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Fluoride metabolism and fluorosis

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Summary *Objectives*. This paper is primarily concerned with the only proven risk associated with water fluoridation: enamel fluorosis. Its purpose is to review current methods of measuring enamel fluorosis, its aetiology and metabolism. A further objective is to identify risk factors to reduce the prevalence of enamel fluorosis and employ methods to manage such risk factors.

Data. The prevalence of enamel fluorosis is increasing in Ireland and internationally. A critical period has been identified at which teeth are most at risk of developing enamel fluorosis: 15–24 months of age for males and 21–30 months of age for females. The data included took these two factors into account.

Source. A thorough narrative review of published literature was conducted to identify studies concerning the aetiology and metabolism of enamel fluorosis. Risk factors for fluorosis were identified from these studies.

Study selection. As it is the pre-eruptive phase of enamel development which represents the greatest risk to developing enamel fluorosis, studies examining sources of fluoride ingestion for young children were selected. These included studies on ingestion of fluoride toothpaste by young children, fluoride supplementation and infant formula reconstituted with fluoridated water.

Conclusions. There is evidence that the age at which tooth brushing with fluoride toothpastes is commenced and the amount of fluoride placed on the brush are important risk factors in the incidence of dental fluorosis. It is recommended that brushing should not commence until the age of 2 and that a pea-sized amount (0.25 g) of toothpaste should be placed on the brush.
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Introduction

The benefits of water fluoridation in controlling dental caries are well documented. Fluoride was first used in water for caries control in 1945 and 1946 in the United States and Canada, respectively. The fluoride concentration in the water supply to four communities was adjusted.[1,2] Each study was designed to be of 10-year duration but after 5 years it became so apparent that the trial cities would duplicate the caries reductions seen in cities of similar natural fluoride concentration that the US Public Health Service gave its endorsement stating that 'communities desiring to fluoridate their communal water supply should be strongly encouraged to do so'.[3]

The British government sent a mission to the United States and Canada in 1952. It reported back

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to the UK government and suggested that studies to demonstrate the dental benefits of water fluoridation should be carried out. These studies began in 1955 in Kilmarnock, Anglesey and in Watford. When these investigations were completed, the findings were in accordance with those of the American studies. Water fluoridation was introduced in Dublin in 1964 and over the next 10 years most urban communities in the Republic of Ireland were fluoridated. In 1961–1963, a baseline epidemiological study was carried out to determine the prevalence of dental caries in the school population of the Republic of Ireland. At this time, the percentage of children with no caries in their permanent teeth was 34, 6 and 2% in 8-, 12- and 15-year-olds, respectively. A further study on Children's Dental Health in Ireland was conducted in 1984.[4] The authors reported a substantial decrease in the caries level in permanent teeth in both fluoridated and non-fluoridated groups. In the 1984 survey, the 'Full Fl' groups contained 69, 23 and 12% of children with no caries in the 8-, 12- and 15-year-old age groups, respectively, and 56, 15 and 8% in the 'Non Fl' group.

All US residents are exposed to fluoride to some degree today and widespread use of fluoride has been a major factor in the decline in the prevalence and severity of dental caries in the US and other economically developed countries.[5] The effectiveness of drinking fluoridated water on coronal decay in children, adolescents and adults has been studied and proven in numerous community trials and economic evaluations in Canada.[6] Approximately 317 million people in 39 countries currently benefit from artificially fluoridated water.[7] An additional 40 million benefit from water supplies that are naturally fluoridated. Community water fluoridation schemes have been in existence in the United States for over 50 years and are employed in 39 countries throughout the world including Spain, Switzerland, Canada, the United kingdom, Israel, Singapore and New Zealand. The success of fluoride in controlling dental caries has led to the production of fluoride-containing products including toothpaste, mouthrinses and professionally applied gels or varnishes.

