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URINARY FLUORIDE AND CALCIUM EXCRETION IN PERSONS SUSPECTED OF FLUORIDE INTOLERANCE*

G. L. WALDBOTT, M.D.

Certain individuals ingesting minute quantities of fluoride in either food or water are unusually susceptible to ill effect^{1,2,3}. Because of the sparsity of objective laboratory data in chronic fluorosis⁴ a clinical test to determine an individual's tolerance to fluoride would be of great value. In an effort to establish such a test urinary excretion studies were undertaken. Whereas no answer can be given as to the validity of this test at this time, other data were sufficiently conclusive to warrant reporting.

FLUORIDE AND CALCIUM

The literature indicates that the tendency for fluorides to accumulate in the system varies greatly from person to person^{5,6}. There is ample evidence that fluoride affects the calcium metabolism in the system: In acute fluoride intoxication blood calcium levels were noted as low as 2.6 mg%⁷ and 5.6 mg%⁸. Leone, Geever and Moran⁹ noted blood calcium levels as low as 6.5 mg. during acute experimental intoxication by the oral and intravenous route.

In chronic protracted intoxication, on the other hand a disturbance, but not necessarily a decrease in calcium in the blood, is apparent. DeSenarclens¹⁰ reported blood calcium levels as high as 14.5 mg% in protracted experimental intoxication.

In animals grazing near factories emanating fluoride¹¹, in men suffering from industrial poisoning⁴ and from drinking fluoridated water¹², the clinical manifestations and laboratory findings of chronic fluorosis coincide markedly with those of hyperparathyroidism. Certain urinary, gastro intestinal and central nervous system manifestations, as well as bone changes characterized by demineralization, are encountered in both diseases. In my own cases of fluorosis a slight but definite increase in blood calcium levels was noted. In contrast to hyperparathyroidism, however, serum phosphorus levels were usually elevated. A disturbance of the calcium metabolism, due to fluoride's strong affinity for calcium, has been suggested by many authors.

In an attempt to establish a test for detection of intolerance to fluoride, it seemed desirable to determine whether or not a coordination exists between excretion of fluoride and that of calcium. A perusal of the literature indicates that no such studies have been made.

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A fluoride tolerance test must take into account the many variables which influence urinary excretion of both calcium and fluoride; the test must be safe and practicable, in other words it should not require too complicated an apparatus and it should be inexpensive.

Fluoride Excretion: It has been demonstrated¹³ that the largest portion of a given dose of fluoride is excreted in the urine; a small fraction (less than 10%) through the bowels, the salivary and sweat glands¹⁴. Under certain conditions more fluoride is stored in the system, whereas at other times more is liberated and excreted¹⁵. The presence of calcium in food and water interferes with fluoride absorption into the blood stream¹⁶. There is a tendency for the body to establish an equilibrium between fluoride intake and output yet, after prolonged ingestion fluoride metabolism may remain in a negative balance for months and even years^{17,18}.

For practical purposes a test pertaining to excretion of fluorides should not extend over a period of more than 2 days. In administering a standard diet preceding the test, we must take into consideration the fact that the fluoride content of some foods, especially certain vegetables, may vary considerably depending upon where they are grown¹⁹ and processed. Therefore, the test dose of fluoride to be ingested must be large enough to overcome such minor variations in fluoride intake; it must be small enough not to induce ill effect.

Calcium Excretion: Calcium excretion in the urine depends largely upon the daily calcium intake. The patient must therefore be placed on a standard calcium intake for at least 3 days. A low calcium diet containing 137 mg. (Albright²⁰) was chosen for the test.

A more exact method of carrying out the test would comprise simultaneous determinations of fluoride and calcium in faeces, sweat and saliva. However, fluoride excretion through channels other than urine constitutes only a small fraction of the total fluoride output. Furthermore, such determinations would not be suitable as a practical clinical test. As to calcium, we are less concerned here with its total output than with its relation to fluoride elimination in the urine.

Some fluoride preparations such as calcium fluoride and calcium fluosilicate are not as readily absorbed from the gastro-intestinal tract as sodium fluoride. Sodium fluoride, therefore, was selected as the compound of choice.

