Dietary fluoride intake for fully formula-fed infants in New Zealand: impact of formula and water fluoride

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Abstract

Objective: A survey of the fluoride content of infant and toddler formulae available on the New Zealand market was conducted. Results were used to estimate the dietary fluoride intake for a fully formula-fed infant.
Methods: Infant and toddler formulae were prepared according to manufacturers' instructions with fluoride-free water and analyzed for fluoride by a modification of the microdiffusion method of Taves. A proportion of samples were reanalyzed after reconstitution with water at fluoride concentrations of 0.7 and 1.0 mg/L. A stochastic model was used to estimate dietary fluoride intake.
Results: The mean fluoride content of prepared infant formulae was 0.069 mg/L. When formulae were prepared with water of differing fluoride concentrations, the fluoride concentration was found to be a simple linear function of water fluoride concentration. Estimates of dietary fluoride intake for infants consuming formulae prepared with fluoride-free water were well below the upper level of intake (UL) for New Zealand and Australia (0.7 mg/day). At water fluoride concentrations of 0.7 and 1.0 mg/L the UL would be exceeded 30 and 93 percent of the time, respectively.
Conclusions: The fluoride content of water used to reconstitute infant formulae has a greater impact on fluoride intake of fully formula-fed infants than the fluoride content of the powdered infant formulae. Infants fully formula-fed on formulae prepared with optimally fluoridated water (0.7-1.0 mg/L) have a high probability of exceeding the UL for fluoride and are at increased risk of dental fluorosis.

Introduction

Infants are dependent on a very narrow range of foods to provide their complete nutrition. The diversity of food intake in the adult tends to protect against imbalances; this protective diversity is not present during the early period of life. Infants also consume more energy per unit body weight than adults. With infants' diets based on comparatively high consumption of a limited range of foods it is particularly important that these foods contain adequate and safe levels of nutrients. For these reasons infant formula products are the most highly regulated and controlled of all commercially available foods.

Infant formula products can be classified in a number of ways. They are primarily classified by the life stage that they are mainly formulated for. The main categories are:

- Starter, for feeding from birth.
- Follow-on, for feeding from 6 months of age.
- Toddler, for feeding from age 1 to 3 years.

It should be noted that toddler formulae are not infant formula products, as defined by the Australia New Zealand Food Standards Code. Infant formulae include a diverse array of products, including milk protein-based (either whey or casein dominant and either bovine or goat's milk) and soy-based products. The milk-based products include some with partially hydrolyzed protein for infants with allergic problems, lactose-free products and products with added long chain polyunsaturated fatty acids.

Fluoride is a naturally occurring element found in water, air, soil and food (1). Fluoride is added to some drinking-water supplies in New Zealand and overseas as a protective measure against tooth decay (2-4). The recommended

fluoride content for drinking-water in New Zealand is in the range of 0.7-1.0 mg/L (5). Fluoride prevents tooth decay by strengthening the tooth surface and inhibiting growth of cariogenic bacteria. It also assists in repairing the early stages of tooth decay (6).

The Nutrient Reference Values for Australia and New Zealand recommend an adequate intake (AI) for infants 0-6 months of 0.01 mg/day and an upper level of intake (UL) of 0.7 mg/day (7). Periodic assessments of fluoride intake from all sources are necessary as fluoride intakes above optimal levels can have negative health outcomes (2-4), whereas low fluoride intake may result in failure to achieve the health benefits of fluoride intake.

Materials and methods

Infant and toddler formula products

As the infant formula products are nationally distributed, all infant formula products were purchased from supermarkets in Christchurch, New Zealand during December 2007. Infant formulae containers were shaken to mix contents. All formulae were made up according to manufacturers' instructions using deionized water. Four formulae with the highest fluoride concentrations were also prepared with water containing 0.7 mg F/L and water containing 1.0 mg F/L.

Of the 32 products analyzed in the current study, 19 were infant formula, 8 follow-on formula and 5 toddler formula. Of the 32 products, 19 products were manufactured in New Zealand, although one soy-based product manufactured in New Zealand was blended from imported ingredients. The remaining 13 products were manufactured in Ireland (8) or France (5).

Fluoride analytical methods

All samples were analyzed for total fluoride by the Fluoride Laboratory, University of Iowa College of Dentistry, Iowa City, IA, USA. Samples were analyzed using a modification (8) of the microdiffusion method of Taves (9). The limit of detection for the method is 0.02 mg/L.

