluorosis, it would affect mainly the second and third molars. Although no evidence of enamel fluorosis has been reported after 8 years of school water fluoridation at 6.2 ppm,[42] the plasma F curves following the ingestion of realistic volumes of this water should be determined.

F supply with foods and beverages of adults

The F supply with ordinary food varies considerably between countries with differing dietary habits. Most data obtained with modern analytical techniques have been reported from the U.S.;[43, 44] however, these studies were made on diets of adults, and in some cases on specialized hospital diets. Hellström and Ericsson[33] calculated the daily doses that would be obtained by infants 8 months through 2 years of age if half of their caloric intake were derived from similar foods as analyzed by San Filippo and Battistone,[43] the other half derived from water-diluted, dry-milk formulas. Their figures give about 0.08 mg/kg of body weight per day if the water F = 1 ppm, or about 0.02 mg/kg/day if the water F = 0.2 ppm (Fig. 1).

F supplies from tablets, drops, etc.

It has generally been suggested that F supplementation should begin as soon after birth as possible in order to obtain maximum beneficial effects for infants who live in nonfluoridated communities. Recommended F dosages have varied;[45] some schemes of actual interest are condensed in Fig. 1. It should be added that the recommendations of the American Dental Association have as a first alternative for children below 2 years the use of water fluoridated in the homes to about 1 ppm F for preparation of beverages and infant foods. The Swedish recommendations, recently adopted, prescribe no fluoride supplementation from birth until 6 months of age when 0.25 mg of F treatment is commenced.

For infants who receive an F supplement in the form of tablets or drops from birth, the total F dosage may be higher than required as the diet of the infant changes from human milk to infant foods at higher F content such as ready-to-feed formulas, concentrates, and powdered milk diluted with fluoridated water. Consequently, many infants may receive more F than was intended, which may lead to mild enamel fluorosis.

F supply with alternative F vehicles

Some staple foods have been proposed as vehicles for F supplementation as alternatives to fluoridated water. They are primarily milk, flour, salt, and sugar. Of these, salt is the only one that has been tested extensively, and it has been used in Switzerland as a supplement for many years. Salt also appears to be the alternative with the greatest prospect of more widespread use within the next decade.

There has been some objection that infants and young children would receive little benefit from salt fluoridation due to their relatively low salt intake. However, with the widespread use of water-diluted

formulas and the increased F intake, salt fluoridation may be an advantage. Both the primary and the permanent teeth appear to be protected significantly by salt fluoridation.[46-48] Fig. 2 shows the dental caries reduction in primary teeth following salt fluoridation in Hungary.[7]

Toth has calculated "optimum" and "tolerable" daily F doses per kilogram of body weight and given the figures 0.045 and 0.073 mg, respectively, for infants below 1 year, and 0.032 and 0.048 mg, respectively, for children 7–9 years of age.[49] Hellström and Ericsson[33] calculated that a consumption of as much as 0.07 g of salt per kg of body weight per day, containing 500 ppm of added F, would give only slightly higher F dosage in the 2–7 age groups than the same food with ordinary salt and water containing 1 ppm of F.

There are no reports of any notable occurrence of enamel fluorosis in conjunction with salt fluoridation, since the F supply with salt occurs only with meals and thus will be absorbed comparatively slowly, the plasma F concentrations following the ingestion of salty foods should be tested (cf. below, "Enamel Fluorosis Associated with Various F Supplies").

F ingestion following oral F applications

This source of F supply is of relatively minor importance with the possible exception of daily use of toothpaste. It has been found that children above 4 years of age generally master their swallowing reflexes and hence can be allowed to use F toothpastes. The amount of F ingested is approximately 25% after 4 years of age.[50] Assuming that 0.5 g of toothpaste containing 0.1% F is used, a total of 125 μg of F may be ingested. In areas with suboptimal water F supply, 4-year-olds may, for example, brush their teeth with a toothpaste containing 0.1% F, provided that they are properly instructed and regularly supervised. Prefer-

