Urinary fluoride excretion in Swiss children aged 3 and 4 consuming fluoridated domestic salt

Summary

Urine from 25 Swiss children aged 3 and 4 was collected during the night of Monday to Tuesday, during the morning, afternoon and evening as well as during the following night. This scheme was repeated from Wednesday evening to Friday morning of the same week. Urinary volumes and fluoride concentrations were determined and urinary excretion rates computed for the 4 nocturnal and the 6 daytime collections. In addition, 24 hour parameters were calculated on the basis of the nocturnal collections on Monday and the following 3 daytime collections; in the same way, 24 hour data were obtained from the nocturnal urine of Wednesday night and the subsequent 3 daytime collections. The complete set of 10 collections was obtained from 17 children; in another 5 children sufficient numbers of collections were obtained to allow at least one 24-hour assessment. In these 22 (17+5) children, the average fluoride excretion was 233 µg/24 h with 95% confidence limits at 181 and 286 µg/24 h. Analysis of the results from the 17 children whose parents handed in the complete set of urinary collections showed that excretions were higher at daytime than at night, and the variation between subjects was considerably larger than within subjects. From a compilation of the currently available data in the literature it emerged that with increasing supply of fluoride there is also an increase of its excretion. This paper supports the hypothesis that monitoring urinary fluoride excretion in children at age 3 may be useful for predicting the level of fluorosis in the permanent teeth.

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Introduction

Over the last 10 years urinary excretion has been studied under various conditions of fluoride exposure in Swiss children aged 10 to 15. Generally, urine was collected during 2–3 school hours in the morning and the subsequent afternoon under supervision of clinic staff while nocturnal urine collections were obtained with the cooperation of the parents (Marthaler et al. 1995). The same procedures were applied to children aged 5 and 6, again under supervision. In the largest of these studies, children living in households where fluoridated domestic salt (250 ppm F) was used, the night and morning averages ranged between 12.6 and 22.1 µg F/h while after lunch, the main meal, the average excretion rate was 28 µg F/h (Aeschbacher 1995).
The purpose of the present study was to obtain 24-hour urinary collections of Swiss children aged 3 and 4 years and to compare the results with data available from the literature.

Material and Methods

Selection of children

From the register of the community of Klingnau (2500 inhabitants) a list of all children aged 2, 3 and 4 years was obtained. Children with names indicating origin from outside Switzerland, Austria, France, Germany and Italy were not included in the sample because of language problems and often limited duration of residence. Of the 50 eligible families, all having been residents in the village for at least 4 years, 34 consented to participate in the study. After exclusion of the children who were still not toilet-trained (mostly the 2-year-olds), 26 children were left, one aged 2 years, 7 aged 3 years and 18 aged 4 years. The

parents of all these children (there were two siblings among them, Nos. 25 and 26) were invited to participate in the study.
Parents were given a questionnaire on the general use of fluoride-containing products which they completed together with the consent form (BINDER-FUCHS 1999). At the start of the urinary study, the parents of the 26 children were given five plastic bottles with screw caps for five consecutive urinary collections between Monday evening (21 October 1996) and Wednesday morning; this included a first nocturnal, three daytime and a second nocturnal collection. On Wednesday morning, the bottles were picked up by a coworker and the parents were given another set of five bottles for repetition of the same procedure from Wednesday night until Friday morning. All bottles were labelled in an appropriate manner to ensure that the time of the micturition was correctly recorded (essentially according to MARTHALER 1999). The second set of five bottles was collected on Friday morning together with completed questionnaires on toothbrushing, meals and drinks consumed during the 4 days. The bottles were brought to the clinic in a cool box within 3 hours, the volume of the urine was measured and approximately 30 ml were transferred to small tubes and deep-frozen until the determinations of fluoride concentration in January 1997.

Fluoride analysis

TISAB IV was prepared in the laboratory according to formula IV of Orion (Instruction Manual, provided with the electrode). In order to prevent interferences by Al, Fe or other metals, 5 g complexon was added to 1 liter of the buffer. One ml of urine was mixed with an equal volume of TISAB IV. After each series of 16 determinations, the ion-sensitive electrodes were again calibrated using solutions 10^{-3}, 10^{-4}, 10^{-5} and 0.5×10^{-5} molar solutions (corresponding to 19, 1.9, 0.19 and 0.095 ppm F, respectively). The electrodes selected showed a linear relation between the millivolt reading and the logarithms of the fluoride concentration down to the lowest concentration of the calibration solution. When the first reading indicated a low fluoride concentration in a urinary sample (readings above 125 mV, indicating less than 0.2 ppm F), TISAB with an added amount of fluoride (10^{-5} molar, or 0.19 ppm F) was used instead of the usual fluoride-free TISAB and the result corrected accordingly. Readings were made in duplicate; if they differed by more than 0.5 mV, further readings were taken until stable results were obtained. When the TISAB with added fluoride was used, four measurements were made. Several samples of the drinking water of Klingnau were analysed. Samples taken before the study and in summer 1998 had fluoride concentrations consistently below 0.1 ppm.

