

Assessing a Potential Risk Factor for Enamel Fluorosis: A Preliminary Evaluation of Fluoride Content in Infant Formulas

Chakwan Siew, Sheila Strock, Helen Ristic, Peter Kang, Hwai-Nan Chou, Jung-Wei Chen, Julie Frantsve-Hawley and Daniel M. Meyer
J Am Dent Assoc 2009;140;1228-1236

The following resources related to this article are available online at jada.ada.org (this information is current as of March 28, 2010):

Updated information and services including high-resolution figures, can be found in the online version of this article at:

<http://jada.ada.org/cgi/content/full/140/10/1228>

Information about obtaining **reprints** of this article or about permission to reproduce this article in whole or in part can be found at:

<http://www.ada.org/prof/resources/pubs/jada/permissions.asp>

Assessing a potential risk factor for enamel fluorosis

A preliminary evaluation of fluoride content in infant formulas

Chakwan Siew, PhD; Sheila Strock, DMD, MPH; Helen Ristic, PhD; Peter Kang, PhD; Hwai-Nan Chou, MS; Jung-Wei Chen, DDS, MS, PhD; Julie Frantsve-Hawley, RDH, PhD; Daniel M. Meyer, DDS

A November 2006 report by the National Research Council¹ cited studies that raised the possibility that infants could receive a greater-than-optimal amount of fluoride by ingesting liquid or powdered concentrate formula that has been reconstituted with water containing fluoride at a time when their developing teeth may be susceptible to enamel fluorosis. In response to this report, the American Dental Association (ADA)² issued interim guidance that advised parents and caregivers to consult with their pediatrician or physician and identified ways to reduce fluoride intake from infant formula. At the same time, the ADA recognized the need for additional research to provide the basis for more definitive recommendations.

This article describes a laboratory study undertaken by the ADA Foundation Research Institute to determine the fluoride concentrations in com-

ABSTRACT

Background. The authors conducted a study to determine concentrations of fluoride in infant formulas, and to estimate fluoride intake in infants consuming predominantly formula. The authors compared estimated fluoride ingestion with the tolerable upper limit and adequate intake level for fluoride recommended by the Institute of Medicine (IOM).

Methods. The authors analyzed fluoride concentrations of powdered and liquid formula concentrates and ready-to-feed formulas. They estimated the total fluoride ingested by infants by considering the fluoride content measured in both the infant formula and various concentrations of fluoridated water. They based consumption volumes on published recommendations. The authors compared estimates for fluoride ingestion with the upper tolerable limit and adequate intake level, which they calculated by using published infant growth charts.

Results. Fluoride concentrations of the different formulas were low and, if reconstituted with low-fluoride water, would not result in ingestion of fluoride at levels exceeding the IOM's upper tolerable limit. Some infants aged between birth and 6 months who consume powdered and liquid concentrate formulas reconstituted with water containing 1.0 part per million fluoride likely will exceed the upper tolerable limit of fluoride.

Conclusions. When powdered or liquid concentrate infant formulas are the primary source of nutrition, some infants are likely to exceed the recommended fluoride upper limit if the formula is reconstituted with water containing 1.0 ppm fluoride. On the other hand, when the fluoride concentration in water used to reconstitute infant formulas is below 0.4 ppm, it is likely that infants between 6 and 12 months of age will be exposed to fluoride at levels below IOM's recommended adequate intake level.

Key Words. Dental caries; dental fluorosis; water consumption; fluoridation; fluoride; infant care; bottle feeding.

JADA 2009;140(10):1228-1236.



When this article was written, Dr. Siew was the senior director, Research and Laboratories, Division of Science, American Dental Association, Chicago. He now is retired.

Dr. Strock is the assistant director of scientific information, Division of Science, American Dental Association, Chicago.

Dr. Ristic is the director of scientific information, Division of Science, American Dental Association, 211 E. Chicago Ave., Chicago, Ill. 60611, e-mail "ristich@ada.org". Address reprint requests to Dr. Ristic.

Dr. Kang is a research associate, Research and Laboratories, Division of Science, American Dental Association, Chicago.

Mr. Chou is the manager, Chemistry, Department of Research and Laboratories, Division of Science, American Dental Association, Chicago.

Dr. Chen is an associate professor, Pediatric Dentistry, School of Dentistry, Loma Linda University, Calif.

Dr. Frantsve-Hawley is the director, Research Institute and Center for Evidence-Based Dentistry, Division of Science, American Dental Association, Chicago.

Dr. Meyer is the senior vice-president, Science/Professional Affairs, American Dental Association, Chicago.

mercially available infant formulas. The study also was aimed at estimating the levels of fluoride exposure in infants whose primary source of nutrition is infant formula reconstituted with water containing from 0.0 to 1.0 parts per million fluoride.