METHOD

After several modifications the following technique was adopted:

Fluoride Intolerance

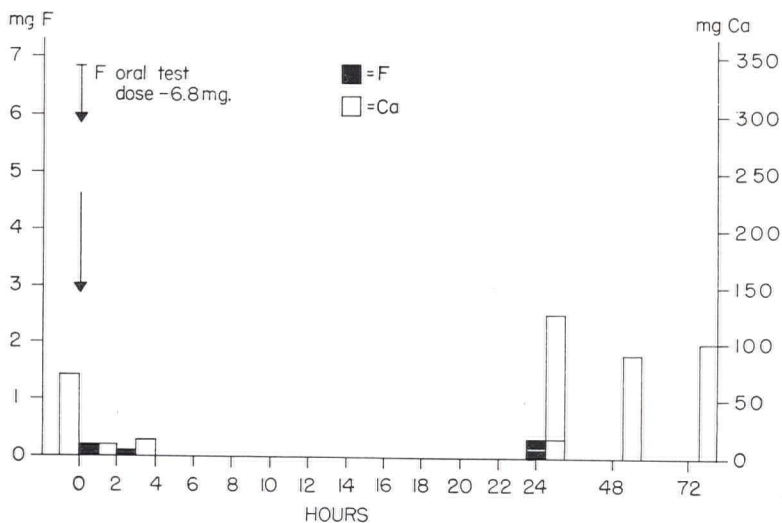


Chart 1

Three Day Course of Fluoride and Calcium Excretion following a test dose of Calcium Fluoride in a Patient with tooth decay. Twenty-four Hour Excretion of F = 4.7% of the Test Dose.

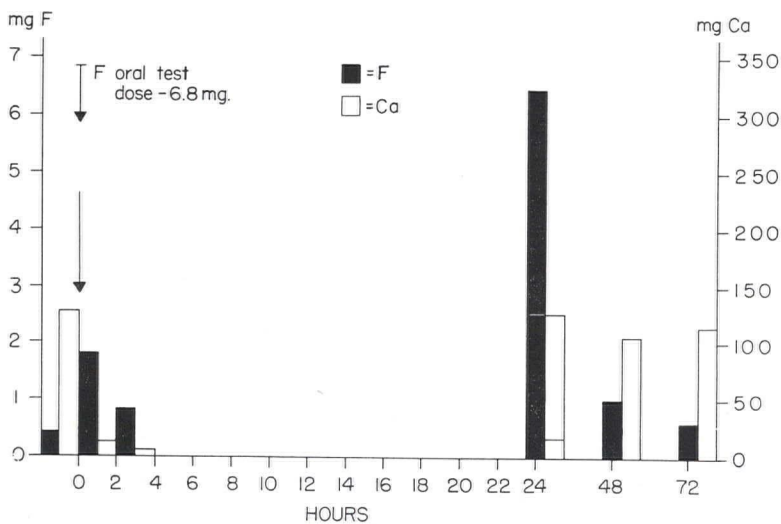


Chart 2

Three Day Course of Fluoride and Calcium Excretion Following a Test Dose of Calcium Fluoride in a Patient with Rheumatoid Arthritis. Twenty-four Hour Excretion of F = 92% of Test Dose.

