Fluoride balance in infants and young children in the UK and its clinical relevance for the dental team

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VERIFIABLE CPD PAPER

IN BRIEF

- Provides an overview of the main sources of fluoride in children.
- Stresses the proportion of fluoride (F) intake from ingestion of toothpaste.
- Draws attention to the implications for oral health of the F balance in infants and young children.
- Illustrates the importance of assessing fluoride exposure at an individual and community level in the context of clinical dental practice.

This paper provides an overview of the main sources of fluoride (F) in children and discusses the importance of assessing F exposure at an individual and community level. It describes some of the methods used to assess F exposure by estimating F intake and excretion, together with the development and use of biomarkers for F and their importance. The paper focuses on what recent F research has shown in terms of significant sources of dietary F intake in UK infants and young children and the proportion of F intake that derives from F ingestion of toothpaste. This information is considered in the context of clinical dental practice and the implications of this research for oral health discussed.

INTRODUCTION

Exposure to fluoride (F) is important for oral health although evidence now suggests that the predominant caries-preventive effects of F occur through its topical rather than systemic effects.[1,2]

In the UK 12% of the population benefit from the topical and systemic effects of F in tap water, while approximately 36,000 nursery and school children receive fluoridated milk on schooldays through school milk fluoridation programmes. Salt as a vehicle for F remains primarily a mainland European approach to dietary F supplementation, while prescription of F tablets is only recommended for a targeted approach to caries prevention in high caries risk children with highly motivated and compliant parental support. Consequently, we may consider that F exposure for the majority of the UK child population is primarily topical, but evidence suggests that children receive significant amounts of F through diet and toothpaste ingestion.

Following the systematic review on water fluoridation in 2000,[3] the Medical Research Council's working group[4] recommended further research to measure F ingestion from all sources, as well as F excretion and retention in children and establish useful biomarkers of internal F dose for use in epidemiological studies of health effect. Although subsequent UK funding for F research to help inform policy and evidence-based practice has been limited, this paper presents evidence on child F exposure from UK-based research and discusses it in a clinical context.

For the purpose of this paper, the following databases were searched for articles on intake (or exposure) and excretion of fluoride: Ovid MEDLINE (in-process and other non-indexed citations and Ovid MEDLINE) for the period from 1946 to January 2013 and EMBASE from 1974 to January 2013. Other data sources of information were relevant publications by the World Health Organisation (WHO), UK Department of Health and the British Association for the Study of Community Dentistry (BASCD). The searches were limited to publications in English and those concerning children. Only UK-based articles reporting fluoride intake (or exposure) and sources of fluoride intake under customary dietary conditions were included. For research articles addressing both intake and excretion of fluoride in children, in view of their limited number, all globally published articles in English were included.

F INTAKE

The common sources of ingested F include fluoridated water, foods and drinks (including infant milk formula) prepared with fluoridated water or containing F naturally. Dietary F supplements (eg fluoridated milk), non-dietary F supplements (eg F tablets), and inadvertent ingestion of fluoridated toothpastes (or other oral health products) comprise other sources of systemic F intake.

Residence in a non-water-fluoridated community does not automatically result in low F intake, nor does residence in a fluoridated community necessarily result in a higher F intake because with increasing fashion for use of bottled waters, greater consumption of soft drinks purchased and consumed away from the home and a shift towards less tap water consumption[5] tap water F may not represent the F concentration of an individual's primary fluid consumption. A study of UK bottled waters[6] showed a mean F concentration of 0.08 mg/L (range 0.010.37 mg/L) and based on average water consumption in UK children[7] bottled water use as a main drinking water source would reduce F intake by a mean of 38% (range 26-48%) for all ages/ both genders compared with a tap water source of 1 mg F/L. In addition, food, drink or even bottled water produced in a fluoridated area may be transported to a non-fluoridated area for consumption and vice-versa.[8] This 'halo effect' has, with

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increasing globalisation, inevitably led to substantial movement of processed food and drink products across water fluoridation boundaries.

