

Fluoride Metabolism in Man

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Fluoride balances were measured in man under strictly controlled dietary conditions before and during the intake of sodium fluoride, and after its discontinuation. Fluoride intake averaged 4.4 mg/day in the control period and 13.8 mg during the addition of an average of 21 mg sodium fluoride/day. The main pathway of fluoride excretion was via the kidney. Urinary fluoride excretion corresponded to about 50 per cent of the fluoride intake in the control study and during the intake of sodium fluoride. Fecal fluoride excretion was very low, averaging 0.29 mg/day in the control period and 0.88 mg/day during the sodium fluoride study. Fluoride balances were positive in all study phases and averaged +1.9 mg/day in the control period and +5.4 mg/day during the addition of 9.1 mg fluoride/day given as sodium fluoride. Fluoride retention corresponded to 42.9 per cent of the fluoride intake in the control period and to 39.3 per cent in the sodium fluoride study. Following the discontinuation of sodium fluoride, the fluoride balances were lower than in the control study. The loss of fluoride in sweat was not determined in these balance studies.

A great deal of information is available on fluoride metabolism in different species of animals [1-5]. Tissue analyses of fluoride, especially of bone and teeth, have been made [6-11], and the fluoride level in urine samples has been determined in man in survey studies [12,13]. However, only few data are available on the metabolism of fluoride studied under controlled dietary conditions. In the present investigation, fluoride balances were measured under constant dietary conditions in control studies, during the addition of sodium fluoride to the diet and after the discontinuation of sodium fluoride.

MATERIALS AND METHODS

Ten ambulatory male patients who were in good physical and nutritional state and who did not have renal, gastrointestinal or skeletal disease were studied under constant dietary conditions on the Metabolic Research Ward. The age of the patients ranged from thirty to fifty-three years, averaging forty-four years (Table 1). All clinical and laboratory tests including the serum levels of calcium, phosphorus and alkaline phosphatase were normal in all patients.

The patients received a basal analyzed low calcium diet which contained an average of 71 gm protein, 325 gm carbohydrate, 71 gm fat, 206 mg calcium and 750 mg phosphorus/day. The calcium intake was raised to an average of 1,448 mg/day by adding calcium

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gluconate tablets to the constant low calcium diet. The phosphorus intake was raised to an average of 1,388 mg/day by adding glycerophosphate to the constant basal diet. These supplements raised the dietary calcium to phosphorus (Ca:P) ratio of the low calcium diet from 1:3.7 to about 1:1. The daily fluid intake was kept constant throughout the studies. The patients were maintained on this constant diet for one to two months on the Metabolic Research Ward prior to the start of the studies. The average fluoride intake of the ten patients in the three study phases is listed in Table I. The daily fluoride intake ranged from 3.57 to 5.37 mg in the control study, from 13.14 to 15.09 mg in the sodium fluoride study and from 3.59 to 5.31 mg/day after discontinuation of sodium fluoride. The fluoride intake derived from the diet and from the drinking water was kept constant in the three study phases of the studies (Table II). In the sodium fluoride study an average of 21 mg/day sodium fluoride (9.06 mg fluoride) was given. The individual sodium fluoride tablets, containing about 1 mg fluoride ion, were administered in clear gelatin capsules, the daily dosage being given in three divided doses with meals. The net absorption of fluoride was determined by the following formula:

$$\text{Net absorption, \%} = \frac{\text{Fluoride intake} - \text{fecal fluoride}}{\text{Fluoride intake}} \times 100$$

The duration of the three study phases averaged twenty-three days, thirty days and twenty days, respectively (Table I).

Complete collections of urine and stool were obtained throughout all studies. Balances of fluoride were determined by analyzing aliquots of six day pools of urine and stool and aliquots of the diet for this element in each six day metabolic period. The drinking water, the individual dietary items and the sodium fluoride tablets were also analyzed for fluoride.