It was previously believed that fluoride needed to be present systemically to be effective in caries prevention. It was assumed that the method of action was due to the incorporation of fluoride into the enamel during enamel formation. This in chemical terms involves the substitution of the hydroxyl ion with the fluoride ion in hydroxyapatite leading to the formation of fluorapatite.[8] It was believed that in order for fluorapatite to be formed it was necessary for the fluoride ion to be present during amelogenesis and hence systemic fluoride was essential. However, later work using sophisticated enamel biopsy and fluoride analysis techniques revealed no simple relationship between enamel fluoride levels and caries experience. This view was upheld by further epidemiological evidence in that caries reductions were found in teeth already erupted at the start of fluoridation programmes.[9,10] It became apparent that reduced enamel solubility is not the sole factor involved in the cariostatic action of fluoride.[11]

At about this time understanding of how a carious lesion develops began to change. It is now known that the early white spot lesion can progress to a cavity, remain static or reverse (remineralise). The presence of fluoride has been shown to promote the remineralisation of white spots and the 'healed' lesion has been shown to be more resistant to caries attack than a similar unchallenged site.[12] Fluoride is also known to have antibacterial effects.[13] It inhibits the process by which cariogenic bacteria metabolise carbohydrates to produce acid. When a low concentration of fluoride is constantly present, *Streptococcus mutans* produce less acid.[14,15] These advances in knowledge have changed thinking on how fluoride works in caries prevention and thus have an impact on the rational use of fluoride in the community.[16] Its method of action is mainly topical but fluoride from water supplies also functions systemically when absorbed and incorporated into developing teeth. Thus, fluoride results in benefits in caries reductions that start in childhood and extend throughout life.

Since the onset of water fluoridation over 50 years ago, there have been numerous claims of harm arising from ingestion of fluoridated water. These have varied from allergic reactions, cancer, birth defects and genetic disorders. The Knox Report 1985[17] concluded that there was no evidence that fluoride occurring either naturally in water or added to water supplies, was capable of inducing cancer. In 2000 Hillier et al.[18] published the results of a population-based case control study, exploring the relationship between fluoride ingestion and the risk of hip fractures. It was concluded that water fluoridated to 1 mg/l does not pose any greater risk of hip fracture. Kaminsky et al. (1990)[19] recorded no evidence of skeletal fluorosis among the general US population exposed to drinking water fluoride concentrations less than 4 mg/l. They also found no evidence of increased renal disease or dysfunction in humans exposed to up to 8 mg fluoride per litre in drinking water. The York Review,[20] concluded that, other than enamel fluorosis, there was no clear evidence of other potential adverse effects associated with water

fluoridation. The Forum of Fluoridation 2002[7] also reiterated that long-term exposures to fluoride does not have an adverse effect on bone strength, bone mineral density or fracture incidence.

The other risk associated with water fluoridation is enamel fluorosis. The original studies conducted by Dean[21] found that the maximum caries reduction in a community served with naturally-occurring fluoride in domestic water supplies was observed at 1 ppm. At this level, however, it was reported that one would expect to see 1% mild fluorosis, 19% very mild and 31% with questionable fluorosis. This gives cumulative total of 51% with some degree of fluorosis and 49% with no change in the appearance of the tooth enamel. At the time of Dean, it was decided that this level of risk (fluorosis) was acceptable taking into account the reduced caries levels. As a result, fluoride was added to the water supplies in 1945 including Grand Rapids, Michigan, Newburgh and New York with Muskegon and Kingston designated as controls. The results of these studies are well known and water fluoridation has subsequently become a widely accepted public health strategy for the control of dental caries. Recently, however, there is increasing evidence from many communities throughout the world that the prevalence of enamel fluorosis is increasing and that in many cases the levels are above those reported by Dean. In the recent systematic review of water fluoridation, the 'York Review',[20] it was concluded that dental fluorosis of aesthetic concern affected 12.5% of residents of fluoridated communities. This was based on a survey of 12-year-old children in the UK.

This paper is primarily concerned with enamel fluorosis. Its purpose is to review current methods of measuring enamel fluorosis, to assess its prevalence and to address its aetiology and metabolism. In doing so, it will be possible to identify risk factors and employ methods to manage such risk factors and thus, to reduce the prevalence of enamel fluorosis.

Defining and measuring enamel fluorosis

Enamel fluorosis is a hypomineralisation of enamel characterised by greater surface and subsurface porosity than in normal enamel as a result of excess fluoride intake during the period of enamel formation.[22] It has also been defined as being 'a dose response effect caused by fluoride ingestion during the pre-eruptive development of teeth'. This change in the enamel is characterised by altered appearance of the tooth ranging from fine white lines to pitting or staining of enamel.

