The Science of the Total Environment, 17 (1981) 1—12
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

STUDIES OF FLUORIDE METABOLISM IN MAN*
A REVIEW AND REPORT OF ORIGINAL DATA

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(Received April 11th, 1980; accepted in final form July 18th, 1980)

ABSTRACT

The dietary intake of fluoride and the fluoride excretions in urine and stool were determined under controlled conditions in man. Fluoride balance studies have shown that the urinary fluoride corresponds to 50—60% of the intake, the fecal fluoride was very low, corresponding to 6% of the intake, and approximately 1 mg fluoride was retained per day during an average fluoride intake of 4.3 mg/day. The fluoride intake depended on the amount of fluoridated water consumed. The dietary fluoride content ranged from 1.2 to 1.5 mg/day. During the intake of supplemental fluoride the fluroide excretions increased but the ratio of the urinary/fecal fluoride was similar. Added fluoride is well retained. Following its discontinuation, very small amounts of the retained fluoride are excreted for several days. Inorganic elements, such as calcium, phosphorus, and magnesium, which have been shown to decrease the intestinal absorption of fluoride in animals were ineffective in man, while aluminum, given as aluminum-containing antacids, markedly decreased the intestinal absorption of fluoride and thereby decreased the retention of fluoride.

INTRODUCTION

In recent years fluoride has been recognized as an essential trace element that affects the growth of animals (Schwarz and Milne, 1972). However, a subsequent publication clarified that the growth-depressing effect of a low fluoride intake can be counteracted by an adequate dietary iron intake (Tao and Suttie, 1976). The concentration of fluoride in natural water varies widely and values ranging from 0.7 to 7.7 ppm have been reported for the United States (WHO Monograph, 1970). Artificial fluoridation of the water supply has been shown to be effective in preventing dental caries (McClure and Likins, 1951; Hayes et al., 1957) and water fluoridation has been introduced as a public health measure, particularly in areas where the natural fluoride content of water is low. Also, fluoride improves the crystal structure of bone (Zipkin et al., 1962). Due to the fact that fluoride is a bone seeker, it may also be of importance for the maintenance of the normal

* Supported by U.S. Public Health Service grant DE-02486.

0048-9697/81/0000—0000/$02.25

skeletal structure. A survey in the United States showed that the incidence of osteoporosis was lower in naturally high fluoride areas than in localities where the fluoride content of water is low (Bernstein et al., 1966). Also, the incidence and extent of aortic calcifications was reduced in the high fluoride areas. Also, a survey in Finland revealed a lower incidence of aortic calcifications in naturally high fluoride areas (Luoma et al., 1973). In view of the fact that fluoride improves the crystal structure of bone (Zipkin et al., 1962) and decreases bone resorption and the solubility of bone, fluoride has been used as a form of treatment for osteoporosis for the past two decades. The metabolic and therapeutic effects of this type of treatment of calcium and fluoride metabolism have been reported (Rich et al., 1964; Rose, 1965; Bernstein and Cohen, 1967; Spencer et al., 1970). However, a recent publication suggests caution and the need for further investigations regarding the use of fluoride for the treatment of osteoporosis (Riggs et al., 1980).

As fluoride enters into the human food chain the metabolism of fluoride in man becomes of importance. This communication therefore deals with the intake of fluoride which is due to the fluoride content of the diet and of the drinking water, with the subsequent disposition of the ingested fluoride from the human body and with the retention of fluoride. The dietary fluoride content and the extent and the pathways of fluoride excretions were determined. These data permitted the calculation of the retention of fluoride in the human body. As various minerals may affect the metabolism of fluoride, the interaction of fluoride with several inorganic elements, such as calcium, phosphorus, magnesium, and aluminum, was investigated in man.