Calculations and statistical procedures

The collections from the first four periods, the nocturnal collection and the subsequent three daytime collections were used for the assessment of 24-hour urine. For the individual 24-hour parameters, the volumes of urine from and the durations of the four collections (night, morning, noon and afternoon) can be added directly. On the other hand, the amount of fluoride in the pool was to be calculated as the sum of the amount of fluoride contained in each of the four urinary collections, i.e. ml×ppm for each period. The pooled daytime excretion of the 17 "complete" children was calculated in the same way.
The 24-hour collections extended in fact from 20 hours and 12 minutes to 25 hours and 30 minutes (average duration 23 hours and 54 minutes); the raw results were adjusted to exactly 24.00 hours. Child No. 14 for example had a total of 24.75 hours (0.75 hours=45 minutes) from the four collection periods of day 1; the urinary volume and fluoride excretion was adjusted by multiplication with 0.970 (=24/24.75). For the other parameters, no corrections were necessary. No "cleaning" of data (MARTHALER 1999) was done in spite of the fact that a few individual results, such as urinary flow rates as low as 2.7 ml/h and a few other values almost as low, indicated incomplete voiding of the bladder at the end of the collection period.
Null hypotheses were tested by using two-way analyses of variance (ANOVA), including paired t-tests of correlation analysis. In view of the skewed frequency distributions of most parameters, the ANOVAs were repeated using the logarithms of the original values.

Results

From the total of 26 children, 20 to 25 valid collections were available from the various periods (Table I) whereby valid means that volume, fluoride concentration and time at the beginning and the end of the collection were available. One subject aged 4 (No. 3) was ill with high fever and was unable to provide urine. Minimal flows were between 2.7 and 4.6 ml/h at night while in the afternoon and evening they were between 8.5 and 10.3 ml/h. The average urinary flow varied from 28.9 to 40.5 ml/h in the six daytime collections whereas in the four nocturnal collections the average flow was only about half as much (14.2–16.1 ml/h). The same pattern emerged from the medians.
Fluoride concentrations ranged between 0.05 and 1.50 ppm. Both median and mean fluoride concentrations showed a weak diurnal variation and ranged from 0.35 to 0.49 ppm, the four nocturnal medians (0.39–0.45) and averages (0.43–0.49) being highest. However, due to the high urinary flow during active periods, average daytime fluoride excretion rates were higher (8.8–13.1 µg/h) than in the four nocturnal collections (6.7–8.0 µg/h). The minimal fluoride excretion rates in single collection periods, particularly those below 2.0 µg/h, occurred in the cases in which urinary flow was minimal, while fluoride concentration was a less important determinant. The coefficients of variation tended to be above 50%, indicating large individual variations. Their averages for urinary flow, fluoride concentration and excretion were 56, 60 and 72%, respectively.
The averages from the 17 children who provided complete sets of

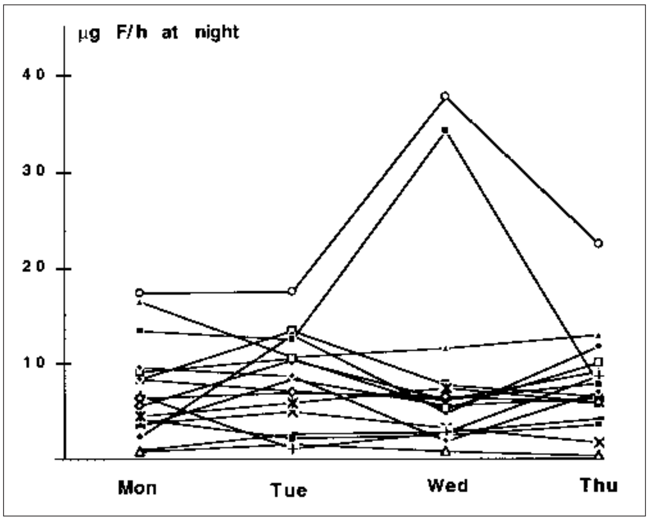

Fig. 1 Urinary excretion of the 17 "complete" children in the 4 subsequent nights

Table I Results of all valid collections

		TUESDAY					THURSDAY			
	Night Monday to Tuesday	**Morning**	**Afternoon**	**Evening**	**Night Tuesday to Wednesday**	**Night Wednesday to Thursday**	**Morning**	**Afternoon**	**Evening**	**Night Thursday to Friday**
Number	**22**	**24**	**25**	**22**	**21**	**20**	**21**	**23**	**21**	**22**
Medians of start of the collection period, hours and minutes										
Median	**2005**	**743**	**1200**	**1740**	**2000**	**2000**	**745**	**1200**	**1647**	**1958**
Duration of collection, hours and one decimal										
Average	**11.2**	**4.4**	**5.6**	**2.8**	**11.7**	**11.4**	**4.5**	**4.9**	**3.2**	**11.9**
SD	**1.0**	**1.7**	**1.6**	**1.1**	**1.4**	**0.8**	**1.3**	**1.1**	**1.3**	**0.9**
Urinary flow, ml/h										
Min	4.6	4.3	10.3	9.3	3.7	2.9	5.3	8.9	8.5	2.7
Max	32.9	96.5	87.5	101.5	45.7	31.9	63.0	86.7	72.6	31.9
Median	14.2	34.7	29.3	29.3	14.4	13.6	27.6	32.0	25.8	13.8
Mean	**14.2**	**40.5**	**35.3**	**38.9**	**16.1**	**14.4**	**32.2**	**36.6**	**28.9**	**14.4**
SD	7.1	27.0	21.4	26.1	10.3	7.8	17.4	17.1	14.8	6.4
CoeVar	50	67	61	67	64	55	54	47	51	44
Mean17	***14.9***	***38.9***	***33.8***	***34.6***	***17.5***	***14.8***	***32.0***	***36.4***	***28.9***	***14.5***
Fluoride concentration, ppm										
Min	0.14	0.10	0.13	0.14	0.14	0.12	0.10	0.08	0.05	0.08
Max	1.45	1.07	0.66	1.08	0.80	1.35	1.06	1.50	0.76	1.00
Median	0.42	0.30	0.37	0.36	0.40	0.39	0.31	0.36	0.28	0.45
Mean	**0.48**	**0.37**	**0.38**	**0.40**	**0.43**	**0.49**	**0.38**	**0.42**	**0.35**	**0.45**
SD	0.29	0.25	0.16	0.24	0.20	0.31	0.25	0.32	0.20	0.25
CoeVar	61	68	42	61	46	63	67	77	58	56
Mean17	***0.46***	***0.37***	***0.40***	***0.40***	***0.48***	***0.52***	***0.36***	***0.47***	***0.36***	***0.52***
Fluoride excretion, µg/h										
Min	0.8	0.6	3.2	3.1	0.8	0.8	2.1	4.7	1.9	0.4
Max	17.4	40.6	41.9	37.6	17.6	37.8	32.4	27.8	17.0	22.4
Median	6.3	10.9	10.0	11.4	7.0	5.6	8.7	11.8	8.5	6.5
Mean	**7.0**	**12.3**	**12.0**	**13.1**	**7.0**	**8.0**	**10.4**	**12.7**	**8.8**	**6.7**
SD	5.0	8.9	7.6	8.5	4.8	9.9	7.4	7.3	4.5	5.0
CoeVar	72	72	63	65	70	125	71	57	52	74
Mean17	***7.1***	***12.1***	***11.3***	***12.3***	***8.1***	***8.7***	***9.6***	***14.0***	***9.3***	***7.8***