Table 1. Fluoride content of infant food, based on estimated average values for the fluoride contents of milk, liquid concentrates, and powder formulas[37]

|	Proportion	F content,	F content in relation to human milk
		mg/kg, mg/l	
Human milk		0.025	
Cow's milk		0.03	
Cow's milk + water, 0.25 ppm F	1 + 1	0.14	5.5×
Cow's milk + water, 1.00 ppm F	1 + 1	0.52	21.0×
Liquid concentrate		0.75	
Liquid concentrate + water, 0.25 ppm F	1 + 1	0.50	20.0×
Liquid concentrate + water, 1.00 ppm F	1 + 1	0.88	35.0×
Powder formula		0.40	
Powder formula + water, 0.25 ppm F	1 + 6	0.32	13.0×
Powder formula + water, 1.00 ppm F	1 + 6	1.07	43.0×
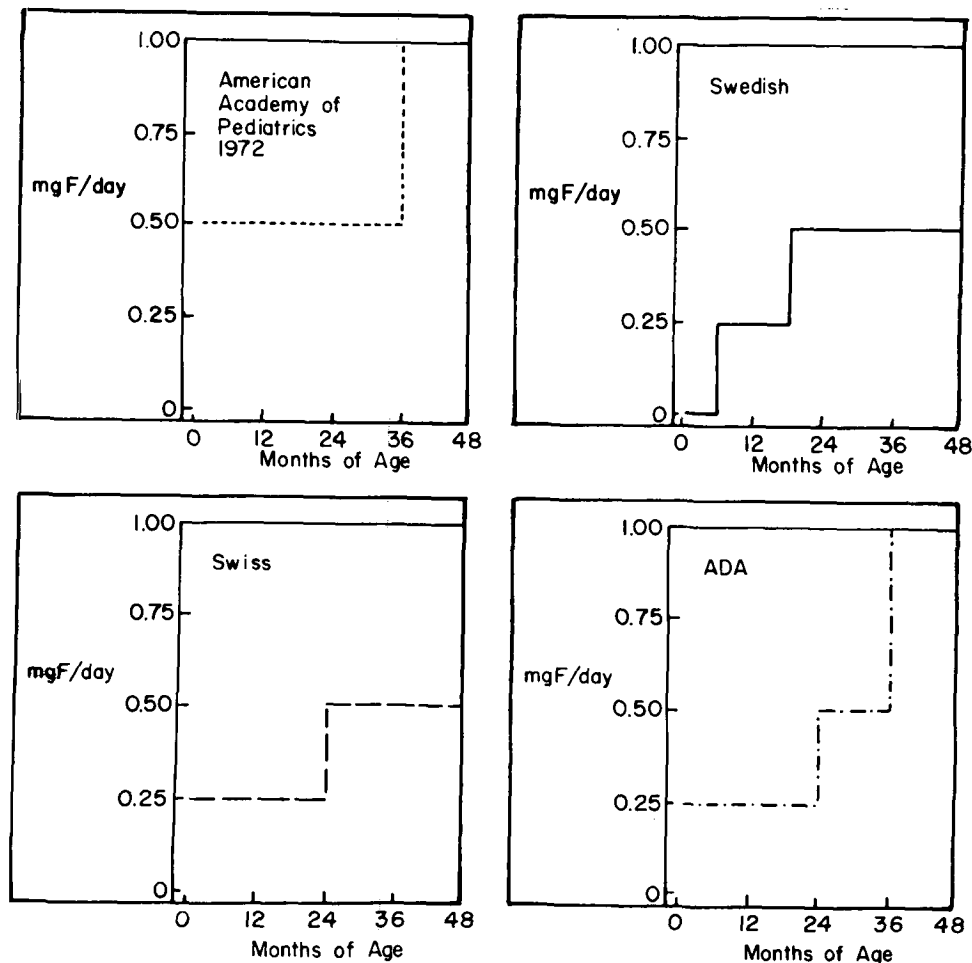
Fig. 1. F tablet dosages recommended for small children by the American Dental Association, the Committee on Nutrition of the American Academy of Pediatrics, the Swedish Board of Health and Social Affairs, and the Swiss Health Authorities.

ably, the volume of toothpaste should be reduced to a pea-size quantity used once daily.