EXPERIMENTAL

The studies of fluoride metabolism in man were carried out in fully ambulatory adult men by analyzing the dietary intake of fluoride and the excretions of fluoride in urine and stool. These studies were performed under strictly controlled dietary conditions in a Metabolic Research Ward. The diet contained an average of 1.6 mg fluoride per day (Spencer et al., 1970; Osis et al., 1974; Osis et al., 1974) but the total fluoride intake was greater due to the intake of water which contained about 1 ppm fluoride. Depending on the amount of water consumed, the total fluoride intake ranged from 3.5 to 5.5 mg per day. The diet and the fluid intake were kept constant throughout the studies and therefore the fluoride intake varied little. Complete collections of urine and stool were obtained and these were analyzed for fluoride by methods previously described (Osis et al., 1974; Singer and Armstrong, 1965). The retention of fluoride was determined by fluoride balance studies, i.e., by relating the fluoride intake to the fluoride output in the excreta. The loss of fluoride in sweat was not determined and, therefore, the retention of fluoride has to be considered as maximal. Studies were also carried out on the metabolic effects of a high fluoride intake which was given orally as sodium fluoride. Three different dosages of fluoride, i.e.,

10, 20, and 45 mg of fluoride, as sodium fluoride, were used in these studies. These fluoride supplements were given daily for several weeks or months under the same strict study conditions. The 45-mg dose of fluoride was given for the treatment of patients with osteoporosis (Spencer, et al., 1970), usually for a 3-month period.

Investigations were also carried out to determine the release of retained fluoride following the discontinuation of fluoride supplements which were given for several weeks. This release was determined by analyzing the fluoride excretions in urine and stool after the fluoride supplements were discontinued and by comparing these excretions with the fluoride excretions prior to the intake of the fluoride supplements. The difference between these fluoride excretions permitted the calculation of the release of the previously retained fluoride.

As the metabolism of fluoride may be altered by the interaction with other minerals, fluoride balance studies were carried out during different intakes of calcium, phosphorus, magnesium, and aluminum. The calcium intake was increased by a factor of 10 by adding calcium gluconate tablets to the constant diet, the phosphorus intake was increased by more than a factor of 2 by adding sodium glycerophosphate and the magnesium intake was increased 3- to 4-fold by the addition of magnesium as the oxide. The effect of aluminum on fluoride metabolism was studied by using relatively small doses of aluminum-containing antacids, i.e., 30 ml given three times daily for several weeks.

All fluoride balance studies were carried out for several weeks. Total fluoride in diet, urine, stool, and plasma was analyzed by a modification (Osis et al., 1974) of the diffusion method of Singer and Armstrong (1965). Extensive experimental studies were carried out in which the validity of this method (Osis et al., 1974) for fluoride analysis of diet and of biological samples was verified. Recoveries of fluoride added to samples of urine ranged from 93—99%, to stool from 91—96% and to diet from 90—100%. In none of the analyses for total fluoride added to diet, urine, or stool were the values higher than these recoveries. Recoveries of fluoride in standards were 99% and the analysis of fluoridated water gave the expected values of 0.9 to 1 ppm. Similarly, analysis of fluoride tablets yielded the declared value of 1 mg. The fluoride values for stool were the same whether these samples were analyzed ashed or unashed (Osis et al., 1974). Similarly, fluoride analysis of ashed and unashed aliquots of the diet yielded values which were in good agreement. A recent report by Debeka et al. (1979) shows very good agreement of the fluoride values of various food items determined by microdiffusion using the ion-specific fluoride electrode with values obtained by macrodiffusion and colorimetry, i.e., by the same method as used in our studies. The analyzed fluoride intake per day in our studies is in agreement with the recent provisionally recommended dietary allowance (RDA) for fluoride*.

* Recommended Dietary Allowances, Office of Publications, National Academy of Sciences, Washington, DC, 1980. Ninth revised edition.