A certified reference material, SRM 2671a, fluoride in freeze-dried urine (The National Institute of Standards and Technology, Gaithersberg, MD, USA) with a designated fluoride content of 0.55 ($\pm$0.03) mg F/kg, was analyzed to demonstrate method accuracy at the low fluoride levels encountered in infant formula products.

Estimation of dietary intake of fluoride

Dietary intake is calculated from the product of the amount of food consumed and the concentration of the component of interest in the food.

While children older than 6 months will sometimes be exclusively formula-fed, weaning usually occurs between 4 and 6 months of age (10). Although exclusive formula feeding of infants up to the age of 6 months is plausible, infants older than 6 months are unlikely to receive their total nutrition from consumption of infant formula only and the analysis of fluoride intake by exclusively formula-fed infants was restricted to infants 6 months of age or less.

Dietary intake estimates were made using a stochastic Monte Carlo simulation model, to allow an assessment of the potential variability in fluoride intakes due to consumption of infant formula. The model was built and run using @Risk software (Palisades Corporation, Ithaca, NY, USA).

Formula consumption information was derived using an approach similar to that of Vannoort and Cressey (11). This approach assumes that infants are receiving their estimated energy requirements (EERs) and that infant formulae are the sole source of nutrition.

EERs for infants are made up of two components:

- Total energy expenditure (TEE), including energy required for basal metabolism, thermoregulation, physical activity and the synthetic cost of growth (12).
- Energy deposition (ED) or the energy cost of growth (ECG). This is, in turn, dependent on the weight gain or weight velocity (g/day) and the energy cost of tissue deposition (kJ/g) (12).

Butte published combined TEE estimates and also separate estimates for breast-fed and formula-fed infants (12). TEE for formula-fed infants can be calculated as:

$$\mathrm{TEE\,(kJ/day)} = 346 \times \mathrm{weight\,(kg)} - 122$$

Data from Kuczmarski *et al.* (13) was used to develop distributions for body weight at 1, 2, 3, 4, 5, and 6 months for males and females. ED was calculated from weight gain for a 1-month period (g/day) distributions from a WHO evaluation (14), combined with energy cost of tissue deposition figures (kJ/g) for 1-, 2-, 3-, 4-, 5-, and 6-month-old males and females (12).

The declared energy density and measured fluoride concentration of infant formulae included in the current survey were modeled as continuous distribution using the Bestfit function of @Risk. The distributions were truncated so that energy density and fluoride values could not fall outside the range observed in the current study.

At each model iteration the Monte Carlo simulation model:

- assigned a gender to the infant, based on a binomial distribution with number of trials equal to one and the probability equal to the proportion of males among live births in 2006 (15);
- assigned an age (in months) using a uniform discrete distribution to give ages of 1, 2, 3, 4, 5, or 6 months;

Table 1 Fluoride Content of Infant and Toddler Formula Products Available in New Zealand

Product type	Mean fluoride concentration (mg/L)	Range of fluoride concentrations (mg/L)
Infant formula	0.069	0.024-0.20
Follow-on formula	0.065	0.044-0.16
Toddler formula	0.081	0.039-0.13

- assigned a body weight and growth rate from the distributions for that age-gender group;
- calculated an EER based on the assigned gender, age, body weight, and growth rate;
- assigned a value from the distribution for the energy density of the infant formula and calculated the volume of infant formula fed per day; and
- assigned a value from the distribution for the fluoride concentration of the infant formula and calculated the estimated daily fluoride intake for the iteration.

The model was run for 20,000 iterations.

Results

Analytical quality assurance

The Fluoride Laboratory of the University of Iowa College of Dentistry is an internationally regarded laboratory for fluoride analysis and was the provider of analyses for the US Department of Agriculture (USDA) National Fluoride Database (16).

Analysis of a freeze-dried urine sample with a certified fluoride content of 0.55 ± 0.03 mg/kg (SRM 2671a, National Institute of Standards and Technology, Gaithersburg, MD, USA) gave analytical results in the range 0.54-0.55 mg/kg. The coefficient of variation (relative standard deviation), determined from duplicate analyses, was 2.6 percent.

Concentrations of fluoride in infant and toddler formula products

A summary of the fluoride content of prepared infant and toddler formula products included in this survey is given in Table 1.

A previous New Zealand survey carried out in 1997 found a mean fluoride content for infant formulae of 0.15 mg/L and for follow-on formulae of 0.098 mg/L (11). Statistical analysis confirmed that the fluoride content of infant formulae available in New Zealand has decreased significantly since 1997.

