

## **National Fluoride Information Centre (NFIC)**

### **Infant Formula Feed, Water Fluoridation and Risk of Dental Fluorosis.**

*March 2007*

#### **Introduction**

This issue has been debated in a number of countries and a definitive statement of risk is not yet available in the UK. There is, however, sufficient information to allow interim conclusions on the degree of risk. The cause of concern is that infants fed formula milk which has been reconstituted using optimally fluoridated water are likely to ingest each day an amount of fluoride, relative to their weight, which could potentially cause mild or moderate dental fluorosis. This concern is largely based on theoretical considerations rather than actual outcome.

One of the most authoritative statements regarding the optimal intake of fluoride was made by the American Academy of Pediatrics (1986) which suggested the total daily intake of fluoride for optimal dental benefits should be 0.05 to 0.07 mgF/kg body weight (b.w.) and no more than 0.1 mg/kg b.w./day to avoid the risk of dental fluorosis. These figures have been endorsed in the UK by the Department of Health (1991), in the report by COMA on dietary reference values and in the European Union by the European Food Safety Authority (2006). Concern about the potential risk of dental fluorosis from infant formula feeds reconstituted with fluoridated water was included in the above reports and in authoritative reports in Australia (NHMRC, 1999) and Ireland (Government of Ireland, 2002).

#### **Estimates of fluoride intake in infancy**

Before weaning at about six months of age, an infant's nutrition comes from breast milk, infant formula feed or a combination of the two. Cow's milk is not recommended for infants. Formula feed can be either 'ready to feed' or as a powder to be reconstituted with water: the latter is more popular in the UK. Breast milk contains a very low concentration of fluoride (about 0.02 mg/litre) and 'ready to feed' formula in the USA contains about 0.2 mg F/litre (Johnson and Bawden, 1987; McKnight-Hanes *et al.*, 1988; Fomon and Ekstrand, 1999; Fomon *et al.*, 2000). Infants would consume low or very low amounts of fluoride from these feeds – about 0.001 mg F/kg b.w./day from breast milk and about 0.03 mg F/kg b.w./day from ready to feed formula (Fomon and Ekstrand, 1999; Fomon *et al.*, 2000).

Historically, powdered infant formula milk was manufactured using the public water supply, which meant powdered formulae made in fluoridated areas contained high concentrations of fluoride. When this was observed, manufacturers changed their methods to use low-fluoride water. This occurred soon after 1978 in the USA, for example, so powdered formulae now contain relatively low concentrations of fluoride.

Today's concern stems from when these powdered formulae are reconstituted using fluoridated water. The following extracts from publications illustrate these concerns over the past 20 years.

In Canada, Lewis and Limeback (1996), estimated fluoride intake could be up to 0.09 mg/kg b.w./day in formula-fed infants, adding that:

*For the formula-fed infants and all other age groups using fluoridated water, the estimates of actual intake greatly exceed the recommended intakes.*

In Australia, Silva and Reynolds (1996) estimated fluoride intake from infant formula feeds. They concluded:

*When formula are reconstituted with water containing the optimal 1.0 ppm F [1.0 mg F/litre] they all provide a daily fluoride intake of above the suggested threshold for fluorosis with intakes up to two to three times the recommended upper limit of 0.07 mg F/kg body mass/day.*

A few years later, the Australian authoritative NHMRC (1999) estimated the fluoride intake in infants fed powdered formula reconstituted with fluoridated water. Their estimate of fluoride intake was high: 0.16 to 0.24 mg/kg b.w./day at three and six months; 0.11 to 0.17 mg/kg b.w./day at nine months. They concluded:

*We can see that formula-fed infants of one year of age and younger living in a fluoridated area exceed the recommended daily intake of not more than 0.1 mg/kg/day fluoride.*

Similarly, Fomon and Ekstrand (1999) and Fomon *et al.* (2000) estimated that infants fed powdered formula reconstituted with fluoridated water would ingest about 0.16 mg/kg b.w./day at birth to two months, about 0.15 mg/kg b.w./day from two to four months and about 0.12 mg/kg b.w./day after four months. Fomon and Ekstrand (1999) recommended:

*To limit fluoride intake to amounts <100 ug/kg/day, it is necessary to avoid use of fluoridated water (1 mg of fluoride per litre) as a diluent for powdered infant formulas (except when such formulas are used as a supplement for breast-fed infants) and as a diluent for concentrated liquid formulas that are to be fed to infants younger than two months of age.*

In Ireland, Anderson *et al.* (2004), estimated fluoride intake in infants consuming powdered formula reconstituted with optimally fluoridated water. They concluded that:

*The average daily intake of fluoride from infant formula reconstituted with fluoridated tap water over the first 4 months of life was estimated to be in the range 0.106-0.170 mg/kg b.w./day, depending on body weight.*

The average figure was 0.13 mg/kg b.w./day which is slightly below the estimates from North America and Australia. Of interest in Anderson's study was they used data on the fluoride concentration in infant formulae from the UK (Vlachou *et al.* 1992).

Thus, reports from several areas of the world have given estimates of fluoride intake from infant formula feed, reconstituted with optimally fluoridated water, which are substantially above the figure of 0.1 mg/kg b.w./day thought to be the threshold for dental fluorosis development.

It should be noted that two studies in the USA some 20 years ago (Johnson and Bawden, 1987; McKnight-Hanes *et al.*, 1988) reported that fluoride concentrations in soy-based formula feeds were higher than other powdered feeds. This was, to some extent, confirmed by Silva and Reynolds (1996) in Australia, although the results were more variable.

### **Studies which have measured fluoride intake in infants.**

Ophaug *et al.* (1980) reported a study into fluoride intake in six-month-old infants in four regions of the USA. In three of the regions, public water supplies contained over 0.65 mg F/litre. They concluded:

*Assuming a body weight of 8.1 kg for the average six-month-old infant, the fluoride intake expressed on a body weight basis ranges from 0.026 to 0.067 mg/kg body weight. Thus, the total daily fluoride intake calculated in this study is not in excess of the levels of 0.05 to 0.07 mg/kg body weight which are generally regarded as optimum and, in some instances may be slightly less.*

More recently in the USA, Levy *et al.* (2001) recorded fluoride intakes in infants and children living in Iowa, where 73% of the water was fluoridated. To quote:

*Mean intake per unit body weight (bw) was about 0.075 mg F/kg bw through three months of age, 0.06 mg F/kg bw at six and nine months, 0.035 mg F/kg bw at 12 and 16 months, and 0.043 mg F/kg bw from 20-36 months.*

The authors point out that some foods, such as ready-to-feed and beverages, were excluded from these figures. The degree of under-recording is difficult to estimate, but is probably small since fluoride from water (to reconstitute formula) and toothpaste was included.

In a further report on these same children, Levy *et al.* (2002) reported the total daily fluoride intake (including reconstituted formula feed) was between 0.05 and 0.06 mg/kg b.w. at four time-points between six weeks and 12 months of age. When describing their group of subjects, they comment that 'the study cohort as a whole had quite low levels of breast-feeding after 6 weeks of age'.

Studying a slightly older age group of 11 to 13 months, in a fluoridated community in New Zealand, Chowdhury *et al.* (1990) reported fluoride intake from foods and drinks was, on average, 0.028 mg/kg b.w./day; when fluoride from toothpaste was included, intake rose to 0.033 mg/kg b.w./day. The authors provide data on the fluoride intake of the three infants consuming cow's-milk-based formula and two infants consuming soy-based formula: their total daily fluoride intake (including from toothpaste) was between 0.03 and 0.06 mg/kg b.w.

Thus, there have been only a few studies of measured fluoride intake in infants and young children. They indicate that measured fluoride intake in groups of infants and children are substantially lower than the estimates given in the previous section.

These studies, though, included all infants, breast-fed and bottle-fed. Lastly, it should be noted that about 65% of fluoride in reconstituted powdered milk formula is absorbed into the blood stream (Spak *et al.*, 1982). Thus, the amount of fluoride which is available to the body is only about two-thirds of that ingested.