Fluoride content was determined by the method of Singer and Armstrong [14]. The preparation of the aliquots of the diet, of urine and stool for fluoride analyses has been described [15]. The coefficient of variation of the fluoride analysis averaged 8.1 per cent for the diet, 5.2 per cent for stool and 2.5 per cent for urine. Calcium in the diet was determined with the atomic absorption spectrophotometer [16,17], phosphorus by the method of Fiske and SubbaRow [18] and nitrogen by the Kjeldahl method [19].

RESULTS

Data on the urinary and fecal fluoride excretions of the ten patients in each of the six day periods in the control study are listed in Table III. The urinary excretion of fluoride varied from patient to patient but was quite constant for each individual patient in the four six-day periods (Table III, upper half). The aver-

TABLE I List of Patients Studied

Patient	Age (yr)	Diagnosis	Studies	Study Days	Fluoride Intake (mg/day)
1	41	Normal, psychoneurosis	Control	24	3.93
			NaF	34	13.27
			After NaF	24	3.59
2	53	Normal, psychoneurosis	Control	22	3.57
			NaF	34	13.14
			After NaF	24	3.65
3	39	Normal, psychoneurosis	Control	24	4.47
			NaF	26	13.46
			After NaF	12	5.00
4	40	Normal, psychoneurosis	Control	24	5.37
			NaF	34	15.09
			After NaF	24	5.31
5	54	Osteoarthritis, slight	Control	22	4.47
			NaF	34	14.03
			After NaF	24	4.31
6	30	Obesity, exogenous	Control	24	4.56
			NaF	42	14.26
			After NaF	22	4.46
7	42	History of alcoholism	Control	22	4.11
			NaF	24	13.56
			After NaF	24	3.87
8	52	History of alcoholism	Control	24	4.50
			NaF	30	13.67
			After NaF
9	50	Osteoporosis, mild	Control	22	4.29
			NaF	28	13.70
			After NaF	24	4.07
10	39	Normal, psychoneurosis	Control	14	4.54
			NaF	22	13.20
			After NaF

age urinary fluoride excretion of the ten patients ranged from 1.51 to 3.09 mg/day, mean 2.26 mg/day, representing approximately half of the fluoride intake. The fecal fluoride excretion (Table III, lower half) was very low in all patients, the average fecal fluoride excretion ranged from 0.19 to 0.43 mg/day, with a mean of 0.29 mg/day. The fluctuations in fecal fluoride excretion in the different six day periods were somewhat greater than the fluctuations in urinary fluoride excretions.

The urinary and fecal fluoride excretions of the ten patients during the intake of sodium fluoride are listed in Table IV. The urinary fluoride excretion was about two to three times higher than in the control study, ranged from 6.0 to 9.27 mg/day and averaged 7.52 mg/day. In the five six-day periods of fluoride supplementation, the urinary fluoride excretion continued to increase slightly with time in most patients. The fecal fluoride excretion was considerably lower than the urinary fluoride excretion but was higher than in the control studies, ranging from 0.56 to 1.56 mg/day and averaging 0.88 mg/day for the ten patients.

TABLE II Fluoride Intake in the Control Study and During and After Sodium Fluoride (NaF) Intake

Patient	Control			NaF				After NaF		
	Fluoride (mg/day)			Fluoride (mg/day)				Fluoride (mg/day)		
	Diet	Water	Total	Diet	Water	NaF	Total	Diet	Water	Total
1	2.17	1.76	3.93	2.38	1.77	9.12	13.27	1.79	1.80	3.59
2	1.99	1.58	3.57	2.52	1.60	9.02	13.14	2.03	1.62	3.65
3	1.99	2.48	4.47	2.14	2.49	8.83	13.46	2.48	2.52	5.00
4	2.17	3.20	5.37	2.56	3.22	9.31	15.09	2.07	3.24	5.31
5	1.99	2.48	4.47	2.41	2.50	9.12	14.03	1.79	2.52	4.31
6	1.45	3.11	4.56	1.78	3.17	9.31	14.26	1.22	3.24	4.46
7	1.99	2.12	4.11	2.40	2.14	9.02	13.56	1.71	2.16	3.87
8	1.81	2.69	4.50	1.98	2.76	8.93	13.67
9	2.17	2.12	4.29	2.54	2.14	9.02	13.70	1.91	2.16	4.07
10	2.74	1.80	4.54	2.50	1.78	8.92	13.20
Average	2.04	2.35	4.39	2.31	2.39	9.09	13.79	1.84	2.39	4.23

