denen biologischen Testobjekten mit anorganischen Fluoriden und organischen Fluorverbindungen unter Einwirkung mehrerer Gegenmittel. Wissenschaftliche Hefte des Pädagogischen Instituts Kothen, 2:233-302, 1973.

13. Elsair, J., Merad, R., Denine, R., Reggabi, M., Alamir, B., Benali, M., Khelfat, K. and Rachedi, M.A.: Effect of Fluorine and an Antidote (Boron) on Respiration of Liver Tissue in Rabbits. Fluoride, 12:172-176, 1979.
14. Elsair, J., Merad, B., Denine, R., Reggabi, M., Benali, M., Alamir, B. and Rachedi, M.A.: Effects of Fluoride Intoxication of Several Months on Hemostasis in Rabbits in the Presence and Absence of an Antidote (Boron). Fluoride, 12:136-143, 1979.
15. Elsair, J., Merad, R., Denine, R., Reggabi, M., Alamir, B., Benali, S., Azzouz, M. and Khelfat, K.: Boron as an Antidote in Acute and Subacute Fluoride Intoxication in Rabbits: Its Action on Fluoride and Calcium-Phosphorus Metabolism. Fluoride, in press 1980.

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FLUORIDE BRIEFS

The authors induced rachitic changes in rats by administering 30 and 100 ppm fluoridated drinking water and a diet free of vitamin D, which contained a calcium and phosphorus ratio of 1:1. By administration of 70 IU of cholecalciferol (vitamin D3) per week, they prevented the rachitogenic effect of fluoride.

Chapman, S.K., Malagodi, M.H. and Thomas, W.C., Jr.:Effect of Vitamin D in Fluoride-Treated Rats. Clin. Orthop. 130:289-296, 1978.

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Twenty commercial bonemeal supplements were analyzed for their mineral content . Their lead concentration ranged between 1.5 and 8.7 µg/g, cadmium 0.05 - 2.5 µg/g. Their fluoride range was between 261 and 921 µg/g.

Capar, S.G. and Gould, J.H.: Lead, Fluoride and Other Elements in Bonemeal Supplements. J. Assoc. Off. Anal. Chem. 62:1054-1061, 1979.

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THE SIGNIFICANCE OF AGE-DEPENDENT FLUORIDE ACCUMULATION IN BONE IN RELATION TO DAILY INTAKE OF FLUORIDE

by

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SUMMARY: Fluoride levels of 600 samples of iliac crest bone in ash weight were correlated with age. They showed a near linearship with age. The yearly rate of accumulation of fluoride in bone was found to be 25.589 µg/g bone ash weight. This accumulation rate could be met by the ingestion of 0.867 mg/day of fluoride. The derivation of this figure is indicated and considered in relation to known ranges of dietary and other levels of fluoride ingestion.

Introduction

In view of the areas of disagreement regarding the significance of fluoride levels in human bone, a survey was undertaken to determine whether fluoride assays of human material can serve as the basis of evaluation of levels of intake and retention. It was also considered advisable to determine whether there is a plateau of fluoride accumulation in bones (1) or a continued lifetime accumulation (2) as expressed by previous workers.

Table 1 presents a compilation of generally acceptable data in categories of intake. These figures indicate a daily fluoride intake in the range of 0.601 to 4.301 mg.

Table 1
Fluoride Intake

	Low Diet	Normal Diet	High Diet
Tea	0	1.6 (4 cups)	2.4 (6 cups)
Food	0.5	0.75	0.9
Water	0.1	0.3	1.0
Air	0.001	0.001	0.001
	0.601	2.651	4.301 mg/day

Other sources such as serious industrial pollution and the use of mineral supplement tablets containing fluorides and fluoride

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toothpaste may further increase the levels of intake. These additional burdens were not included. From this type of data 2.5 mg/day are usually considered the average daily intake in western countries. In the W.H.O. Report (3), categories of intake are linked to clinical manifestations as given in Table 2; these data are generally accepted.