1. *Dietary fluoride intake of adults*

Prior to water fluoridation the dietary fluoride intake was estimated to range from 0.5 to 1.5 mg per day (Machle et al., 1942; McClure, 1949; Hodge and Smith, 1965). In London, England, the total daily dietary fluoride intake was higher, ranged from 1.3 to 1.8 mg, while after water fluoridation it ranged from 2.2 to 3.2 mg/day (Longwell, 1957). In other studies, the total dietary fluoride intake, calculated from analyzed individual food items, ranged from 2 to 5 mg per day (Marier and Rose, 1966). In a survey of the contents of shopping baskets of four young men the dietary fluoride intake ranged from 2.1 to 2.4 mg, including dietary beverages and fluoridated drinking water (San Fillippo and Battistone, 1971). Fluoride analyses of diets used for metabolic studies and of hospital diets in the Chicago area have been reported (Osis et al., 1974). In five years the average fluoride content of metabolic diets ranged from 1.6 to 1.8 mg/day and of the hospital diets from 1.2 to 2.4 mg/day, exclusive of the fluoride content of drinking water. In a study of fluoride content of diets from several areas in the United States (Kramer et al., 1974), the dietary fluoride varied widely, ranging from 1.7 to 3.4 mg/day, exclusive of the drinking water in fluoridated localities and averaged 0.9 mg/day in non-fluoridated areas. The variability in dietary fluoride in fluoridated areas may be due to the varying fluoride content of fluoridated water (Shannon and Wescott, 1975) used in the preparation of processed foods. Other reports indicate a daily intake of fluoride of adults, ranging from 0.85 to 1.44 mg/day, exclusive of the fluoride content of beverages and from 1.46 and 2.57 mg/day including beverages (Singer et al., 1978). Certain food items, for instance, tea, have a high fluoride content (McClure, 1949) and seafood (Schwarz and Milne, 1972).

2. *Excretion of fluoride*

The major pathway of fluoride excretion is via the kidney and the urinary fluoride excretion corresponds to 50—70% of the fluoride intake (Machle et al., 1942; Spencer et al., 1970). These excretions increase with increasing fluoride intake. The fecal fluoride excretion is very low, corresponding to about 5% of the fluoride intake, particularly during a low fluoride intake of 4 mg/day. During the higher fluoride intakes, the fecal fluoride excretion increases but it also accounts for only 5—9% of the fluoride intake, the highest excretion was observed during the highest fluoride intake. In view of the low fecal fluoride excretion, even during a high fluoride intake, the retention of fluoride mainly depends on the magnitude of urinary fluoride excretion. Table 1 shows data of the urinary and fecal fluoride excretions and of the fluoride balances expressed as milligram per day and as percent of the fluoride intake. During a low fluoride intake of 4 mg/day, the main pathway of excretion of fluoride is via the kidney, the fecal fluoride is very low, and the fluoride balance is positive. Increasing the fluoride intake from 4 to 14, 25, and 45 mg per day by adding sodium fluoride to the constant diet, resulted in a progressive increase of both the urinary and fecal fluoride excretion, the urinary fluoride being high during all fluoride intakes. Here

TABLE 1
FLUORIDE EXCRETIONS AND BALANCES DURING DIFFERENT FLUORIDE INTAKES IN MAN

Study days	Fluoride, mg per day				Fluoride, % of intake		
	Intake[a]	Excretions		Balance	Urine	Stool	Retained
		Urine	Stool				
28	4	2.5	0.3	1.2	63	8	30
32	14	7.5	0.8	5.7	54	6	41
90	25	14.0	1.5	9.5	56	6	38
76	44	21.0	4.5	18.5	48	10	42

[a] The fluoride intake of 4 mg/day was due to the fluoride content of the diet and drinking water. All other fluoride intakes were due to the addition of sodium fluoride.

again, the main pathway of the excess excretion of fluoride was via the kidney. The fluoride balance also increased with increasing fluoride intake and was most positive during the highest fluoride intake. When the fluoride excretions were expressed as percent of the fluoride intake, the urinary fluoride ranged from 48% during the highest intake to 63% during the lowest intake, the percent fecal fluoride varied from 6% to 10% during the different fluoride intakes. The fluoride retention, expressed as percent of the fluoride intake, did not differ greatly during the different fluoride intakes and ranged from 30% to 42%; however, the actual amount of retained fluoride increased with increasing fluoride intake. The fluoride retention, determined by fluoride balance studies, must be considered maximal as the secretion of fluoride in sweat was not determined.