TABLE III Urinary and Fecal Fluoride Excretion in the Control Study

Period	Patient									
	1	2	3	4	5	6	7	8	9	10
Urinary Fluoride Excretion (mg/day)										
1	1.65	1.45	2.60	3.15	2.15	2.25	2.00	2.70	1.95	...
2	1.70	1.40	2.40	3.20	1.95	2.45	1.90	2.20	2.90	...
3	2.00	1.70	2.20	2.90	2.10	2.30	1.95	2.65	2.15	2.47
4	2.00	1.50	2.45	3.10	2.15	2.20	1.80	2.70	2.20	2.54
Average	1.84	1.51	2.41	3.09	2.09	2.30	1.91	2.56	2.30	2.51
Fecal Fluoride Excretion (mg/day)										
1	0.17	0.23	0.29	0.58	0.19	0.32	0.29	0.67	0.28	...
2	0.21	0.22	0.30	0.43	0.25	0.39	0.28	0.16	0.28	...
3	0.22	0.13	0.31	0.29	0.19	0.42	0.28	0.30	0.22	0.41
4	0.18	0.18	0.20	0.29	0.14	0.38	0.21	0.34	0.21	0.45
Average	0.19	0.19	0.27	0.40	0.19	0.38	0.26	0.37	0.25	0.43

NOTE: Average fluoride intake = 4.39 mg/day. A metabolic period = six days.

TABLE IV Urinary and Fecal Fluoride Excretion During the Intake of Sodium Fluoride

Period	Patient									
	1	2	3	4	5	6	7	8	9	10
Urinary Fluoride Excretion (mg/day)										
1	6.90	5.31	7.52	9.17	6.50	7.59	6.34	6.71	7.46	6.51
2	7.15	6.36	7.68	9.03	6.70	7.53	6.70	7.95	7.62	6.80
3	7.80	6.13	7.60	9.02	6.91	7.94	6.70	7.70	7.75	7.45
4	8.02	6.65	7.97	9.56	7.19	8.20	6.50	7.73	8.22	...
5	8.52	6.04	...	9.62	7.68	8.29	6.50	...	8.48	...
Average	7.59	6.01	7.71	9.27	6.94	8.12*	6.53	7.43	7.85	6.85
Fecal Fluoride Excretion (mg/day)										
1	0.48	0.56	0.56	0.92	0.53	1.48	0.74	0.83	0.40	0.87
2	0.32	0.66	0.60	0.72	0.50	1.50	1.16	1.06	0.91	0.98
3	0.99	0.65	0.60	1.29	0.61	1.72	1.10	1.59	0.47	1.15
4	0.57	0.74	0.70	0.90	0.70	1.51	1.17	1.14	0.52	...
5	0.65	0.58	...	0.94	0.61	1.78	0.98	...	0.59	...
Average	0.59	0.63	0.62	0.95	0.58	1.56†	1.01	1.11	0.56	0.98

NOTE: Average fluoride intake/day = 13.79 mg.

* Average includes two additional periods in which the urinary fluoride was 8.56 and 8.93 mg/day, respectively.

† Average includes two additional periods in which the fecal excretion of fluoride was 1.32 and 1.58 mg/day, respectively.