SD: standard deviation
Mean17: means from the 17 complete cases
CoeVar: coefficient of variation

10 urinary collections («Mean17», Table I) were very similar to those obtained from all valid collections from 20 to 24 children. For these children, the individual excretion results at night are shown in Fig. 1. While the majority of the nocturnal excretions were below 15, there were a few high values, particulary in the third night. The variations at daytime were much larger (Fig. 2), and high excretions were frequent. Due to the few high individual excretions the frequency distributions were skewed and averages were slightly higher than the respective medians (Table I).

Table II lists 24-hour data, available from 22 children. Besides the 17 children with the full set of 10 collections, one child (No. 17) provided two complete 24-hour collections, but they were not subdivided into all the separate periods as requested. From another four children (Nos. 7, 18, 25, 26), at least one night, one morning, one afternoon and one evening collection was available, enabling the construction of four additional complete 24-hour cycles. The five children aged less than four years excreted amounts of fluoride similar to the 4-year-olds (Fig. 3); among them, the child aged 2 (No. 10, exact age 26 months) had results close to the average. The 24-hour urinary flow data varied between 310 and 1052 ml. On average, fluoride excretion was 233 µg/24h, with 95% confidence limits at 181 and 286 µg/24h. In the 24 hour urine, fluoride concentrations varied between 0.14 and 0.78 ppm, the median and average being 0.35 and 0.38 ppm. The coefficient of variation was lowest for the urinary flow (28%), whereas those for fluoride exretion were almost twice as high (51 and 52%).

Among the 22 children providing 24-hour data there were seven non-users of fluoridated salt. Their mean excretion was 208 µg F/24 h while the remaining 15 excreted 245 µg F/24 h on average (difference not significant, $P>0.1$). No relation was apparent between the reported usages of fluoride-containing products or mineral waters as coded in Table 2 and the individual urinary fluoride excretion. Of the two siblings (Nos. 25 and 26), the female excreted more than twice as much fluoride than her male counterpart, and her urinary flow was more than twice as high; accordingly, the two siblings may be regarded as independent.

Several statistical analyses were made on the per hour excretion data of the 17 children who provided all 10 collections. There was no significant difference ($p>0.1$) between the excretions in the four subsequent nights (Table III) whereas the variation between the individuals was highly significant ($p>0.01$). Likewise, there was no significant difference between the six daytime excretions, three on Tuesday and three on Thursday, but there was again significance between subjects.

Additional analyses were done on collections exactly two days

Table II Complete list of the children, basic data, 24-hour urinary results as available from 22 children (with 95% confidence limits) and fluoride exposure

Child no.	Gender	Age	Body weight kg	*Urine flow and F excretion §* Results/24 h ml urine	µg F	Results/hour ml	µg F	ppm F**	24 h µg F per kg	*Coded fluoride exposure §§* F in salt	F in paste	F tabl.	F rinse	Mineral
1	*m	4	15.5	729	103	30.4	4.3	0.14	6.6	No	1	No	No	0
2	*f	4	17	595	245	24.8	10.2	0.41	14.4	Yes	3	No	No	1
4	*f	4	20	625	221	26.0	9.2	0.35	11.1	Yes	1	No	No	2
5	*m	4	17	345	154	14.4	6.4	0.45	9.0	Yes	3	No	No	1
6	*f	4	14	815	378	34.0	15.8	0.46	27.0	Yes	1	No	No	0
7	f	3	13	1052	298	43.8	12.4	0.28	22.9	Yes	1	Spor.	No	0
8	*m	4	18	582	117	24.3	4.9	0.20	6.5	Yes	1	No	No	1
9	f	3	14							No	1	No	No	1
10	*f	2	13	559	226	23.3	9.4	0.40	17.3	Yes	1	Yes	No	1/2
11	*m	4	20	669	522	27.9	21.7	0.78	26.1	Yes	2	No	No	1
12	f	3	12							Yes	1	No	No	1
13	m	3	18							No	1	No	No	0/1
14	*m	4	20	409	126	17.0	5.3	0.31	6.3	Yes	1	No	No	1
15	*m	4	19	539	248	22.5	10.3	0.46	13.0	Yes	1	No	Yes	2
16	*f	4	20	615	224	25.6	9.3	0.36	11.2	No	1	No	No	0
17	f	4	22	690	197	28.8	8.2	0.29	9.0	Yes	1	No	No	0/1
18	m	3	12.5	310	138	12.9	5.7	0.45	11.0	Yes	1	No	No	0
19	*f	4	24	367	94	15.3	3.9	0.26	3.9	No	1	No	No	1
20	*f	4	19	583	179	24.3	7.5	0.31	9.4	Yes	1	No	No	1
21	*f	4	16.5	666	470	27.8	19.6	0.71	28.5	Yes	1	No	Yes	0/1
22	*f	4	17	544	158	22.7	6.6	0.29	9.3	Yes	1	No	Yes	1
23	*f	3	14	756	218	31.5	9.1	0.29	15.5	No	1	No	No	1
24	*f	3	15	552	186	23.0	7.7	0.34	12.4	No	1	No	No	1
25	m	4	16	583	199	24.3	8.3	0.34	12.4	No	1	No	No	0
26	f	4	18	848	433	35.3	18.1	0.51	24.1	No	1	No	No	2
N		**25**	**25**	**22**	**22**	**22**	**22**	**22**	**22**	16	22	2	3	
Min		2	12.0	310	94	12.9	3.9	0.14	3.9	Yes	"1"	Yes	Yes	
Max		4	24.0	1052	522	43.8	21.7	0.78	28.5					
Median		4	17.0	589	208	24.5	8.7	0.35	11.8					
Mean		**4.1**	**17.0**	**610**	**233**	**25.4**	**9.7**	**0.38**	**14.0**					
Stand.dev.			3.1	172	119	7.2	4.9	0.15	7.3					
Coefficient of variation				28	51	28	51	39	52					
Standard error				37	25	1.5	1.1	0.03	1.6					
Lower limit				**534**	**181**	**22.2**	**7.5**	**0.32**	**10.7**					
Upper limit				**687**	**286**	**28.6**	**11.9**	**0.45**	**17.2**					