Estimation of total daily F intake is important when recommendations for F use are being considered for dental caries prevention while minimising risk of dental fluorosis. This involves being able to estimate F intake from diet and from toothpaste ingestion.

Table 1 Summary of literature on sources of total daily F intake (TDFI) for infants and young children in the UK

	Zohoori *et al.* (2006)[60]	Maguire *et al.* (2007)[18]			Zohoori *et al.* (2012)[59]	
Age (years)	1-3	6-7			6-7	
Water F concentration (mg/L)	0.81	0.08	0.47	0.82*	0.3	1.06**
Number of children	7	18	8	5	21	12
TDFI mg/day mg/kg bw/day	0.71 0.05	0.736 0.031	0.883 0.038	1.043 0.047	0.945 0.038	1.707 0.076
F ingested from diet mg/day mg/kg bw/day Percentage of TDFI	0.26 0.02 37	0.188 0.008 43	0.349 0.016 65	0.565 0.025 53	0.341 0.014 44	0.578 0.026 41
F ingested from toothbrushing mg/day mg/kg bw/day Percentage of TDFI	0.45 0.03 63	0.549 0.023 57	0.534 0.022 35	0.478 0.022 47	0.606 0.024 56	1.130 0.050 59

*Artificially fluoridated water; **naturally fluoridated water

Table 2 Summary of main sources of daily dietary F intake presented as mean (µg/day) and as percent of total daily dietary intake in six to seven-year-old UK children (from Zohoori *et al.* 2006)[60]

Sources of dietary F intake	Mean daily dietary F intake by F concentration of tap water (n = no. of children)					
	0.7 mgF/L (n = 6)		0.3–<0.7 mgF/L (n = 9)		<0.3 mgF/L (n = 18)	
	µg/day	%	µg/day	%	µg/day	%
All foods	209	41	139	45	126	67
Rice, pasta, boiled veg.	117	16	54	17	16	9
Fruit and raw veg.	15	2	19	8	16	7
Bread	12	5	20	6	20	12
Confectionery, cakes, sweets	11	2	10	3	15	9
Meat and meat products	5	2	6	2	17	9
Breakfast cereals	2	1	5	1	6	3
Soup and gravy	2	<1	<1	<1	<1	<1
Fish and sea-foods	<1	<1	2	<1	7	2
Others	45	12	22	6	28	15
All drinks	382	59	210	55	62	32
Bottled water	<1	<1	<1	<1	<1	<1
Squash and cordials	214	31	95	24	10	7
Tap water	83	11	81	24	7	4
Tea	29	3	0^a	0^a	9	3
Carbonated soft drinks	28	6	12	4	23	11
Coffee	20	4	2	<1	0^*	0^*
Non-carbonated soft drinks	4	2	4	1	8	4
Milk	3	1	2	<1	2	1
Hot chocolate	<1	<1	15	4	2	1
All food and drinks	591	100	349	100	188	100

*Not consumed

F intake from diet

Two main methods are used to estimate F intake through diet:

1. A full three-day dietary history, including portion size and fluid volumes, which is collected, usually by a nutritionist, and analysed using a previously populated database containing the F concentrations of all commonly consumed foods and drinks, producing an estimated mean daily F intake for that individual
2. A duplicate plate method in which an exact copy of an individual's daily food and drink intake is collected and weighed. Solid foods are then homogenised together in a laboratory and a F concentration for the sample recorded using a F-ion selective electrode.[9] A similar process is undertaken for drinks so that a total daily F intake from diet as a whole can be calculated for the individual.