TABLE V Fluoride Balances in the Control Study, During the Intake of Sodium Fluoride and After Its Discontinuation

Period	Days	Patient 1				Days	Patient 2				
		Fluoride (mg/day)					Fluoride (mg/day)				
		Intake	Urine	Stool	Balance		Intake	Urine	Stool	Balance	
Control Study											
1	6	4.33	1.65	0.17	+2.51	4	3.97	1.45	0.23	+2.29	
2	6	3.80	1.70	0.21	+1.89	6	3.45	1.40	0.22	+1.83	
3	6	3.85	2.00	0.22	+1.63	6	3.57	1.70	0.13	+1.74	
4	6	3.73	2.00	0.18	+1.55	6	3.30	1.50	0.18	+1.62	
Average	24	3.93	1.84	0.19	+1.90	22	3.57	1.51	0.19	+1.87	
During Sodium Fluoride Intake											
5	10	12.95	6.90	0.48	+5.57	10	12.70	5.31	0.56	+6.83	
6	6	13.22	7.15	0.32	+5.75	6	13.14	6.36	0.66	+6.09	
7	6	13.30	7.80	0.99	+4.51	6	13.13	6.13	0.65	+6.35	
8	6	13.44	8.02	0.57	+4.85	6	13.37	6.65	0.74	+5.98	
9	6	13.70	8.52	0.65	+4.53	6	13.63	6.04	0.58	+7.01	
Average	34	13.27	7.59	0.59	+5.09	34	13.14	6.01	0.63	+6.50	
After Sodium Fluoride Intake											
10	6	3.79	2.98	0.38	+0.43	6	3.90	2.29	0.27	+1.34	
11	6	3.58	2.52	0.23	+0.83	6	3.66	2.12	0.18	+1.36	
12	6	3.53	2.05	0.20	+1.28	6	3.49	1.57	0.20	+1.72	
13	6	3.47	2.18	0.25	+1.04	6	3.57	1.70	0.19	+1.68	
Average	24	3.59	2.43	0.26	+0.90	24	3.65	1.92	0.21	+1.52	

Data of the individual six day fluoride balances in the three study phases are shown for two patients in Table V. In the control study, the urinary fluoride excretion was quite constant in the various periods and ranged from 1.65 to 2.0 mg/day in Patient 1 and from 1.40 to 1.70 mg/day in Patient 2. The fecal fluoride excretion of the two patients was very low and fluctuated within a narrow range in the various metabolic periods, from 0.17 to 0.22 mg/day for Patient 1 and from 0.13 to 0.23 mg/day for Patient 2. The fluoride balances of the two patients were also fairly constant in the various periods and ranged from +1.55 to +2.51 mg/day for Patient 1 (average, +1.90 mg/day) and from +1.62 to +2.29 mg/day for Patient 2 (average, +1.87 mg/day). The addition of sodium fluoride to the diet promptly increased the urinary fluoride excretion three- to fourfold. The urinary fluoride excretion continued to increase slightly during the period of fluoride supplementation. The urinary fluoride excretion ranged from 6.90 to 8.52 mg for Patient 1 (average, 7.59 mg/day) and from 5.31 to 6.65 mg/day for Patient 2 (average, 6.01 mg/day). The fecal fluoride excretion also increased but remained relatively low and averaged 0.59 mg/day in Patient 1 and 0.63 mg/day in Patient 2. The fluoride balances became more positive and fluctuated within a narrow range, from +4.51 to +5.75 mg/day in Patient 1 and from +5.98 to +7.01 mg/day in Patient 2. After discontinuing sodium fluoride, the urinary fluoride excretion of both patients was slightly higher in the first two six-day periods than in the control study and returned to con-

control levels thereafter. The fecal fluoride excretion also decreased after the discontinuation of sodium fluoride, but was slightly higher than in the control study in the first period after discontinuing sodium fluoride in Patient 1 and returned to baseline levels thereafter. In Patient 2, the fecal fluoride excretion returned to control levels in the first six-day period after the discontinuation of sodium fluoride. The fluoride balances were slightly lower after the discontinuation of fluoride than in the control study, particularly in the first two six-day periods, and this decrease was more marked in Patient 1 than in Patient 2. In the other eight patients, the patterns of the urinary and fecal excretions and the fluoride balances were similar to those of Patients 1 and 2 in the different metabolic periods in the control, sodium fluoride and after sodium fluoride studies.