Fluoride content of formulae from the current survey are generally similar to or lower than those reported for equivalent studies internationally. Table 2 summarizes results from relevant comparative studies. Wherever possible data have been restricted to powdered infant formulae reconstituted with fluoride-free water according to manufacturers' instructions.

Impact of water fluoride on formula fluoride concentration

The four infant formula products with the highest fluoride concentrations, when reconstituted with deionized water (0.14, 0.15, 0.16, and 0.20 mg/L), were reanalyzed after reconstitution with water at 0.7 and 1.0 mg/L fluoride concentrations. Results are summarized graphically in Figure 1.

Table 2 Summary of Results from International Studies on the Fluoride Content of Infant Formula Products

Country	Year	Number of samples	Fluoride concentration, Mean (range), mg/L	Reference
New Zealand (current study)	2008	19	0.069 (0.024-0.20)	
New Zealand	1997	18	0.15 (0.03-0.37)	(11)
Australia	1988		0.24 (0.03-0.53)	(17)
Brazil	2001	10	0.14 (0.01-0.75)	(18)
Brazil	2004	4	0.16 (0.08-0.21)	(19)
Brazil	2006	7	0.15 (0.04-0.33)	(20)
Japan	2004	10	0.07 (0.04-0.12)	(21)
Turkey	2001	5	0.10 (0.01-0.19)	(22)
USA	1985	29	0.12 (0.03-0.24)	(23)
USA	1988	3	0.07 (0.06-0.10)	(24)
USA	1992-1993	17	0.14 (0.05-0.28)	(8)

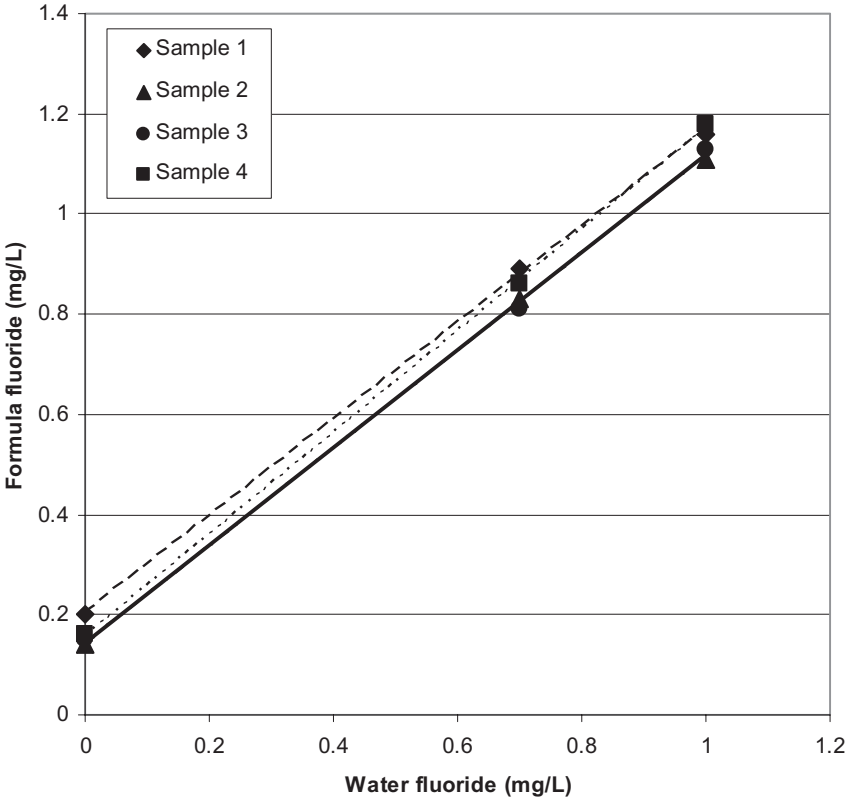

Figure 1 Comparison of infant formula fluoride content at three make-up water fluoride concentrations.

Regression lines for formula fluoride against water fluoride are all highly linearly correlated ($R^2 > 0.999$) with slopes close to unity (0.96-1.02).

Dietary intake of fluoride – fully formula-fed infants (0-6 months); formulae prepared with fluoride-free water

Figure 2 shows the results of the Monte Carlo simulation to estimate the dietary fluoride intake for infants 0-6 months consuming only infant formula prepared with fluoride-free water. The mean estimated dietary fluoride intake was 0.059 mg/day (5th-95th percentiles 0.019-0.129 mg/day). When expressed on a body weight basis the mean estimated dietary fluoride intake is 0.010 mg/kg body weight/day (5th-95th percentiles 0.003-0.023).

