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DIETARY INTAKE AND BIOAVAILABILITY OF FLUORIDE

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INTRODUCTION

Ample current epidemiologic evidence indicates that community water fluoridation in the last 3–4 decades has resulted in a significant decrease (50–60%) in the prevalence of dental caries in the United States and other developed nations of the world (65, 100, 142). However, recent studies suggest that the prevalence of caries is also declining in communities where drinking

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water is not fluoridated (65, 66, 84, 100, 117, 142, 183, 207). This phenomenon may be primarily related to a recent increase in the use of dentifrices containing fluoride (F) (about 80% of dentifrices currently sold in the United States contain F) and F supplements (65, 66, 85, 100, 120). Secondarily, it may be related to systemic exposure to F of individuals in nonfluoridated areas resulting from an increase in F in the food chain from the use of fluoridated water in commercial food processing (54, 56, 79, 91, 93, 107, 123, 129, 137, 138, 164, 167, 189), use of infant formulas and baby foods with significant F content (2, 3, 55, 135, 136, 165, 166, 204), and unintentional ingestion of F from dentifrices (11, 13, 39, 41, 58) and mouthwashes (13).

The enhanced F exposure from diet and other sources may have led to some increase in the prevalence of mild dental fluorosis among children in communities with fluoridated water (4, 33, 57, 100, 120, 144, 195, 198, 199). Dental fluorosis is a non–life-threatening tooth surface imperfection that is considered cosmetically unesthetic. This has provided additional fuel to the long-standing fluoridation controversy (75, 193), with arguments being made for and against a need for reassessing (20, 43, 53, 81, 98, 100, 155) the currently accepted optimal range at 0.7–1.2 ppm F in drinking water (190). The lower F level in the recommended range is for the warmest temperature zones; the range increases to the higher level for the coldest zones to account for differences in temperature and water consumption patterns.

Because of the modern multiple sources of F ingestion, the F content of drinking water alone may not accurately reflect current daily total F intake, as was the case at the beginning of the community water fluoridation program. Besides occurrence of endemic dental fluorosis in regions where natural F levels in water exceed the optimal range considered beneficial for dental health (20, 125, 125a, 197), there have been isolated reports of debilitating effects resulting from ingestion of excessive F through accidentally contaminated food and water (194). Although trace levels of F are normally found in the modern food chain, there is no current consensus on the level of F acceptable in various foods and beverages consumed on a daily basis. To achieve such a consensus, it is essential to have accurate estimates of the F contents of foods and beverages. More importantly, data on their bioavailability must be obtained, because two items containing identical amounts of F may exhibit very different F bioavailability. This information will provide a more accurate estimate of the daily total F intake of individuals residing in communities with fluoridated and nonfluoridated water.

This chapter reviews the world literature on the F content of foods and beverages, with emphasis on studies involving F intake and bioavailability. The health and disease aspects of F in drinking water and other sources have been the subject of several reviews (19, 36, 80, 87, 90, 153, 206) including one in an earlier volume in this series (149).

METHODOLOGY FOR FLUORIDE ANALYSIS

In contrast to fluoridated water, in which all of the F is in ionic or free form, foods and beverages contain both ionic and nonionic, or bound, forms of F (10, 35, 134, 164, 170). Similarly, the body fluids and tissues of animals and humans ingesting F also contain free and bound F. The ratio between the two forms of F depends on such factors as the F content, nature of the food or beverage, and time after its consumption (70, 133).

The analysis of ionic F in drinking water samples is relatively straightforward and usually involves the use of the F ion-specific electrode (104). However, no convenient and adequate method is generally accepted for the analysis of free and bound F in foods and beverages at this time.