CARIES PREVENTION AND DENTAL FLUOROSIS

Exposure to systemic fluoride during pre-eruptive tooth development, and to topical fluoride post-eruption, reduces the risk of dental caries.³⁻⁵ Cariostasis results from the uptake of systemic fluoride by enamel crystallites during pre-eruptive tooth development, as well as the uptake of topical fluoride through repetitive demineralization and remineralization cycles in the oral cavity after tooth eruption. Fluoride uptake allows for the formation of fluorohydroxyapatite, which is less susceptible to acid attack than is hydroxyapatite, which is found in normal tooth enamel.⁶⁻¹⁰

Although use of fluoride has been important in the prevention and control of dental caries, it also introduces the risk of development of enamel fluorosis. Fluoride ingested during tooth development can lead to structural changes in enamel that result in dental fluorosis.^{1,6,11-13} Dental fluorosis is characterized by increased hypomineralization or porosity of the subsurface enamel, causing the enamel to appear opaque. The opaqueness can range from barely discernible fine white lines to an entirely chalky-appearing tooth surface. The very mild and mild forms of enamel fluorosis appear as chalklike, lacy markings across the enamel surface that are not readily apparent to the affected person or the casual observer. In the moderate form of fluorosis, more than 50 percent of the enamel surface is opaque white. With severe fluorosis, the enamel becomes pitted and brittle and may develop areas of brown staining.¹¹⁻¹⁵

The risk of developing dental fluorosis is increased early in life if total fluoride intake exceeds the recommended upper tolerable limit.^{1,6,12,16-21} Results of clinical studies suggest that the critical period for development of fluorosis is during the postsecretory or early maturation phase of tooth development.^{19,21,22} Because teeth develop at different times, a child is potentially at risk of developing fluorosis of the permanent incisors through systemic exposure to fluoride from birth to age 3 or 4 years for early-erupting teeth and to age 7 or 8 years for late-erupting teeth.^{16,18-21,23-25}

On the basis of the cariostatic effect of fluoride, the Institute of Medicine (IOM),¹⁶ Washington, established the adequate intake level, which is the level of fluoride intake expected to reduce the occurrence of dental caries maximally in a population without causing unwanted side effects, including moderate dental fluorosis. For infants from birth to 6 months of age, the IOM set the adequate intake level at the level of fluoride found in mother's milk (0.01 milligrams per day). For infants aged from 7 to 12 months, the IOM established an adequate intake level of 0.05 mg per kilogram per day. Because the milder forms of enamel fluorosis are considered a cosmetic effect, the IOM selected moderate enamel fluorosis as the critical adverse effect for susceptible age groups (infants, toddlers and children). The IOM identified a fluoride intake of 0.10 mg/kg/day as the lowest-observed-adverse-effect level (LOAEL) for moderate enamel fluorosis in children from birth through the age of 8 years, the age at which there is no additional risk of developing fluorosis of the anterior teeth. The IOM derived the upper tolerable intake limit from the LOAEL of 0.10 mg/kg/day and an uncertainty factor of one. Uncertainty factors are used in risk assessment when extrapolating study results to the entire population. The IOM¹⁶ selected an uncertainty factor of one because

- the relationship between fluoride intake and enamel fluorosis is based on results from studies of humans;
- enamel fluorosis is considered a cosmetic effect rather than an adverse functional effect.

Fluoride exposure. Researchers working with the Centers for Disease Control and Prevention (CDC),²⁶ Atlanta, reported an increase of 9 percentage points in the prevalence of very mild or greater fluorosis among children and adolescents aged 6 through 19 years between the mid-1980s and the early 2000s. They compared data from the National Institute of Dental Research 1986-1987 survey of school children with data they collected from 1999 through 2002 and found that the prevalence of very mild or greater fluorosis rose from 23 to 32 percent, with most of the fluorosis being very mild or mild. Infants and children can be exposed to fluoride in water from

ABBREVIATION KEY. ADA: American Dental Association. CDC: Centers for Disease Control and Prevention. IOM: Institute of Medicine. LOAEL: Lowest-observed-adverse-effect level.

sources beyond the home or school, such as child care settings,^{17,27} as well as from beverages, foods, toothpastes and other dental products. These multiple exposure sources may contribute to the increased prevalence of dental fluorosis in the United States.^{22,27-29}

Although results of the CDC's National Immunization Survey showed that rates for breastfeeding initiation and duration increased for children born in 2004 compared with those born in 2000,³⁰ the major dietary source of fluoride for many infants shortly after birth is infant formula and the water used to reconstitute it.^{20,30,31} The prevalence of breastfeeding during the early postpartum period (defined as the in-hospital period before discharge), at 6 months postpartum and at 12 months postpartum were approximately 74 percent, 43 percent and 21 percent, respectively, according to 2006 CDC provisional data.³² However, only 32 percent of infants born in 2005 were exclusively breastfed through the age of 3 months. The CDC also noted disparities in rates of exclusive breastfeeding, associating lower breastfeeding rates with mother's lower income, lower education and younger age.³⁰ As infants are weaned from breast milk, most receive their nutrition from infant formula, especially in the first four to six months of life before they are introduced to solid foods.²⁴ Semisolid or solid foods also can provide some exposure to fluoride, and a few foods can have high fluoride levels (for example, baby foods containing fluoride-rich chicken byproducts that are incorporated into infant food during preparation).³³ Dry cereals generally have acceptable fluoride concentrations (approximately 0.4 ppm). However, when reconstituted with 1.0-ppm fluoridated water, this food source also could contribute to the potential for infants to ingest excessive amounts of fluoride.¹⁸