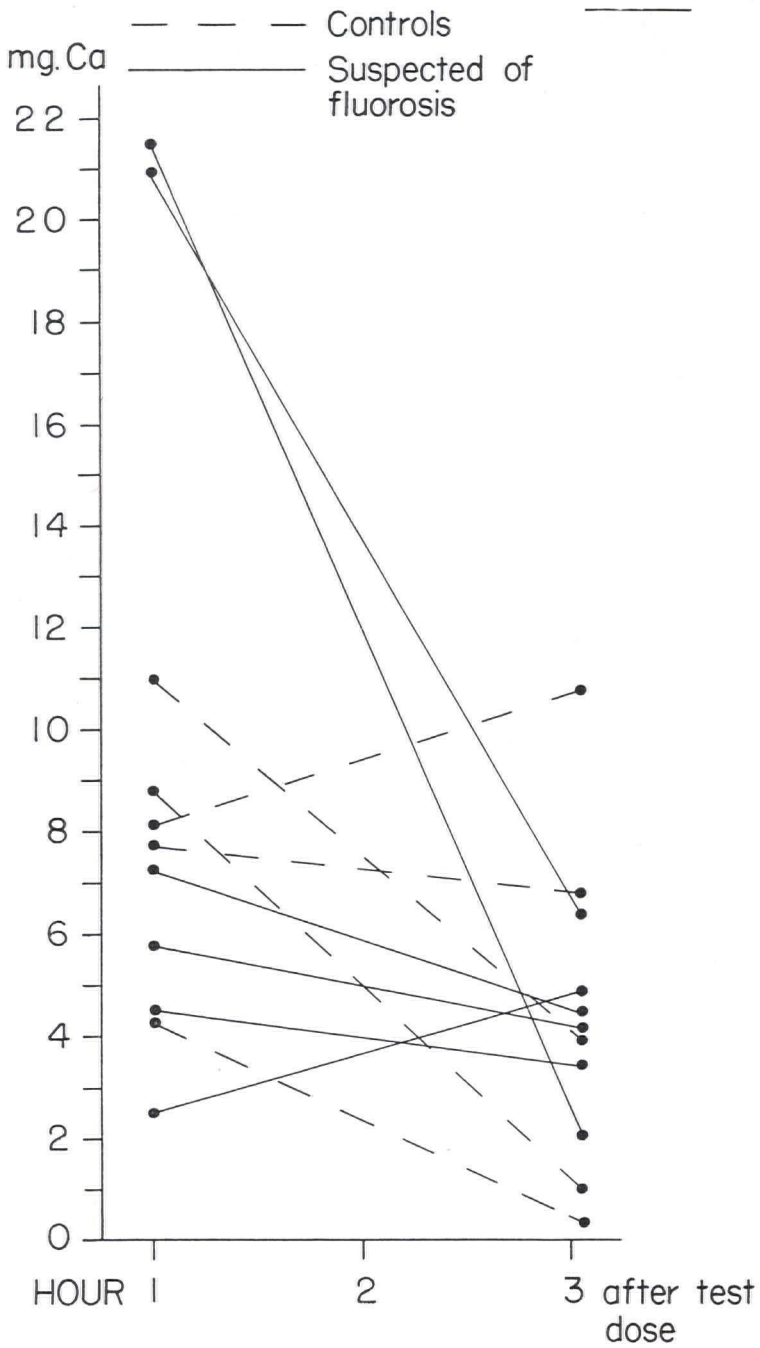


Chart 3

Urinary Calcium Excretion during first hours after Fluoride test dose. Eleven cases.

Fluoride Intolerance

The Albright diet is administered for three days prior to and during the test. On the fourth day the 24 hour specimen of urine is collected for baseline determinations of calcium and fluoride; 15 mg. of Na F (6.8 mg. F) is when administered on a fasting stomach in 400 c.c. of water in two portions, 15 minutes apart. Urine collections are made after 1-1/2 hours, 3 hours, 24 and 48 hours.

The urine is collected in a glass or plastic container with a plastic top. Contact with metal may interfere with the correct determination.*

Dividing the test dose into two portions of 7-1/2 mg each is a precautionary measure to detect any outward symptoms before administering the total dose.

As much as 6.8 mgm of F is given in order to counter minor analytical errors which might be encountered in the small sized specimens collected during the first 3 hours.

The following data were charted: (Charts 1 and 2).

- a) The total baseline urinary fluoride and calcium output on the day before the test.
- b) The amount of the two collections within the first three hours.
- c) The total 24 and 48 hour urinary fluoride and calcium excretion.
- d) The proportion of urinary calcium to fluoride excretion initially, within the first 3 hours and during the total test period.

Among 13 patients (Table 1) seven had suggestive symptoms of fluorosis, six were controls. Two of the seven had minor ill effects and two a more sustained recurrence of former symptoms of fluorosis following the tests. None of the three others and none of the controls had any discomfort whatsoever following the test dose.

RESULTS

The following results can be recorded so far:

1. There were great individual variations in total fluoride output during the 24 hours. The lowest 24 hour excretion was 4.7%; the highest 99% of the 6.8 mg test dose.

*Fluoride determinations were made according to Official Methods of Analysis of the Association of Official Agricultural Chemists; Eighth Edition, 1955, P.O. 540, Benjamin Franklin Station, Washington 4, D.C.

Table 1

Urinary Fluoride and Calcium after the Oral Fluoride test in thirteen patients.

| Case | Symptoms Suggestive of Fluorosis | Volume | 24 Hour Urinary Excretion F in Mg | % of Total Intake | Ca Mg |
|-------------------------|--------------------------------------------|-----------|--------------------------------------|-------------------|----------|
| ° 1. Mrs. E. S. 58 | G. I. and Neurological | 1965 | 2.23 | 33% | 133.4 |
| ° 2. Mrs. M. J. 37 | G. I. Neurological, Stomatitis Migraine | 3665 | 2.71 | 40% | 160 |
| ° 3. Mr. R. R.* 43 | Joint Swellings | 1747 | 3.80 | 56% | 480 |
| ° 4. Mr. F. L. P. 60 | Stomatitis, Migraine and Joint Swelling | 1870 | 1.17 | 16% | 79 |
| 5. Mrs. D. M. 25 | Urinary and Joint Symptoms | 3000 | 3.24 | 48% | 41 |
| 6. Mrs. A. L. 46 | Urinary and Joint Swellings | 1407 | .52 | 7.6% | 114.7 |
| 7. J. M. 7 | Mottled Teeth | 1621 | .77 | 11% | 111.4 |
| | | | av. = 2.06 | | |
| Controls | | Diagnosis | | | |
| ° 8. Mr. L. L. 33 | Psoriasis | 1935 | 6.77 | 99% | 360.1 |
| ° 9. Mrs. R. B. 61 | Gastro-intestinal Allergy | 3272 | 3.56 | 52% | 178 |
| ° 10. Mrs. T. W. 43 | Arthritis, Respiratory Allergy | 680 | 2.17 | 32% | 101.5 |
| 11. Mr. A. J. B. 60 | Rheumatoid Arthritis | 1929 | 6.23 | 92% | 134.8 |
| 12. D. K. 11 | Rapid Tooth Decay, Respir. Allergy | 1680 | .321 | 4.7% | 128.7 |
| 13. Mrs. I.K. 41 | Urticaria | 1040 | .610 | 9% | 41.8 |
| | | | av. = 3.27 | | |

*Urinary Ca excretion closely paralleled F. output in this patient.