However, any hazard by small children's use of such toothpastes is entirely hypothetical and may be eliminated by the use of dentifrices with lower F content.

Effects on caries from various F supplies

There is voluminous literature on this subject which has also been extensively reviewed recently. Consequently, reference is made here to the reviews.[45, 51, 52] The age of F supply and the relationship between caries and fluorosis will be briefly discussed.

Of critical importance is the question of the child's age when the F supply has to be introduced in order to provide maximal or near-maximal protection of the dentition. The earliest clinical trials with water fluoridation indicated that the permanent teeth would receive equally good protection whether the children were 2–3 years old or newborn at the time of fluori-

dation (Fig. 3). This is not surprising considering the facts that most caries-prone enamel surfaces are mineralized after the age of 2 and that all permanent tooth surfaces accumulate F for years before eruption.

Concerning the deciduous dentition, the F supply from birth might be assumed to be of importance, but there seems to be very little evidence supporting this contention. The possibility that formula-fed children in an area with about 0.2 ppm of water F had obtained a greater caries resistance than breast-fed infants (owing to the much higher F supply of the former group) was negated by a Swedish study[53] and an American study[54] in a fluoridated community which showed a caries increase in long-term bottle-fed children. Hennon et al.[55] reported 55–70% caries reductions in the deciduous teeth 1–3 years after starting F tablet supply at 1–1½ years of age.

These results indicate the possibility that the local F effect on the enamel surface after eruption gives sufficient caries protection.
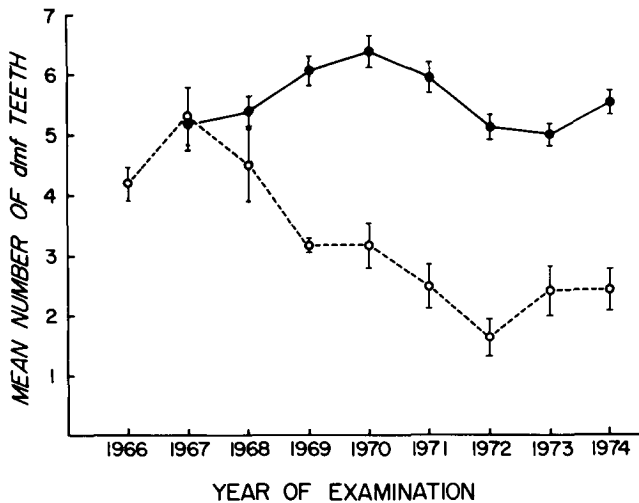
Fig. 2. Caries reduction in primary teeth from salt fluoridation in Hungary.[47] O- - -O, test children; ●———●, control children (2-6 years).

F has often been administered to children in the U.S. together with supplemental vitamins in the form of tablets or drops. Available data indicate no difference in anti-caries effect from F administration alone.[19]

Although it is well known that the dental caries rate is significantly reduced when the water F concentration reaches 1 ppm, a much less publicized finding is that when the F content in the water exceeds 4-5 ppm, resulting in moderate to severe enamel fluorosis, there is an increasing caries rate in the permanent teeth of affected individuals.[56, 57] Experiments on rats with a high pre-eruptive F dosage have confirmed this observation.[58-60] In Forsman's study,[57] however, there was no relationship between fluorosis and caries in the primary teeth.

Williams[61] found highly permeable structures in mottled enamel from teeth of residents in Colorado Springs long before this condition was known to be caused by excessive intake of F, and many later investigations have confirmed these structural defects. Thus, the increased caries resistance of dental enamel with a high F content seems to be negated when the structural defects become excessive, resulting in greatly increased permeability of the enamel.[6]

Enamel fluorosis associated with various F supplies

It is generally agreed that enamel fluorosis is a specific type of hypoplasia which constitutes the first clinical sign of incipient F overdose and that this hypoplasia is of no general health concern, *per se*.