Infant formulas today. Investigators have identified reconstitution of infant formulas with fluoridated water as a risk factor for the development of dental fluorosis.³⁴⁻³⁶ In the 1970s, results of a number of studies raised concerns about the high and variable fluoride levels in commercial infant formulas.^{12,34-36} In response to those studies, in 1979, the ADA convened a meeting with the manufacturers of infant formulas and public

health advocates.³⁷ Since that time, most infant formula manufacturers voluntarily have reformulated their products to ensure low levels of fluoride.³⁴⁻³⁷ Nevertheless, formulas still have some fluoride that will contribute to the daily fluoride intake.^{36,38-41} Also, depending on the type and amount of formula consumed, one should consider the fluoride content of the water source used to reconstitute the formula.^{12,20,21,31,34-38} For example, soy-based infant formulas, recommended for infants with lactose intolerance, are rich in fluoride-binding tricalcium phosphates and phytates and, therefore, may potentially contain fluoride levels higher than those of the milk-based formulas.^{36,38-40,42}

We conducted a study to determine fluoride

concentrations in commercially available powder concentrate, liquid concentrate and ready-to-feed milk-based and soy-based infant formulas. We also undertook to estimate fluoride intake in infants whose primary source of nutrition is infant formula reconstituted with water containing from 0.0 to 1.0 ppm fluoride.

MATERIALS AND METHODS

Infant formula. We purchased 49 commercially available infant formulas in the Chicago area: nine ready-to-feed formulas, 13 liquid

concentrate formulas and 27 powdered formulas. These formulas included both milk-based and soy-based varieties. Table 1 lists the brands, product names and types of formulas studied. It was not possible to measure batch consistency in this convenience sample; however, we purchased three different lots of each type of formula to determine if any significant variability existed within this limited sample.

Fluoride concentration of formula. We reconstituted powdered and liquid concentrate formulas using deionized water according to the manufacturers' instructions. For powdered formulas, we reconstituted one scoop of formula with 2 ounces of deionized water. We diluted liquid concentrates 1:1 with deionized water. We analyzed the ready-to-feed formulas as they were. To analyze the total fluoride content of the formulas, we used a procedure modified from the diffusion method developed by Taves⁴³ to allow accurate detection of small fluoride concentrations.

Most infant formula manufacturers voluntarily have reformulated their products to ensure low levels of fluoride; nevertheless, formulas still have some fluoride that will contribute to the daily fluoride intake.

TABLE 1

Fluoride concentrations of infant formulas tested.

FORMULA TYPE	BASE	BRAND NAME	FLUORIDE CONCENTRATION		
			Parts per Million	Mean ± SD*	P Value†
Powdered Concentrate	Milk	Baby's Only Organic‡	0.11	0.12 ± 0.08	.44
		Earth's Best Organic§	0.11		
		Enfamil A.R. Lipil¶	0.09		
		Enfamil EnfaCare Lipil	0.10		
		Enfamil Gentlease Lipil	0.26		
		Enfamil Lactofree Lipil	0.21		
		Enfamil Lipil	0.06		
		Enfamil Nutramigen Lipil	0.25		
		Enfamil Pregestimil Lipil	0.26		
		Enfamil With Iron	0.04		
		Nestlé Good Start Supreme#	0.07		
		Nestlé Good Start Supreme DHA & ARA	0.07		
		Parent's Choice Milk Based**	0.05		
		Parent's Choice Gentle	0.07		
	Parent's Choice Lactose-Free	0.13			
	Parent's Choice Organic	0.06			
	Similac Advance††	0.05			
	Similac Alimentum	0.27			
	Similac Lactose Free	0.17			
	Similac Neosure	0.13			
Similac Organic	0.03				
Soy	Baby's Only Organic	0.20	0.16 ± 0.09		
	Earth's Best Organic	0.12			
	Enfamil ProSobee Lipil	0.29			
	Nestlé Good Start Supreme Soy DHA & ARA	0.06			
	Parent's Choice Soy	0.08			
	Similac Isomil Advance Soy	0.18			
Liquid Concentrate	Milk	Enfamil Lipil	0.48	0.27 ± 0.18	.01
		Enfamil with Iron	0.39		
		Nestlé Good Start Supreme	0.37		
		Nestlé Good Start Supreme DHA & ARA	0.38		
		Parent's Choice Milk Based	0.01		
		Parent's Choice Milk-Based With Iron	0.39		
	Similac Advance	0.08			
	Similac With Iron	0.07			
	Soy	Enfamil ProSobee Lipil	0.57	0.50 ± 0.08	
		Nestlé Good Start Supreme Soy DHA & ARA	0.51		
Similac Isomil Soy		0.41			
Similac Isomil Advance Soy		0.43			
Similac Isomil Advance Soy With Iron	0.57				
Ready-to-Feed	Milk	Enfamil Lipil With Iron	0.14	0.15 ± 0.06	.46
		Enfamil Nutramigen Lipil	0.21		
		Similac Lactose Free	0.23		
		Similac Organic	0.08		
		Similac Sensitive R.S.	0.13		
		Similac With Iron	0.10		
	Soy	Enfamil ProSobee Lipil	0.32	0.21 ± 0.10	
		Parent's Choice Soy Based	0.16		
		Similac Isomil Advance	0.13		

* Mean fluoride concentrations for milk-based formulas are compared with those for soy-based formulas for each type of infant formula (that is, powder concentrate, liquid concentrate and ready-to-feed). SD: Standard deviation.