Table 2

Fluoride Ingestion Associated with Dental and Skeletal Changes

0.5 - 2 mg/day	No evidence of abnormal bone density.
2.0 - 8 mg/day	Some mineralization of teeth. Over long periods, bone density increased.
Over 8 mg/day	Skeletal fluorosis

Experimental Method

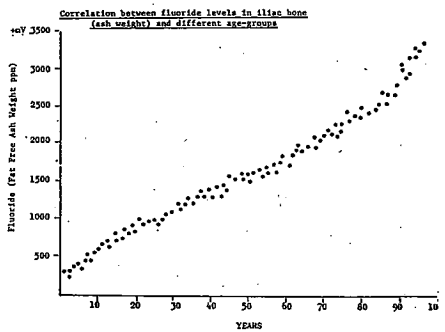
An assessment of age-related fluoride data and an approximate daily intake of fluoride was carried out by means of the fluoride ion selective electrode method (7). Six hundred samples of iliac crest bone obtained at autopsies were examined for their fluoride content. As with previous investigations, the samples obtained from the age groups 1 - 20 years and 80 - 99 years were limited to 3 to 5 for each group. For the age range 21 - 79 years, there were between 5 and 7 samples for each year group. All samples were obtained from hospitals in the London Health Authority Area from residents of South East England supplied with nonfluoridated water. The samples were analyzed by extraction with dilute perchloric acid and acetate buffer at pH 5.4. The instrument used was the Corning EEL pH meter model 12.

Bone Fluoride

The fluoride levels (in ppm) in dry fat free ash weight from ages 1 to 99 were approximately linear a good correlation coefficient of 0.99079 is shown in Figure 1. The significance is 0.00001,

Fig. 1

Correlation between fluoride levels in iliac bone (ash weight) and different age-groups



the intercept 314.79 and the slope 25.589. This result supports previous findings that fluoride levels increase with advancing age. Calculations based on observed rate of fluoride accumulation in bone is found to be 25.589 µg/g bone ash weight/year. Table 3 in conjunction with Figure 1 permitted the calculation of this value which could be satisfied by an intake of 0.867 mg/person/day.

Table 3

Mean Fluoride Levels in Bones (ppm)

Age	Mean F^- Level	Age	Mean F^- Level	Age	Mean F^- Level
1	260	34	1310	67	2050
2	240	35	1320	68	1950
3	280	36	1300	69	2140
4	348	37	1350	70	1960
5	380	38	1420	71	2100
6	345	39	1300	72	2200
7	445	40	1450	73	2350
8	500	41	1300	74	2200
9	450	42	1400	75	2200
10	540	43	1300	76	2250
11	600	44	1550	77	2330
12	650	45	1420	78	2320
13	700	46	1310	79	2000
14	648	47	1530	80	2500
15	800	48	1540	81	2400
16	700	49	1530	82	2320
17	750	50	1540	83	2450
18	850	51	1520	84	2450
19	800	52	1680	85	2600
20	900	53	1720	86	2600
21	1000	54	1600	87	2720
22	950	55	1680	88	2730
23	950	56	1600	89	2800
24	980	57	1700	90	2820
25	1020	58	1710	91	3100
26	900	59	1730	92	2800
27	1000	60	1800	93	3000
28	1050	61	1875	94	3030
29	1150	62	1830	95	3300
30	1200	63	1900	96	3400
31	1210	64	1900	97	3350
32	1250	65	1950	98	3400
33	1230	66	1970	99	3405

Accumulation of Fluoride in Bone in Relation to Age Group

Iliac bone samples were taken from postmortem subjects of different age groups who resided in areas where fluoride in water ranged from 0.15 to 1.0 ppm. The mean levels of their bone fluoride levels are shown in Table 3.

If the accumulation rate is 25.589 µg F/g bone ash per year, the total accumulation in a 7 kg skeleton would be 89.56 mg/year. It is assumed that a constant level is maintained in tissue and that the iliac crest is a good indicator bone for the calculation of total accumulation of fluoride in the skeleton.

