

ALLERGY TO FLUORIDE

by

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SUMMARY: Clinical data presented here indicate that fluoride can induce urticaria, dermatitis, allergic stomatitis and gastro-intestinal manifestations. The differential diagnosis between allergy and intolerance to fluoride is outlined.

Fluorine is the most electro-negative of all elements and will combine with almost any element to form many different compounds. It has a high affinity for calcium. When introduced into the body, either by inhalation or ingestion, the fluoride ion acts as a hapten by combining with serum proteins. Taves (1) has demonstrated two forms of fluoride in human blood serum. Of the total 0.14 ppm normally found, 0.02 ppm is present as free ion capable of entering into any number of potential reactions whereas the remainder is protein-bound. To date, not much is known about protein-bound fluoride which normally accounts for about 85 percent of the total fluoride in human serum. It has been suggested (2) that this bound fluoride consists of covalently-bonded organic fluoride.

In considering allergic manifestations due to fluoride, it is necessary to differentiate between allergy and toxicity of a drug. Toxicity, a reaction specific for each drug, is essentially a function of excessive dosage and of individual tolerance often due to decreased excretion of the drug. Allergy to a drug, on the other hand, produces a specific group of symptoms regardless of the composition of the drug.

Toxicity

Acute fluoride poisoning, either accidental or suicidal, is an example of excessive dosage. For instance, in 1974 (3) 12 adults and 201 students from a rural school in Stanly County, North Carolina, experienced nausea and vomiting shortly after drinking orange juice prepared with tap water and ice. Due to malfunction of the fluoride pump, which was feeding the solution of sodium fluoride into the water supply the water contained 125 mg/liter of fluoride; the orange juice 270 mg/liter. A similar outbreak occurred in Hungary in 1965 (4).

Another form of toxic reaction to fluoride, not necessarily due to excessive dosage, is dental fluorosis, a defect in the development of the enamel of the teeth which occurs in some children who ingest a fluoride

compound during the period of tooth development. According to Dean (5) up to 10 percent of the children drinking water fluoridated at 1 ppm from birth "show very mild or more severe types of mottled enamel."

In 1956, Waldbott (6) recorded a series of cases of incipient fluoride poisoning from drinking water at the 1 ppm concentration, in 18 out of 52 of which a history of allergic manifestations was observed. The symptoms of these cases described in detail by Waldbott cleared completely when the patients were placed on nonfluoridated water for drinking and cooking, and reappeared with the resumption of fluoridated water. He also observed that allergic individuals have a lowered tolerance to drugs (7).

Grimbergen's cases of poisoning by fluoridated water, established by a double-blind study, constitute intolerance to fluoride (8). His preliminary results with 60 patients out of a group of 300 indicate that certain individuals are intolerant to fluoride and develop reproducibly gastrointestinal symptoms, stomatitis, joint pains, polydipsia, headaches and visual disturbances. Petraborg (9) presented additional data on this disease.

Drug Allergy or Hypersensitivity

Hypersensitivity or allergy, however, is an immunological phenomenon peculiar to the affected individual, not necessarily related to dosage or to the normal action of the drug. The allergic manifestation results from the interaction of specific antibodies with the drug localized in tissue cells whence allergic mediator substances such as histamine or complement are released. Allergic symptoms usually continue, and in some cases become more severe, as long as the drug is being administered. The presence of tissue and blood eosinophilia, allergic edema, prompt response to epinephrine, and positive intradermal and/or patch tests aid in the differentiation. The double-blind test with the use of nonfluoridated water in appropriate dilutions, constitutes a specific diagnostic tool.

Rapaport and Linde (10) state in their book: "A few patients have been reported sensitive to fluoride. They had some allergic symptoms from using toothpaste or vitamin preparations containing fluoride."

Urticaria has been reported by Lidbeck, Hill and Beeman (11), Fischer (12) and Geiger (13) as one of the symptoms in acute fluoride intoxication. Waldbott observed chronic urticaria which he was able to trace to fluoridated water (14). A case of urticaria in a pregnant woman taking

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fluoride tablets was reported by Zanfagna (15) in 1965 to the U. S. Food and Drug Administration. Its director informed him that reports had been received which establish fluoride as the cause of dermatitis.