* These were the 17 children who provided complete data for the 10 collection periods
§ In the 18 children who provided two 24-hour collections, the average of ml urine and µg F was taken and ppm F obtained from the 2 averages
§§ Codes for fluoride exposure. F in (tooth)paste: 1=250 ppm, 3=1500 ppm, 2=both, but 250 ppm on urine collection days.
Fluoride tablets: spor=sporadically 0.25 mg F; yes=0.25 mg F/day.
Mineral and drinking water: 0=no mineral water, low drinking water intake; 1=no mineral water, but high drinking water intake; 2=mineral water 0.7–2.0 ppm F in use

apart (middle part of Table III). The ANOVA of the Monday/Wednesday nocturnal fluoride excretion data resulted in a 5 times higher Interaction MS than the one of Tuesday/Thursday. As evident from Figure 1, this was essentially due to two children who had very high excretions on Wednesday night (night 3). After logarithmic transformation, the disparities between the two ANOVAs vanished largely and the strong individual component and lack of differences between nights was again borne out. The ANOVAs of the pooled daytime collections showed again a strongly significant individual component ($p<0.05$ on the numerical scale, $p<0.01$ on the logarithmical one). The large Interaction MS (Mean Square) of 40.31 from the six separate daytime collections was reduced by the pooling to only 12.01. In the ANOVAs of the logarithms of the excretions, the Interaction MS of the daytime pools (1.34) were in fact smaller than those of the nocturnal collections (4.59, 4.46 and 5.00). On the whole, the average nocturnal excretion rate (7.92 µg F/h) was lower ($p<0.01$) than that during daytime (10.90, average from the two daytime pools).

The last ANOVA of Table III shows that the fluoride excretions between the first and the second 24-hour periods were strongly correlated ($F>7$, $P<0.001$). Figure 4 illustrates this correlation in those 18 children who provided two complete 24-hour urinary collections ($r=0.78$, $p<0.001$). By contrast, there was no obvious

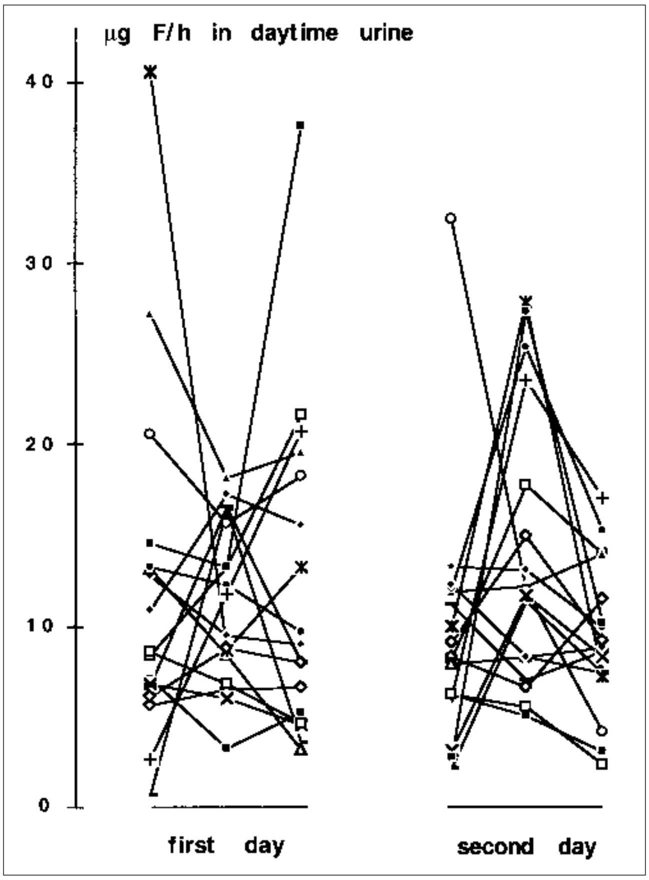

Fig. 2 Urinary excretion of the 17 "complete" children in the 3 daytime collection on Tuesday and Thursday

