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Monitoring salt fluoridation programs through urinary excretion studies

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Summary

This paper reviews problems associated with urinary collection for the estimation of fluoride exposure and recent findings in this context. After intake of a salted meal at noon, children aged 9 to 14 excreted on average 45 µgF/h. Morning and nocturnal excretions were only 16 µgF/h with the exception of those children who ate bread made with fluoridated salt (25 µgF/h). Fluoride excretions in children consuming drinking water with 0.6 to 0.8 ppmF were similar, but the variations within the 24 h period were smaller. When it is not feasible to obtain reliable 24 h urinary collections, fairly precise extrapolations of 24 h excretions can be obtained from three separate collections lasting about 16 hours, which should cover morning, early afternoon and the whole night. Three- to six-year-old children benefitting from optimal fluoride supply through water or milk excreted approximately 0.35 to 0.40 mgF/24 h; this range seems to correspond to an optimal usage of fluorides. Studies on urinary fluoride excretion, like those on total fluoride intake, cannot be carried out on random samples. Due to the necessity of close cooperation of parents and children, such studies were done with "convenience" samples. In westernized countries with now low caries prevalence, intermittent high urinary excretions occur frequently. Possible sources are fluoride intake from concentrated oral care products (fluoride gels, fluoride chewing gums) or from dentifrices (containing 1,000 to 1,500 ppmF), mineral waters, industrial tea preparation or fluoride tablets (or other supplements). These problems do not affect the amount of fluoride in fingernail clippings which appear to be suitable for the routine monitoring of fluoride exposure.

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Introduction

Blood plasma, ductal saliva and urine are useful fluids for monitoring fluoride exposure or rather intake (WHO 1994). Fluoride ingested with solid food and fluids passes rapidly into the blood, the absorption already beginning in the stomach. Following absorption part is deposited in the bones while another part is excreted with the urine. With the feces, about 10% of ingested fluoride is excreted (WHITFORD 1996).

Figure 1 illustrates the fluoride concentration in plasma and the corresponding urinary excretion. The initial plasma concentration is low because in such studies the rule is that subjects are not allowed to eat during the preceding six hours. The plasma fluoride then reflects the steady-state concentration ratio between plasma and the exchangeable pool in bone. The usual procedure is to have study subjects ingest one or several milligrams of fluoride, in solution or with food. In the plasma, the highest concentration is usually reached approximately one hour after ingestion and decreases during the following hours. Such studies with single doses were published by numerous authors (for instance Trautner 1989, Trautner & Einwag 1989, Whitford 1996). In urine collections beginning at the time of the fluoride intake and lasting for two hours fluoride excretion will be highest because the maximal plasma concentration lies within this two-hour period. A second urinary collection lasting for another two hours will still be higher than the pre-experimental level. Five to eight hours after fluoride intake fluoride in plasma will have almost reverted to its original levels. It should be noted that the higher excretion is exclusively due to the rise in the fluoride concentration of the plasma. The fluoride concentration in the plasma does not affect urinary flow.

In the case of fluoridated salt (FS) for domestic usage, supplemental fluoride is ingested through meals cooked at home. Its intake is highest with the main cooked meal which in countries like Germany and Switzerland is lunch. Accordingly, peak excretions of 43.3 µgF/h occurred in the early afternoon (Tab. I, Geneva). In contrast, fluoride excretions throughout the morning and night were less than half as high (16.2 and 16.5 µgF/h) since in these periods of the day little or no supplemental fluoride was ingested. On the other hand, children from Lausanne (Canton of Vaud) had benefitted from a universal salt fluoridation scheme comprising the salt used by bakeries, school canteens and restaurants, introduced in 1970. The peak excretion of 47.8 µgF/h in the afternoon was similar to that of the Geneva children, whereas morning and nocturnal excretions were approximately 50% higher than in Geneva (25.3, 24.6 µgF/h). In children consuming fluoridated water, variations between morning, afternoon and nocturnal fluoride excretions and concentrations were lowest (Tab. I).