The average fluoride balances of the ten patients in the three study phases are listed in Table VI. In the control study, on an average intake of 4.39 mg fluoride/day, approximately half of the intake, 2.26 mg/day, was excreted in urine and an average of only 0.29 mg/day was excreted in stool. The fluoride balances were positive in all patients, ranging from +1.57 to +2.19 mg/day and averaging +1.84 mg/day. During the intake of sodium fluoride the average urinary fluoride excretion ranged from 6.01 to 9.27 mg/day and averaged 7.52 mg/day, again representing approximately half of the average intake of 13.79 mg fluoride/day. The fecal fluoride excretion increased during the intake of sodium fluoride to 0.88 mg/day

TABLE VI Fluoride Balances Before, During and After Sodium Fluoride (NaF) Supplementation

Patient	Control				NaF				After NaF			
	Fluoride (mg/day)				Fluoride (mg/day)				Fluoride (mg/day)			
	Intake	Urine	Stool	Balance	Intake	Urine	Stool	Balance	Intake	Urine	Stool	Balance
1	3.93	1.84	0.19	+1.90	13.27	7.59	0.59	+5.09	3.59	2.43	0.26	+0.90
2	3.57	1.51	0.19	+1.87	13.14	6.01	0.63	+6.50	3.65	1.92	0.21	+1.52
3	4.47	2.41	0.27	+1.79	13.46	7.71	0.62	+5.13	5.00	3.45	0.60	+0.95
4	5.37	3.09	0.40	+1.85	15.09	9.27	0.95	+4.87	5.31	3.39	0.37	+1.55
5	4.47	2.09	0.19	+2.19	14.03	6.94	0.58	+6.61	4.31	2.45	0.21	+1.65
6	4.56	2.30	0.38	+1.88	14.26	8.12	1.56	+4.58	4.46	2.78	0.47	+1.21
7	4.11	1.91	0.26	+1.94	13.56	6.60	1.11	+5.85	3.87	2.15	0.33	+1.39
8	4.50	2.56	0.37	+1.57	13.67	7.79	1.25	+4.63
9	4.29	2.30	0.25	+1.74	13.70	7.90	0.48	+5.32	4.07	2.35	0.24	+1.48
10	4.54	2.51	0.43	+1.60	13.20	6.85	0.98	+5.37
Average	4.39	2.26	0.29	+1.84	13.79	7.52	0.88	+5.39	4.23	2.56	0.32	+1.35

as compared to 0.29 mg/day in the control study, both values representing 6.4 and 6.6 per cent of the fluoride intake, respectively. The fluoride balances of the ten patients were markedly positive, ranged from +4.58 to +6.61 mg/day and averaged 5.39 mg/day. After discontinuation of sodium fluoride, the fluoride balances were determined in eight patients. The urinary fluoride excretion of these patients was slightly higher in this study phase than in the control study whereas the fecal fluoride excretions were similar to those of the control study except for the higher excretion of Patient 3 who had an episode of diarrhea in this study phase. The fluoride balances of all patients were somewhat lower after the discontinuation of sodium fluoride than in the control study, averaging +1.35 mg/day versus +1.84 mg/day in the control study.

The urinary and fecal fluoride excretions expressed as per cent of the fluoride intake are listed in Table VII. In the control study, the urinary fluoride excretion ranged from 42.3 to 57.5 per cent and averaged 51.0