When data from F intake studies of young UK children (Table 1) are considered, it can be seen that UK children aged six to seven years ingest between 0.188 mg and 0.578 mg F per day through their diet. This represents between 0.008 and 0.026 mg/kg bw/day depending on local water F concentration. Diet contributes 37% of total daily F intake (TDFI) in one-year-olds and between 43% and 65% of TDFI intake in 6-7-year-olds depending on drinking water F concentration. This is consistent with similar studies undertaken in other countries and confirms that solid foods contribute a significant proportion of dietary fluoride intake.[10] Main dietary F sources for UK six- to seven-year-olds vary according to whether they receive a fluoridated tap water supply (Table 2). For those receiving >0.7 mgF/L water, squashes and cordials, carbonated soft drinks and tap water together account for 48% of dietary F intake while in <0.3 mgF/L areas, these drinks contribute only 22%. In contrast, for those children living in a <0.3 mgF/L, solid foods (particularly bread) provide the main dietary F source and contribute 67% of the daily dietary fluoride intake, while in a higher water F areas, rice, pasta and boiled vegetables are the main solid food contributors.

With regard to infant feeding, breastfeeding, with exclusive breastfeeding for the first four to six months, is recommended in most European countries including the UK, although for a number of reasons in many cases this may be impractical. As a result 55% of newborns are fed with infant formula and this proportion increases to 93% at four months and almost 100% at six months.[11] In addition, as infants are weaned from breastfeeding they now receive the bulk of their nutrition from infant formula before moving on to cow's milk, which is now not recommended as a substitute for breast milk or infant milk formula until the age of one year.[12] For infants and very young children there is evidence that the choice of feeding method can have a profound impact on their dietary F intake. Dental fluorosis has been reported to be more prevalent in the permanent teeth of children who had been fed powdered infant milk formula diluted with the local fluoridated water supply during the first four months of life than in those who had been breastfed.[13,14] Recent studies[15,16] have shown a greater impact of the F in water used to reconstitute infant powdered formula on F intake of formula-fed infants than the F content of the powdered formula itself. However, there are trends towards greater use of convenient ready-to-feed infant products and a study of UK ready-to feed infant foods[17] has shown some of these to contain a relatively high F concentration (eg ready-to-feed meat-based weaning foods: 1.20 µgF/g). More research in this area is needed since body F burden (body retention) is key to determining risk but is technically highly challenging and time-consuming in infants and young children who are not toilet-trained.

F intake from toothbrushing

Recording toothpaste ingestion is also challenging but a valid and reproducible method is available that involves measuring the amount of toothpaste dispensed onto a toothbrush and then collecting the expectorated paste and saliva produced during brushing.[18] By analysing the weighed, expectorated saliva and paste for F and subtracting this value from the amount of F dispensed within the toothpaste, an estimate of inadvertent ingestion of F through toothbrushing can be made.

On average, toothbrushing with a fluoridated toothpaste accounted for 63% of TDFI in one-year-olds while for six to seven-year-olds in the UK the proportion was less, but still substantial, at between 35% and 59%, and up to 90% at an individual level (Table 1). The international literature also shows wide variations in toothpaste's contribution to TDFI from 22% in six-year-olds in Iowa[19] to 69% four to five-year-old Columbian children.[20] In a recent study, conducted after the Department of Health/BASCD guidelines[21] were published, F usage from fluoridated toothpaste by four to six-year-old children in a fluoridated area of the UK was investigated[22] and showed that the mean weight of toothpaste dispensed was 0.67 g with no gender difference, while boys swallowed more toothpaste (0.0174 mg/kg bw/day or 44% of dispensed paste/brushing) than girls (0.0165 mg/kg bw/day; 38%). The latter study also revealed that the majority of children used, on average, more than double the Department of Health/BASCD[21] recommended pea-sized amount (0.25 g). F intake per toothbrushing session was significantly influenced by the weight of toothpaste dispensed, its F concentration and the child's age.