### **Epidemiological studies which have related consumption of infant formula feed to the occurrence of dental fluorosis.**

There are about eight studies which have examined the relationship between consumption of infant formula feed and the subsequent occurrence of dental fluorosis in primary and permanent teeth. These have been undertaken in Nordic countries, North America and Australia.

Two reports by Forsman investigated dental caries and dental fluorosis in Swedish children who had been either breast-fed or formula-fed and who lived in low fluoride areas (Forsman and Ericsson, 1974) or high fluoride areas (Forsman, 1974). Children in the low fluoride areas (<0.2 mg F/litre) did not have dental fluorosis in their permanent teeth regardless of the method of feeding.

The second report (Forsman, 1974) described the prevalence and severity of dental fluorosis in people in communities in Sweden which had received high and very high concentrations of fluoride in drinking water, and also analysed the effect of infant feeding practices on the occurrence of dental fluorosis. The communities were placed in three groups (about 10, 5 and 1 mg F/litre) according to drinking water supply. Severe dental fluorosis was prevalent in the 10 and 5 mg F/litre communities. Regarding infant feeding, the author concluded that:

*Duration of breastfeeding influenced the degree of fluorosis in areas up to about 5 ppm [5mg F/litre] in both the primary and secondary dentitions; in areas with about 10 ppm F only the primary dentition was influenced, while the permanent teeth in these areas showed severe fluorosis even with long duration of breastfeeding.*

In other words, breast-feeding provided some protection from dental fluorosis development in the communities with relatively lower fluoride concentrations in drinking water. No statistical analysis was reported.

Three years later, Forsman (1977) reported a study of the occurrence and severity of dental fluorosis in communities in Sweden receiving different concentrations of fluoride in drinking water. The influence of several factors, in addition to water fluoride concentration were studied, including whether the children had been breast-fed or with water-diluted powdered formula. In the community Eskilstuna, which received drinking water containing 1.2 mg F/litre, prevalence and severity of dental fluorosis was higher in permanent incisors of the formula-fed children. To quote:

*[T]here was a markedly greater frequency and severity of fluorosis in the children in Eskilstuna who had received water-diluted formula powder from an early age (0-5 months) compared with those who had been breastfed at least six months and/or received milk-diluted gruel.*

However, the severity of dental fluorosis, recorded using Dean's index, was 'very mild' (1) or 'mild' (2); to quote 'The fluorosis registered as Grade 2 had not in most cases been observed by the patients or their acquaintances'. The author estimated the daily fluoride intake of these children living in Eskilstuna when they were six months and two and a half months old had been about 0.005mg/kg b.w. for breast-fed infants and 0.22 to 0.24 mg/kg b.w. for the formula-fed infants – these were estimates not measurements.

Walton and Messer (1981) reported a study of the relationship between infant feeding practice and the occurrence of dental fluorosis in children living in optimally fluoridated areas of Minnesota, USA. No fluorosis was observed in primary teeth, but a relation between infant feeding practice and fluorosis severity was recorded for permanent teeth: to quote, regarding permanent teeth:

*A ranking of the levels of fluorosis in terms of infant feeding shows that children breast-fed for three months or more showed the lowest mean fluorosis index (0.08); those breast-fed for less than three months and those bottle-fed for less than 12 months showed similar indices (0.14 and 0.16, respectively), and those bottle-fed for more than 12 months showed the highest mean index (0.27).*

There are two comments made by the authors to note:

*Among all dentitions showing fluorosis, none showed any cosmetic disfiguration which was of aesthetic concern to the child, parent or dental staff. In no instance did the index for any tooth or dentition exceed 1.50 and the majority of affected dentitions were either questionable (score 0.25) or very mild (score 0.50). On the scale used, only scores between 2.5 and 4 were considered un-aesthetic [Moller, 1965].*

*Since the initiation of the present study, several manufacturers of commercial infant foods and formulas have instituted changes in the manufacturing process to significantly lower the fluoride content of these preparations.*

Osuji *et al.* (1988) conducted a case-control study among schoolchildren living in a fluoridated community in Ontario, Canada. The occurrence of dental fluorosis was related to the exposure of fluoride in infancy. The authors expressed the risk of dental fluorosis in terms of the 'odds ratio'. Compared with breast-fed children, the odds of formula-fed children having dental fluorosis was 3.5. The odds were higher (5.6) in those who were given formula feed for over 12 months compared with those who had been fed formula for less than 12 months.