The results of the current simulation modeling suggest that dietary fluoride intakes for fully formula-fed infants will fall within the range of the AI and UL (0.01-0.7 mg/day) on greater than 99 percent of occasions. Of the 20,000 iterations none simulated an intake of greater than 0.7 mg/day and less than 0.3 percent of iterations were less than 0.01 mg/day.

The formula feeding rates used in the calculations carried out to produce Figure 2 represent mean fluid intakes ranging from approximately 180 mL/kg body weight/day (5th-95th percentiles 119-260 mL/kg) for a 1-month-old infant to 130 mL/kg body weight/day (5th-95th percentiles 90-175 mg/kg) for a 6-month-old infant. Infants 0-6 months of age may typically consume 140-160 mL/kg body weight/day, with some consuming as much as 180 mL/kg body weight/day.

Dietary intake of fluoride – impact of water fluoride concentration

The simple linear relationship between water fluoride and formula fluoride was used to recalculate all formula fluoride concentrations on the basis of water fluoride concentrations of 0.7 and 1.0 mg/L. The mean slope of the regression lines for the four analyzed infant formulae (0.982) was used for this recalculation. Recalculated fluoride concentrations were then fitted to lognormal distribution for use as inputs to the simulation model. Cumulative probability plots for three water fluoride concentration (0.0, 0.7, and 1.0 mg/L) are shown in Figure 3.

Mean estimated fluoride intakes are 0.059, 0.66, and 0.91 mg/day at 0.0, 0.7, and 1.0 mg/L water fluoride concentrations, respectively. While exceeding the UL is clearly an improbable event for infants consuming infant formula prepared with fluoride-free water, for formula prepared with water containing 0.7 mg/L fluoride simulation modeling suggests that the UL would be exceeded approximately