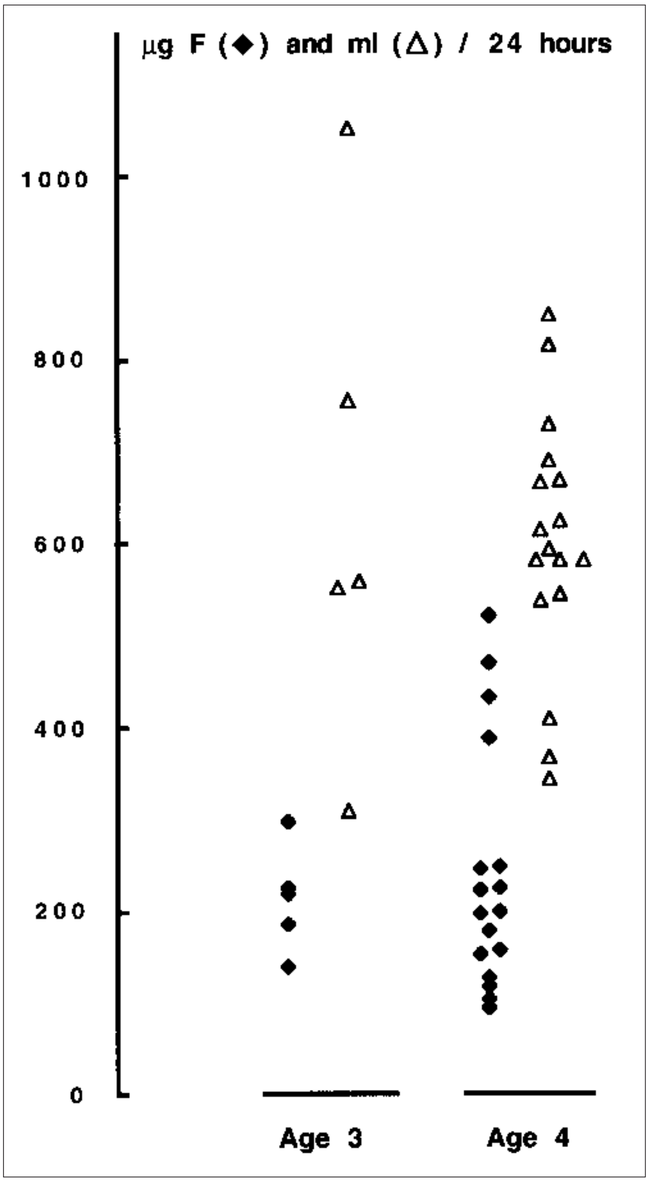

Fig. 3 Fluoride excretion and urinary flow in 24 hours according to age (one of the children shown as being 3 years old was only 26 months old), data from 22 children (Table II)

correlation between urinary flow on the first and second days (Figure 5, p>0.1).

Discussion

The participation of 34 families out of a total of 50 (68%) was attained due to the fact that the author doing the field work (MB-F) had been living in the village up to adulthood. Since dietary habits are fairly homogeneous throughout the resident population in the German-speaking part of Switzerland, the representative quality of the sample is satisfactory with respect to the majority of Swiss families (20% of the residents in Switzerland are non-citizens). The percentage of users of fluoridated salt, 16 of 25 households (64%), was lower than its overall market share of 84% (1996) in Switzerland (difference not significant). Since fluoride excretion in the non-users of fluoridated salt was not much lower than in the users, the estimate of 233 µg or 0.23 mg of daily excreted fluoride, with confidence limits (p=0.95) at 0.18 and 0.29 mg may be regarded as valid for Northeastern Switzerland. For the fluoride excretion in terms of body weight, the corresponding estimate is 14.0 µg F/kg with a confidence interval of 10.7–17.2 µg F/kg (p=0.95).

The large "between subjects" mean squares when compared to the interaction document the strong individual component of fluoride excretion. This is most obvious from the figures 1 and 2 which show that there are a few individuals whose fluoride excretion is consistently low. For this survey, this means that if the total of 40 collections of 24-hour urines had come from 40 different children, the confidence interval would have been noticeably narrower. For routine monitoring of fluoride excretion in general, it is thus advisable to obtain only one 24-hour collection from each subject but to include as many subjects as possible.

There were two exceptionally high nocturnal excretions in the night of Wednesday to Thursday (37.8, 34.2 µgF/h, the other 83 nocturnal excretions being below 23, see Fig. 1). The two high excretions were due to both high urinary flow (28 and 32 ml/h) and high fluoride concentrations (1.35, 1.07 ppm F). The detailed records kept on food intake and oral hygiene (most children brushed their teeth two or three times a day) did not reveal direct clues for these two outliers. Nevertheless, in these two children customary use of a 1500 ppm F toothpaste (case 11, Table II) and fluoride rinses (case 21) may explain in part the high fluoride concentrations, whereas reasons for the high urinary flow were not available.

In recent years, several investigations on the fluoride excreted via urine by children aged 3 to 6 have been published. Available results of the studies on children aged 2–6 and providing

Table III Two-way analyses of variance of the excretion data, Degrees of Freedom (DF), Mean Squares (MS), F is the variance ratio. The square root of the Interaction MS is the residual standard deviation (s), given in parantheses