† The P value is based on a t test (unpaired data) comparing the mean fluoride concentrations in milk-based formulas with those in soy-based formulas.

‡ All Baby's Only Organic formulas are manufactured by Nature's One, Lewis Center, Ohio.

§ All Earth's Best Organic formulas are manufactured by Hain Celestial Group, Melville, N.Y.

¶ All Enfamil formulas are manufactured by Mead Johnson Nutrition, Glenview, Ill.

All Nestlé Good Start formulas are manufactured by Nestlé Infant Nutrition, El Paso, Texas.

** All Parent's Choice formulas are manufactured by PBM Nutritionals, Georgia, Vt.

†† All Similac formulas are manufactured by Abbott Laboratories, Abbott Park, Ill.

TABLE 2

Formula volume consumed and body weights of infants (from birth to age 12 months).

AGE (MONTHS)	FORMULA INTAKE RANGE (OUNCES)	BODY WEIGHT (KILOGRAMS), ACCORDING TO SEX AND GROWTH CHART PERCENTILE					
		Girl			Boy		
		10th Percentile	50th Percentile	90th Percentile	10th Percentile	50th Percentile	90th Percentile
0-4	21-29	2.7-5.2	3.4-6.2	4.0-7.1	2.8-5.7	3.6-6.7	4.2-7.8
4-6	29-32	5.2-6.2	6.2-7.2	7.1-8.4	5.7-6.8	6.7-7.9	7.8-9.2
6-9	30-32	6.2-7.4	7.2-8.5	8.4-9.8	6.8-8.0	7.9-9.3	9.2-10.8
9-12	24-30	7.4-8.3	8.5-9.5	9.8-11.0	8.0-9.0	9.3-10.3	10.8-11.9

Two of the authors (P.K., H.-N.C.) placed 1 milliliter of formula, reconstituted formula or fluoride standard and 2 mL of deionized water in a petri dish (60 × 15 millimeters, polystyrene, Falcon 1007, Becton Dickinson, Franklin Lakes, N.J.). They removed the three spacers on the cover of the petri dish and drilled a hole (2-mm inner diameter) through the cover. The base trap was composed of 50 microliters of 0.05 normal sodium hydroxide placed as five drops on the inside of the cover. The investigators ringed the inside periphery of the cover with a thin layer of Vaseline Petroleum Jelly (Unilever, Englewood Cliffs, N.J.) to form an airtight seal with the bottom of the petri dish. They added 1 mL of 3 normal sulfuric acid saturated with hexamethyldisiloxane to the bottom through the hole on the cover. They immediately sealed the hole with a piece of sealing film. After the sample underwent 16 hours of diffusion at room temperature, the investigators removed the cover. They added 50 µL of 0.05 normal acetic acid and 100 µL of total ionic strength adjustment buffer to the sodium hydroxide trap and adjusted the total volume to 200 µL by adding deionized water. They transferred 200 µL of the solution to a sample vial cap (15.3-mm outer diameter), and they measured the fluoride concentration by using a fluoride-specific electrode (Orion Fluoride Combination Electrode, Thermo Scientific, Beverly, Mass.). They determined the fluoride concentrations of various formulas from the linear regression analyses of fluoride standards. They analyzed duplicate samples from three lots of each product and calculated fluoride exposure by using the mean fluoride concentrations of the samples.

Calculating fluoride exposure from infant formulas reconstituted with water containing from 0.0 to 1.0 ppm fluoride. Two of

the authors (H.-N.C. and H.R.) estimated total fluoride intake for female infants at different ages by calculating the amount of fluoride ingested from the water source used to reconstitute the formula (that is, whether the water contained 0.0, 0.4, 0.5, 0.7 or 1.0 ppm fluoride) and from the formula itself. To estimate the amount of formula ingested per day, they used the feeding guidelines for infants recommended by Hendricks and Duggan’s⁴⁴ Manual of Pediatric Nutrition, considered a standard in pediatrics. These guidelines are age-based estimates (birth-4 months, 4-6 months, 6-9 months and 9-12 months) for total formula consumption during the first year of life (Table 2). The investigators compared the potential fluoride ingestion per age group with the upper tolerable limits and adequate intake levels set by the IOM by using the body mass index-for-age percentiles published by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion.⁴⁵ They calculated fluoride intake limits for infants from birth to 12 months of age in the 10th and 90th percentiles for body mass and compared them with the potential fluoride ingestion per age group described above. On the basis of the formula consumption and body weight data in Table 2, it appears that female infants will have a slightly greater exposure in each age group; therefore, the researchers used only data for girls in their calculations. However, Table 2 also presents the data for boys as a point of comparison.