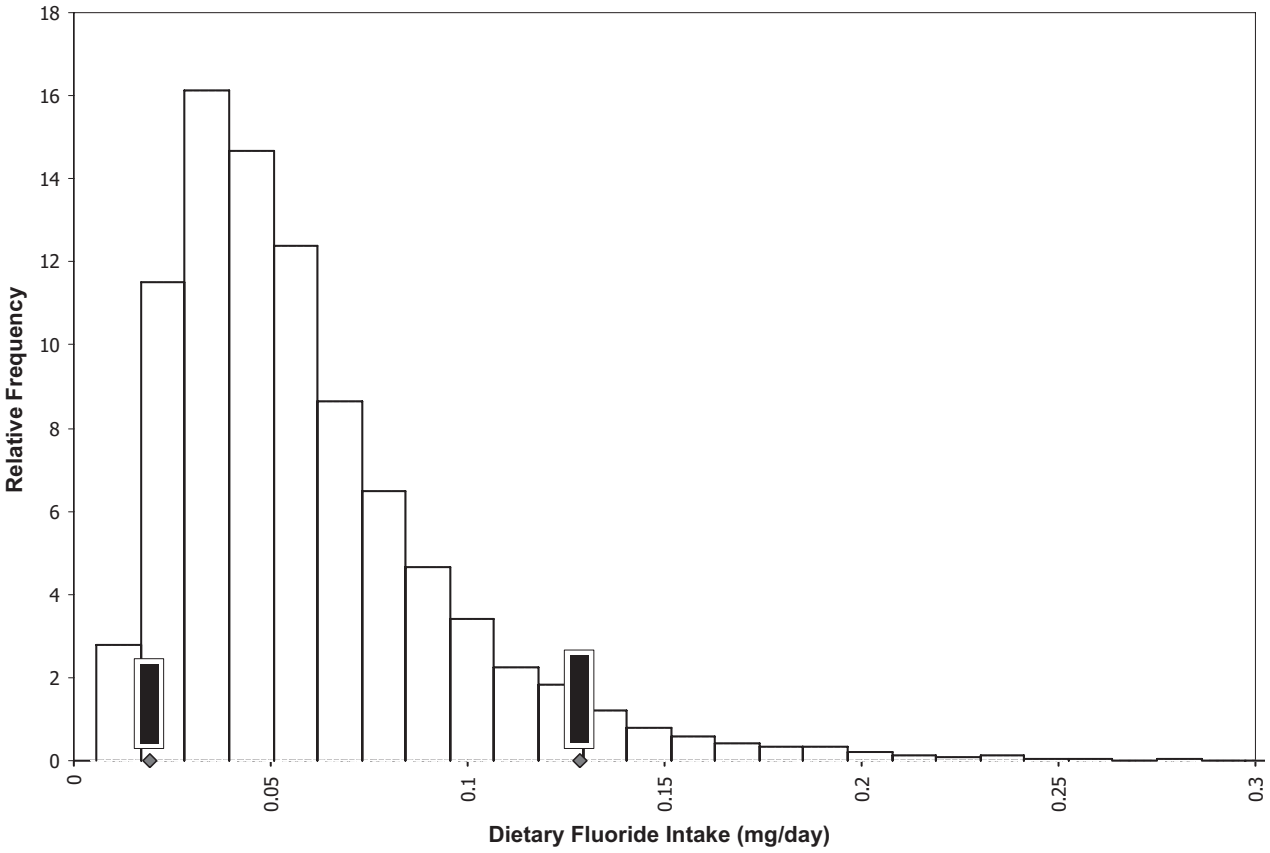

Figure 2 Dietary fluoride intake for fully formula-fed infants (1-6 months). Formula prepared with fluoride-free water.

30 percent of the time, while at a water fluoride concentration of 1.0 mg/L the UL would be exceeded 93 percent of the time.

Discussion

The fluoride content of infant formulae available in New Zealand in 2007 has decreased significantly since the last survey, conducted in 1997. This is consistent with anecdotal evidence from infant formula manufacturers, that they were making efforts to reduce the fluoride content of their products.

The fluoride content of infant formula products appears to be remarkably consistent between countries and across time. This is perhaps not surprising as infant formula products are a heavily internationalized food, with products from large manufacturers available in a wide range of countries. Given this observation, the approximate halving of the fluoride concentration of infant formula products available on the New Zealand market should be viewed as a significant development. The fluoride content of infant formulae available in New Zealand appears to be at the lower end of the range observed internationally.

When prepared with water of differing fluoride concentrations, the fluoride concentration in the formula is related to the fluoride concentration in the water in a simple linear manner. While this appears self-evident, there is little evidence that this relationship has been demonstrated previously. Consequently, in regions with fluoridated water supplies, the fluoride intake of fully formula-fed infants will be largely due to fluoride from water used for reconstitution, rather than fluoride from the infant formula product.

Consumption of formulae prepared with unfluoridated water results in estimated dietary intake of fluoride well below the UL for infants (0.7 mg/day), with a mean intake of 0.059 mg/day. As a point of comparison Chowdhury *et al.* (25) estimated that the mean daily intake of fluoride of a breastfed New Zealand infant would be 0.003 mg/day. However, according to the intake model used in this study, formula prepared with water fluoridated at 0.7 mg/L would result in a mean fluoride intake for fully formula-fed infants in the first 6 months of life of 0.66 mg/day, with a 30 percent probability of exceeding the UL. At a water fluoride concentration of 1.0 mg/L, there is a near certainty of fully formula-fed infants exceeding the UL.