	DF	MS	F	Sig. #	MS on Log §	F	Sig.
Comparisons based on the original collection periods							
Four subsequent nocturnal collections							
Between the 17 subjects	16	125.37	6.42	**	44.68	9.74	**
Between the 4 nights	3	6.91	0.35	ns	2.19	0.48	ns
Interaction	48	19.51	(s=4.42)		4.59	(s=2.14)	
3 daytime collections Tuesday, 3 on Thursday							
Between the 17 subjects	16	120.02	2.98	**	20.58	3.40	**
Between the 6 collections	5	53.32	1.32	ns	8.34	1.38	ns
Interaction	80	40.31	(s=6.35)		6.05	(s=2.46)	
Comparisons of corresponding collections 2 days apart							
First (Mon) versus third night (Wed)							
Between the 17 subjects	16	107.47	3.61	**	26.75	6.00	**
Between the 2 nights	1	19.99	0.67	ns	0	0.00	ns
Interaction	16	29.76	(s=5.46)		4.46	(s=2.11)	
Second (Tue) versus fourth night (Thu)							
Between the 17 subjects	16	40.76	6.88	**	22.24	4.45	**
Between the 2 nights	1	0.73	0.12	ns	0.53	0.11	ns
Interaction	16	5.93	(s=2.43)		5.00	(s=2.24)	
First daytime pool (Tue) vs second daytime pool (Thu)							
Between the 17 subjects	16	32.98	2.75	*	5.92	4.41	**
Between the daytime pools	1	0.71	0.06	ns	0.03	0.02	ns
Interaction	16	12.01	(s=3.47)		1.34	(s=1.16)	
First versus second 24 hour period							
Between the 17 subjects	16	51.91	7.44	**	9.07	7.74	**
First vs second day	1	2.27	0.33	ns	0.28	0.24	ns
Interaction	16	6.89	(s=2.64)		1.17	(s=1.08)	

\# Significances: *means p<0.05; **means p<0.01; ns: not significant, p>0.1
§ log (10) of µg F/h were used, multiplied by 10 to obtain similar magnitudes of MS

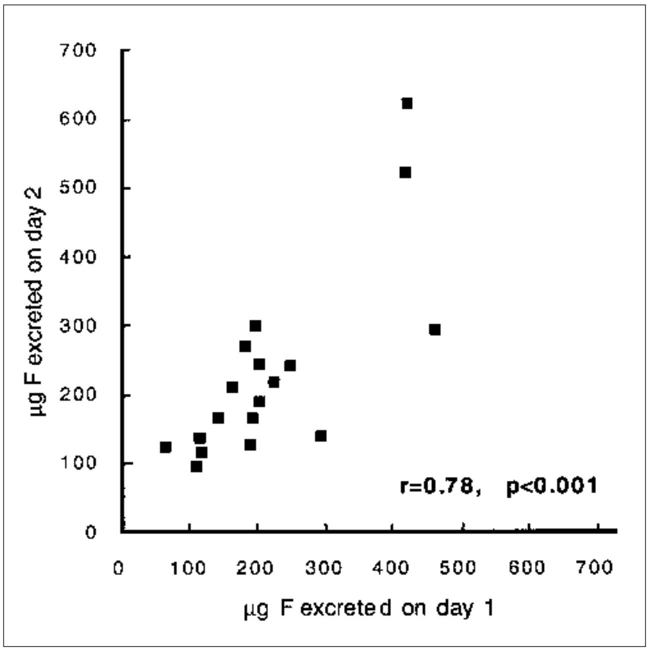

Fig. 4 Fluoride excretion during the first 24-hour period versus the second 24-hour period, N=18

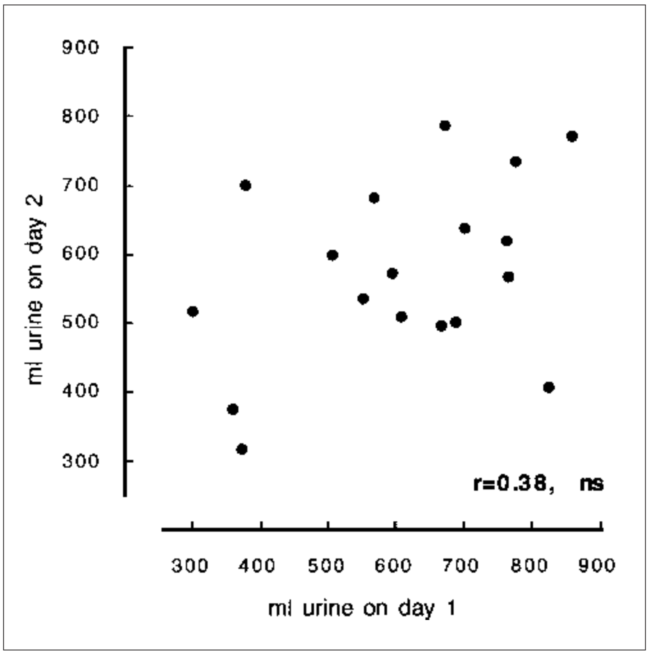

Fig. 5 Urinary flow during the first 24-hour period versus the second 24-hour period, N=18

Table IV Summary of reported urinary fluoride (F) data from children 2–6 years of age

Years			*Urinary flow*		Conc.	*Fluoride excretion*			Fluoride exposure
survey	Age	N	ml/24 h	ml/h	ppm F	F/24 h	Period	µg F/h	explanations in footnote*
									Low exposure
1994	3–6	41				204		8.5	Low-F DW, FP, Germany (1)
									Exposure mainly via water
1995/6	4	78	465	19	0.73	339		14.1	0.33 ppm F DW, Iran (2)
	3–4	20	406	17	0.93	358		14.9	0.6 ppm F DW, Chile (3)
1993/4	2	132	225	9	0.80	175		7.3	0.8 ppm F DW,
	4	132	282	12	0.86	229		9.5	24 collections, in part
	6	126	303	13	0.89	265		11.0	incomplete? Saudi Arabia (4)
1991	4	44	449	19	1.02	420		17.5	0.8–1.0 ppm F DW, FP, England
	4	53	504	21	1.19	550		22.9	0.6–1.1 ppm F DW, Sri Lanka (5)
1997	5–7	22	633	26	1.34	749		31.2	1.2 ppm F DW, FP, Texas, USA (6)
1995/6		16	473	20	5.88	2659		110.8	≈ 4 ppm in DW, Iran (7)
									Exposure mainly via salt
1996	3–4	22	610	25	0.38	233		9.7	Present study, FDS (250 ppm), FP
1993	5–6	37					morning	19.5	FDS (250 ppm), FP,
		36					afternoon	28.0	average from two days,
		37					night	12.9	Embrach, Switzerland (8)
1997	3–5	43	446	19	0.83	446		18.6	FDS (250 ppm), Uruguay (9)
1995	4	16					morning	16.6	FDS (250 ppm) and lunch
							afternoon	39.8	prepared with fluoridated salt
							night	16.7	(250 ppm), FP, Germany (10)