Atopic Dermatitis: Feltman (16) reported allergic manifestations caused by fluoride tablets. One percent of a series of 1,100 cases, presented evidence of undesirable side-effects from fluoride therapy, namely atopic dermatitis, headaches, epigastric distress, varying from slight discomfort to bloody vomiting.

Contact Dermatitis: In 1948 Abelson (17) reported typical contact dermatitis with vesiculopapular pruritic lesions on the first and second phalanges and the thumb of the right hand of a dentist. It occurred immediately upon application of a 2% solution of NaF to his patient's teeth. The author has observed repeatedly the pattern of dermatitis on the fingers such as Abelson described in dentists, contact-sensitive to medication applied to teeth. A 4-plus positive patch test reaction to a 2% solution of sodium fluoride was obtained. Monocaine applied simultaneously with the fluoride solution as a patch test gave a negative reaction.

Stomatitis: Douglas (18) observed stomatitis in 133 cases from fluoride-containing toothpastes. The patients' ages ranged from 3 1/2 to 92 years. His series included one family of six and another of four, every member of which was adversely affected by fluoride toothpastes. All were refractory to antibiotic therapy and to local medications. The lesions cleared only when a nonfluoride toothpaste was substituted for the fluoride-containing one. In 32 patients the stomatitis was reproduced by reapplying the fluoride dentifrice, in some as often as six times.

Lee (19) encountered in a family consisting of a grandmother, son and grandson, what appeared to be allergic lesions in the mouth, on the tongue and throat due to the use of fluoridated water. All lesions cleared with the use of nonfluoridated water for drinking and cooking. The grandmother, however, had a recurrence of the lesions when she resumed the use of fluoridated water. A similar case due to the use of fluoridated water was reported by Kailin (20). This patient also showed a hypersensitivity to iodides and to bromides.

Shea et al. (21) recorded allergic reactions to fluoride in six children and one adult. They exhibited the following conditions after the use of toothpaste and vitamin preparations containing fluoride: urticaria, exfoliative dermatitis, atopic dermatitis, stomatitis, gastrointestinal and respiratory allergy.

Case Reports: Mrs. M. E. T., age 48, consulted her family physician while residing in Michigan in 1966 for muscular weakness, progressive fatigue associated with a loss of appetite, marked polydipsia, diarrhea alternating with constipation, hearing loss and loss of weight. She was known to be sensitive to penicillin and to the phenothiazines. She was hospitalized for a medical checkup including extensive laboratory tests, x-ray examinations and cardiac evaluation. Her physician considered her symptoms due to allergy of unknown origin.

In 1968, she visited at an air base in New York where she drank fluoridated water for several days. She promptly developed an acute generalized urticaria the cause of which was not determined. In 1969 after she had moved to Pittsburgh she consulted a dentist for periodontal disease. The dentist noticed a hyperemia and edema of the tongue which he attributed to drinking fluoridated water. Her physician concluded after reviewing the case history that most of the symptoms had cleared by the use of nonfluoridated water for drinking and cooking and agreed with the dentist that the patient was allergic to fluoride. Despite her precautions, the patient developed another attack of urticaria. The cause was traced to fluoridated water in Cola drinks.

In 1972, the patient was again exposed to fluoridated water while in the Carney Point area of New Jersey. She developed convulsions and became unconscious necessitating a week's stay at a hospital. A thorough evaluation with extensive laboratory tests were unrevealing. The patient now resides in Brookfield, Mass. and is using well water containing less than 0.2 ppm fluoride for all purposes. She also attempts to avoid beverages and food contaminated by fluoride. Most of her symptoms have cleared and she has been gradually gaining weight. Sensitivity to fluoride was confirmed by positive challenge tests.