3. *Retention of fluoride*

Studies were carried out to determine whether the human body continues to retain large amounts of fluoride which are given for relatively prolonged periods of time. This information is important as fluoride is used for the treatment of patients with osteoporosis for several months or even years. In fluoride balance studies carried out in this Research Unit the retention of fluoride was determined during a period of several weeks or months of continued fluoride administration. Fluoride supplements were given in doses of 10, 20, or 45 mg/day as sodium fluoride (Spencer et al., 1975). During the intake of 10 mg fluoride per day, the fluoride balance was high, averaged 4.6 mg/day in the first 6 days of fluoride administration compared to an averge of 1.6 mg/day prior to the intake of the fluoride supplements. The initial balance during the high fluoride intake remained the same throughout the period of the high fluoride intake which extended for several weeks. Similarly, during a higher fluoride intake of 20 mg/day, the fluoride balance increased to approximately 8—10 mg/day in the first 6 days, depending on the retention of a given individual, and this fluoride retention persisted

throughout the 3 months of this fluoride intake. When the fluoride intake was increased further to 45 mg/day, given for 3 months to patients with osteoporosis, the retention of fluoride increased further, ranging from 12 to 18 mg/day. This high fluoride retention persisted throughout the 3 months of this high fluoride intake. Even when a 3-month course of 20 mg fluoride per day preceded the intake of a 45-mg dose of fluoride which was given daily for 3 months, the retention of fluoride during the 3 months of the higher fluoride intake was as high as the fluoride retention of persons who did not receive supplemental fluoride prior to the intake of the large dose of 45 mg per day (Spencer et al., 1975).

The question arises whether and how much of the retained fluoride is released from depot sites, most probably from bone, and is excreted. Other investigators reported that large amounts of fluoride are excreted for prolonged periods of time by persons who lived in a high fluoride area for many years and who subsequently moved to a low fluoride area (Likins et al., 1962). The knowledge of the release of previously deposited fluoride is relevant as fluoride is used as a form of treatment for osteoporosis (Rich et al., 1964; Rose, 1965; Bernstein and Cohen, 1967; Spencer et al., 1970). It was therefore important to investigate under controlled conditions the release of retained fluoride following cessation of the fluoride therapy. In a study performed in this Research Unit, only a very small fraction of the retained fluoride was excreted after the discontinuation of the high fluoride intake (Spencer et al., 1975). When a 10-mg dose of fluoride was given for several seeks only approximately 6—10% of the previously retained fluoride was excreted and most of this small excess was excreted in the first 6 days after the discontinuation of the fluoride supplements. It was also observed that the main pathway of the excess fluoride excretion was via the kidney, while only negligible amounts were excreted via the intestine.

Table 2 shows data of the excess excretion of fluoride, i.e., data on the

TABLE 2

EXCRETION OF RETAINED FLUORIDE AFTER THE DISCONTINUATION OF FLUORIDE SUPPLEMENTS

Fluoride intake and retention	Excretion of retained fluoride		
	6-day period[a]	Excess excretion, mg/6 days[b]	
		Urine	Stool
Fluoride intake = 14 mg/day[c]	First	5.1 ± 0.65	0.9 ± 0.22
Duration of fluoride intake = 32 days	Second	2.6 ± 0.71	0.5 ± 0.34
Fluoride balance = 3.6 mg/day	Third	0.3 ± 0.60	0.2 ± 0.14
Fluoride retention = 114 mg	Total excess excretion	8.0 ± 1.36	1.2 ± 0.57

[a] Following discontinuation of 10 mg fluoride as sodium fluoride per day.
[b] Study carried out in 10 patients.
[c] Fluoride intake due to the intake of 10 mg fluoride as sodium fluoride per day.