Total daily fluoride intake (TDFI)

Although there is currently no international consensus on the maximum safe daily dose of F, a total F intake of 0.05-0.07 mg/kg bw/day in children younger than 12 years of age is regarded as optimum for dental health benefits.[23] It is also generally agreed that intakes of F should not exceed 0.1 mg/kg bw/day during infancy, to minimise the risk of dental fluorosis.[23,24]

As Table 1 shows, the mean TDFI for six to seven-year-olds living in UK areas where the mean water F concentration ranged from 0.08 to 1.06 mgF/L was between 0.031 and 0.076 mg/kg bw/day, while in one-year-olds living in a 0.8 mg F/L area TDFI was estimated to be 0.05 mg/kg bw/day. However, all these values represent means and the variation in TDFI at an individual level is high. This places some children potentially at risk of developing dental fluorosis if a higher F intake is sustained over a critical period of tooth development and, conversely, at the lower end of the scale provides inadequate F exposure to help prevent caries.

F EXCRETION

Faeces, urine, and sweat represent the three different routes for the elimination of F from the body. Approximately 10% of our total daily F intake is not absorbed systemically and is consequently excreted through faeces.[25,26] Urine is the most important metabolic pathway for removal of absorbed F from the body. Sweat is a quantitatively minor route of F excretion as its F concentrations are very low (1-3 µmole/L), similar to those in plasma[27] and under most conditions daily volumes are very low.

Urinary F excretion

The kidneys are the principal route for elimination of F that is absorbed systemically from the gastrointestinal tract (GIT) but not taken up by bone/other mineralised tissue, hair or nail. Under conditions of constant F intake approximately 50% of daily absorbed F becomes associated with calcified tissues within 24 hours and the rest is excreted from the body.[28] However, urinary F excretion is dependent on urinary flow rate and F concentration of the urine. Urinary flow rate varies through the day depending on fluid intake, while urinary F concentration at any point in time is related to timing of F ingestion. Therefore, the best estimate of daily urinary F excretion (DUFE) is via a 24-hour urine sample and recommended by the WHO for monitoring community fluoridation schemes,[29] with collection over a shorter time period if a 24-hour urine is not practical. Several F studies assessing salt fluoridation schemes have collected urine samples over 8 or 14-16 hours.[30,31] In addition, although a spot (an untimed 'single-void') urine sample is not a valid basis for extrapolation to 24-hour data,[32] the mean of two or three daily spot urine samples may provide a guide to DUFE[33] and the F/creatinine ratio of a morning spot urine sample may be used to estimate mean DUFE in children who are not-toilet trained.[34]

Faecal F excretion

Under normal dietary intake conditions and absence of foods/drinks containing high amounts of divalent or trivalent cations such as calcium, aluminium and magnesium, which can form complexes with F in the GIT, approximately 80-90% of ingested F is absorbed from the GIT.[35] Faecal F excretion in children is generally assumed to be 10% of total daily F intake. However, this assumption is based on just two studies with small numbers of very young children. A mean faecal F excretion of 11% of F intake, ranging from 2% to 15%, was reported for five breast-fed infants, whereas the corresponding mean (range) was 2% (0.5% - 5.0%) for five formula-fed infants.[25] In another study Ekstrand *et al.*[36] reported faecal F excretion from 2% to 34% of intake for formula-fed infants aged 5-11 months receiving a F supplement (0.25 mg/day) with a feed. There has been no research on faecal F excretion in UK children.