The three methods in current use for F analysis in foods utilize the F ion-specific electrode for determination of F after its isolation by (*a*) perchloric acid diffusion from unashed samples (27), (*b*) similar acid diffusion from samples ashed in open crucibles (164), or (*c*) silanol extraction after ashing in a closed oxygen bomb (191). A recent comparison (134, 164, 166) of the three methods indicated that method *c* gave the best results, which were $47.0 \pm 6.1\%$ and $19.0 \pm 4.9\%$ higher than those of methods *a* and *b* respectively. This suggests that earlier studies using methods *a* and *b* for F analysis may have significantly underestimated the bound F in various food samples investigated. However, a different conclusion was reached during a similar comparison of F analyses of 93 individual food items using samples ashed in covered platinum crucibles and unashed samples (181). This study found no discrepancy between the two methods with the exception of analyses of two dry cereals and of black pepper, which showed significantly higher F after ashing.

Colorimetric methods for F analysis of foods were routinely used in the 1960s and earlier, before the general availability of the F ion-specific electrode. There is now evidence that these methods may have overestimated F content due to the presence of interfering substances in some of the foods analyzed (164, 165, 180, 181). Thus, development of a generally accepted method for accurate and precise estimation of F in foods and beverages should be a high priority for future research. The recently reported proton activation analysis for the measurement of F in foods, which measures total F content not perturbed by its chemical form (160), is a step in this direction. Also, application of the oxygen bomb ashing method (164, 191) in conjunction with gas (10, 12) and ion (9, 60) chromatographic determinations of total F in foods and beverages deserves attention.

It is noteworthy that a recent collaborative study by the Association of Official Analytical Chemists (26) has recommended a method based on acid diffusion from unashed samples (method *a*, above) for determining F in infant foods (27).

FLUORIDE CONTENT OF FOODS AND BEVERAGES

The earliest reports on the F content of foods in the United States appear to be those published from 1939 to 1949 (6, 106, 112, 113), approximately the time when fluoridation of public water supplies was initiated. As one would have expected, these initial studies indicated that the daily intake of F through foods was low, about 0.5 mg or less. Consequently, dietary sources of F received only occasional attention for the next decade or so (21, 28, 62, 72, 110). However, there was a resurgence of interest in the subject in the 1960s, with the reports that the use of fluoridated water enhanced the F content of foods and beverages (22, 42, 78, 94, 107, 192). Since then, a steady stream of studies on dietary sources of F has appeared in the literature around the world (3, 23, 24, 49, 52, 54–56, 71, 79, 83, 85, 91, 93–96, 123, 126, 127, 130, 132, 135–139, 151, 165–167, 181, 188, 189, 197, 204). The 1979 review (164) appears to be the most current one on the subject.

Baby Formulas and Foods

The most recent estimates of F in baby formulas and foods sold in the United States appear to be those reported in 1981 (166). This study used samples collected in 1978 belonging to ten food groups fed to infants and toddlers in four dietary regions (Table 1). Among the commercially available solid infant foods, such as various meat products, vegetables, and fruits, only chicken products had extremely high and variable F contents (0.62–10.6 ppm), probably as a result of the inclusion of varying amounts of bone fragments (166). The mean F contents of fruits (0.048 ppm) was less than that of the vegetables (0.23 ppm) and meat products other than chicken (0.32 ppm). For these solid food groups, F content was not related to the F concentration in water used in their processing.

In contrast, the F levels in dry infant cereals, fruit juices, and milk formulations processed in plants using fluoridated water were significantly higher than those processed in plants employing nonfluoridated water (3, 56, 166). The ranges of F levels in products processed in the fluoridated and nonfluoridated plants were, respectively: dry cereals, 3.85–6.35 and 0.93–2.11 ppm; ready-to-feed milk formulations, 0.57–0.76 and 0.08–0.31 ppm; and fruit juices, 0.35–1.22 and 0.014–0.21 ppm. The substantial increase in F content of infant cereals processed in plants using fluoridated water is attributed to the initial use of water for slurrying ingredients that are later dried. Appropriate steps are now being taken by some infant formula manufacturers to monitor and keep F levels within an acceptable range.