There is some evidence to indicate a specific sensitivity of the ameloblasts to varying concentrations of F. Enamel formation is damaged much earlier than is

dentin formation by increasing F dosage in spite of the much greater F accumulation in the dentin. The specificity may be due to the epithelial nature of the ameloblasts and their particular pattern of mineralization. It is notable, for example, that the shark's "mesenchymal enamel," which is nearly pure fluorapatite with over 100 times more F than human mottled enamel, is formed without disturbances. However, in spite of numerous investigations, the pathogenesis and mechanisms of dental fluorosis are still largely unknown.[6]

The relationships between the different baby feeding schemes, F supply, and enamel fluorosis have recently been investigated in Sweden. Children of ages 8 and 9 years in communities with water F ~1.2 ppm who had been either typically breast-fed or typically formula-fed during infancy were examined.[62] The amount of F ingested by the formula-fed children was calculated to be nearly 50-fold higher than the F dose of the breast-fed children for at least 5 months of the first year of life. However, the clinical study found only small and statistically nonsignificant differences between the two groups in the degree of enamel fluorosis.

Analysis of shed primary teeth from children in the Uppsala study, which had been mineralized in part during their first year of life, showed 2-3 times higher F content in the enamel and crown dentin than the formula-fed group.[63]

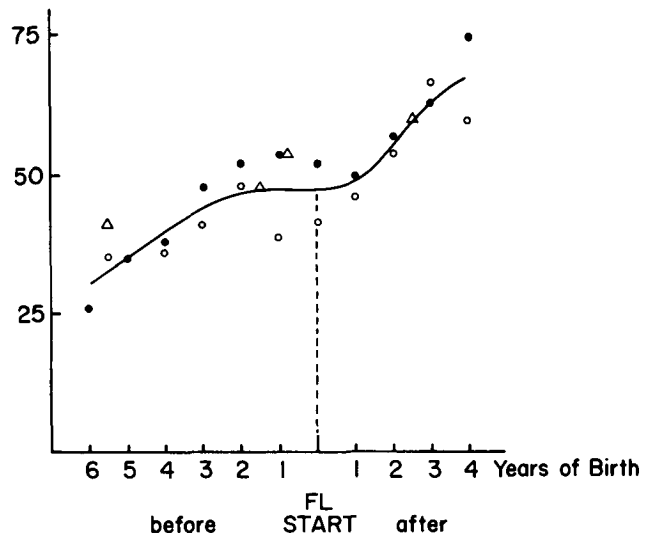Later studies by Forsman[38, 56] in areas with about 1,

Fig. 3. Percent caries reduction in the permanent teeth of children born 6 years before through 4 years after start in 1945 of water fluoridation in Grand Rapids, Michigan[84] (●), Newburg, New York[85] (△), and Brantford, Ontario[86] (O). Note the apparently equal effect in children born 2-3 years before through 1 year after the start.

5 and 10 ppm of water F have shown a clear-cut tendency to a higher degree of enamel fluorosis with shorter periods of breast feeding followed by reciprocally longer periods of feeding water-diluted powder formulas in the two regions with 1 and 5 ppm of F. No such difference was found in the 10 ppm community where all children had high degrees of fluorosis. Thirty-two percent of the formula-fed children in two low-F areas showed slight enamel fluorosis, with both frequency and degree of fluorosis increasing markedly in those who had obtained F supplementation from shortly after birth.

Primary teeth appear to be more protected from the toxic effects of excessive amounts of F, but fluorosis was found in many primary teeth in 5 and 10 ppm of F areas[56] with some teeth affected to the degree of moderate (3) or severe (4) fluorosis.

Forsman[56] reported prenatal fluorosis in primary teeth of children who resided in areas with 10 ppm of F. However, it is difficult to be certain that enamel fluorosis does occur during the prenatal period because fluorosed enamel resembles normal immature enamel at the microscopic and ultrastructural levels.[64] It is well known that the labial surfaces of maxillary central incisors are the most prone to enamel fluorosis. These same areas have been noted to be normally hypomineralized and highly porous at birth,[65, 66] and might be prevented from maturation by a high F supply from birth.