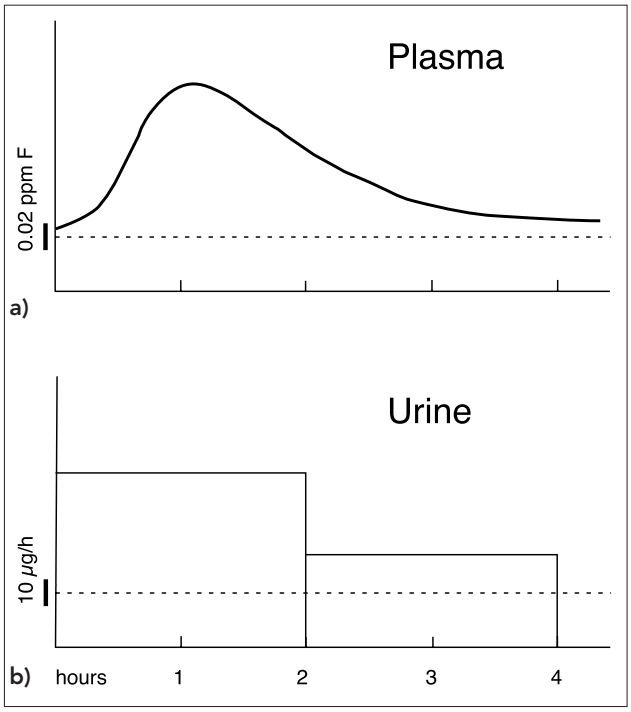

Fig. 1 Fluoride levels in a) plasma: typical pattern of fluoride concentration after intake of 2 mg of fluoride by fasting subjects; the interrupted line shows the concentration under fasting conditions; b) urine: typical pattern of urinary fluoride excretion in 2 h collections corresponding to the plasma concentration curve shown in a), the interrupted line shows the excretion under fasting conditions

Tab. I Urinary fluoride excretion, fluoride concentration and urinary flow of children age 9–14 (numbers between 47 and 74)

	Morning	Afternoon	Night
Fluoridated salt only for domestic use (Geneva 1988)			
µgF/h	16.2	43.3	16.5
ppmF	0.70	1.21	0.76
urine, ml/h	30	46	23
Fluoridated salt for domestic use and bakeries (Vaud 1985)			
µgF/h	25.3	47.8	24.6
ppmF	0.80	1.32	1.14
urine, ml/h	36	42	23
Fluoridated water from the Canton of Basel-Stadt (1989)*			
µgF/h	23.5	33.3	19.0
ppmF	0.63	0.82	0.71
urine, ml/h	43	48	28

* The study took place in Binningen (Canton of Basel-Landschaft) which is provided with drinking water from Basel-Stadt, required to contain 0.8 to 1.0 ppmF. On the day of the urinary collections, however, it happened to contain only 0.6 ppm fluoride. Source of data: Marthaler et al. (1995).

Problems associated with the collection of urine

Collections of 24 h urine are ideal for assessing daily fluoride excretion. While it is relatively easy to obtain 24 h urines in hospitals, this is difficult or impossible to obtain from the population at large. Nevertheless, studies by Rugg-Gunn et al. (1993) and Zohouri & Rugg-Gunn (2000) used 24 h collections, and the results corresponded to the existing knowledge on quantitative fluoride metabolism. However, 24 h urines do not provide information on the hours with low or high fluoride excretion during the day.

Fairly reliable assessments of 24 h fluoride excretion can be obtained when using three defined collection periods spread over the day. Nocturnal urinary collections from children in "stable families" are fairly easy to obtain. Techniques and possibilities of timed urinary collections for assessing the fluoride exposure or rather total uptake of fluoride have been described in detail (Marthaler 1999). Often it is possible to obtain supervised collections in the morning and afternoon in schools, kindergartens or other pre-school institutions. In westernized cultures, morning, afternoon and nocturnal collections cover 13 to 16 hours and provide bases for fairly reliable extrapolations of the 24 h fluoride excretion. A collection period of several hours following the main intake of salted food provides data for the period of highest fluoride excretion. The bias that may occur through extrapolations to 24 h was shown to be quite small (Marthaler et al. 1992, Baez et al. 2000, Marthaler 1999). Excretion studies using three collection periods were performed in connection with salt fluor-

idation (Marthaler et al. 1995, Aeschbacher 1995, Marthaler et al. 2000). For part of the material, extrapolations for 24 h urinary output have not been computed. In fact, automated programs for carrying out the respective computations were presented in 1999 only (Marthaler 1999), and since then the programs have been further developed. Urinary fluoride excretion studies have also been used in connection with milk fluoridation (Ketley & Lennon 2001, Ketley et al. 2002).