When liquid concentrates and evaporated milk formulas for infants and toddlers are used, the F level of the final preparation is obviously related to the F content of the water in the home (2, 82, 166). The F level in both human (169)

Table 1 Fluoride contents of different food groups fed to infants and toddlers in the United States[a]

Food group	F ppm Infants mean (range)	F ppm Toddlers mean (range)
Drinking water[b]	— (0.37–1.04)	— (0.37–1.04)
Milk	0.02	0.02
Other dairy products, substitutes	0.42 (0.24–0.68)[c]	0.13 (0.08–0.19)
Meat, fish, poultry	0.33 (0.19–0.47)	0.38 (0.22–0.48)
Grain, cereal products	1.71 (0.39–3.84)	0.32 (0.23–0.47)
Potatoes	0.08 (0.04–0.11)	0.12 (0.04–0.19)
Vegetables	0.37 (0.23–0.45)	0.20 (0.17–0.24)
Fruits, juices	0.12 (0.08–0.20)	0.18 (0.11–0.25)
Oils, fats	0.26	0.28 (0.15–0.45)
Sugar, adjuncts	0.21 (0.11–0.35)	0.32 (0.24–0.44)
Beverages[b]	— (0.40–0.94)	— (0.54–1.19)

[a]Market basket studies from North Central, South, Northeast and West Dietary Regions analyzed in 1978. Adapted from Ref. 166.
[b]Mean F values varied with location.
[c]Values are high because of inclusion of ready-to-feed milk formulations.

and cows' milk (10) is generally low (< 0.1 ppm) and thus does not significantly contribute to the total F ingested by babies (52, 53, 72, 166, 195). There is also indication that water fluoridation does not affect F levels in human milk (169).

Adult Foods

A recent study (164) of F contents of 12 food groups consumed by young adults (16–18 years old) in the United States compared collections analyzed in 1971 (147) and in 1978 (164). The F levels in the two collections seven years apart were remarkably similar (Table 2). However, these recent F estimates for foods appear generally lower than those reported for similar food groups in 1959 (21) and 1949 (113). This may well be due to the better analytical specificity of methods used in the newer studies (see the section on Methodology for Fluoride Analysis, above).

It may be concluded that F in foods is not a major source of F exposure for adults and that this situation has not significantly changed over the past four decades despite community water fluoridation. As was discussed above, this is in contrast to the F levels of infant and toddler formulas and cereals, where a significant increase in F content attributable to water fluoridation is documented.

A study of the effect of cooking vessel composition on F levels suggests that the use of those coated with teflon, an F polymer, may release F during

Table 2 Fluoride contents of different food groups reported in the United States, 1949–1978[a]

Food group	F range ppm 1949[b]	1959[c]	1971[d]	1978[e]
Dairy products	0.07– 0.22	0.04– 0.55	0.11–0.22	0.05–0.07
Meat, fish, poultry	0.1 –12.1	<0.10–24	0.42–1.04	0.22–0.92
Grain, cereal products	0.20– 0.71	0.10–20	0.26–0.59	0.29–0.41
Potatoes	< 0.20	—	0.13–0.20	0.08–0.14
Green, leafy vegetables	0.1 – 0.7	—	0.13–0.85	0.10–0.15
Legumens	0.11– 0.60	—	0.19–0.25	0.15–0.39
Root vegetables	0.01– 0.60	0.10– 3.0	0.06–0.22	0.09–0.10
Other vegetables, vegetable products	0.2 – 0.4	—	0.70–0.41	0.06–0.17
Fruits	0.15– 0.26	0.02– 1.32	0.10–0.11	0.06–0.13
Fats, oils	1.5	0.4 – 1.50	0.12–0.45	0.13–0.24
Sugar adjuncts	0.00– 1.00	0.10– 0.32	0.30–0.56	0.21–0.35

[a]Adapted from Ref. 164.
[b]Adapted from Ref. 113.
[c]Adapted from Ref. 21.
[d]Adapted from Ref. 147.
[e]Adapted from Ref. 164.

cooking, e.g. the F level of water boiled for 15 min in such a vessel increased by 2 ppm (61). In contrast, utensils made out of aluminum decreased F levels by about 30% (61).

Beverages

Unlike foods, the basic constituent of beverages is water. As one would expect, the F content of these products is significantly higher when processed with fluoridated water (56, 154, 157, 164, 179). Analyses of 24 different soft drinks processed in four different plants in Houston, Texas showed that their F contents (0.05–1.31 ppm) closely paralleled the F levels of the water used in their processing (0.07–1.47) (157). The F content of carbonated beverages that were processed with the same water was the same whether they were packaged in bottles or cans.