°These cases were on a regular diet previous to test.

Table 2

Serum Calcium, Phosphorus and Alkaline Phosphatase
Values following Ingestion of 15 mg Na F (6.8 mg F)

| Name - Age | J. S.* 35 | | S. C.* 8 | | M. N.* 50 | | M. D.* 57 | | W. H.* 16 | | K. K. 13 | | I. K. | | J. C. 70 | |
|-------------------------|-------------------------------|----------------|-------------------|----------------|-----------------------|----------------|-------------------------|----------------|---------------------------|----------------|------------------|----------------|-----------|----------------|-----------------|----------------|
| Diagnosis | Sterility Mottled Teeth | | Hearing Defect | | Arthritis Migraine | | Arthritis Br. Asthma | | Tetaniform Convulsions | | Stained Teeth | | Urticaria | | Pruritus Ani | |
| Blood | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After | Before | 2 Hr. After |
| Calcium | 10.2 | 11 | 11.2 | 11.4 | 10.3 | 11.3 | 9.2 | 10 | 10.3 | 10.1 | 10 | 10 | 10.8 | 10.2 | 10.3 | 10.4 |
| Phosphorus | 2.9 | — | 4.4 | 4.7 | 3.5 | 3.9 | 3.2 | 4.4 | 5.4 | 5 | 4 | 4.1 | 2.6 | 2.6 | 2.8 | 2.9 |
| Alkaline Phosphatase | 4.4 | 6.3 | 10.5 | 6 | 1.5 | 1.1 | 4 | 4 | 11.3 | 15.4 | 6.7 | 7.7 | 4.2 | 4.2 | 3 | 4.4 |

All patients had been on a low calcium diet (137 mg) 3 days prior to test.

*Suspected of Fluoride Intolerance.

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2. In 9 out of 11 cases there was an initial drop in calcium excretion during the first 3 hours (Chart 3). During this time between 5.3% and 35.3% of the total 24 hour urinary F output was eliminated.
3. The total 24 hour urine output ranged from 680 cc to 3665 cc.

COMMENT

Whereas in most of seven patients suspected of fluoride intoxication the 24 hour urinary fluoride output was low, (average 2.06 mg, extremes 3.80 mg and .52 mg) it is still too early to decide whether or not this procedure will meet the requirements of a clinical test. Great variations in the excretion curves were noted in the 6 control cases without previous evidence of intoxication (average 3.27 mg; extremes 6.77 mg and .32 mg) as well as in those afflicted. Fluoride excretion and fluoride storage may not necessarily parallel the production of symptoms and their severity. In some individuals even minute doses of fluoride might affect certain body structures merely by virtue of "streaming through," rather than due to accumulation in these structures.

Whether decreased fluoride output in some individuals indicates that less fluoride was absorbed into the blood stream or that more fluoride was stored in the system must await further exploration.

If the urinary fluoride and calcium excretion parallels the production of symptoms, this test will serve as a tool for additional studies on fluoride excretion as well as for other types of clinical investigation. It could be employed especially in cases with vague gastro-intestinal symptoms, (gastritis, colitis, stomatitis), in nephrolithiasis and pyelitis, in arthritis, especially of the lower spine and in migraine like headaches of unexplained origin.

In 8 cases blood calcium, phosphorus and alkaline phosphatase levels were determined within 1-1/2 hours after the test dose. Whereas this study is still incomplete there is a definite tendency to a rise in calcium and phosphorus values as indicated in Table 2, both in cases suspected of fluorosis and the controls. In some, blood phosphorus levels increased simultaneously with the blood calcium.

8 cases suspected of incipient fluorosis and 6 controls were given orally 15 mg of Na F (6.8 mg of F). Fractional fluoride and calcium determinations in the urine were made after 1-1/2, 3 and 24 hours.

The 24 hour fluoride excretion ranged widely from 4.6% to 99% of the test dose; the total urinary volume from 680 cc to 3665 cc.

Fluoride Intolerance

In 9 out of 11 cases there was an initial decrease of urinary calcium output within the first 3 hours.

Further studies are in progress to determine whether or not this test can be utilized as a tool for detection of intolerance to fluorides.

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