release of previously retained fluoride in the body. When a 10-mg dose of fluoride as sodium fluoride was given daily for 32 days, a total of 114 mg fluoride was retained. After the discontinuation of this fluoride supplement, a total of 5.1 mg fluoride was excreted in urine in the first 6 days, 2.6 mg in the second 6 days, and very little, 0.3 mg fluoride, was excreted in the third 6-day period. The total excess fluoride excretion in urine in these 18 days was 8 mg of 7% of the retained fluoride. Very little of the excess fluoride excretion was passed in stool and these small amounts could only be detected in the first two 6-day periods, so that a total of only 1.2 mg fluoride was recovered after the first 12 days. The total excess fluoride excretion in both urine and stool was 9.2 mg in 18 days or a total of 8% of the previously retained fluoride. After this period of time the fluoride excretions in urine and stool had returned to control levels and no further excess excretion could be detected. Similar results were also obtained after the discontinuation of a large dose of 45 mg fluoride per day which was given daily for 90 days. During this period of time the calculated fluoride retention, estimated from fluoride balance data, was more than 800 mg. The excess fluoride excretion after the discontinuation of this dose of fluoride was very low and the total excess excretion corresponded only to 2% of the retained fluoride. This excess was excreted in the first 8 days, mainly via the kidney, and no further excess excretion could be detected in subsequent weeks.

4. *Effect of inorganic elements on fluoride metabolism*

a. *Calcium and phosphorus.* Both calcium and phosphorus, used singly or combined, have been reported to inhibit the intestinal absorption of fluoride in animals (Largent, 1954; Greenwood, 1961; Wagner and Muhler, 1960). In studies in man, calcium and/or phosphorus decreased the absorption of fluoride when fluoride was given as bone meal, cryolite, or calcium fluoride (Machle and Largent, 1943; McClure et al., 1945). However, studies carried out in this Research Unit have shown that these observations are not applicable to man when daily calcium supplements are given for several weeks (Spencer et al., 1975). These studies were carried out during a relatively low fluoride intake of about 4 mg/day which was due to the fluoride content of the diet and drinking water as well as during a high fluoride intake of an average of 13.8 mg/day which was due to supplementation of the constant diet with sodium fluoride. These studies have shown that increasing the calcium intake level from 200 to 1500 and 2000 mg/day did not significantly change the urinary fluoride excretion. The fecal fluoride increased only slightly but this increase was small and not significant. The fluoride balances did not change during the high calcium intake. Table 3 shows the changes of the fluoride balance during different calcium and phosphorus intakes. The fluoride balance studies show again that fluoride is primarily excreted via the kidney during all calcium intakes. The fecal fluoride excretion is very low, particularly during the low calcium intake of 200 mg per day and the fluoride balance was slightly positive. Increasing the calcium intake from 200 to 1500 mg/day resulted in a slight decrease of the urinary fluoride

TABLE 3
EFFECT OF CALCIUM AND OF PHOSPHORUS ON THE FLUORIDE BALANCE

Calcium intake, mg/day[a]	Phosphorus intake, mg/day[b]	Fluoride, mg/day			
		Intake	Urine	Stool	Balance
200	800	4.0	2.9	0.13	+ 0.9
	1400	4.0	2.6	0.17	+ 1.2
1500	800	4.0	2.6	0.17	+ 1.2
	1400	4.3	2.5	0.26	+ 1.5
2200	800	3.9	2.9	0.20	+ 0.7
	1400	4.4	2.9	0.31	+ 1.2

[a] The low calcium intake was due to the calcium content of the constant diet. All higher calcium intakes were due to the addition of calcium gluconate tablets.
[b] The phosphorus intake of 800 mg/day was due to the phosphorus content of the diet; the 1400-mg phosphorus intake was due to the intake of sodium glycerophosphate.

excretion and a slight increase of the fecal fluoride. However, the overall fluoride balance was similar during the two calcium intakes, 0.9 to 1.2 mg per day, respectively. Increasing the calcium intake further, to 2000 mg/day, did not affect the urinary fluoride, while the fecal fluoride excretion had increased slightly; however, the fluoride balance was the same during the 2000-mg calcium intake and during the 200-mg calcium intake. With regard to the effect of phosphorus on the fluoride balance during the different calcium intakes, increasing the phosphorus intake did not affect the urinary fluoride during the different calcium intakes, while the fecal fluoride increased slightly during the higher calcium intakes. The data show that adding 600 mg phosphorus to the low calcium intake did not change the fecal fluoride excretion, while adding phosphorus to the higher calcium intakes increased the fecal fluoride more than during the addition of calcium alone. However, the fluoride balances were similar during the high phosphorus intake and in the control studies, irrespective of the calcium intake. The lack of change of the fluoride balance during the combined use of calcium and phosphorus is due to the fact that the increase in fecal fluoride was very small in relation to the much greater dietary fluoride intake. The observation that the overall retention of fluoride remained unchanged during the various calcium and phosphorus intakes was made both during a low fluoride intake of about 4 mg/day and a high fluoride intake of 14 mg/day.