Three points are worth considering. First, the risk of dental fluorosis from early use of fluoride toothpaste was much greater than from consumption of formula feed.

Second, the severity of dental fluorosis was low in all children. Out of the total of 633 children, 551 (87%) had no fluorosis. Of the 82 'cases', 63 (77%) had score one fluorosis (very mild) on the Thylstrup-Fejerskov index; 14 (17%) had a score of two; four a score of three and one child a score of four. Scores of three or over might be considered likely to be of aesthetic concern.

Third, the authors point out that manufacturers had recently lowered the fluoride content of their formula feed and the children in this study would not have benefited from this reduction.

Larsen *et al.* (1988) compared the occurrence of dental fluorosis in children living in an optimally fluoridated community in Greenland (1.1 mg F/litre drinking water) and who had received powdered formula reconstituted with tap water, with children in a community in Denmark where public water contained 1.4 to 1.6 mg F/litre and who had been fed with cow's milk (<0.02 mg F/litre) in infancy. The prevalence of dental fluorosis was higher in primary teeth of children living in Greenland, and highest in the second molar teeth. The severity of dental fluorosis in these teeth was low – the vast majority being grade one on the Thylstrup-Fejerskov index. The severity of dental fluorosis in the permanent dentition was higher in the children in Denmark, probably due to the higher fluoride concentration in drinking water.

Pendrys and Katz (1989) reported a case-control study involving 850 children in non-fluoridated Massachusetts and Connecticut. While mild to moderate dental fluorosis was strongly associated with ingestion of fluoride dietary supplements during the first six years of life (odds ratio = 4.0), positive associations with use of infant formula (odds ratio = 1.7) and fluoride dentrifice (odds ratio = 2.9) during the first year of life were statistically not significant. The authors comment that the results for infant formula were 'suggestive' and:

Are, therefore, not inconsistent with the decision to reduce the fluoride concentration in infant formula.

The Australian Research Centre for Population Oral Health (ARCPOH) has carried out several epidemiological studies of infant feeding practice and dental fluorosis. Recently, ARCPOH (2006) published a policy document '*The use of fluorides in Australia: guidelines*'. It contained the following:

*Historically, infant formula powder was manufactured with a varying but relatively high fluoride content. When reconstituted with fluoridated water and consumed by infants, there was a potential for exposure to relatively high levels of fluoride in relation to body weight. Infant formula now has very low amounts of fluoride. While the workshop did not review information about fluoride content of infant formulas, evidence from Australian population-based studies reveal no association between consumption of infant formula and levels of dental fluorosis.*

From the above epidemiological investigations, it can be concluded that several studies reported the prevalence of dental fluorosis was higher in children who had been fed powdered formula reconstituted using water containing optimal or higher concentrations of fluoride compared with children who were breast-fed.

Two studies (Walton and Messer; Osuji *et al.*) reported that continuing use of formula feed after 12 months was a particular risk. Some caution is needed in interpreting some studies since only three (Osuji *et al.*; Pendrys and Katz; ARCPOH) employed multivariate analysis. In studies in optimally fluoridated communities, the severity of dental fluorosis in formula-fed children was generally mild or very mild and seldom likely to be of aesthetic concern.

### **Authoritative statements**

#### ***The European Union***

The panel did not establish an UL [upper limit] for infants. Breast-fed infants have very low fluoride intakes from human milk (2-40 mg/day) and are not at risk of developing enamel fluorosis even when given fluoride supplements of 0.25 mg/day.

The Panel notes that the Scientific Committee on Food has recommended a maximum fluoride level of 0.6-0.7 mg/L [litre] in infant formula and follow on formula, equivalent to an intake of about 0.1 mg/kg body weight per day in infants during the first six months of life (body weight 5 kg). For powdered formula, this maximum will be exceeded if water containing more than 0.7 mg/L is used for its preparation. (European Food Safety Authority, 2006).