There are two main methods for recording enamel fluorosis. The first are the aetiological indices. These are an unusual family of epidemiological indices as the examiner diagnoses the defect as being enamel fluorosis. The diagnosis of fluorosis is a controversial one and as enamel opacities can be caused by a variety of other causes (for example rickets, caeliac disease, malnutrition, high altitude and premature birth) descriptive indices are now used to prevent misclassification of defects. Such indices describe the appearance or features of a range of defects without assuming the aetiology of the defects. They record all enamel opacities (thought to be developmental in origin) including those caused by fluoride.

Dean observed a correlation between fluoride in the drinking water and mottled enamel and from this he devised Dean's Index of Fluorosis.[21] This scores the two teeth that are most affected. The index grades fluorosis from very mild, mild, moderate or severe and notes the percentage of the labial surface that is affected by fluorosis. Despite criticisms,[23] Dean's Index has proven to be a robust classification and is recommended for use by the World Health Organisation in its publication Oral Health Surveys-Basic Methods 4th Edition.[24] Thylstrup et al.[23] proposed a modification of Dean's index known as the TF index. This classifies clinical features of fluorosis that reflect histopathological changes following histological examination using ordinary and polarized light of affected enamel. The index requires that the teeth be dried before examination. Tooth Surface Index of Fluorosis (TSIF) described by Horowitz et al.[25] provides an analysis based on aesthetic concerns and examines teeth when wet. The Fluorosis Risk Index (FRI), developed by Pendrys, 1990[26], is designed to produce an accurate association between age-specific exposures to fluoride and the development of fluorosis. It divides the enamel surface of the permanent teeth into two developmentally related groups of surface zones. Code 1 began formation during the first year of life and code 2 began during the third to sixth years of life. Scores are recorded for each zone.

The second methods for recording fluorosis are the descriptive indices. The descriptive index developed by Young[27] formed the basis of several indices that were to be developed later. He used three features to define the clinical characteristics of enamel defects: location, colour and hypoplasia. He also attempted to ascribe an aesthetic severity to the opacities within his index. The indices used by Al-Alousi et al.[28] Jackson et al.[29] and Murray and

Shaw[30] were all modifications of the descriptive method proposed by Young in 1973.[27] Differences include the tooth surfaces recorded and a condensing of category groups. The Developmental Defects of Enamel (DDE) was developed in 1982 by the Federation Dentaire Internationale[31] and has since been modified.[32] It divides defects into three types: demarcated, diffuse and hypoplastic. The diffuse opacity category probably contains most of the fluoride-related opacities. However, this group is also likely to contain some non-fluoride opacities as well and no attempt is made to differentiate these types. The modified version of the DDE index suggested that the extent of the defect should be recorded in thirds of the tooth surface area and that a limit in size of greater than 1 mm in diameter should be used to distinguish between normal and abnormal enamel.

Prevalence of enamel fluorosis

In recent years it has been noted that the level of enamel fluorosis is increasing. A study recording the level of enamel fluorosis in the Eastern Health Board in Ireland between 1993 and 1997 was conducted amongst 12-year-olds (Table 1).[33] A decrease in the percentage of 12-year-olds categorised as having no dental fluorosis and an increase in the percentage categorised as having very mild, mild or moderate fluorosis was recorded. In the Eastern Health Board the prevalence of fluorosis has increased for 8-year-olds (Table 2) and 15-year-olds from 7 to 3%, respectively, in the children's dental health survey of 1984[4] to 22 and 25% in 1993 mainly at the questionable level.[34] A study assessing the decrease in dental caries in Belgium among 12-year-old children recorded an increase in fluorosis from 5 to 30% of the subjects between 1983 and 1998.[35] Fomon et al.[36] referred to an increase in fluorosis in the US over the previous 30 years both in fluoridated and non-fluoridated communities.

There have been few studies on enamel fluorosis in primary teeth. It has been established that the prevalence of primary tooth fluorosis increases with increasing levels of water fluoride.[37,38] Dental fluorosis in the primary dentition is often described as being 'less severe' than fluorosis in the permanent dentition.[39] As the primary dentition is exfoliated, fluorosis in deciduous teeth is seen to be of little importance. However, Mann et al.[40] found that occurrence of primary tooth fluorosis was closely associated with fluorosis in the permanent dentition. Milsom et al.[41] reported that children with fluorosis of their primary second molars were 1.86 times as likely to develop fluorosis in their permanent incisors than those with no primary molar fluorosis.

Table 1 Enamel fluorosis in the Eastern Health Board.