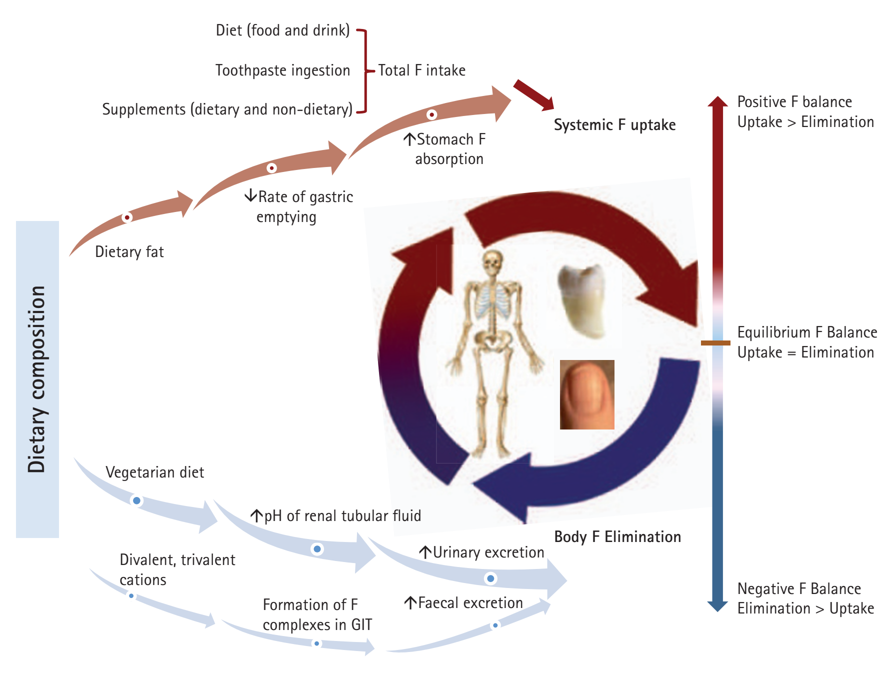

Fig. 1 Dietary factors affecting fluoride balance

Table 3 Summary of literature on total daily F intake (TDFI), daily urinary F excretion (DUFE) and fractional urinary F excretion (FUFE) by age group and country

Country	F exposure		Age (years)	No. of children	TDFI (mg/d)	DUFE (mg/d)	FUFE* (%)
	Source	Concentration (mg/L) or (mg/kg)					
Chile[55]	Water	0.5-0.6	3-5	20	1.02	0.358	35.5
Colombia[56]	Table salt	180-220	4-5	96	1.55	0.414	33
Germany[57]	Salt & F tablets	0.25-1.0	3-6	11	0.931	0.476	51.5
Iran[58]	Water	0.30-0.39	4	78	0.428	0.339	80
Sweden[25]	Water	1.0	0.19-0.54 0.15-0.31	5 Breast-fed 4 Formula-fed	0.011 0.927	0.030 0.359	359 39
UK[34]	Water	0.81	1-3	7	0.71	0.33	48
UK[18]	Water	0.08 0.47 0.82	6-7	18 8 5	0.736 0.883 1.043	0.277 0.333 0.420	44 40 32
UK[59]	Water	0.30 1.06	6-7	21 12	0.945 1.707	0.297 0.393	30 40
USA[42]	Water	Optimal	3-4	10	0.33	0.28**	NR***
USA[26]	Water	1.0	0.19-0.89	4 Formula-fed	0.190	0.144	78

*DUFE as a % of TDFI; **including faeces; ***not reported

F BALANCE, BODY BURDEN, AND BIOMARKERS

As Figure 1 illustrates, F balance represents the difference between systemic F uptake and body elimination. When total F intake is greater than total F excretion, the F balance is positive and F is retained in the body. Conversely, when F excretion is greater than F intake, the balance is negative and F is lost from the body. Several factors are known to influence the degree of F absorption and excretion, and consequently its retention and balance.

Dietary composition and the form of ingested F can affect F absorption. The absorption of sodium fluoride (NaF), a soluble F compound, added to water is almost 100%. However, the degree of absorption is reduced when F is taken with foods and drinks (such as milk) containing substantial amounts of divalent or trivalent cations due to formation of insoluble complexes that increase faecal F excretion.[37] The extent of F absorption from disodium monofluorophosphate (NaMFP) and NaF in dentifrices has been suggested to be similar. However, since F in NaMFP needs to first be released by enzymatic reaction of intestinal phosphatase this can result in lower and delayed peak plasma F concentrations. In the stomach, F is mainly absorbed as hydrogen fluoride (HF) and therefore gastric F absorption is inversely associated with stomach pH. A high dietary fat intake may increase F absorption from the stomach by reducing the rate of gastric emptying.[27]