RESULTS

Fluoride content in milk-based and soy-based infant formulas. In this study, we compared the fluoride concentrations in soy-based versus milk-based powdered concentrate, liquid concentrate and ready-to-feed formulations. Soy-

based formulas generally were higher in fluoride content than were milk-based formulas. This difference was not statistically significant for powdered concentrate and ready-to-feed formulations; however, the fluoride concentration of the liquid concentrate soy formulas tested was significantly higher than that of milk-based liquid concentrate formulas ($P < .05$, t test analysis for unpaired data) (Table 1). The fluoride content in different batches of the same product was fairly consistent.

Estimated fluoride exposure resulting from infant formula consumption. The figure illustrates the estimated fluoride intake resulting from infant formula consumption compared with the IOM's recommendations. The lines in each portion of the figure indicate the adequate fluoride levels and upper fluoride intake limits according to body weight percentile.

The hatched boxes represent the estimated daily intake of fluoride from powdered concentrate, liquid concentrate and ready-to-feed formulas reconstituted with 0.0-ppm, 0.4-ppm, 0.5-ppm, 0.7-ppm and 1.0-ppm fluoridated water. Most infants will exceed the upper tolerable limit if they exclusively are fed powdered infant formula reconstituted with 1.0-ppm fluoridated water. There is minimal risk of exceeding the upper tolerable limit for fluoride ingestion if powdered and liquid concentrate infant formulas are reconstituted with water containing fluoride at levels below 0.5 ppm (Figure, D and E). However, infants aged between 6 and 12 months are unlikely to reach the adequate intake of fluoride if they are fed ready-to-feed formula or powdered or liquid concentrate infant formulas reconstituted with water that contains less than 0.4 ppm of fluoride. Results also show that the infant formulas themselves (powdered concentrate, liquid concentrate and ready-to-feed) did not contain fluoride at levels that would exceed the IOM's upper limit (0.10 mg/kg/day) with normal consumption (Figure, E).

DISCUSSION

We found that the infant formulas themselves (powdered concentrate, liquid concentrate and ready-to-feed) did not contain fluoride at levels that would exceed the IOM's upper tolerable limit

(0.10 mg/kg/day) with expected consumption volumes when prepared with deionized water. In addition, soy-based formulas generally had a fluoride content higher than that of milk-based formulas, but this difference was statistically significant only for the liquid concentrate formulas tested, not for ready-to-feed and powdered concentrate formulas. This finding is consistent with previous reports indicating that soy-based formulas in general contain more fluoride than do milk-based products.^{36,38-40,42}

We compared calculations of estimated fluoride intake levels with the IOM's adequate intake level and upper tolerable limit. The IOM established an adequate fluoride intake level on the basis of estimated intake levels that have been shown to maximize the preventive effect of fluoride in the reduction of dental

caries. The IOM established upper tolerable limits to protect against moderate and severe dental fluorosis. The results suggest that when powdered or liquid concentrate formulas are the primary sources of nutrition for infants from birth to age 12 months, some infants likely will exceed the recommended upper tolerable limit for fluoride ingestion if these formulas are reconstituted with water containing fluoride at levels from 0.7 to 1.0 ppm. Therefore, this exposure places these infants at increased risk of developing enamel fluorosis. Only when water containing less than 0.5 ppm fluoride is used to

reconstitute infant formulas is it likely that most infants will ingest fluoride at levels below the recommended upper tolerable limit.

The data also indicate that ingestion of liquid concentrate formulas likely will not result in fluoride intake that exceeds the IOM's upper tolerable limit for most infants when reconstituted with water containing fluoride at a level less than 0.7 ppm. Because ready-to-feed formulas are not reconstituted and the data suggest that these products have consistently low fluoride levels, their use will not result in fluoride intake that exceeds the IOM's upper tolerable limit.

If infants receive primarily ready-to-feed formulas or powdered or liquid concentrate formulas that are reconstituted with fluoride-free or low-fluoride water, they likely will not achieve the

**If infants
 receive primarily
 ready-to-feed
 formulas or powdered
 or liquid concentrate
 formulas that are
 reconstituted with
 fluoride-free or
 low-fluoride water,
 they likely will not
 achieve the adequate
 intake level
 of fluoride.**