Dean's Index (%)	1993	1997
Questionable	20	14
Very mild	2	6
Mild	1	3
Moderate	0	1

Permanent incisors of 12-year-olds.

Table 2 Enamel fluorosis in the Eastern Health Board.

Dean's Index (%)	1984	1993
Questionable	5	19
Very mild	2	2
Mild	0	1
Moderate	0	0

Permanent incisors of 8-year-olds.

Studies of primary tooth fluorosis have been conducted in certain high water fluoride areas in Africa and Europe.[42,43] The results of these studies have demonstrated universal presence of primary tooth fluorosis in these locations. The primary molars, particularly the primary second molars were most frequently and severely affected. Studies of primary tooth fluorosis in industrialized nations in Europe with levels of water fluoride at 2 ppm are less common. Harding et al.,[44] carried out a study investigating the levels of enamel fluorosis in primary teeth in 5-year-old children residing in both fluoridated and non-fluoridated communities in Ireland. The authors concluded that the prevalence of enamel fluorosis in primary teeth was significantly higher in the fluoridated group (29.4%) as compared to the non-fluoridated group (1.2%). The majority of the fluorosis was confined to the second deciduous molars as compared to the first deciduous molars.

Fluoride metabolism and enamel fluorosis

It is necessary to look at the method by which fluoride acts on enamel to gain an understanding of the way it induces enamel fluorosis. Fluorosed enamel is characterised by a retention of amelogenins in the early maturation stage of development and the formation of a more porous enamel with a subsurface hypomineralisation.[45]

Table 3 Primary teeth chronology.

	Incisors	Canines	First molars	Second molars
Calcification commences	3rd–5th month IU	5th month IU	5th month IU	6th–7th month IU
Completion of crown	Age 4–5 months	Age 9 months	Age 6 months	Age 10–12 months
Appearance in mouth	Age 6–8 months	Age 16–20 months	Age 12–16 months	Age 21–30 months

IU, in utero.

Secretory enamel is believed to be more susceptible to acute fluoride exposure. The transition/early maturation stage of enamel formation is the most susceptible to chronic fluoride ingestion above the threshold levels.

To explain the mechanism of fluorosis metabolism, a number of hypotheses exist. Many studies have been conducted to focus on the effects of fluoride on apatite nucleation and crystal growth. Fluoride has been shown to have the following effects: increase the size of apatite crystals, improve the crystallinity of apatite and to increase the driving force towards apatite nucleation and growth.[46,47] Scanning and electron micrographic studies of fluorotic enamel have revealed alterations in crystallite morphology and crystal defects.[48] Increasing evidence of late has supported the hypothesis that excess fluoride in the extracellular fluids can result in delay of the cleavage and removal of amelogenin matrix proteins during enamel maturation.[49,50] An enzyme involved in hydrolysis of amelogenins may also be inhibited by fluoride.[51] These collective studies suggest that excessive concentrations of fluoride in developing enamel partially inhibit the proteinases that split the larger molecular weight amelogenins. This results in retention of amelogenins and effects on crystal growth.[52] Inhibition at the critical stage of enamel formation could have major effects on the structural appearance of the fully formed enamel.

It is important to assess the calcification and eruption dates of primary and permanent teeth in order to identify when developing teeth are at most risk of enamel fluorosis (Tables 3 and 4).[53] Fluoride ingested during tooth development can result in changes in enamel opacity because of hypomineralisation.[54] The occurrence of enamel fluorosis is strongly associated with cumulative fluoride ingestion during enamel development but the severity of the condition depends on the dose, timing and duration of the fluoride intake.[55] Permanent incisors begin calcifying at 3–4 months and this is completed at 4–5 years. Completion of crowns of primary molars overlaps with commencement of calcification of permanent incisors at around 4 months of age.

Evans et al.[56] examined data to determine the critical time frame during which developing maxillary central incisors are most prone to fluoride challenge. The authors found that the secretory and early maturation phases of amelogenesis is the period when enamel is most vulnerable to developing fluorosis. A series of epidemiologic 'windows' or time frames of differing lengths were identified and these were used to establish the presumed start of enamel mineralisation (at birth), and ranged from 0 to 60 months later. Thus the most susceptible time for developing enamel to be influenced by changes in water fluoride concentrations was localised. The greatest risk was associated with a 4-month critical period starting at 22 months after birth. The authors concluded that fluoride exposure during the months prior to this period carry less risk than continued exposure for up to 36 months beyond this critical time. However, this finding was from the analysis of whole tooth-based assessments of fluorosis using Dean's index[21] and at that time it was generally held that fluorosis distribution on incisors was more dense incisally than cervically. Uncertainty thus existed surrounding the tooth-based estimate of susceptibility due to bias arising from the supposedly more affected incisal third.[57]

Table 4 Permanent teeth chronology.