The total fluoride retained in the skeleton is derived from the 28.3% considered by Stookey (8) to be the retention figure. In cases of renal malfunction the retention figure may be higher but in this experiment the effect on the results would be to catagorize them as having high intakes. Thus, the accumulation rate found by analysis could be provided by 0.867 mg/day ingested from all sources according to the for mula.

$$\frac{89.56 \times 100}{28.3} = 316.47 \text{ mg/year}$$

Discussion and Conclusions

Balance studies which provide retention data do not take into account bone fluoride turnover. The use of any retention figure provides a mechanism to relate accumulation data to the various dietary levels cited in the literature and by experimentation. To what extend bone fluoride turnover and the state of mineralization in the very young and the very old accounts for the apparent daily intake in the region of 2.5 mg yielding an apparently low net accumulation has not been determined.

Analysis and theoretical appraisal of dietary and other levels of fluoride indicate ranges from 0.6 mg to 4.3 mg of fluoride per day. This has led to the use of the widely quoted 2.5 mg per day. It is, however, known that in some areas of the world the intake per day is considerably higher. Some clinical manifestations are believed to occur at 2 mg per day intake which is subsequently progressive up to 8 mg per day, when skeletal fluorosis may be expected. The demonstrated figure of a daily fluoride intake of 0.867 mg is lower than the 2.5 mg average. Therefore it appears to be unwise to use dietary means for calculation of fluoride tolerance from additional sources.

All age-related graphs dealing with fluoride accumulation in bones, demonstrate a wide scatter of results consistent with multivariable factors but the current study confirms that lifetime accumulation is progressive.

The fact that the data produced from a best fit curve produces a result below the average daily intake strongly suggests that total fluoride ingestion follows an asymetric distribution which is positively skewed with a long tail to the right. This would mean that the majority of subjects in this survey appear to have ingested less fluoride than generally supposed, namely between 0.6 and 1.02 mg.

In view of the widespread concern about the effect of further increase in fluoride from water supplies and industrial pollution, it may

be considered more hazardous to impose additional fluoride burdens on a skewed distribution peaked at 0.867 mg than on a normal distribution peaked at 2.5 mg.

In this survey, the lifetime accumulation levels are below the generally recommended 4000 ppm for western populations with adequate dietary calcium. More precise surveys are needed to determine the exact shape of the asymetric distribution curves of ingestion in order to determine the size in any population of the group "at risk". This would be taken as that number ingesting above 2 mg per day in view of the progressive nature of fluorosis with increasing levels of intake.

This survey suggests a population group in a satisfactory position and provides a useful data base for comparison with populations in areas of industrial fluoride pollution or with high fluoride levels in water naturally.

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Bibliography

1. Jackson, D. and Weidmann, S.M.: Fluoride in Human Bone Related to Age and the Water Supply of Different Regions. J. Path. and Bact. 76:461, 1958.
2. Smith, F.A., Gardner, D.E. and Hodge, H.C.: Age Increase in Fluoride Content in Human Bone. Fed. Proc., 12:368, 1953.
3. Fluorides and Human Health. World Health Organization Monograph Series No. 59, Geneva, 1970, pp. 32-40.
4. Waldbott, G.L., Burgstahler, A.W. and McKinney, H.L.: Fluoridation: The Great Dilemma. Coronado Press, Inc. Lawrence, Kansas 1978, pp. 36-42.
5. Marier, J.R. and Rose, D.: Environmental Fluoride. Nat. Res. Council of Canada Publication 12:226, 1971.
6. Mohamedally, S.M.: Ph.D. Thesis (to be submitted). Section related to bone disease.
7. M.A.F.F. Central Veterinary Laboratory, Method Sheet. Fluoride Analysis, Weybridge U.K.
8. Stookey, G.K.: Unpublished data reported in W.H.O. Monograph, Ref. 3, p. 41.

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