Although the amount of F excreted in urine is directly influenced by the amount of F intake, the daily urinary F excretion (DUFE) can be affected by several other factors. After ionic F enters the renal tubules, between 10-90% of the ion is reabsorbed and returned to the systemic circulation.[38] Urinary flow rate and the pH of renal tubular fluid affect the amount of F reabsorption. With acidic tubular fluid, more ionic F is converted to HF, which is diffusible across the tubular epithelium. Conversely, with an alkaline renal tubular fluid, most F exists in ionic form and remains within the tubule to be excreted.[39] Dietary composition has been shown to influence urinary pH. A meat-based diet promotes a more acidic urine, whereas a vegetarian diet renders urinary pH relatively alkaline.[40] Other factors that could influence acid-base status and urinary pH include certain drugs, high altitude, some respiratory diseases, metabolic diseases such as diabetes mellitus and levels of physical activity.[39]

Studies on the F balance in children are limited due to the difficulty of collecting 24-hour urine and faeces samples from children and the available F balance data are conflicting. Ekstrand *et al.*[25] found that breast-fed infants, with daily F intakes ranging from 0.005 to 0.019 mg, were in negative F balance. In contrast, they found a positive F balance for formula-fed infants who received daily F intakes ranging from 0.891 to 1.012 mg, a finding in agreement with Ericsson *et al.*[41] who also reported a negative F balance in breast-fed infants. In another study, in three to four-year-olds residing in a fluoridated community in California F excretion in urine and faeces almost equalled F intake, and net F retention was minimal with an average F balance of +0.05 mg/day.[42] Due to the practical difficulties in sampling and analysis of 24-hour faecal samples and its assumed minor role in F metabolism, most F retention and balance studies have focused their balance calculations on urinary F excretion rather than total F excretion.

Determining F body burden is important when assessing optimal F exposure for oral health benefit and conversely, dental fluorosis risk. However, collection of dietary and toothpaste ingestion data at a community level is time consuming, costly and requires a high level of expertise and therefore the development and use of biomarkers for F has been useful. This topic is extensively and comprehensively described elsewhere,[43] but it is useful to summarise the widely accepted classification for biomarkers for F as it helps focus on the need for their future development as a means of improving assessment techniques for monitoring and evaluating individual- and community-based prevention. Contemporary biomarkers for F are those that assess present or very recent exposure to F; for example, blood, bone surface, saliva, milk, sweat and urine, while chronic or sub-chronic exposure to F can be assessed by recent (eg nail and hair) and historical (eg dentine and bone) biomarkers for F body burden. Urine is the current preference for estimating acute (very recent) exposure while F in nail shows some promise as a biomarker for chronic exposure and dentine in exfoliated primary teeth has been used to assess F body burden.

DUFE has been suggested as an index or biomarker for F intake. In order to clarify the ability of DUFE to predict TDFI and, therefore, the risk of development of dental fluorosis in children, a recent study examined published data on concurrent measurements of TDFI and DUFE for 212 children and suggested that children under seven years of age, on average, excrete 45% of their ingested F in the urine.[44] However, studies of TDFI and DUFE have shown a wide variation in fractional urinary F excretion (FUFE), that is, the proportion of F intake that is excreted, (FUFE = [DUFE/TDFI] × 100), ranging from 32% for six to seven-year-olds to 359% for breast-fed infants as summarised in Table 3. The wide range can be explained by differences in dietary composition as well as dietary and oral hygiene habits of children studied, since these factors affect F absorption from gastrointestinal tract and urinary excretion of F, as discussed previously. Since growth rate and body size (skeletal mass) can also influence F retention, it is important to adjust the data on F intake, excretion and retention based on body weight.