	Central incisors		Lateral incisors		Canines		First molars	
	U	L	U	L	U	L	U	L
Calcification commences	3-4 m	3-4 m	10-12 m	3-4 m	4-5 m	4-5 m	Birth	Birth
Completion of crown	4-5 y	4-5 y	4-5 y	4-5 y	6-7 y	6-7 y	2.5-3 y	2.5-3 y
Appearance in mouth	7-8 y	6-7 y	8-9 y	7-8 y	11-12 y	9-10 y	6-7 y	6-7 y

U, upper jaw; L, lower jaw; m, months; y, years (Berkowitz[53]).

A measurement system that accounted for the differential distribution of fluorosis signs on the enamel surface and its chronological development was suggested.[57] In 1993, Evans developed the Chronological Fluorosis Assessment (CFA) Index to investigate the chronological development of enamel fluorosis.[58] Evans et al.[57] refined the estimated time for enamel fluorosis to occur. The authors indicated that drinking fluoridated water during an 8-month period, centred around 19 or 20 months of age for males and 25 or 26 months of age for females was critical in relation to the degree of fluorosis that subsequently developed on the incisal, middle and cervical thirds of maxillary central incisors. It was concluded that the critical period of susceptibility would be related to the timing of enamel secretion corresponding to any given point on the tooth crown, as apposed to mainly focussing on the incisal third. The critical period for exposure to fluoride is of about 4-months duration for each third. It is also worth noting that fluorosis may develop in teeth exposed to a fluoride challenge in periods exclusive of the critical period. The critical period is the period when risk of enamel fluorosis is at a maximum.

Risk factors for developing enamel fluorosis

A certain degree of enamel fluorosis is inevitable with water fluoridation. Dean regarded an increased prevalence of enamel fluorosis as an acceptable risk when compared to the benefits to oral health that would result from the introduction of this public health measure. However, other fluoride-containing products, such as toothpastes, have become available to the public for consumption since the time of Dean and now there is clear evidence that fluorosis is increasing in the US and worldwide. As the fluoride level in water has remained relatively stable, the increase in fluorosis is likely to be related to increased consumption of fluoride-containing products by children <6 years.[59] However, excessive intake of fluoride may result from drinking water where technical problems with dosing in smaller plants may result in fluoride levels over and above the upper limit of 1 ppm.

Fluoride toothpastes

Fluoridated toothpaste, since its introduction into the European market in the 1970s, now occupies over 95% of the toothpaste market. It has led to a marked decrease in caries in all countries.[24] EU guidelines state that fluoride toothpastes sold over the counter should contain no more than 1500 ppm.[7] Over the last 10 years it has been noted that an increasing number of infants and very young children have tended to swallow toothpaste and this is likely to be contributing to the increasing level of enamel fluorosis. This could be due to parents brushing their babies' teeth with toothpaste at too young an age (before 18 months to 2 years when baby molars appear in the mouth) or when children have not learned how to adequately rinse out their mouths and they, in turn, ingest too much toothpaste (Table 5).[53] Also, a pea-sized amount of toothpaste on the brush is more than adequate to clean young children's teeth but this amount (0.25–0.3 g) is often exceeded. The amount of fluoride ingested depends on the amount of toothpaste on the brush and the concentration of fluoride in the toothpaste.

Table 5 Flint EU Project: 8-year-olds. Age at which parents began brushing children teeth %.

Cities	*N*	<1 year	1–2 years	$2\pm$ years
Cork	100	36	47	20
Reykjavik	150	24	20	6
Oulu	202	11	60	29
Knowsley	200	78	19	1
Almada	200	2	50	48

Children over 6 years have developed a more sophisticated swallowing reflex and thus are more able to control inadvertent swallowing of fluoride toothpaste and mouthwash. Certain posterior teeth are still at critical stages of enamel development when a child is over 6 years, but the position of these molars means that fluorosis is less aesthetically objectionable. Children who begin using fluoride toothpaste under 2 years of age are at a higher risk of enamel fluorosis than those who do not use fluoride toothpaste at all or begin to use it later. Excess fluoride can be ingested if children inadvertently swallow too much toothpaste.[60] In order to assess the risk factors of dental fluorosis, Osuji et al.[61] interviewed parents about their children's first 5 years of existence, their diet and preventive caries practices in Ontario. It was concluded that those who brushed their teeth before the age of 25 months were 11 times more likely to develop fluorosis compared to those who began brushing later.