Specific hypotheses of experiments may necessitate subdivisions of the 24 h period. A two-year study of adults consuming lunch cooked with fluoridated salt in a canteen may serve as an example (Schulte et al. 2002, see also Schulte 2005). The afternoon collections yielded a higher fluoride excretion than those from night and morning, indicating that the lunch was in fact noticeably enriched in fluoride. In addition, the results showed that the increased fluoride intake after lunch did not affect excretion at night and in the morning. A mere 24 h excretion study would not have revealed the increased fluoride excretion after lunch. In fact, the 24 hour excretion values were subject to additional variations masking the higher fluoride excretion in the afternoon. An interpretation would have been uncertain because of the non-significant results.

When time of the beginning of the collection (always after a urination) and of its end are correctly recorded, an uncertainty remains as to whether the urination left the bladder completely empty at the start or at the end of the collection time. Nocturnal urines are least affected by this insecurity because the amounts of urine not passed are relatively small when compared to the amount of urine produced during seven to ten hours of sleep.

Urinary excretions when fluoride exposure is approximately in the optimal range

In a strict sense, an optimal range of fluoride exposure is difficult to define because very low intakes of fluoride as occurring in all continents do apparently not entail health disadvantages except for being associated with higher caries prevalence. Nevertheless, full use of fluorides is indicated because caries can and does attack teeth throughout life. This means that as long as fluoride intake is low, there is room for more intensive usage of fluoride for improving preventive effectiveness; the term "optimal level" of fluoride exposure, supply or intake will be used in this sense. Under conditions of low fluoride intake – low fluoride drinking water, no sources of fluoride from dental care products – children aged two to six excrete 6–10 µgF/h, corresponding to approximately 0.2 mgF/24 h (unpublished data of 1993 of T.M. Marthaler). In 1992 and 1994 in Eastern Germany, similary low excretions (four averages in the range 7.2 to 8.6 µgF/h) were still found in children receiving neither fluoride tablets nor FS (Hetzer et al. 1994). In a recent European study, 67 children aged 1.5 to 3.5 years from five countries using neither water nor salt fluoridation had an average daily excretion of 0.23 mgF/h (confidence limits 0.18, 0.27, Ketley et al. 2004). In view of the very low age of the children this may indicate a slightly increased fluoride intake from fluoridated toothpastes.

It is of primary interest to look at the fluoride excretion of children who have been living under stable conditions of optimal fluoride exposure or intake for at least one year. The first five lines of Table II list average fluoride excretions under conditions of mostly optimal fluoride levels in water.

Tab. II Urinary fluoride excretions at various levels of supplemental fluoride intake

Age	Morning µgF/h	Afternoon µgF/h	Night µgF/h	In 24 hours mgF/24h	In 24 hours µgF/h	Source of supplemental fluoride
4				0.36	14.9	0.6 ppmF in water (1)
3				0.37	15.4	0.8–1.0 ppmF in water (2)
4				0.42	17.5	0.8–1.0 ppmF in water (3)
4				0.55	22.9	0.9–1.1 ppmF in water (3)
5–7				0.75	31.2	1.0–1.3 ppmF in water (4)
4				2.66	110.8	≈ 4 ppmF in water (5)
4				0.30	12.5	0.5 mg F in milk (6)
5				0.33	13.8	0.5 mg F in milk (7)
5–6				0.26	13.0	0.5 mg F in milk (7)
5–6				0.36	15.0	1.0 mg F in milk
5–6				0.45	18.8	1.5 mg F in milk
5–6				0.61	25.4	2.0 mg F in milk
2–4	10.4	12.6	8.0	0.23	9.7	250 ppmF dom. salt (8)
3–5				0.45	18.6	250 ppmF dom. salt (9)
5–6	19.5	28.0	12.9			250 ppmF dom. salt (10)
4	16.6	39.8	16.7			250 ppmF salt (11)