b. *Magnesium.* The studies of the effect of magnesium on fluoride metabolism were carried out both during a low fluoride intake of 5 mg/day and a high fluoride intake of 25 mg/day. Fluoride balances were determined in control studies and during the addition of magnesium to the diet (Spencer et al., 1978). The magnesium intake averaged 300 mg/day in the control study and 800 mg/day during the high magnesium intake. This higher magnesium intake was due to the addition of magnesium oxide to the constant

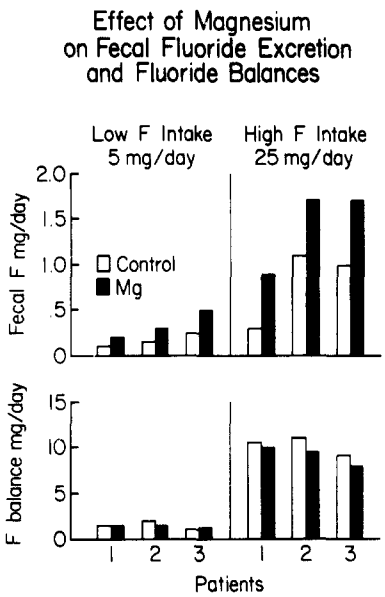

Fig. 1. The fluoride intake of 5 mg/day was due to the fluoride content of the diet and drinking water. The high fluoride intake of 25 mg/day was due to the intake of 20 mg fluoride per day, given as sodium fluoride.

diet. During the increased magnesium intake the urinary fluoride excretion remained unchanged during both the low and high fluoride intake, while the fecal fluoride excretion increased. Figure 1 shows data of the effect of magnesium on the fecal fluoride excretions and on the fluoride balance during a low and high fluoride intake. The fecal magnesium excretion increased in each of the three patients studied during a low fluoride intake of 5 mg/day and during a high fluoride intake of 25 mg/day. However, the added magnesium had little effect on the fluoride balance as the increase of the fecal fluoride was small, particularly in relation to the fluoride intake. There was no change of the fluoride balance during the low fluoride intake and the slight decrease during the high fluoride intake was not significant. Similar observations were made during the addition of magnesium to a high calcium or high calcium–high phosphorus intake. It can be concluded that a substantial increase in magnesium intake does not alter the metabolism of fluoride in man. This is in contrast to results obtained in animals.

c. *Aluminum.* In animal studies, aluminum sulfate decreased the intestinal absorption of fluoride, it decreased the concentration of fluoride in bone, and diminished the pathologic effects of fluorosis (Hobbs et al., 1954). Aluminum has been reported to be a highly effective complexing agent for fluoride in water (Brudevold et al., 1972). The possibility that aluminum may inhibit the absorption of fluoride in man has been considered (Hodge, 1961), however, no data have been reported. In one study, the urinary fluoride excretion was found to be lower following the oral intake of Al-EDTA than the fluoride excretion following the intake of sodium fluoride. This

TABLE 4
EFFECT OF ALUMINUM HYDROXIDE ON FLUORIDE METABOLISM

Study	Study days	Fluoride, mg/day				Fluoride excretion % of fluoride intake		Net absorption %
		Intake	Urine	Stool	Balance	Urine	Stool	
Control	26	4.4	2.8	0.2	+1.4	64	5	96
Aluminum hydroxide[a]	22	5.4	2.2	3.2	0	41	59	41

[a] Dose of aluminum hydroxide = 30 ml three times daily.