A study in Cork, Ireland[62] developed a standardised epidemiological method for collecting

information on young children using individual variables that may affect fluoride ingestion from toothpaste over 7 European countries: Ireland, UK, Finland, Greece, Iceland, Netherlands and Portugal. These variables include fluoride concentration and weight of toothpaste used, frequency of brushing and body weight of the child. The overall aim of the Biomed 2 Flint Project[62,63] was to assess the link between fluoride ingestion from toothpaste by young children and dental fluorosis. The authors concluded that 60% of the 1.5–2.5 year-olds who participated in the study swallowed between 70 and 100% of the toothpaste placed on the brush. The level of fluoride intake from all sources beyond which 'unacceptable' dental fluorosis will occur has been estimated as 0.05–0.07 mgF/kg body weight/day.[22] If it is accepted that the daily fluoride intake should not exceed this level, then the mass of fluoride ingested from toothpaste should not exceed 0.022 mg–0.036 mgF/kg body weight/day.

Fluoride supplements

Fluoride supplements are a risk factor for fluorosis in young children when used inappropriately and not conforming to appropriate dosing schedules. The use and availability of fluoride supplements in Ireland does not appear to be an issue of concern.

Before the American Dental Association (ADA) supplementation schedule, American infants (less than 6 months), who were breast fed, were often prescribed fluoride tablets containing 0.25 mg fluoride per day.[55] Mothers would sometimes finish breastfeeding and continue to give their children the fluoride supplements, unknown to the prescribing dentist. These infants, if consuming 29 oz of soy-based liquid concentrate formula prepared with 1 ppm water and a dietary supplement, could consume as much as 1.35 mg of fluoride per day. The authors noted that a daily fluoride intake in excess of 0.1 mg/kg/body weight will give rise to enamel fluorosis. Many studies have reported a clear association between supplement use by children aged <6 years and enamel fluorosis.[64–66] Pendrys and Katz[67] noted that mild-to-moderate fluorosis was strongly associated with fluoride supplementation during the first 6 years of life. Subjects who used fluoride supplements during the first 6 years of life had a 28-fold increase in the risk of fluorosis as compared to unexposed subjects.

Infant formula

Larsen et al.[68] compared the prevalence of fluorosis in primary and permanent teeth of a population of Danish children who had either been breastfed or fed on cow's milk during the first year of life with that of children from Greenland who had been fed with infant formula reconstituted with fluoridated water containing 1.1 mg/l fluoride. The Greenland children examined (exposed to fluoridated water in infancy) had a higher prevalence of fluorosis in primary teeth, whereas the Danish children (not exposed to fluoridated water until after the first year of life but then exposed to water fluoridated to 1.5 mg/l fluoride) had a higher prevalence of fluorosis of the permanent teeth. This supports the findings of Evans et al.[57] who suggested that the most critical period for developing dental fluorosis of the permanent central incisors is between 15 and 24 months for males and 21–30 months for females.

Osuji et al.[61] carried out a case control study of children living in the fluoridated community of East York, Ontario. The authors reported that prolonged use of infant formulas (13–24 months) was associated with 3.5 times the risk of fluorosis of the anterior permanent teeth, compared with less or no formula use. In this study, children who brushed their teeth with a fluoride toothpaste before the age of 25 months had 11 times the risk of fluorosis of the anterior permanent teeth. The authors estimated that early tooth brushing with a fluoride toothpaste and prolonged use of infant formula reconstituted with fluoride water were responsible for 72 and 22%, respectively, of the cases of fluorosis in their study. Overall the authors concluded that the ingestion of infant formula reconstituted with fluoridated water is only a risk factor for enamel fluorosis when the formula was consumed for a period of 13–24 months. The Food Safety Authority of Ireland has concluded that the risk of moderate dental fluorosis of the primary and permanent teeth is very low in exclusively formula-fed infants aged 0–4 months residing in areas in which the level of fluoride in water does not exceed the statutory level.