(1) Villa et al. (2000), Chile (Santiago), 0.6 ppmF was considered optimal for the climate
(2) Ketley et al. (2002), Cork, Ireland
(3) Rugg-Gunn et al. (1993), Newcastle, England
(3) Rugg-Gunn et al. (1993), Dambulla, Sri Lanka, hot climate
(4) Baez et al. (2000), children in Southern Texas, USA, hot climate
(5) Zohouri (1997), natural high fluoride in Iran
(6) Ketley et al. (2002), Knowsley
(7) Ketley & Lennon (2001), experiment with increasing F-dosages in milk in one group of children
(8) Marthaler et al. (2000), Switzerland, pre-kindergarten children living at home
(9) Pucci & Dol (1997), Uruguay
(10) Aeschbacher (1995), Switzerland, supervised collection during morning and afternoon at kindergarten
(11) Hetzer et al. (1996), Germany, supervised collection at kindergarten, meal cooked with F-salt, used also at home

In temperate climates, they ranged from 0.36 to 0.42 mgF/24 h. For the children in Cork, the confidence limits were 0.32 and 0.42 mgF/24 h ($P > 0.95$). The higher excretion associated with water at 0.9–1.1 ppmF in Sri Lankan children (0.55 mgF/24 h) and in southern Texas, with water at 1.0–1.3 ppmF, may be explained by both the hot climate and the slightly higher fluoride levels in the drinking water. Exceptionally high excretion was found in Iranian children consuming water containing 4 ppmF. The middle part of Table II presents data available from milk fluoridation studies. With a supplement of 0.5 mg fluoride, average 24 h excretions varied between 0.26 and 0.33 mgF/24 h. Higher dosages increased the excretion, which was 0.61 mgF/24 h when the supplement was 2.0 mg fluoride. Based on these data, the excretion of 0.35 to 0.40 mgF/24 h seems to be the optimal range. Excretion data associated with domestic salt fluoridation (lower part of Tab. II) were fairly low (0.23 mgF/ 24 h) in Swiss pre-kindergarten children, but the average excretion by Uruguay children was 0.45 mgF/24 h. It should be noted that in Switzerland (and much of Western Europe), industrially processed and presalted food substitutes part of the domestic salt.

The fraction of fluoride excreted from the ingested fluoride is still a matter of research (Villa 2004). The data of Table II avoids this complex problem and allows conclusions whether in a given salt project fluoride excretion is low, optimal or above the limit, possibly leading to frequent enamel fluorosis. At this time, there are no reports of undesirable levels of enamel fluorosis in countries using FS (Menghini 2005).

Further sources of fluoride affecting urinary fluoride excretion

In Western Europe fluoride-containing products for caries prevention (tablets, toothpastes, gels, rinses) have been easily accessible for decades. The concentrated preparations are sold in drug stores (but rarely in supermarkets) depending on regulations in the different countries. A liberal policy regarding concentrated fluoride preparations for oral care like fluoride gels and frequent topical applications as well as intake of high-fluoride mineral water (Schulte et al. 1996, Behnrendt et al. 2002, Freund & Thumeyer 2005) or iced tea products (Behrendt et al. 2002) will lead to frequent high fluoride excretions, particularly in short collection periods. In children three and four years of age studied by Marthaler et al. (2000), 11 daytime excretions between 21 and 41 µgF/h were recorded among a total of 136, but all of the adjacent collections in the same children showed excretions below 20 µgF/h.

Even at night, two children had excretions of 34 and 38 µgF/h in the third of four consecutive nights. A sudden rise in nocturnal fluoride excretion must be due to a high intake just prior to bed rest in order to be discernible in a nocturnal period of 11 hours. An excretion of 36 µgF/h during 11 hours corresponds to 0.4 mg excreted fluoride; these two children may have swallowed adult toothpaste (containing 1,500 ppmF as a rule) or may have consumed mineral water; no intake of a fluoride tablet was reported. The same two children had excreted less than 20 µgF/h in the two preceding nights; in the fourth night, one excreted 22.4 µgF/h, the other less than 10 µgF/h (Figs. 1 and 2 in Marthaler et al. 2000). Nocturnal plasma fluoride concentration (if not preceded by unusual fluoride intake before bedrest) in children can "serve as a biomarker for the chronic level of fluoride intake and the total amount of fluoride in the body" (Whitford 2005), and urine collected during the night may fulfill this role, but less accurately than plasma fluoride. Questionnaires completed by the parents of these children designed to identify possible sources did not provide hints as to the reasons for the high excretions. Occasional high fluoride intakes have no physiological consequences, but the ensuing high excretions increase the standard deviation, which lowers the precision of the averages.