* Abbreviations: DW=drinking water, FP=common use of fluoride-containing toothpaste, FDS=use of fluoridated domestic salt

(1) SCHULTE et al. (1995)
(2) ZOHOURI & RUGG-GUNN (2000)
(3) VILLA et al. (2000)
(4) RUGG-GUNN et al. (1998)
(5) RUGG-GUNN et al. (1993)
(6) BAEZ et al. (2000)
(7) ZOHOURI (1997)
(8) AESCHBACHER (1995)
(9) PUCCI & DOL (1997)
(10) HETZER et al.(1996)

average 24-hour excretion or presenting at least morning, afternoon and nocturnal averages are compiled in Table IV. Three to 6-year-old German children whose only exposure to fluoride was through fluoride dentifrices (most of them with 250–500 ppmF) had excretion levels of 8.5 µg F/h or 204 µg F/24h (SCHULTE et al. 1995). A total of 78 Iranian children consuming water containing 0.33 ppm fluoride excreted 339 µg F/24 h on average (ZOHOURI & RUGG-GUNN 2000). These values were obtained from duplicate assessments, one in summer and one in winter. When questioning led to the suspicion that micturations were missed, the 24-hour collection was repeated. Studies of creatinine excretion confirmed that on the whole, the 24-hour urinary collections were likely to have been complete.

VILLA et al. (2000) studied fluoride excretion in 3- and 4-year-old children (N=20) in Santiago, Chile, where the drinking water contains 0.6 ppm fluoride. The average 24-hour fluoride excretion was 358 mg. In Saudi Arabian children aged 4 years, the average 24-hour urinary fluoride concentrations were 0.80, 0.86 and 0.89 ppm at the ages 2, 4 and 6, respectively (RUGG-GUNN et al. 1998). These concentrations were in accordance with the simple rule that they should be equal to that in drinking water which contained in fact 0.8 ppm. On the other hand, the average fluoride excretions, 175, 229 and 265 µg/24 h, respectively, were clearly below expectations. The data compiled in Table IV show that on average only 225, 282 and 303 ml urine (age 2, 4 and 6, respectively) were collected during the 24-hour period. This suggests that for some of the children the 24-hour collection may have been incomplete, which in turn would explain the low excretion. In fact, if an urinary flow of 500 ml in a day's time is assumed, which would be expected in 4-year-old children, multiplication with 0.86 ppm fluoride (Table IV, age 4) would result in 430 µg fluoride excreted in 24 hours; this would be in agreement with the other data.

Four-year-old children consuming drinking water containing 0.8–1.1 ppm fluoride had average fluoride excretions of 420 (Newcastle, England, 0.8 ppm F, mean maximum air temperature 12 °C) and 550 µg F/24 h (Dambulla, Sri Lanka, 1.1 ppm F, 27 °C) (RUGG-GUNN et al. 1993). In subtropical southern Texas (USA), children of San Isidro were exposed to higher than optimal concentration of fluoride in the drinking water. Samples of drinking water obtained from 28 households dispersed over a wide area revealed an average concentration of 1.32 ppm fluoride, with the second and third quartile (middle 50%) of the sources ranging from 0.74 to 1.65 ppm. In the early morning the children were bused to school where they had breakfast and lunch and remained until mid-afternoon; there the water contained 1.0–1.3 ppm fluoride. Average excretion was 749 µg F per day or 31.2 per hour (BAEZ et al. 2000). Iranian children using drinking water with approximately 4 ppm fluoride excreted 2.66 mg fluoride per 24-hours (ZOHOURI 1997).

With respect to children living in households using fluoridated salt (lower part of Table VI) the present study resulted in a 24-hour excretion of 233 µg F/24 h or 9.7 µg F/h. Only the morning and afternoon excretion averages, 10.4–12.7 µg F/h of the 3–4-

year-old children were higher than the 8.5 µg F/h (obtained from 24-h urine) in the German sample with low-fluoride exposure; however, the German children were on average older as their age range was 3–6. The average fluoride excretion of 43 Uruguayan children was 446 µg/24 h or 18.6 µg/h, which is twice the average of the present results (Pucci & Dol 1997). Their fluoride exposure comprised both suboptimal fluoride in the drinking water and fluoridated domestic salt (250 ppm) while their use of fluoride toothpaste may have been below the level common in affluent countries. In 16 German children of the same age who had a salted meal at school, excretion during the afternoon reached 39.8 µg F/h (average based on two different days, Hetzer et al. 1996), while excretion during the morning and night were at 16.6 µg F/h. Obviously, these children had eaten meals prepared with more plain, i.e. cheap, salt than may be customary in private households where plain salt is often substituted by pre-packaged spices and bouillon cubes which are not fluoridated. These children did brush their teeth after the meal, which is known to go along with some inadvertent fluoride ingestion from toothpaste. This source of fluoride, however, must be assumed for most subjects on which Table IV is based except for those in Iran, Saudi Arabia and Sri Lanka.