Beverages labeled as natural sparkling mineral waters contained considerably higher concentrations of F (1.7–6.5 ppm) which depended on the geographic location of their natural sources (105, 156). Since children tend to drink any soft drinks that are brought into the household, there is a need to alert regular users of mineral waters to the high F content of these beverages.

Tea also contains significant amounts of natural F (23, 34, 88, 130, 143, 151, 163, 179, 184). The F content of teas grown in different parts of the world varies widely, ranging from 0.11 to 4.18 ppm when infused in F-free water. The following levels of F were reported in a survey of teas currently sold in the

United States: regular and green teas, loose or in bags, 1.32–4.18 ppm; instant teas, 1.0–1.5 ppm; herbal teas, < 0.02 ppm (184). If fluoridated water is used for brewing, the F content of the resulting tea beverage is enhanced by the amount present in the water used. It is noteworthy that herbal teas, now gaining popularity as caffeine-free "natural" beverages, contained insignificant amounts of F (G. S. Rao and Y. S. Tong, unpublished results).

The F content of beer, wine, and other alcoholic beverages generally reflected that of water used in their brewing (130, 151, 179).

The United States Food and Drug Administration (FDA) recently established the following limits on the F content of bottled water: domestic with no F added, 1.4–2.4 ppm; domestic with F added, 0.8–1.7 ppm; imported with no F added, 1.4 ppm; imported with F added, 0.8 ppm (189a).

Fluoridated Food Ingredients and Beverages

Since fluoridation of community water is shown to be a practical, cost-effective means of achieving significant decreases in the prevalence of dental caries (32, 87, 153, 206), the addition of F to foods and beverages as an alternative or supplemental mode of F delivery has gained only limited acceptance around the world (2, 14, 50, 53, 83, 108). In the United States, any claim of therapeutic efficacy attributable to F as a food ingredient has yet to be approved by the FDA.

In recent years, fluoridated salt (51, 109, 119, 122, 185, 186, 200), sugar (140), flour (50), milk (29, 145, 150, 174, 175, 208), and citrus beverages (63, 77) have been tested, especially in several European and South American countries. In some instances, successful reductions in caries prevalence comparable to those achieved with water fluoridation have been reported. Fluoridated salt (250 ppm F) is currently used in Switzerland and Hungary. It is noteworthy that natural salt and sugar in some parts of the world contain significant levels of F. The sea salt used in Bombay, India is reported to contain 40 ppm F (159), and salts used in various cities in the Soviet Union are known to contain 10–141 ppm F (62). The F levels in cane sugars sold in Australia range from 0.76 to 2.13 ppm (148).

Selective fluoridation of dietary constituents, such as salt and milk, has the major advantage of utilizing much smaller quantities of F for a given population than the fluoridation of an entire water supply, of which only about 1% is actually used for drinking (87). Two major disadvantages of fluoridated food ingredients and beverages are the wide individual variations in their use and the difficulties in providing them to children, the main target population, in all socioeconomic groups.

Miscellaneous Products

Significant amounts of F may be ingested through habitual use of certain products such as chewing tobacco, snuff, and betel nuts and leaves (67, 126, 127, 158). A recent survey of tobacco products sold in the United States showed a wide range in their F contents: chewing tobaccos (pouch and plug types) had 0.19–9.30 ppm F, and snuff had 0.120–0.196 ppm F (67). Similar studies reported F levels of 3.1–38.0 ppm in chewing tobaccos and 7.0–12.0 ppm in betel nuts and leaves sold in India (126, 127).

Fluoridated chewing gums (0.25–0.50 mg F/stick) have been tested as a vehicle for systemic F delivery (18), but they have not been marketed.