Statistical considerations and the question of representativeness

One weakness, however, is common to studies on fluoride excretion and on fluoride intake as well: it is not practical or even feasible to draw subjects randomly. Franco et al. (2005) actually used probabilistic sampling and subsampling but their final choice was "non-probabilistic (convenience), given that data collection required high cooperation from parents …". In practice, it is difficult to organize food samples and information as to the amounts of each item of food eaten or drunk, as was done for instance by Rojas-Sanchez et al. (1999). Collecting urinary samples is considerably easier but it also requires parental cooperation and at least a minimal educational level of the parents.

Individual fluoride excretions and concentrations are very variable. Coefficients of variation are typically in the range of 60% to 90% for individual collections.

However, after combining three collections into the 24 h estimate, coefficients of variation are approximately halved. This is due to the fact that unusually high excretions in one or even two collections will be less pronounced after the combination of all three collections into a single estimate, valid for 24 hours. The number of children should not be below 30 in order to reduce the confidence intervals sufficiently. Children who do provide only two or even a single collection can also be used for the evaluation and need not be excluded.

On the other hand, it would seem to be very easy to obtain fingernail clippings from subjects selected at random. The clippings are to be put into small plastic bags with proper identification and anamnestic data and can be stored until analysis in a specialized laboratory is carried out. Individual variations will be lower because the fluoride concentration in fingernails is determined by the average plasma level during one to three weeks (Whitford 2005b). It is expected that for routine monitoring in nationwide salt fluoridation projects and comparisons with water fluoridation schemes fingernail studies will be preferred in the future.

Zusammenfassung

Diese Arbeit diskutiert Probleme bei Urinsammlungen zur Schätzung der Fluoridexposition und diesbezügliche neuere Befunde. Nach der Einnahme einer mit fluoridiertem Salz zubereiteten Hauptmahlzeit am Mittag schieden 9- bis 14-jährige Kinder im Mittel 45 µgF/h aus. Im Morgen- und Nachturin waren es dagegen nur rund 15 µgF/h mit Ausnahme derjenigen Kinder, deren Brot mit fluoridiertem Salz hergestellt wurde (25 µgF/h). Bei Kindern, die Trinkwasser mit 0,6 bis 0,8 ppmF verwendeten, waren die Befunde ähnlich, die Schwankungen innerhalb der 24-Stunden-Periode jedoch geringer. Wenn 24-Stunden-Sammlungen von Urin nicht machbar sind, lassen sich aus drei getrennten Urinsammlungen am Morgen, Nachmittag und über die ganze Nacht, die sich über insgesamt 12 bis 16 Stunden erstrecken sollten, recht genaue Extrapolationen für die 24-Stunden-Ausscheidung gewinnen. Drei- bis sechsjährige Kinder, welche von optimaler Fluoridzufuhr aus Trinkwasser oder Milch profitierten, schieden rund 0,35 bis 0,40 mgF/24 h aus; dieser

Bereich entspricht somit einem optimalen Einsatz von Fluoriden zur Kariesvorbeugung. Studien zur Fluoridausscheidung lassen sich nicht an Zufallsstichproben durchführen. Da man auf die Mitarbeit zuverlässiger Eltern und Kinder angewiesen ist, muss man auf ausgewählte Familien zurückgreifen (convenience samples). Dies gilt in vermehrtem Masse für Studien zur Fluorideinnahme. In westlichen Ländern mit nunmehr niedriger Kariesprävalenz wurden oft kurzzeitige hohe Fluorid-Ausscheidungswerte gemessen. Als Quelle dafür kommen Mundpflegepräparate mit hohen Fluoridkonzentrationen (Gelées, Lösungen), Mineralwässer oder Fluoridtabletten in Frage. Die Bestimmung des Fluoridgehaltes in Fingernagelproben erscheint für das Routine-Monitoring der Fluoridversorgung vorteilhaft.