Research summarized by Murray et al. (1991, pages 269–270) seemed to indicate that under conditions of fairly constant fluoride intake, approximately 50 percent of ingested fluoride will be excreted by the urine. If this were the case, at least in specific age groups, fluoride excretion multiplied by two would provide an estimate of total fluoride intake, allowing to predict the level of later fluorosis if enough data were available. However, recent research has produced conflicting results in the age group 3 to 4 years. Whereas Zohouri & Rugg-Gunn (2000) reported that of 426 µg F ingested per day, 339 µg F equal to 80% were excreted in Iranian (vegetarian) children, Villa et al. (2000) found that of 1.019 mg fluoride ingested, only 0.358 mg or 35% were excreted. Based on data from the literature and their own material, Villa et al. (2000) derived a formula which for a given level of fluoride intake should predict the percentage of excreted fluoride in the urine. For the Iranian children with a daily fluoride intake of 0.426 mg F equal to 31 µg F/kg (Zohouri & Rugg-Gunn 2000), only 52% would be expected according to the formula instead of the observed 80%. In the Iranian children with the very high fluoride intake of 3.363 mg/day (equal to 0.240 µg F/kg, Zohouri 1997), 79% of the ingested fluoride were excreted whereas according to the formula only 33% would have been expected. A discussion of these conflicting results and other recent studies on the subject is not within the scope of this paper. The booklet on "Monitoring of renal fluoride excretion in community preventive programmes on oral health" (Marthaler 1999) avoids this discussion and is based on the assumption of an approximately stable relation between small children's 24-hour excretion of fluoride and dental fluorosis.

The usefulness of quantitative assessments of fluoride excretion to serve as a marker, in monitoring studies, for prediction of the level of fluorosis is based on the assumption that the factors influencing the quantitative metabolism of fluoride, as investigated and described in detail by Whitford (1996), tend to level out in surveys comprising a suitable number of subjects. It is obvious, however, that more surveys studying relations between fluoride ingestion and excretion are needed, preferably from small children in regions where water fluoridation has been well controlled and the prevalence of dental fluorosis was monitored. This would provide improved bases for estimating the supposed quantitative relations between fluoride intake, excretion and dental fluorosis.

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Zusammenfassung

Urin von 25 3- und 4-jährigen Kindern wurde gesammelt in der Nacht von einem Montag auf den Dienstag, anschliessend am Morgen, Nachmittag und Abend sowie in der Nacht von Dienstag auf Mittwoch. Ab Mittwochabend bis Freitagmorgen erfolgten nochmals fünf separate, zeitlich gleich angesetzte Urinsammlungen. Das Urinvolumen und die Fluoridkonzentration der einzelnen Urinsammlungen wurden bestimmt und die Fluoridausscheidung errechnet. Darüber hinaus wurden auch die 24-Stunden-Parameter aus den Urinsammlungen von Montagnacht und den drei anschliessenden tagsüber gesammelten Proben berechnet; ebenso wurde für die 24-Stunden-Periode von Mittwochabend bis Donnerstagabend verfahren. Der vollständige Satz von zehn Urinsammlungen liess sich von 17 Kindern erhalten; bei weiteren fünf Kindern waren genügend Sammlungen vorhanden, welche mindestens eine volle 24-Stunden-Ausscheidung erlaubten. Bei diesen 22 (17+5) Kindern lag die mittlere Ausscheidung bei 233 µg/24 h Fluorid, mit 95%-Vertrauensgrenzen bei 181 und 286 µg F/24 h. Anhand der 17 Kinder mit vollständigen Daten liess sich eruieren, dass tagsüber mehr Fluorid ausgeschieden wurde als in der Nacht, und dass die Variabilität deutlich höher war zwischen den einzelnen Kindern als innerhalb der Kinder. Aus der Zusammenstellung mit vorhandenen Daten in der Diskussion geht hervor, dass sich mit steigender Fluoridversorgung auch die Fluoridausscheidung erhöht. Diese Arbeit stützt die Hypothese, dass die Fluoridausscheidung über den Urin von 3- und 4-jährigen Kindern als nützlicher Indikator für die Vorhersage des Fluoroseniveaus der später durchbrechenden bleibenden Zähne benützt werden kann.

Résumé

Des prélèvements d'urine ont été effectués chez 25 enfants de 3 et 4 ans, dans la nuit d'un lundi à un mardi, ainsi que le matin, l'après-midi, le soir et la nuit du mardi au mercredi. Ce procédé a été répété du mercredi soir au vendredi matin de la même semaine. Les volumes d'urine et la concentration en fluorure des échantillons ont été mesurés et l'excrétion urinaire de fluorure a été déterminée. En outre, les paramètres de 24 heures ont été calculés, d'après les prélèvements nocturnes du lundi et les trois diurnes des jours suivants; de même, les données de 24 h ont été tirées des échantillons du mercredi soir et des trois prélèvements diurnes subséquents.

Une collection complète de 10 prélèvements a pu être réalisée chez 17 enfants; auprès de 5 autres sujets, un nombre suffisant d'échantillons a permis de déterminer au moins une donnée de 24 h. Chez ces 22 enfants (17+5), l'excrétion moyenne de fluorure était de 233 µg/24 h (limites de confiance entre 181 et 286 µg F/24 h). Chez les 17 sujets avec collection complète, l'analyse a montré des excrétions diurnes plus élevées que les nocturnes, ainsi que des variations entre sujets nettement plus

marquées que chez un même sujet. D'après les données de la littérature, l'augmentation de l'apport de fluorure s'accompagne d'une excrétion plus élevée.
Ce travail soutient l'hypothèse d'une forte dépendance entre excrétion urinaire et apport total de fluorure. Cette excrétion pourrait être un bon indice de prédiction du niveau de fluorose des dents permanentes.

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