decrease was interpreted to reflect a decrease of the intestinal absorption of fluoride by Al-EDTA but the fecal fluoride excretion was not determined (Mellberg, 1965). No information was available on the effect of aluminum on fluoride metabolism in man up to the recent past. Studies carried out in this Research Unit have demonstrated that commonly used commercially available aluminum-containing antacids markedly decrease the intestinal absorption of fluoride in humans. This was demonstrated by a significant increase of the fecal fluoride excretion (Spencer and Lender, 1979) which results in a signficant decrease of the intestinal absorption of fluoride. Examples of the increase of the fecal fluoride excretion and of the decrease of the fluoride balance during aluminum hydroxide administration are shown in Table 4. In the control study the fluoride intake averged 4.4 mg/day. The urinary fluoride excretion corresponded to 64% of the fluoride intake, the fecal fluoride excretion was very low, averaging 0.2 mg/day or 5% of the intake, and the average fluoride balance was positive. During the intake of a relatively small dose of aluminum hydroxide of 30 ml given three times daily, the fluoride intake was 1 mg greater than in the control studies due to the fluoride content of this antacid. The major effect of aluminum hydroxide on fluoride metabolism was a significant increase of the fecal fluoride excretion, from 0.2 mg/day in the control study to 3.2 mg/day during the administration of aluminum hydroxide. This increase was highly significant, $P < 0.001$. Due to this increase, there was a significant decrease of the net absorption of fluoride, from 96% of the fluoride intake in the control study to 41% during the intake of aluminum hydroxide. The urinary fluoride was lower during the intake of aluminum hydroxide and corresponded to 41% of the fluoride intake vs. 64% in the control study. The fluoride balance decreased significantly from a positive value to equilibrium. The observation of the inhibition of fluoride absorption indicates that the fluoride intake derived from the food and from drinking water is only utilized in part. It should also be kept in mind that the absorption of large doses of fluoride which are used as a form of treatment for patients with

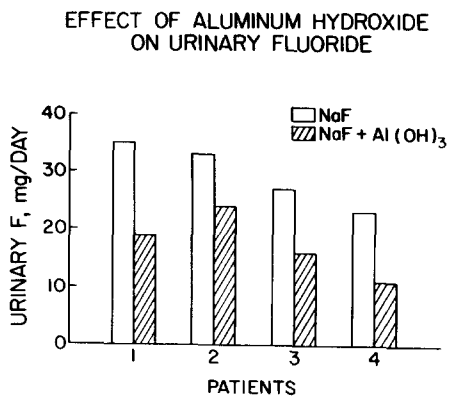

Fig. 2. The studies were carried out in patients with osteoporosis who received a daily dose of 45 mg fluoride as sodium fluoride.

osteoporosis would be utilized only in part should aluminum hydroxide be used as a medication at the same time. Figure 2 shows that this inhibition of fluoride absorption by aluminum hydroxide is reflected by a marked decrease of urinary fluoride excretion during the high fluoride intake.