Résumé

Après le repas de midi, préparé avec du sel fluoruré (SF), l'urine des enfants de 9 à 14 ans excrétait en moyenne 45 µgF/h, alors que le matin et le soir leur urine ne contenait que 15 µgF/h, à l'exception des enfants qui mangeaient du pain préparé avec du SF (25 µgF/h). Les résultats étaient similaires parmi les enfants qui buvaient de l'eau contenant de 0,6 à 0,8 ppmF, les écarts en l'espace de 24 h étant toutefois moins importants. Si les collections d'urine dans un tel espace ne sont pas praticables, on parvient à des résultats approximatifs assez sûrs en effectuant trois collections séparées: le matin, l'après-midi et la nuit (soit pendant une période de 12 à 16 heures). Des enfants de trois à cinq ans profitant d'un excellent ravitaillement en fluorure dans l'eau ou le lait excrètent 0,35–0,40 µgF/24 h, ce qui correspond à l'effet optimum de fluorure pour la prévention de la carie. Etant donné qu'il est nécessaire de s'assurer de la coopération digne de la part de parents et enfants, on a dû choisir des familles exemplaires. C'est à dire que des échantillonnages au hasard ne peuvent être réalisés. Cette considération s'applique aussi tout particulièrement aux études de l'absorption totale de fluorure. En effet, dans les pays occidentaux, on constate souvent des excrétions de fluorure très élevées mais de brève durée. Ce phénomène peut être dû à l'emploi de produits de soins bucco-dentaires à haute concentration de fluorure (gelées, solutions), d'eau minérale ou de cachets de fluorure. Quant au contrôle efficace de l'approvisionnement en fluorure, il paraît avantageux d'en déterminer la présence dans les ongles.

References

Aeschbacher M: Fluorid- und Natriumausscheidung im Urin von fünf- bis sechsjährigen Kindern einer Zürcher Gemeinde. Med Diss, Zurich (1995)

Baez R M, Baez M X, Marthaler T M: Urinary fluoride excretion by children 2–6 years old in a South Texas commmunity. Pan Amer J Publ Health 7: 242–248 (2000)

Behrendt A, Oberste V, Wetzel W E: Fluoride concentrations and pH of iced tea products. Caries Res 36: 405–410 (2002)

Franco A M, Martignon S, Saldarriaga A, Gonzalez M C, Arbelaez M I, Ocampo A, Luna L M, Martinez Mier E A, Villa A E: Total fluoride intake in children aged 22–35 months in four Colombian cities. Community Dent Oral Epidemiol 33: 1–8 (2005)

Freund U, Thumeyer A: Fluoride im natürlichen Mineralwasser. Oralproph & Kinderzahnheilk 27: 24–32 (2005)

Hetzer G, Walde J U, Dude H: Zur Fluoridversorgung der Vorschulkinder durch fluoridiertes Speisesalz. Dtsch Zahnärztl Z 49: 889–92 (1994)

Hetzer G, Straube H, Neumeister V: Zur Verwendung fluoridierten Speisesalzes in der Gemeinschaftsverpflegung. Dtsch Zahnärztl Z 51: 679–682 (1996)

Ketley C E, Lennon M A: Urinary fluoride excretion in children drinking fluoridated school milk. Int J Paediatr Dent 10: 260–270 (2000)

Ketley C E, Lennon M A: Determination of fluoride intake from urinary fluoride excretion data in children drinking fluoridated school milk. Caries Res 35: 252–257 (2001)

Ketley C E, Cochran J A, Lennon M A, O'Mullane D M, Worthington H V: Urinary fluoride excretion of young children exposed to different fluoride regimes. Comm Dent Health 19: 12–17 (2002)

Ketley C E, Cochran J, Holbrook W P, Sanches L, Van Loveren C, Oila A-M, O'Mullane D M: Urinary fluoride excretion by preschool children in six European countries. Community Dent Oral Epidemiol 32: 62–68 (2004)