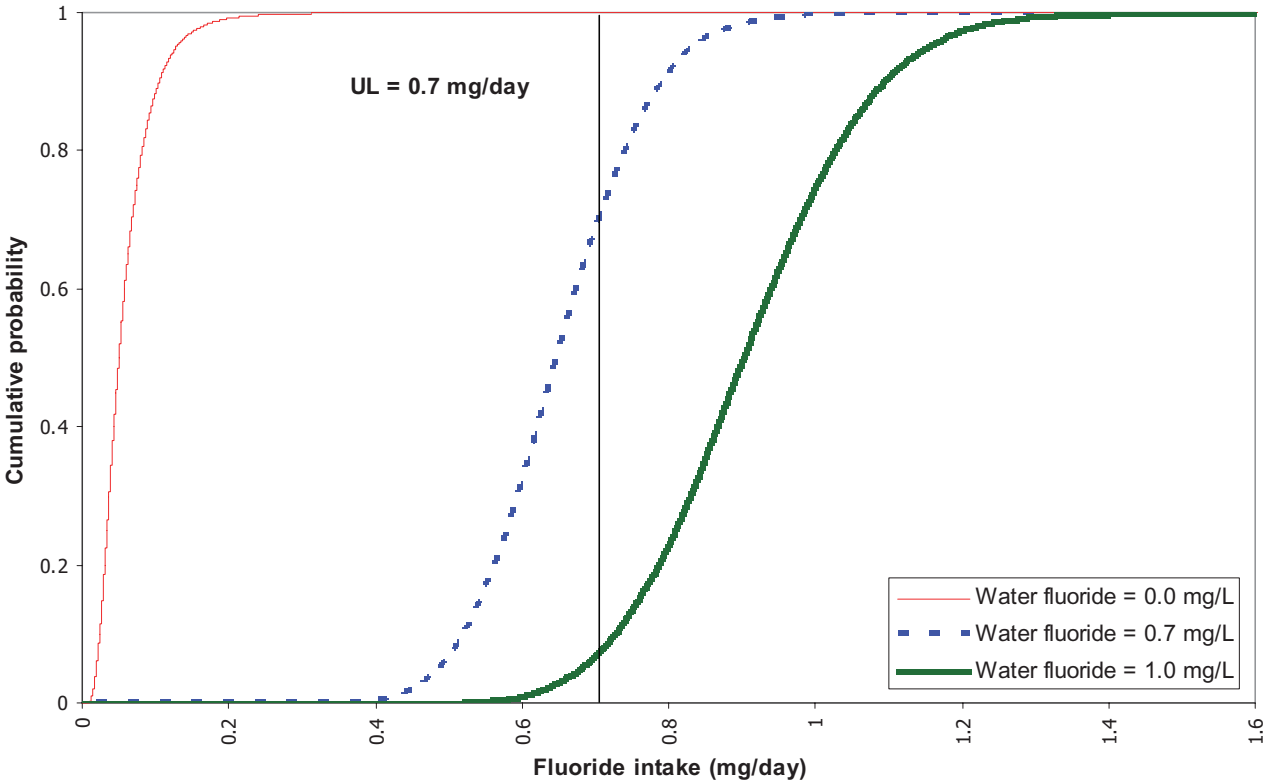

Figure 3 Cumulative probability of fluoride intake for fully formula-fed infants at varying water fluoride concentrations.

Anderson *et al.* (26) also used a stochastic approach to estimate the dietary intake of formula-fed infants to fluoride in Ireland. Based on an average prepared formula fluoride concentration of 0.84 mg/L, they estimated the dietary intake during the first 4 months of life to be 0.132 mg/kg body weight/day (2nd-98th percentiles 0.106-0.170). This is analogous to the scenario of formula prepared with water at 0.7 mg/L fluoride in our model. This scenario resulted in an average formula fluoride content of 0.76 mg/L and an average fluoride intake for the first 6 months of life of 0.11 mg/kg body weight/day (5th-95th percentiles 0.08-0.16). Despite significant differences in the modeling approach used, the two studies give near identical estimates when differences in formula fluoride are accounted for. These similarities reflect the dominant contribution of water fluoride concentration to dietary fluoride intake for exclusively formula-fed infants.

Levy *et al.* (27) estimated fluoride intakes for 192 children at the ages of 6 weeks, 3 months, 6 months, and 9 months, based on diet diaries. Fluoride intake from formula consumption decreased from a mean of 0.43 mg/day (range 0-1.24 mg/day) at 6 weeks to 0.32 mg/day (range 0-1.07 mg/day) at 9 months. Given that the fluoride content of the waters used to prepare the formulae ranged from 0.02 to 1.00 mg/L, these results are not inconsistent with the results of the current study.

Ophaug *et al.* (28) used a "market basket" approach to estimate the dietary intake of fluoride by 6-month-old infants. Market baskets from cities with water supplies containing greater than 0.7 mg fluoride per liter gave an average dietary intake of 0.42 mg/day, whereas market baskets from cities with water supplies containing <0.3 mg fluoride per liter gave an average dietary intake of 0.23 mg/day. The approach of Ophaug *et al.* (1985) differed from the current approach in considering a diverse diet, rather than infant formula alone. An earlier study by the same authors produced similar results (29), with average dietary intakes of 0.35 and 0.54 mg fluoride per day for 6-month-old infants from areas where water supplies contained low and high levels of fluoride, respectively.

The results of the current study suggest that infants fully formula-fed on formula prepared with optimally fluoridated water will be at increased risk of dental fluorosis. There is still considerable uncertainty about the key exposure period to fluoride resulting in fluorosis of permanent dentition (26,30), but it appears likely that elevated fluoride intakes during the first 6 months of life may cause fluorosis in deciduous teeth, without impacting on permanent teeth (26,30). There is also good evidence to suggest that, although the rates of dental fluorosis are higher in regions with fluoridated water supplies, the fluorosis observed is almost universally "mild" or "very mild" (30).

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