REFERENCES

Bernstein, D. S. and P. Cohen, J. Clin. Endocrinol Metab., 27 (1967) 197.
Bernstein, D., H. Sadowsky, D. M. Hegsted, C. Guri and F. Stare, JAMA, 193 (1966) 499.
Brudevold, F., E. Moreno and Y. Bakhos, Arch. Oral Biol., 17 (1972) 1155.
Dabeka, R. W., A. D. McKenzie and H. B. S. Conacher. J. Assoc. Off. Anal. Chem., 62 (1979) 1065.
Greenwood, D. A. Quoted by E. J. Largent (Ed.), in Fluorosis, The Health Aspects of Fluoride Compounds, Ohio State University press, Columbus, 1961, p. 74.
Hayes, R. L., N. W. Littleton and C. W. White. Am. J. Publ. Health, 217 (1957) 192.
Hobbs, C. S., R. P. Moorman, Jr., J. M. Griffith, J. L. West, G. M. Merriman, S. L. Hansard, C. C. Chamberlain, W. H. MacIntire, L. J. Hardin and L. S. Jones (Editors), Fluorosis in Cattle and Sheep, (Bulletin No. 235), The University of Tennessee Agricultural Experiment Station, Knoxville, 1954, pp. 87—101; 119—143; 144—152.
Hodge, H. C., JAMA, 177 (1961) 313.
Hodge, H. C. and F. A. Smith, in J. H. Simons (Editor), Fluorine Chemistry, Vol. 4, Academic Press, New York, 1965, p. 155, p. 171.
Kramer, L., D. Osis, E. Wiatrowski and H. Spencer, Am. J. Clin. Nutr., 27 (1974) 590.
Largent, E. J., in J. H. Shaw (Editor), Fluoridation as a Public Health Measure, American Association for the Advancement of Science, Washington, DC, 1954.
Likins, R. C., F. J. McClure, and A. C. Steere, in F. J. McClure (Editor), Fluoride Drinking Water, U.S. Government Printing Office, Washington, DC, 1962, Public Health Service Publication No. 825, p. 287.
Longwell, J., Roy. Soc. Health J., 77 (1957) 361.
Luoma, H., S. K. J. Helminen, H. Ranta, I. Rytomaa and J. H. Meurman. Scand. J. Clin. Lab. Invest., 32 (1973) 217.
Machle, W. and E. J. Largent, J. Ind. Hyg. Toxicol., 25 (1943) 112.
Machle, W., E. W. Scott and E. J. Largent, J. Ind. Hyg. Toxicol., 24 (1942) 199.
Marier, J. R. and D. Rose, J. Food Sci., 31 (1966) 941.

McClure, F. J., Publ. Health Rep., 64 (1949) 1061.
McClure, F. J. and R. C. Likins, J. Dent. Res., 30 (1951) 172.
MClure, F. J., H. H. Mitchell, T. S. Hamilton and C. A. Kinser, J. Ind. Hyg. Toxicol., 27 (1945) 159.
Mellberg, J. R., J. Pharm. Sci., 54 (1965) 615.
Osis, D., L. Kramer, E. Wiatrowski and H. Spencer., J. Nutr., 104 (1974) 1313.
Osis, D., E. Wiatrowski, J. Samachson and H. Spencer, Clin. Chim. Acta, 51 (1974) 211.
Rich, C., J. Ensinck and P. Ivanovich, J. Clin. Invest., 43 (1964) 545.
Riggs, B. L., S. F. Hodgson, D. L. Hoffman, P. J. Kelly, K. A. Johnson and D. Taves, JAMA, 243 (1980) 446.
Rose, G. A., Proc. Roy. Soc. Med., 58 (1965) 436.
San Fillippo, F. A. and G. C. Battistone, Clin. Chim. Acta, 31 (1971) 453.
Schwarz, K. and D. B. Milne, Bioinorg. Chem., 1 (1972) 331.
Shannon, I. L. and W. B. Wescott, N. Carolina Dent. J., 58 (1975) 15.
Singer, L. and W. D. Armstrong, Anal. Biochem., 10 (1965) 495.
Singer, L., R. H. Ophaug, B. F. Harland and R. Marts, J. Dent. Res., 56 (1978) 335.
Spencer, H., L. Kramer, D. Osis and E. Wiatrowski, J. Appld. Physiol., 38 (1975) 282.
Spencer, H., L. Kramer, E. Wiatrowski and D. Osis, Am. J. Physiol., 234 (1978) E343.
Spencer, H. and M. Lender, Gastroenterology, 76 (1979) 603.
Spencer, H., I. Lewin, D. Osis and J. Samachson, Am. J. Med., 49 (1970) 814.
Spencer, H., I. Lewin, E. Wiatrowski and J. Samachson, Am. J. Med., 49 (1970) 807.
Spencer, H., D. Osis and E. Wiatrowski, J. Nutr., 105 (1975) 733.
Spencer, H. D. Osis and E. Wiatrowski, Clin. Chem., 21 (1975) 613.
Tao, S. and J. W. Suttie, J. Nutr., 106 (1976) 1115.
Wagner, M. J. and J. C. Muhler. J. Dent. Res., 39 (1960) 49.
WHO Monograph Series No. 59. Geneva, 1970, p. 17.
Zipkin, I., A. S. Posner and E. D. Eanes, Biochim. Biophys. Acta, 59 (1962) 255.