DIETARY INTAKE OF FLUORIDE

The presence of F in the enamel of teeth was first reported in 1805 by the French chemists Gay-Lussac and Berthollet. Dental fluorosis (mottled teeth) was recognized as an endemic developmental imperfection of the tooth surface in the early 1900s (16, 37), and by the 1940s the causative agent was proven to be ingestion of drinking water containing F at concentrations of 2 ppm or greater (30, 31, 118). Concurrently, at the beginning of the 1940s, the health benefit of about 1 ppm F in drinking water in preventing dental caries without producing enamel fluorosis was established (7, 64, 112). Thus began fluoridation of drinking water as an unprecedented public health measure designed to improve the dental health of an entire community (114, 168).

As early as 1939 (106), it was recognized that F in foods may contribute to the daily total F ingested in communities where drinking water naturally contained F. By the time large-scale community water fluoridation became a reality in the 1950s, it was apparent that many common foods contain significant quantities of F, and numerous studies were conducted to assess the daily total F intake originating from both drinking water and other dietary sources (73, 74, 91, 94, 101, 135–139, 164–167, 180, 188, 204).

Tables 3 and 4 summarize data on daily intake of F from dietary sources in communities around the world with and without water fluoridation. In view of the fact that some of the early colorimetric analyses of F in foods may have overestimated F levels in some foods, it is remarkable that the daily intake of F in the United States in general has not changed significantly during the period 1942–1981 (Table 3). As expected, the daily F intake estimates from dietary sources in the fluoridated areas were consistently higher than those in the nonfluoridated areas.

A current estimate of the contribution of individual food groups to the daily total intake of F in a fluoridated area (181) is presented in Table 5. This study found that the observed F intake from foods is approximately one fourth of the total daily intake, a value which is close to the ratio of bone (210), urine (115), and serum (182) F concentrations of nonfluoridated and fluoridated community residents.

There is some indication that household detergents, pesticides, and fertiliz-

Table 3 Estimates of dietary fluoride intake in the United States, 1942–1981

Age group	Mean and/or range F intake[a] mg/day	Year	Reference
Infants			
< 2 months	0.32 –0.57	1975	204
2 months	0.05 –0.63	1975	165
4 months	1.02	1975	204
	0.102–0.680	1979	165
6 months	1.23	1975	204
	0.094–0.763	1979	165
	0.153–0.763	1981	166
Toddlers			
2 years	0.196	1943	112
	2.1–2.4	1971	147
	0.78–1.03[b]	1974	93
	1.73–3.44	1974	93
	0.315–0.610	1978	136
Young adults			
16–19 years	1.0–2.0	1966	107
	0.912[b]	1975	167
	1.213–1.720	1975	167
	1.636	1977	167
Adults	0.27–0.32[b]	1942	6
	0.20–0.50[b]	1949	113
	0.86;0.73–0.94[b]	1967–1972	138
	1.96;1.23–2.41	1967–1972	138

[a]Values are for residents of fluoridated communities unless otherwise noted.
[b]Values are for residents of nonfluoridated communities.

ers containing F may be additional sources of F exposure (91, 131). However, currently such sources appear to contribute insignificantly to the daily dietary F intake.

In specific subgroups of the population, such as children, dietary F may significantly contribute to the daily total F intake, e.g. baby formulas and foods may provide as much as 0.763 mg F/day (164–166, 203). A recent survey of tea-drinking households in Newcastle, England indicated that the average intake of F from tea among children (from under one year to about eight years) was 0.4 mg/day, while in adults it was 4.4 mg/day (G. N. Jenkins, unpublished results). In the British population there appears to be a steady increase in tea consumption, and hence in F intake, with age (34).

The Council on Dental Therapeutics of the American Dental Association recommends the following supplemental fluoride according to F concentration

Table 4 Estimates of dietary fluoride intake in different countries[a]

Country	Mean or range F intake mg/day	Year	Reference
Canada			
Infants			
4 months	0.169[b], 0.459[c]	1950	72
12 months	0.564[b], 1.123[c]	1950	72
Adults	0.429–0.792	1954	74
England	0.6–1.8	1957	101
India			
Children 5–8 yrs	0.7	1972	126
Japan	0.47–2.66	1959	21
Norway			
Children	0.22	1956	28
Adults	0.31	1956	28
Sweden	0.9	1959	21
Switzerland	0.5	1948, 1959	54, 21
Soviet Union	0.6–1.2	1951	62
West Germany	0.2–0.4	1970	130

[a]Values are for adults unless otherwise noted.
[b]Low-F area.
[c]High-F area.