Case 2: Mrs. J. G. of Methuen, Mass. reported severe, allergic reaction in her 4 year-old son caused by ingestion of a fluoride tablet. Within minutes after taking a fluoride pill, sudden extreme edema of lips and tongue was followed promptly by severe periorbital edema and swelling in the pharynx and nasal passages, dyspnea and wheezing. Whereas no further data could be obtained on this case, the outbreak of this episode is so characteristic of allergic shock from fluoride that its report here is believed to be warranted.

Fluoride as a constituent of vitamin preparations, dentifrices and drinking water can cause symptoms of allergy or intolerance in a segment of the population. Atopic individuals with known sensitivities and those suffering from specific chronic illnesses appear to be most susceptible.

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Bibliography

1. Taves, D. R.: Evidence that there are Two Forms of Fluoride in Human Serum. *Nature*, 217:1050-51, 1968.
2. Taves, D. R.: Electrophoretic Mobility of Serum Fluoride. *Nature*, 220:582-3, 1968.
3. Clarke, R. et al.: Morbidity and Mortality Weekly Report, 23:199, 1974. (from the Communicable Disease Center, U.S. P. H. S., Atlanta, Georgia.)
4. Horvath, I., Palicske, J., and Hanny, I.: Mass Intoxication with Fluoride in Soda Water. *Orvosi Hetilap*, 108:306-7, 1967.
5. Dean, H. T., Elvove, E.: Studies on the Minimal Threshold of the Dental Sign of Chronic Endemic Fluorosis (Mottled Enamel). *Public Health Report*, 50, 1719-29, 1935.
6. Waldbott, G. L., Incipient Chronic Fluoride Intoxication from Drinking Water. II. Distinction Between Allergic Reactions and Drug Intolerance. *Intern. Arch. Allergy and Applied Immun.*, 9: 241-49, 1956.
7. Waldbott, G. L., Blair, K. E., and McKeever, R.: Drug Tolerance in Asthma. Fatal Salicylate Poisoning from A Physiologic Dose. *Annals of Allergy*, 11:199-203, 1953.
8. Grimbergen, G. W.: A Double Blind Test for Determination of Intolerance to Fluoridated Water (Preliminary Report), *Fluoride*, 7:3, 1974.
9. Petraborg, H. T.: Chronic Fluoride Intoxication from Drinking Water (Preliminary Report). *Fluoride*, 7:47-52, 1974.
10. Rapaport, H. G., and Linde, S. M.: *The Complete Allergy Guide*, Simon and Shuster, New York, 1970.
11. Lidbeck, W. L., Hill, I. B., and Beeman, J. A.: Acute Sodium Fluoride Poisoning. *J. Am. Med. Ass.*, 121:826, 1943.
12. Fischer, H.: Uber Fluornatrium Vergiftung; *Deutsch Ztschr. Gerichtl. Med.*, 1:501, 1933.

13. Geiger, J. C.: Poisoning Due to the Ingestion of a Mixture of Sodium Bicarbonate-Sodium Fluoride, *California and West Med.*, 44:81, 1936.
14. Waldbott, G. L.: Urticaria Due to Fluoride. *Acta Allergologica*, 13:456-68, 1959.
15. Sadusk, J. F., Jr.: Medical Director, U.S. Food and Drug Administration, June 3, 1965.
16. Feltman, R. and Kosel, G.: Prenatal and Postnatal Ingestion of Fluorides- Fourteen Years of Investigation-Final Report. *J. of Dent. Med.*, 16:190-99, 1961.
17. Abelson, J. H.: A Case of Hypersensitivity to Sodium Fluoride in a Dentist. *Fortnightly Rev. Chicago Dental Soc.* 16, 8:6, 1948.
18. Douglas, T. E., Fluoride Dentifrice and Stomatitis, *Northwest Medicine*, 56:107, 1957.
19. Lee, C. H.: Letters of the International Society of Allergists, 35:9, January 1972.
20. Kailin, E.: Letters of the International Society of Allergists, 34:150, December 10, 1971.
21. Shea, J. J., Gillespie, S. M., and Waldbott, G. L.: Allergy to Fluoride. *Annals of Allergy*, 25:388-91, 1967.