### ***American Dental Association***

While more research is needed before definitive recommendations can be made on fluoride intake by bottle-fed infants, the American Dental Association issues this guidance because we know that parents and other caregivers are understandably cautious about what is best for their children. Parents, caregivers and health professionals who are concerned have some simple and effective ways to reduce fluoride intake from infant formula:

- (a) feeding infants breast milk, widely acknowledged as the most complete form of nutrition for infants;
  - (b) for infants who get most of their nutrition from formula during the first 12 months, choosing ready-to-feed formula over formula mixed with fluoridated water to help ensure that infants do not exceed the optimal amount of fluoride intake;
  - (c) if liquid or powdered concentrate infant formulas is the primary source of nutrition, it can be mixed with water that is fluoride free or contains low levels of fluoride to decrease the risk of fluorosis, including water that is labelled purified, demineralised, deionised, distilled or reverse osmosis filtered water (many grocery stores sell these types of drinking water for less than \$1 per gallon);
  - (d) the occasional use of water containing optimal levels of fluoride should not appreciably increase a child's risk for fluorosis.
- (American Dental Association, 2006).

### ***Australia***

Infant formula nowadays is safe for consumption by infants when reconstituted using fluoridated water. (ARCPOH, 2006).

### ***Ireland***

It is recommended that parents continue to reconstitute infant formula with boiled tap water until the results of ongoing research are available. (Government of Ireland, 2002).

The Expert Body emphasised that there is no health risk to any member of society including babies from consumption of fluoride in breast milk, infant formula, water or food at levels of fluoride observed in Ireland. It expressed concern on the confusion regarding potential health risks associated with the use of fluoridated water to reconstitute baby formula and states these concerns are unfounded. Advice to parents remains unchanged. The use of fluoridated tap water in Ireland to make up baby formula is considered safe.

Based on the conclusion of a Food Safety Authority of Ireland risk assessment published in 2002, the Expert Body accepts that the risk of moderate dental fluorosis of the permanent dentition is very low in formula-fed infants aged 0-4 months residing in areas where fluoride levels do not exceed the statutory limit. (Irish Expert Body on Fluorides and Health, 2007).

## **Conclusion**

Estimates of consumption of fluoride by infants fed exclusively on powdered infant formula reconstituted with optimally fluoridated water indicate that they exceed the presumed and widely accepted threshold level of 0.1 mg F/kg body weight/day.

These estimates are consistent and appear in many publications from several countries over the past 30 years.

There have been few measurements of fluoride intake by infants fed powdered formula reconstituted with optimally fluoridated water. These indicate actual intake may be much lower than the theoretical estimates. While most children in these studies will have been formula-fed, average intakes for the groups include both breast- and formula-fed infants.

About eight epidemiological studies have been reported which have related infant feeding practice to the prevalence and severity of dental fluorosis. They have generally compared children who either were breast-fed or fed formula reconstituted with fluoridated water, or a combination of both of these. Dental fluorosis was more prevalent in children fed formula than in breast-fed children. The teeth affected were the late-forming primary teeth (second molars) and early-forming permanent teeth (incisors and first molars). The severity of the dental fluorosis was mild or very mild and unlikely to be of aesthetic concern in nearly all cases.

Many of the studies were carried out before manufacturers reduced the fluoride concentration in their powdered infant formula.

Some of the studies indicated the importance of other sources of fluoride in infancy, such as early use of fluoride toothpaste and fluoride dietary supplements. Few studies controlled for potential confounding factors making interpretation difficult in some studies.

In conclusion, there is a recognisable theoretical cause for concern, although a limited number of studies indicate these high fluoride intakes in infancy may not occur in reality. Epidemiological studies indicate the occurrence of mild and very mild dental fluorosis in some children fed powdered formula reconstituted with optimally fluoridated water in infancy.

The quality of the evidence is not high and further research is required now that powdered formula contains little fluoride and the early use of excessive amounts of high fluoride toothpaste in young children is discouraged. It is noted that none of the studies identified were from the UK.

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