CLINICAL RELEVANCE OF F EXPOSURE IN CHILDREN

Chronic excessive F intake from birth to four years of age is considered to be a key contributor to dental fluorosis development in permanent maxillary central incisors.[45,46] Furthermore, Levy *et al.*[47] have suggested that the six to nine-month-old period is most important in dental fluorosis aetiology for the primary dentition, while Warren *et al.*[48] determined that the critical period for development of fluorosis in late developing primary teeth is from four months *in utero* until 11 months of age.

Burt *et al.*[49] cautioned against too precise definitions of age of greatest risk of fluorosis because there is increasing evidence that developing tooth germs may be vulnerable to F over a longer period, including their initiation period.[19,50]

It is important to recognise that there are a number of sources of fluorides (dietary and non-dietary) to which infants and young children may be systemically exposed during their dentally formative years. The dental impact of these sources is confounded by a number of factors relating to F metabolism and consequently F balance, described in previous sections. As the Iowa fluoride study[51] has shown, the true risk factor for dental fluorosis is total F intake, which, in turn, is dependent on feeding patterns, F concentration of infant milk formula and weaning foods/drinks in infants, as well as the impact of dentifrice usage and toothbrushing habits in infants, toddlers and young children. Information on F exposure throughout the whole period of aesthetically important tooth development is critical so that contributors to dental fluorosis risk during particularly vulnerable periods can be highlighted and parents advised accordingly.

Despite the best infant feeding practice being breastfeeding, some infants may be fed exclusively on formula milk for the first six months of age. Recent guidelines from the American Dental Association in 2011 advised the parents of infants consuming reconstituted infant formula to continue using optimally fluoridated drinking water in feed preparation while being mindful of the potential risks of development of dental fluorosis.[52] The guidelines also advise parents resident in a fluoridated area who are concerned about potential dental fluorosis risk to reconstitute powdered formula milk with F-free or low-F water or use ready-to-feed infant milk products. A similar approach has been adopted in the UK[53] with advice to parents with concerns about dental fluorosis risk, which includes the use of suitable bottled waters for reconstituting powdered infant formula. The NHS Choices website[12] provides further advice with regard to infant feeding and bottled waters stating the importance of checking the label and ensuring the sodium concentration is less than 200 mg/L and the sulphate content is not higher than 250 mg/L. It also reminds parents that bottled water is not usually sterile so that if it is being used to make up an infant feed it still needs to be boiled, like tap water, before the feed is prepared.

With regard to toothpaste use and toothbrushing, recent revisions in child toothpaste formulations and associated toothbrushing habits together with the introduction of the toolkit for prevention[21] and Scottish Dental Clinical Effectiveness Programme's guidelines for the prevention and management of decay in children[54] have impacted children's exposure to F. These evidence-based guidelines are designed to increase and maintain the topical F concentration in the mouth for a more prolonged period through the higher toothpaste F concentration and 'spit, don't rinse' advice. However, to minimise the effect of F dose (dose = concentration × amount) on fluorosis risk from the inevitable inadvertent ingestion of toothpaste in children, it has become increasingly crucial that parents and children comply with manufacturers' instructions and parents are pro-actively advised to read the instructions carefully and limit the amount of toothpaste dispensed according to the child's age. Dispensing paste across the brush, rather than down the brush's long axis can help with this instruction, but toothpaste manufacturers could also help by improving the dispensing system for toothpastes.

CONCLUSION

Although dental fluorosis is not considered an adverse health effect, but a side-effect of chronic excessive F exposure, the rational use of F requires careful monitoring since the dental fluorosis risk to caries reduction benefit 'dose gap' is relatively narrow. Health professionals need to be fully aware of recent and historical F histories of their young patients and families in order to assess their main sources of F exposure and other factors that may impact on body F burden. In this way they can ensure that their advice for parents and carers will be fully informed and appropriate for maximum prevention of dental caries while minimising risk of dental fluorosis in their child patients.

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