per cent of the fluoride intake. During sodium fluoride supplementation the excretion values were similar, ranging from 45.7 to 61.5 per cent and averaging 54.5 per cent. After discontinuation of sodium fluoride, the urinary fluoride excretion expressed as per cent of the fluoride intake was higher than in the other two studies, ranging from 52.6 to 69.0 per cent and averaging 60.1 per cent. The fecal fluoride excretion was considerably lower than the urinary excretion, ranging from 4.3 to 9.5 per cent of the fluoride intake in the control study, from 3.5 to 10.9 per cent in the sodium fluoride study and from 4.9 to 12.0 per cent after the discontinuation of sodium fluoride. The average values for fecal fluoride excretion were 6.6 and 6.4 per cent in the control and sodium fluoride studies, respectively, and slightly higher in the study after sodium fluoride was discontinued, 7.4 per cent. The value of 12 per cent for Patient 3 was omitted from the group average because this patient had diarrhea in the study period after sodium fluoride was discontinued

TABLE VII Fluoride Excretions and Balances in Per Cent of Fluoride Intake

Patient	Urinary Fluoride (% Intake)			Fecal Fluoride (% Intake)			Fluoride Balance (% Intake)		
	Control	NaF	After NaF	Control	NaF	After NaF	Control	NaF	After NaF
	1	46.8	57.2	67.7	4.8	4.4	7.2	48.4	38.4
2	42.3	45.7	52.6	5.3	4.8	5.8	52.4	49.5	41.6
3	53.7	57.3	69.0	6.0	4.6	12.0	40.0	38.1	19.0
4	57.5	61.5	63.8	7.4	6.3	7.0	34.5	32.3	29.2
5	46.8	49.5	56.8	4.3	4.1	4.9	48.9	47.1	38.3
6	50.4	56.9	62.3	8.3	10.9	10.5	41.2	32.1	27.1
7	46.5	48.5	55.6	6.3	8.2	8.5	47.2	43.1	35.9
8	56.9	57.8	...	8.2	9.3	...	34.9	33.9	...
9	53.6	57.6	57.7	5.8	3.5	5.9	40.6	38.8	36.4
10	55.3	51.9	...	9.5	7.4	...	35.2	40.7	...
Average	51.0	54.5	60.1	6.6	6.4	7.4	42.9	39.3	31.9
S.E.M.	±1.7	±1.6	±2.1	±0.5	±0.8	±0.9	±1.8	±1.7	±2.7

NOTE: Average duration of studies: control, twenty-three days; NaF, thirty days; after NaF, twenty-two days. S.E.M. = standard error of mean.

and this study phase was considerably shorter (twelve days) than that of the other patients. The fluoride balances ranged from 34.5 to 52.4 per cent in the control study (average, 42.9 per cent), from 32.1 to 49.5 per cent during sodium fluoride intake (average, 39.3 per cent), and from 19.0 to 41.6 per cent after the discontinuation of fluoride (average, 31.9 per cent).

The values for the net absorption of fluoride in the three study phases are listed in Table VIII. These values were similar for the individual patients in the three study phases and averaged 94, 94 and 92 per cent for the control, sodium fluoride and after sodium fluoride studies.

COMMENTS

The present study has shown that the urinary fluoride excretion corresponded to about 50 per cent of the fluoride intake during the low or higher intake of fluoride. Other investigators have reported that the entire fluoride intake is eliminated in urine on a fluoride intake of about 1 mg/day [20], but on a higher intake of fluoride the urinary fluoride excretion has been reported to be 40 and 60 per cent of the fluoride intake [21,22]. The remarkable constancy of the urinary fluoride excretion in successive study periods of the control study in the different patients is noteworthy. During the intake of sodium fluoride the urinary fluoride excretion increased promptly on the first day of fluoride administration and continued to increase gradually during fluoride supplementation. A comparison of the urinary fluoride excretion during the first six day period of sodium fluoride supplementation with that during the last period of fluoride intake shows an increase that is statistically highly significant ($P < 0.001$). The marked increase in urinary fluoride excretion during sodium fluoride administration contrasts with the small increase in fecal fluoride excretion. After the discontinuation of sodium fluoride the urinary fluoride excretion was only slightly higher than in the control study for one to two six-day periods in most patients. The return to baseline excretion levels after this initial phase of fluoride excretion of slight excess indicates that the retained fluoride is released from bone only to a small extent. The rapid incorporation of fluoride into bone of man has also been demonstrated by the use of radiofluoride [3].