Table 5 Daily fluoride intake from individual food groups in the United States[a]

Food group	Mean ± SD F intake mg/day
Dairy products	0.013
Meat, fish, poultry	0.044 ± 0.035
Grain, cereal products	0.241 ± 0.153
Potatoes	0.018
Leafy vegetables	0.027 ± 0.019
Legumens	0.037
Root vegetables	0.010
Fruits	0.006
Oils, fats	0.003 ± 0.001
Sugar, adjuncts	0.001
Total, all foods	0.400
Beverages	1.383 ± 0.0411
Total, foods & beverages	1.783

[a]Six-day diets from a hospital in a fluoridated area, collected in 1977. Data adapted from Taves (181).

of drinking water: for areas with < 0.3 ppm F in water, 0.25, 0.50, and 1.00 mg F/day for age groups birth to 2, 2–3, and 3–13 years, respectively; for areas with 0.3–0.7 ppm F in water, 0.25 and 0.50 mg F/day for age groups 2–3 and 3–13 years, respectively; for areas with > 0.7 ppm F in water, no supplement for any age group (1).

In children, the total dietary intake, including drinking water, should provide 0.05–0.07 mg F/kg of body weight for optimal dental health benefit. The apparent threshold of 2.0 ppm F in drinking water at which dental fluorosis becomes evident corresponds to a daily intake of about 0.1 mg F/kg of body weight up to the age of 12 years.

The systemic exposure of children to F from F-containing dentifrices and mouthwashes is significant (11, 13, 39, 41, 58). Thus a recent study of children 7–13 years old found 0.4–1.2 mg F retention after brushing with a F-containing dentifrice, while the use of a F-containing mouthwash led to retention of 0.2–0.4 mg F (13). This indicates the importance of accurately estimating the total daily F intake in children from diet, water, and other F sources such as oral hygiene aids before prescribing F supplements.

In adults, a dietary intake of 4.0–5.0 mg F/day is considered to be without any health hazard (116). The United States National Research Council has recently recommended 1.5–4.0 mg F/day as a "safe and adequate" intake for adults (143a).

BIOAVAILABILITY OF DIETARY FLUORIDE

Bioavailability of F in foods and beverages may be defined as the efficiency with which consumed F is absorbed from the oral cavity and the gastrointestinal tract and is thus available for use or storage in the body. Since the bioavailability of NaF in humans is essentially 100% when it is ingested in water or tablets (40), it is generally used as a standard in reporting F bioavailability from foods and beverages.

Several biological markers have been used to assess bioavailability of F from dietary sources: F levels in blood (5, 51, 70, 106b, 139, 162, 170, 182), saliva (18, 139), plaque (69, 89), teeth (49, 99, 111, 141, 159, 209) and bones (15, 47, 124, 176, 178, 196, 209, 210) as indicators of uptake; and F levels in urine (17, 48, 106, 106a, 106b, 116, 143, 171–173, 187, 201, 202), feces (17, 106a, 106b, 116, 139, 171, 172) and sweat (116) as indicators of elimination. F balance in the body is the difference between its uptake and elimination.

For practical reasons, F levels in blood, urine and feces are commonly used in bioavailability studies involving human subjects, while hard tissue uptake is usually used only in investigations on experimental animals. The radioactive isotope ^{18}F has been utilized in both animals and humans to assess bioavailability of F in milk (44). Extracted teeth have been studied for in vitro estimates of uptake and disposition of F from selected dietary items (45, 92).

Pharmacokinetic calculations may be employed to estimate the bioavailability of F in foods and beverages from plasma uptake or urine excretion data (170). Background plasma and urine F levels must be determined during the control period prior to the experiment. These values are subtracted from those obtained after ingestion of the test food or beverage and NaF in water, which is used as a standard. The net area under the plasma F concentration vs time curve (ΔA) is then estimated using the trapezoidal rule for both test and standard F groups.