Marthaler T M (Ed): Monitoring of renal fluoride excretion in community preventive programmes on oral health. World Health Organization, Geneva (1999)

Marthaler T M, Menghini G D, Steiner M, Sener-Zanola B, De Crousaz P: Excreción urinaria de fluoruro en niños suizos que consumen suplementos de fluoruro en la sal o el agua (Urinary fluoride excretions in Swiss children consuming supplemental fluoride in salt or drinking water). Archivos de Odontoestomatología Preventiva y Comunitaria 4: 27–35 (1992)

Marthaler T M, Steiner M, Menghini G, Sener B, De Crousaz P: Urinary fluoride excretion in children with low fluoride intake or consuming fluoridated salt. Caries Res 29: 26–34 (1995)

Marthaler T M, Binder-Fuchs M, Baez R J, Menghini G: Urinary fluoride excretion in Swiss children aged 3 and 4 consuming fluoridated domestic salt. Acta Med Dent Helv 5: 9–17 (2000) (in: Schweiz Monatsschr Zahnmed Vol. 110, No. 6, June 2000)

Menghini G, De Crousaz P, Steiner M, Helfenstein U, Sener B: Excrétion urinaire de fluorures chez des écoliers de Genève et Lausanne, en relation avec la fluoration du sel. Schweiz Monatsschr Zahnmed 99: 292–298 (1989)

Menghini G: Dental fluorosis in salt fluoridation projects. Schweiz Monatsschr Zahnmed 115: in press (2005)

Pucci F W, Dol I: Estudio de excreción urinaria de fluor in niños de 3 a 5 años. Ministerio de Salud Pública, Montevideo, Uruguay (1997)

Rojas-Sanchez F, Kelly S A, Drake K M, Eckert G J, Dunipace A J: Fluoride intake from foods, beverages and dentifrices by young children in communities with negligibly and optimally fluoridated water: a pilot study. Community Dent Oral Epidemiol 27: 288–297 (1999)

Rugg-Gunn A J, Nunn J H, Ekanajake L, Saparamadu K D G, Wright W G: Urinary fluoride in 4-year-old children in Sri Lanka and England. Caries Res 27: 478–483 (1993)

Schulte A, Schiefer M, Stoll R, Pieper K: Fluoridkonzentration in deutschen Mineralwässern. Dtsch Zahnärztl Z 51: 763–767 (1996)

Schulte A, Gräber R, Kaspek C, Koch M J, Staehle H J: Influence of fluoridated salt on urinary fluoride excretion of adults. Caries Res 36: 391–397 (2002)

Schulte A: Fluoridation in Germany since 1991. Schweiz Monatsschr Zahnmed 115: 659–662 (2005)

Trautner K: Influence of food on relative bioavailability of fluoride in man from Na_2FPO_3-containing tablets for the treatment of osteoporosis. Int J Clin Pharm Ther Tox 27: 242–249 (1989)

TRAUTNER K, EINWAG J: Influence of milk and food on fluoride bioavailability from NaF and Na_2FPO_3 in man. J Dent Res 68: 72–77 (1989)

VILLA A, ANABALON M, CABEZAS L: The fractional urinary fluoride excretion in young children under stable fluoride intake conditions. Community Dent Oral Epidemiol 28: 344–355 (2000)

VILLA A: Critical evaluation of previously published data on the fractional urinary fluoride excretion in your children. Comm Dent Health 21: 155–160 (2004)

WHITFORD G M: The Metabolism and Toxicity of Fluoride. 2nd edition, Karger, Basel (1996)

WHITFORD G M: Monitoring fluoride exposure with fingernail clippings. Schweiz Monatsschr Zahnmed 115: 685–689 (2005)

WHO, World Health Organization: Fluorides and Oral Health. WHO Technical Report Series No. 846, Geneva (1994)

ZOHOURI F V: Fluoride intake and excretion in 4-year-old Iranian children. PhD-thesis, University of Newcastle, United Kingdom, Oct. (1997)

ZOHOURI F V, RUGG-GUNN A J: Total fluoride intake and urinary excretion in 4-year-old Iranian children residing in low-fluoride areas. Brit J Nutr 83: 15–25 (2000)