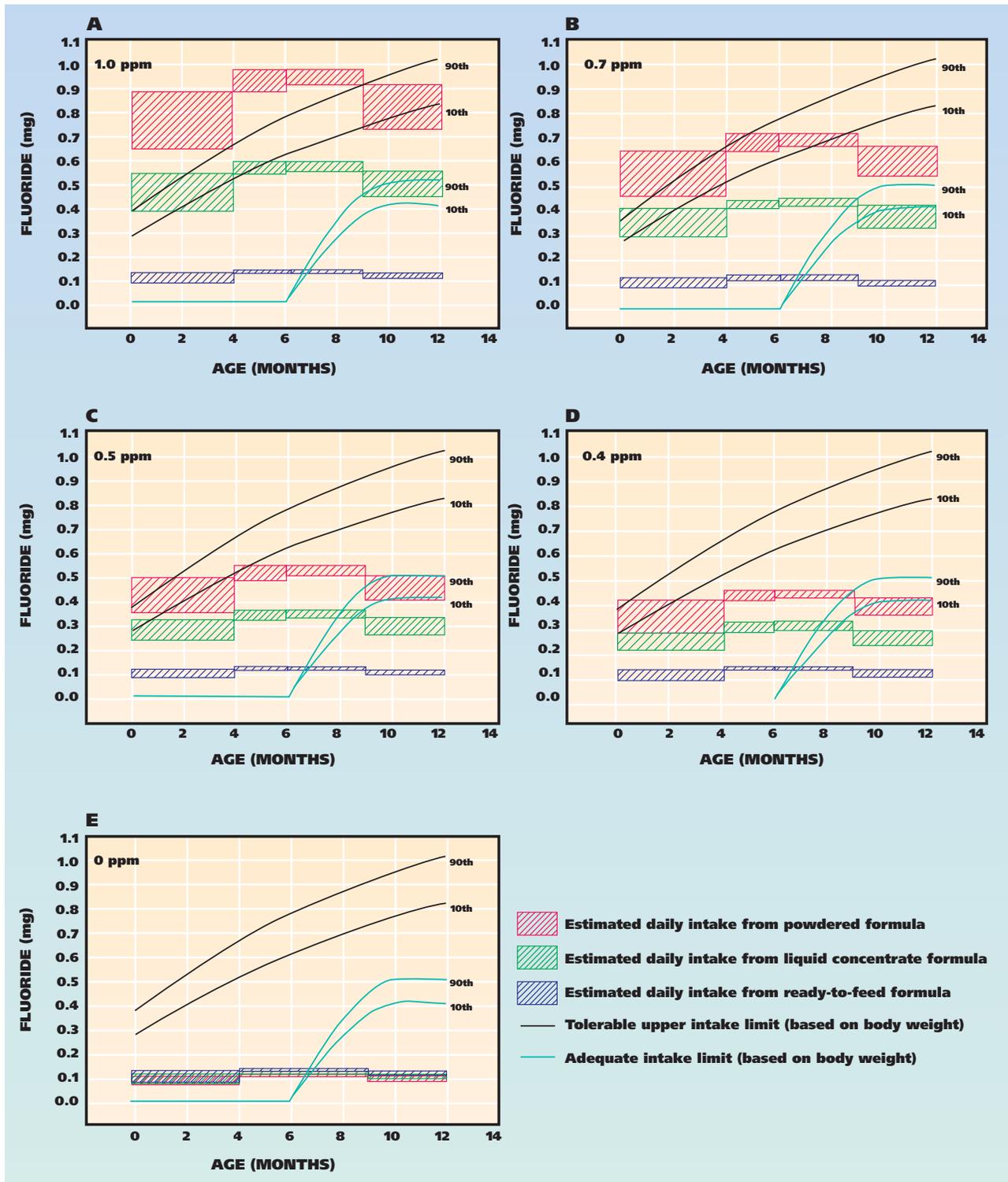


Figure. Graphs illustrating the calculated daily fluoride intake range for female infants resulting from ingestion of formulas in powdered (pink hatched boxes), liquid concentrate (green hatched boxes) and ready-to-feed (blue hatched boxes) formulas reconstituted with water containing varying concentrations of fluoride in relation to the tolerable upper intake limits (black line) and adequate intake levels (green line) of fluoride established by the Institute of Medicine¹⁶ on the basis of body weight percentiles (from the 10th to the 90th). **A.** Formulas reconstituted with water containing 1.0 part per million fluoride. **B.** Formulas reconstituted with water containing 0.7 ppm fluoride. **C.** Formulas reconstituted with water containing 0.5 ppm fluoride. **D.** Formulas reconstituted with water containing 0.4 ppm fluoride. **E.** Formulas reconstituted with water containing 0.0 ppm fluoride. mg: Milligrams.

adequate intake level of fluoride as recommended by the IOM. On the basis of the current ADA dietary fluoride supplementation schedule,⁴⁶ these infants would be candidates for supplementation beginning at age 6 months. It seems unreasonable to recommend the use of supplements for children residing in a community with fluoridated water. In addition, infants from 7 to 12 months of age may exceed the upper tolerable limit for only a short period, because most infants are weaned from formula at around the age of 12 months. Under these circumstances, the risk of developing fluorosis attributable to infant formula is not known. These issues will need to be considered more thoroughly by the ADA expert panel that is developing evidence-based recommendations on the use of fluoridated water for reconstitution of infant formula to assist health care providers in guiding patients. (Publication of the recommendations is anticipated in spring 2010.)

It is important to note that our estimates of fluoride intake from infant formula assume exclusive formula feeding during the first year of life. In addition, the intake limits set by the IOM are an expert panel's best estimates, based on cross-sectional studies. Therefore, we do not know the significance of exceeding the upper tolerable limit or not meeting the adequate intake level, especially for short periods, with respect to the development of fluorosis or prevention of caries.

When a child is 4 to 6 months of age, his or her diet rapidly expands to include other semisolid and solid dietary sources that can contain fluoride. Therefore, deriving precise dose-response relationships or estimates of fluoride intake that are based on all sources of fluoride is difficult unless longitudinal studies are conducted in which people are monitored carefully for at least several years from birth to age 4 years.^{26,40} Such a study is being conducted (S. Levy, unpublished data, 1999).