The apparent bioavailability of F in the test product based on plasma data (B_p) is given by equation 1:

$$B_p\% = \frac{\Delta A_t/F_t}{\Delta A_s/F_s} \times 100, \tag{1.}$$

where F_t and F_s are F concentrations in the test food or beverage and the water standard, respectively.

Similarly, the apparent bioavailability of F in the test product based on urine data (B_u) is given by equation 2:

$$B_u\% = \frac{\Delta U_t/F_t}{\Delta U_s/F_s} \times 100, \tag{2.}$$

where ΔU_t and ΔU_s are the net amounts of F excreted in the urine during the experimental period after ingestion of the test product and the water standard, respectively.

The ratio between ΔU and ΔA gives the renal clearance of F. The bioavailability of F when administered as NaF in water standard is assumed to be 100% in these calculations.

Factors Affecting Fluoride Bioavailability

Since foods and beverages contain both free and bound forms of F, the bioavailable F depends on the ratio between the two forms. In general, the higher the free F, the greater its bioavailability. Thus, any factor that influences the ratio between free and bound F will also have a corresponding effect on F bioavailability. Some of these factors are

1. Nature of food and beverage, e.g. protein-rich milk vs tea and other soft drinks (38, 63, 99, 124, 141, 152, 170, 209)
2. F concentration and its chemical form (inorganic vs organic) (49, 52, 68, 70, 76, 77, 86)
3. Presence of other elements and constituents that influence F uptake and metabolism, e.g. Al, Ca, Mg, and chloride reduce F uptake, while P

and sulfate increase F uptake (15, 25, 45, 47, 97, 102, 103, 121, 146, 173, 176, 196)
4. Previous and/or concurrent F exposure from other sources (46, 70, 106b, 133)
5. Physiological and pathological state of individuals, e.g. age (child vs adult and geriatric population) (46, 178), acid-base balance status and urine pH (40a), and disease state, especially diseases of the kidney, the major organ for F clearance in the body (40, 59)

Factors such as these should be considered in interpreting the results of bioavailability studies on dietary F conducted in different laboratories under different conditions and with diverse populations of the world.

In general, unbound F in water is more bioavailable than protein-bound, organic F in foods, milk, and other proteinaceous beverages. Also, factors that interfere with F absorption or its release from organic F in the body will decrease F bioavailability; impaired kidneys will have an opposite effect due to higher F retention. Limited clinical studies suggest that pregnancy may not significantly alter dietary F metabolism (106a).

Studies in Laboratory Animals

Because it is difficult to test F bioavailability in individual food items and impractical to assess F uptake in critical hard tissues such as teeth and bones, laboratory animals have been utilized as models to simulate possible bioavailability and uptake in humans. Rats appear to be the most widely used animal species (44, 46, 47, 86, 97, 102, 103, 124, 128, 152, 162, 178, 196, 205, 209), although cows (177), dogs (68), chickens (15), guinea pigs (176), and mice (146) have been employed occasionally.

Milk (44, 124, 141), tea (152), citrus beverage (99), and fish products (209) are some examples of individual dietary items that have been studied in animals for F bioavailability. In general, these studies indicate that F in foods and beverages appears less bioavailable than equivalent F in water as NaF. This is in agreement with similar clinical studies in humans.

A comprehensive rat bioassay procedure for determining total F bioavailability in foods was recently reported (128). It is based on the method of standard additions and uses weanling rats. The control group is fed a low-F diet, while the test group is fed the same diet plus the test food. Both groups are further divided into subgroups supplemented with 0, 5, 10, 20, or 40 ppm F as NaF and offered deionized water for a period of 10 days. The rats are then killed and femur and tibia analyzed for F content. The F contents of the two hard tissues are plotted against the amounts of F added to the diets. With the aid of weighted regression equations describing the linear relationship between the variables, these data can then be used to calculate the bioavailability of F in the test food.

This appears to be a sensitive and precise bioassay procedure for studying bioavailability of F in foods.