A possible interpretation of the moderate effects of water-diluted formulas was that F could be less available from dry-milk formulas than from human milk, but this hypothesis was negated by a metabolic investigation on four infants from Uppsala whose intake and total excreta were measured during 2 weeks of formula-feeding and breast-feeding.[67] It is possible, however, that water-diluted powder formulas in 1 ppm of F areas may give a high total absorption of F without causing excessive plasma peak F concentrations. F ingestion with milk has been shown to give a protracted absorption with much lower plasma peak compared to ingestion with water.[28, 29, 30]

No data on the availability of F from formulas based on soy protein seem to exist. There is a likelihood that the combination of a 0.5 mg single dose F tablet with the increased F supply from powder formulas may be the cause of mild enamel fluorosis of the permanent teeth, especially maxillary central and lateral incisors and first molars. If a carefully controlled study is not conducted, and considering the subjective method of assessment of fluorosis, many of the very mild to mild categories of enamel fluorosis may easily be overlooked or underestimated. However, an increased frequency of enamel fluorosis is indicated by several clinical observations and studies. Aasenden and Peebles[68] reported as high a frequency as 67% in children

who received a daily F supplement from birth to 3 years of 0.5 mg, and 1 mg from age 3 and up.

Furthermore, 14% of these children had moderate enamel fluorosis although no discoloring or pitting of the enamel was reported. These authors concluded that the dosage of F supplement during the first year of life was at the very borderline of the tolerable level and that consideration should be given to reducing this dosage. Similarly, Hotz[69] reported observations of mild enamel fluorosis in Switzerland when children were supplemented with 0.5 mg of F per day from birth to age 4, and 1 mg afterward.

Hennon et al.[70] recently published an investigation of small groups of 7-year-old children in an area with 0.7 ppm of water F who had received a NaF-vitamin preparation daily since an average age of 6–7 months. The F dosage had been 0.5 mg daily in one of the groups, and in another group the same dosage was given to 3 years of age and then 1 mg daily. The fluorosis indices of these groups were 0.19 and 0.25, respectively, significantly higher than that of a control group but still much lower than reported by Aasenden and Peebles.[68] Further study of larger groups is desirable.

In one Swedish study[71] of enamel fluorosis in children who had obtained half as large a tablet F dosage as in the studies of Aasenden and Peebles, no significant difference from control children was found. However, in another study[72] using a similar F tablet dosage in Denmark, 42% enamel fluorosis, mostly of the very mild type, was found in the test children compared to 15% in the control children.

There are several animal studies which showed that elevated concentrations of plasma F may be mainly responsible for the effects on the enamel organ.[73–76] The two former groups of authors found that a certain dosage during a shorter period of time produced more enamel mottling than the same dosage given over an extended period of time. Suttie et al.[74, 75] found that plasma F concentrations around 0.3 μg/ml caused severe mottling.

Ericsson et al.[76] found in two series of experiments that the minimal mottling dose in rats caused plasma peaks of about 0.2 μg of F per ml without a noticeable rise of the steady state of plasma F levels. Although similar F peaks have been demonstrated in human plasma following F ingestion,[77, 78] it is not known which height, frequency or duration of these elevations would cause enamel fluorosis.

F supplements as tablets or drops have generally been recommended to be given as single daily doses, or even as twice as large single doses every second day. This must give considerably higher plasma F peaks than the divided doses obtained with fluoridated drinking water, particularly if the doses are administered between meals.[29, 78] This deviation from the die-

tary supply of small amounts of fluoride with foods and beverages may, to a great extent, explain the increased occurrence of enamel fluorosis with the F tablet programs. Unfortunately, the reports on effects of F supplement programs have seldom indicated whether the tablets or drops were given with or between meals, and they have not indicated whether the infants consumed water-diluted formulas along with the supplements. These data appear essential for judging the dose-effect relationship.

Other data indicate that moderately elevated continuous plasma F levels may also cause enamel fluorosis. For example, Lindemann[79] found such changes in rat incisors mineralized several weeks after cessation of high F ingestion. Ericsson et al.[80] found that fasting plasma F levels are a function of the skeletal F content in both humans and rats, which may explain the secondary effect on rat ena..el mineralization from a high skeletal F load.