The fluoride content of the infant formulas tested in this study, which we purchased in the Chicago area, generally are consistent with those found in a study conducted between 1992 and 1993 in Iowa.³⁶ Results of more recent studies conducted in Brazil^{35,47,48} also showed similar fluoride concentrations in Brazilian infant formulas. However, investigators in two Brazilian studies found higher fluoride concentrations in soy-based powder concentrates (0.70-0.75 ppm) than those we found in this study (0.16 ppm).^{35,48} Although one limitation of our study was the use of a

regional sample of infant formula products, the consistency of its results with those of the Iowa study and the fact that the formula manufacturing plants are centralized make it likely that the results can be extrapolated to other parts of the country. In this study, we calculated fluoride intake by using estimates of formula consumption according to body weight and age rather than by measuring actual fluoride intake. Therefore, there are limitations in using these results to identify an optimal water-fluoride concentration for reconstituting infant formula.

CONCLUSIONS

The findings of this study support those of other studies^{35,36,47,48} suggesting that the intake of fluoride by infants will be influenced more by the water used to reconstitute formulas than by the formulas themselves. The ready-to-feed formulas that we tested all had fluoride concentrations that were relatively low and, therefore, would not be expected to contribute significantly to any risk of developing fluorosis. One can conclude that most infants from birth to age 12 months who consume predominantly powdered and liquid concentrate formulas are likely to exceed the upper tolerable fluoride limit if the formula is reconstituted with optimally fluoridated water (0.7 to 1.2 ppm); however, the validity of this upper tolerable limit in protecting against moderate-to-severe fluorosis is uncertain. Conversely, because of the low inherent level of fluoride in the formulas, reconstitution with deionized water (0.0 ppm fluoride) likely will result in infants' not achieving adequate fluoride intake, if fluoride intake from other nutritional sources is low. ■

Disclosure. None of the authors reported any disclosures.

The laboratory study described in this article was undertaken by the American Dental Association (ADA) Foundation Research Institute under the direction of the ADA Council on Scientific Affairs.

1. National Research Council of the National Academies. Fluoride in drinking water: a scientific review of EPA's standards. Washington: National Academies Press; 2006.
2. American Dental Association. Interim guidance on fluoride intake for infants and young children. "www.ada.org/prof/resources/positions/statements/fluoride_infants.asp". Updated Nov. 8, 2006. Accessed Aug. 20, 2009.
3. Margolis HC, Moreno EC. Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. *J Dent Res* 1990;69(special issue):606-613.
4. Fejerskov O, Larsen MJ, Richards A, Baelum V. Dental tissue effects of fluoride. *Adv Dent Res* 1994;8(1):15-31.
5. Singh KA, Spencer AJ. Relative effects of pre- and post-eruption water fluoride on caries experience by surface type of permanent first molars. *Community Dent Oral Epidemiol* 2004;32(6):435-446.
6. Fejerskov O, Manji F, Baelum V. The nature and mechanisms of dental fluorosis in man. *J Dent Res* 1990;69(special issue):692-700.
7. Driessens FC. Mineral aspects of dentistry. *Monogr Oral Sci* 1982; 10:1-215.