Studies in Human Subjects

The earliest clinical study in the United States on the bioavailability of F in food appears to be that reported in 1939 (106). Based on urinary F levels, this study showed that F in food plays a minor role in the production of dental fluorosis when compared to F in drinking water. This conclusion is generally in agreement with those of most subsequent investigations including current ones (20, 33, 125, 144, 198, 199).

The 1945 study (116) on F (3.0–5.0 mg, total) ingested from various foods and water by young men reported that F excretion in urine, sweat, and feces accounted for most of the F intake; urine was the major excretory vehicle, followed by sweat and feces. It was thus concluded that a daily dietary intake of 4.0–5.0 mg F was without any health hazard since no significant retention of F occurred in the body at these levels. This original study continues to be the basis for estimating the safe range of dietary F intake.

The most recent study (17) in 3- and 4-year-old children living in an optimally fluoridated community in California also found that F excretion in urine and feces paralleled F intake, and that net retention in the body was minimal. The children's average dietary F intake and output were 0.33 ± 0.14 mg/day and 0.28 ± 0.08 mg/day respectively, with an average F balance of $+0.05 \pm 0.08$ mg/day.

In addition to the various studies on F intake in the diet as a whole (8, 17, 49, 72–74, 106a, 106b), several investigators have evaluated the bioavailability of F in individual foods and beverages. These include items naturally containing F, such as tea (23, 34, 88, 143), fish products (171, 172), and fluoridated milk (38, 44, 145, 170, 174, 175, 208) and salt (48, 51, 76, 187, 200–202). These clinical studies have employed subject populations belonging to all age groups, from infants to the elderly.

In general, most investigators have found that, for all age groups studied, bioavailability of F in foods and beverages is less than that of equivalent F in water as NaF. Several explanations have been offered for the decreased bioavailability of F from dietary sources: (*a*) binding of F to the food constituents through physical sequestration or chemical bond (164, 181); (*b*) food acting as a physical barrier preventing F access to the mucosal surface of the oral cavity and the gastrointestinal tract (170); (*c*) the modulating effect of stomach contents under strong acidic conditions, e.g., coagulation of milk and formation of CaF_2, which has a low solubility and thus causes F to become substantially less bioavailable (44).

An exception to the above generalization is the bioavailability of F in fluoridated salt (48, 51). A recent Swedish clinical study (51) involving age groups from one-year-old to adult consuming fluoridated salt (380 mg F/kg) in 14 different staple food categories found F bioavailability, as measured by plasma F levels, to be comparable to that of the corresponding F concentrations in drinking water.

Based on data from F bioavailability and F analyses of individual food items, a nomogram has been constructed that permits estimation of permissible intake of food items, depending on the desired or planned F supply (161). The practical applicability of this novel approach in monitoring dietary F intake awaits further studies.

SUMMARY AND CONCLUSIONS

After almost 40 years of water fluoridation in the United States, its effect in the food chain is now being appreciated. Current surveys indicate significant increases in the F content of infant formulas, toddler cereals, fruit juices, and popular beverages, largely because fluoridated water is used in their processing. According to the best estimates, the daily total F intake of children from foods, beverages including water, and other sources such as unintentional ingestion of dentifrices containing F is on the rise, although it is generally within the currently accepted range for this age group. It is encouraging to note that appropriate steps are now being taken by some manufacturers of infant formulas to monitor F levels and keep them within an acceptable range.

Because of the increasing contribution of dietary F to total F intake, dietary F should be included in any estimate of daily total F intake in children before F supplements are prescribed, whether the children live in communities with fluoridated or nonfluoridated water. To achieve this goal, it is essential to develop a generally accepted, sensitive method for the analysis of F in foods and beverages. This should help develop the bioavailability profiles for individual foods and beverages essential for accurate assessment of dietary F intake.

Fluoridated salt, used in some European countries, appears to be the only food ingredient currently in use as an alternative to water fluoridation. Attempts to utilize staple foods and beverages as vehicles for systemic F delivery have generally failed because of the decreased bioavailability of F in such products, and because it is difficult to make them available to the general population and especially to the lower socioeconomic segments of the population.

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