Possible skeletal effects associated with enamel fluorosis

Although there is considerable evidence to indicate a specific sensitivity of the enamel-forming cells to F, it has not been possible to exclude that there may be early borderline effects on dentin and bone formation as well.[6]

In a study comparing formula-fed and breast-fed infants in Uppsala (water F 1.2 ppm), Hellström[15] found significantly higher values for plasma F and alkaline phosphatase in the formula-fed infants. She also interpreted the higher values of plasma alkaline phosphatase, the increased growth rate and the increased number of ossification centers, which were reported from a previous study in Northern Sweden,[81] as a possible F effect. Further studies should attempt to confirm or negate the indirect evidence that higher F doses during infancy may have a temporary, and perhaps also a stimulatory, influence on bone formation.

Clinical implications and recommendations

The notable occurrence of very mild to mild enamel fluorosis in relation to different forms of baby feedings and some F supplementation programs warrants a revision of the recommendations for F supply to infants and small children.[82] Although the evidence for a causal effect of temporarily elevated plasma F levels cannot be regarded as conclusive, there appears to be enough information to develop principles for F supply to small children that will deviate as little as possible from the well established supply and dosage distribution obtained with fluoridated water.

Detailed rules may be dependent on the availability and acceptance of foodstuffs and F supplements in different countries, but the following principles appear well-founded.

The total F supply from various foods and substitutes should closely resemble that obtained in areas with optimal caries-preventive water F content and well established, scientifically accepted feeding schemes, including 4 to 6 months of breastfeeding.

The F supply should be derived principally from water and ordinary foods, produced at home or commercially. When the F ingestion from dietary sources and water is deficient, then special supplements such as tablets or drops may be used.[82-86]

Water exceeding the optimal caries-preventive F content should not be used for dilution of infant formulas. Water exceeding twice this content should be avoided during the entire childhood.

Special F supplements should be prescribed only with knowledge of and in accordance with the F content of the individual's water supply. Such supplements should not be given during periods dominated by water-diluted formula feeding.

Special F supplements should probably be given in such ways that (a) large and rapidly absorbed single doses are avoided, and (b) optimal contact with the surfaces of erupted teeth is obtained. Administration of F with meals will retard absorption and reduce plasma F peaks.

Oral applications of F preparations should consider F retention by inadvertent swallowing, particularly before 3–4 years of age.

Areas for further research

There are many areas that will need additional research regarding the effects of F in infants and young children, particularly when deviations are made from nature's supply of F with the drinking water. These include:

a. Total doses and effects obtained with simultaneous F supplies, e.g., water-diluted formula + supplement.
b. Plasma F kinetics following different dosage regimens.
c. The effects of plasma F peaks vs. lower continuous elevations of plasma F concentrations.
d. Optimal F dosage regimens for caries resistance without enamel fluorosis.
e. Relationship of plasma to bone F concentrations.
f. The relationship of plasma and salivary F concentrations.
g. The mechanisms of F effects on the ameloblasts and enamel formation.
h. The possible effect of F on osteogenesis.
i. Special implications of new F vehicles such as table salt.

Some of these suggested investigations may be ac-

F content of drinking water	Birth to age 2	Daily dosage age 2–3	(F ion) age 3–14
ppm	*mg*	*mg*	*mg*
Less than 0.3	0.25	0.50	1.00
0.3 to 0.7	0	0.25	0.50
Over 0.7	Fluoride dietary supplements unnecessary		

complished by use of already existing clinical material or routine hospital analyses of blood and tissue samples.

Examples of progress in this area include:

1. The major baby formula manufacturers in the U.S. have been and are taking active steps to reduce and standardize the fluoride content of baby formulas to an average of less than 0.1 mg of F per liter of formula.[87]

2. The Committee on Nutrition (CON) is reviewing their F supplement recommendations and will probably revise their schedule to a slightly lowered dosage very similar to the one used by the Council on Dental Therapeutics of the American Dental Association (Table 2).

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