The fecal fluoride excretion in the present study was very low, about one-tenth that of the urinary fluoride excretion in the control study, similar to results reported previously [21]. The fecal fluoride excretion has previously been reported to be 3 and 12 per cent of the fluoride intake [21,22], increasing with increasing fluoride intake [23]. In the present study, the fecal fluoride excretion corresponded to about 6 or 7 per cent of the fluoride intake during both the low and higher levels of fluoride intake. These low values of fecal fluoride excretion may suggest that the ingested

TABLE VIII Net Absorption of Fluoride Before and During the Intake of Sodium Fluoride

Patient	Net Absorption (%)*		
	Control	NaF	After NaF
1	95	96	92
2	94	95	88
3	95	96	94
4	93	95	94
5	96	94	93
6	92	96	95
7	94	89	89
8	92	92	...
9	94	93	91
10	91	93	...
Average	94	94	92

$$* \text{ Net absorption} = \frac{\text{Fluoride Intake} - \text{Fecal Fluoride}}{\text{Fluoride Intake}} \times 100.$$

fluoride is almost completely absorbed and that the small amounts excreted in stool are of endogenous origin. This possibility is supported by the observation that the fecal fluoride excretion after the discontinuation of sodium fluoride was similar to the fecal fluoride excretion in the control study. If the fecal fluoride excretion was due to unabsorbed fluoride one would expect that considerably larger amounts of fluoride would be excreted in the stool in some of the patients for one or two six-day periods after the discontinuation of sodium fluoride, due to delayed fecal passage of fluoride. The assumption that the fecal fluoride may be of endogenous origin cannot be tested since suitable isotopes of fluorine are not available which would permit counting of the fecal radioactivity for a sufficiently long period of time for determination of the endogenous fecal fluoride excretion. The low fecal fluoride excretion during the intake of sodium fluoride observed in the present series of patients is in agreement with findings of others who reported that the intestinal absorption of fluoride given in aqueous solution ranged from 93 to 97 per cent [23].

The present studies have shown that the fluoride balances were positive in all patients during the intake of fluoride contained in the diet and drinking water, and that the retention of fluoride increased when fluoride supplements were given. Fluoride retention, expressed as per cent of the fluoride intake, varied little during low or higher intake levels of fluoride.

The fluoride balances described do not take into account the loss of fluoride in sweat. Under conditions of induced perspiration associated with a weight loss up to 1 kg in an eight hour period, i.e., at a temperature of 84° to 85°F and a humidity of 49 to 50 per cent, the loss of fluoride in sweat has been reported to range from 13 to 23 per cent of the fluoride intake [22]. However, the environmental conditions in our Meta-

bolic Ward were such as to minimize sweating. Despite these precautions one must assume that some loss of fluoride occurred in insensible perspiration. Therefore, the average fluoride balance of 42.4 per cent of the fluoride intake in the control study, of 39.2 per cent in the sodium fluoride study and of 32.5 per cent after the discontinuation of sodium fluoride represent maximal values.

This is in contrast to results reported in a study in which the fluoride balance was zero on a fluoride intake ranging from 0.5 to 1.5 mg/day [20]. However, on a fluoride intake of 6 mg/day Machle et al. [21] reported a fluoride retention of 57 per cent, which is

higher than the retention in our studies. Also, the absorption and retention of fluoride was shown to depend on the form in which fluoride was given [23]. Our findings indicate that the body store of fluoride, presumably the skeleton, has the ability to accept and retain fluoride for prolonged periods, possibly for many years. The fact that the fluoride is not released to any great extent after discontinuation of sodium fluoride further strengthens the supposition that fluoride is firmly incorporated in the bone crystal [24-26]. The low excretion of fluoride in urine after discontinuing sodium fluoride is in contrast to findings reported by other investigators [23,27].

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