8. Groeneveld A, Van Eck AA, Backer Dirks O. Fluoride in caries prevention: is the effect pre- or post-eruptive? *J Dent Res* 1990;69(special issue):751-755.
9. Thylstrup A. Clinical evidence of the role of pre-eruptive fluoride in caries prevention. *J Dent Res* 1990;69(special issue):742-750.
10. Chow LC. Tooth-bound fluoride and dental caries. *J Dent Res* 1990;69(special issue):595-600.
11. Pendrys DG, Stamm JW. Relationship of total fluoride intake to beneficial effects and enamel fluorosis. *J Dent Res* 1990;69(special issue):529-538.
12. Fomon SJ, Ekstrand J, Ziegler EE. Fluoride intake and prevalence of dental fluorosis: trends in fluoride intake with special attention to infants. *J Public Health Dent* 2000;60(3):131-139.
13. Cutress TW, Suckling GW. Differential diagnosis of dental fluorosis. *J Dent Res* 1990;69(special issue):714-720.
14. Thylstrup A, Fejerskov O. Clinical appearance of dental fluorosis in permanent teeth in relation to histologic changes. *Community Dent Oral Epidemiol* 1978;6(6):315-328.
15. Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. *MMWR Recomm Rep* 2001;50(RR-14):1-42.
16. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride. Washington: National Academies Press; 1997:288-313.
17. Levy SM, Kohout FJ, Guha-Chowdhury N, Kiritsy MC, Heilman JR, Wefel JS. Infants' fluoride intake from drinking water alone, and from water added to formula, beverages, and food. *J Dent Res* 1995;74(7):1399-1407.
18. Heilman JR, Kiritsy MC, Levy SM, Wefel JS. Fluoride concentrations of infant foods. *JADA* 1997;128(7):857-863.
19. Hong L, Levy SM, Warren JJ, Broffitt B, Cavanaugh J. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. *Caries Res* 2006;40(6):494-500.
20. Levy SM, Warren JJ, Davis CS, Kirchner HL, Kanellis MJ, Wefel JS. Patterns of fluoride intake from birth to 36 months. *J Public Health Dent* 2001;61(2):70-77.
21. Mascarenhas AK. Risk factors for dental fluorosis: a review of the recent literature. *Pediatr Dent* 2000;22(4):269-277.
22. Burt BA. The changing patterns of systemic fluoride intake. *J Dent Res* 1992;71(5):1228-1237.
23. Bårdsen A. "Risk periods" associated with the development of dental fluorosis in maxillary permanent central incisors: a meta-analysis. *Acta Odontol Scand* 1999;57(5):247-256.
24. Hong L, Levy SM, Broffitt B, et al. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dent Oral Epidemiol* 2006;34(4):299-309.
25. Ismail AI, Messer JG. The risk of fluorosis in students exposed to a higher than optimal concentration of fluoride in well water. *J Public Health Dent* 1996;56(1):22-27.
26. Beltrán-Aguilar ED, Barker LK, Canto MT, et al. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis: United States, 1988-1994 and 1999-2002. *MMWR Surveill Summ* 2005;54(3):1-43.
27. Levy SM, Zarei-M Z. Evaluation of fluoride exposures in children. *ASDC J Dent Child* 1991;58(6):467-473.
28. Szpunar SM, Burt BA. Trends in the prevalence of dental fluorosis in the United States: a review (published correction appears in *J Public Health Dent* 1987;47[3]:155). *J Public Health Dent* 1987;47(2):71-79.
29. Clark DC. Trends in prevalence of dental fluorosis in North America. *Community Dent Oral Epidemiol* 1994;22(3):148-152.
30. Centers for Disease Control and Prevention. Breastfeeding trends and updated national health objectives for exclusive breastfeeding: United States, birth years 2000-2004. *MMWR Morb Mortal Wkly Rep* 2007;56(30):760-763.
31. Fomon SJ, Ekstrand J. Fluoride intake by infants. *J Public Health Dent* 1999;59(4):229-234.
32. Centers for Disease Control and Prevention. Breastfeeding Among U.S. Children Born 1999-2006. CDC National Immunization Survey. "www.cdc.gov/breastfeeding/data/NIS_data/index.htm". Accessed July 28, 2008.
33. Fein NJ, Cerklewski FL. Fluoride content of foods made with mechanically separated chicken. *J Agric Food Chem* 2001;49(9):4284-4286.
34. Marshall TA, Levy SM, Warren JJ, Broffitt B, Eichenberger-Gilmore JM, Stumbo PJ. Associations between Intakes of fluoride from beverages during infancy and dental fluorosis of primary teeth. *J Am Coll Nutr* 2004;23(2):108-116.
35. Buzalaf MA, Granjeiro JM, Damante CA, de Ornelas F. Fluoride content of infant formulas prepared with deionized, bottled mineral and fluoridated drinking water. *ASDC J Dent Child* 2001;68(1):37-41.
36. Van Winkle S, Levy SM, Kiritsy MC, Heilman JR, Wefel JS, Marshall T. Water and formula fluoride concentrations: significance for infants fed formula. *Pediatr Dent* 1995;17(4):305-310.
37. Levy SM. Review of fluoride exposures and ingestion. *Community Dent Oral Epidemiol* 1994;22(3):173-180.
38. Johnson J Jr, Bawden JW. The fluoride content of infant formulas available in 1985. *Pediatr Dent* 1987;9(1):33-37.
39. Ekstrand J. Fluoride intake in early infancy. *J Nutr* 1989;119(12 suppl):1856-1860.
40. Adair SM, Wei SH. Supplemental fluoride recommendations for infant based on dietary fluoride intake. *Caries Res* 1978;12(2):76-82.
41. Koparal E, Ertugrul F, Oztekin K. Fluoride levels in breast milk and infant foods. *J Clin Pediatr Dent* 2000;24(4):299-302.
42. McKnight-Hanes MC, Leverett DH, Adair SM, Shields CP. Fluoride content of infant formulas: soy-based formulas as a potential factor in dental fluorosis. *Pediatr Dent* 1988;10(3):189-194.
43. Taves DR. Separation of fluoride by rapid diffusion using hexamethyldisiloxane. *Talanta* 1968;15(9):969-974.
44. Hendricks KM, Duggan C, eds. *Manual of Pediatric Nutrition*. 4th ed. Hamilton, Ontario, Canada: BC Decker; 2005:148-150.
45. Kuczmarowski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: Methods and development. *National Center for Health Statistics. Vital Health Stat* 2002;11(246):20. "www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf". Accessed Aug. 21, 2009.
46. American Dental Association. Interim guidance on fluoride intake for infants and young children. "www.ada.org/prof/resources/positions/statements/fluoride_infants.asp". Updated November 2006. Accessed Aug. 27, 2009.
47. Buzalaf MA, Damante CA, Trevizani LM, Granjeiro JM. Risk of fluorosis associated with infant formulas prepared with bottled water. *J Dent Child (Chic)* 2004;71(2):110-113.
48. Pagliari AV, Moimaz SA, Saliba O, Delbem AC, Sasaki KT. Analysis of fluoride concentration in mother's milk substitutes. *Braz Oral Res* 2006;20(3):269-274.