The No Observed Adverse Effect Limit (NOAEL) is defined as the highest dose of a chemical in a single study, found by experiment or observation, which causes no detectable adverse health effect.[7] The NOAEL is based on long-term studies, preferably of ingestion of drinking water. The NOAEL is 0.05 mgF/kg/body weight in the case of enamel fluorosis. Thus for children at risk of developing fluorosis (<8 years), it is accepted that the daily intake of fluoride which will not produce mild fluorosis in permanent teeth is 0.05 mgF/kg body weight/day. The lowest

observed adverse effect limit (LOAEL) is the lowest dose of a chemical in a single study that causes a detectable adverse health effect. In the context of enamel fluorosis, the LOAEL is 0.1 mgF/kg/body weight. An intake slightly above this LOAEL for an extended period of time during tooth development is likely to produce dental fluorosis. Bazalef et al.[45] concluded that dilution of infant formula with water fluoridated at 1 ppm will result in intake of fluoride >0.1 mg/kg/body weight and could result in increased prevalence of enamel fluorosis.

Risk management for enamel fluorosis

It can be seen from the above that a major risk factor in enamel fluorosis is inappropriate use of fluoride toothpaste at a young age. In the US non-compliance to an appropriate dosing schedule of fluoride tablets can lead to an increased prevalence of enamel fluorosis. The fluoride level in drinking water in Ireland should be less than 1 ppm to comply with the Drinking Water Regulations 2000. Having reviewed data from more recent studies, Heller et al.,[69] found that little decline in caries levels was observed between 0.7 and 1.2 ppm fluoride in water, while an increase in fluorosis was seen at this level. The authors suggested that a suitable trade-off between dental decay and fluorosis appears to occur at 0.7 ppm. Further work is needed to establish the effectiveness of water fluoridated at between 0.6 and 0.8 ppm. According to the Forum on Fluoridation 2002, lowering the fluoride level in drinking water to between 0.6 and 0.8 ppm will be sufficient to bring about considerable reductions in dental decay while reducing the risk of dental fluorosis.[7]

It is recommended that parents continue to reconstitute infant formula with boiled tap water.[7] The Food Safety Authority of Ireland has investigated the overall contribution to the development of fluorosis attributable to infant formula. Continued use of infant formula diluted with fluoridated water beyond 6 months of age is likely to be associated with fluorosis in permanent incisors. Bottle-feeding does not protect against infection in the same way that breast feeding does. Human breast milk of mothers living in fluoridated and non-fluoridated areas contains negligible amounts of fluoride. Increased breast feeding would lead to a significant decrease in the level of fluorosis.[7]

Children <6 years should not use fluoride mouth rinse without prior consultation with a dentist as fluorosis could occur if such mouth rinses are swallowed. Fluoride supplements can be prescribed for children at high risk of dental caries. For children aged <6 years, dentists should weigh the risk for caries without fluoride supplements, the caries prevention offered by supplements and the potential for enamel caries if considering the use of fluoride mouthrinses.[60]

In a study on risk of fluorosis from fluoride toothpaste, children brushing <2 years of age were reported to have an increased risk for prevalence or severity of fluorosis.[70] A recent study in Cork[62] Ireland found that 60% of the 1.5–2.5 year old children swallowed between 70 and 100% of the toothpaste placed on the brush. Use of fluoride toothpaste should continue due to the additive benefit from the combination of fluoridated water and toothpaste. The Forum on Fluoridation 2002 recommends that parents should be advised to use simply a toothbrush and water to brush the teeth of children <2 years of age. Parents should consult professional advice with regard to the use of fluoride toothpaste when children are perceived to be at a high risk of dental decay. Children aged between 2 and 7 years of age should be supervised when brushing and only a pea-sized amount of toothpaste should be used. The use of paediatric toothpastes with low concentrations of fluoride requires further research before they can be recommended.[7] The child should also be encouraged to spit out excess toothpaste.[60]

Conclusion

When used appropriately, fluoride is a safe and effective method of reducing dental caries. It is needed throughout life to prevent and control dental decay. To ensure continued use of fluoride toothpaste and water fluoridation, the risks associated with excessive ingestion of fluoride need to be monitored. Use of toothpaste from a young age would seem to be a greater risk for enamel fluorosis than use of infant formula diluted with water. Further research is required to establish the relative contribution of these two factors to the increased levels of enamel fluorosis.

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