

## Allergy to Fluoride

Six children and one adult exhibited various allergic reactions after the use of toothpaste and vitamin preparations containing fluoride. The following conditions were encountered: Urticaria, exfoliative dermatitis, atopic dermatitis, stomatitis, gastro-intestinal and respiratory allergy.

The literature contains little information concerning allergic reactions to the fluorine ion. Indeed some have questioned the possibility that fluoride in such a small amount as is present in vitamin tablets, toothpastes or water could act as a sensitizer. Two other halogens, iodine and bromine are recognized as sources of allergic manifestations.

Feltman and Kosel [1] noted atopic dermatitis, urticaria, epigastric distress, emesis, and headache in one per cent of 672 pregnant women and children to whom they had administered fluoride tablets as a prevention of dental caries. Waldbott reported urticaria and dermatitis due to fluoride in drinking water. The causal relationship of these diseases to fluoride was established 'by blind and double blind tests. Epstein [4] encountered a case of general dermatitis in one out of 20 patients with acne to whom he administered, on an experimental basis, 1 mg of fluoride per day for one to eleven weeks.

Douglas [5] presented an account of stomatitis in 133 cases due to fluoride containing dentrifices. The patients' ages ranged from 2 1/2 to 92 years. His series included a family of six and another of four, every member of which was adversely affected by fluoride toothpaste. Several of these patients

had gastro-intestinal disturbances. The ulcers in the mouth were refractory to antibiotic therapy and to local medication, but cleared up promptly when a nonfluoride toothpaste was substituted for the fluoride toothpaste. In 32 patients Douglas reproduced the stomatitis by reapplying the dentifrice, in some cases as often as six times.

The following is a report of allergy to fluoride-containing toothpaste confirmed by a double-blind test.

### Case Reports

Case 1: Mr. E. H., age 48, consulted one of us (JJS) on May 9, 1961, because of giant urticaria of one month's duration. The lesions involved mainly hands and feet and at times the entire body surface. At the first visit the lips and gums showed a marked edema. The lesions usually occurred about one hour after breakfast. The patient had been using a fluoridated toothpaste at that time. Because of a tendency to hyperglycemia, he had been on a high protein, low carbohydrate diet. Otherwise, his history was unremarkable. He was asked to discontinue the fluoride toothpaste and not to take any medication. Three days later, he reported having had only a single hive and slight residual pruritus. Six days later (May 18), he was completely free of symptoms.

In June 1964, three years later, this patient experienced another episode of generalized urticaria. In the morning he had inadvertently brushed his teeth with a toothpaste used by his family without realizing that it was a fluoride brand. The hives appeared within one hour of

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its-use. The patient consented to a double-blind test in order to establish whether or not fluoride had caused his hives. A local pharmacist prepared three identical bottles, which be labeled #1, #2 and

#3. Two of the bottles contained plain distilled water, the third contained distilled water to which had been added NaF in the proportion of 2.2 mg NaF per 15 cc of water, the equivalent of 1 mg F per tablespoon of fluid. This solution was without taste, color or odor. Only the pharmacist knew which bottle contained fluoride. On May 19, 1965, the patient was instructed to take daily before breakfast one tablespoonful (15 cc) from bottle #1 for one week, one tablespoonful from bottle #2 the following week and one tablespoonful from bottle #3 the third week.

On the fourth day on bottle #2, he developed generalized pruritus and edema in the distal joints of his extremities. Never-the-less, he continued taking the water from bottle #2 for another three days during which he developed hives on the right elbow and pains in the lumbo-sacral area, followed by an outbreak of generalized urticaria. These symptoms disappeared two days after the patient discontinued the use of bottle #2, which unknown to the patient contained fluoride.

The following cases deal with allergic reactions to fluoride containing vitamins and toothpastes:

*Case 2: C.E.O.*, a seven-month-old female child, had been taking Tri-Vi-Flor daily for five weeks since January 4, 1966. About that time she developed an exudative, pruritic dermatitis on the neck, face and in the antecubital and retropliteal areas accompanied by diarrhea, abdominal cramps and bloody stool. The parents noted that the cramps occurred exclusively, shortly after the afternoon feedings when the baby received the fluoride drops. The drug, therefore, was discontinued. The skin immediately began to clear up. Within one week the eruption had healed, no medication had been prescribed. The child has been in good health ever since.

*Case 3: E.A.*, a 6-week-old female, had been placed on Tri-Vi-Flor when she was three weeks old. During the 5th week of life, the

mother noticed an acute erythematous, diffuse pruritic exanthema. She consulted one of us (SMC) on October 14, 1966, five days after the onset of the rash. The baby appeared seriously ill. An exfoliative dermatitis covered nearly the whole body surface. During the examination the child had a dark brown bowel movement, suggestive of enteric bleeding. The urine contained numerous red cells. The blood count showed slight anemia, a leucopenia, a 10 per cent eosinophilia and a normal leucocyte-lymphocyte ratio. Benadryl (25 mg) was administered for symptomatic relief. Since S.M.G. had encountered two other cases of dermatitis due to Tri-Vi-Flor drops, they were discontinued. Within five days the exanthema disappeared. The baby was placed on Tri-Vi-Sol without fluoride and no further symptoms occurred.

*Case 4: B.W.*, an 8-week-old female, presented an eczematoid eruption on the face and trunk. She had been on an evaporated milk formula and Tri-Vi-Flor since the second week of life, and on cereal since the third. As a therapeutic trial, the milk was discontinued and soybean broth substituted. When there was no improvement, the cereal was eliminated from the baby's diet. However, the dermatitis persisted with increasing severity. At that time the fluoride drops were discontinued. Within 3 days there was visible fading of the eczema. The child has since been on plain vitamin drops and has had no further illness.

*Case 5: D.J.D.*, a 9-year-old female, was seen by one of us (GLW) on March 21, 1964, because of frequent urticaria, allergic conjunctivitis and minor asthmatic- attacks. She had a dry dermatitis on both lips with considerable fissuring and pruritus accompanied by constant episodes of ulcers up to pea-size, distributed throughout the oral cavity. The abdomen was distended and slightly tender upon palpation. Intradermal skin tests gave two and three plus reactions to several antigens, including ragweed pollen and certain fungi. Patch tests were done for chewing gum, Lifesavers, a fluoride toothpaste which she had been using since the onset of the lesions and a non-fluoride toothpaste. The fluoride toothpaste gave a two plus reaction. During the development of the positive patch test reaction the patient experienced a flareup of the oral

lesions associated with severe abdominal pain.  
The smear from the ulcer revealed a normal

Table I.

1.	E. H.	M	48 yrs.	Toothpaste	Urticaria	JJS
2.	C. E. O.	F	7 mos.	Vitamin Drops	Dermatitis; Diarrhea;	SMG
				Blood in Stool		
3.	E. A.	F	6 Wks,	Vitamin Drops	Exfoliative Dermatitis;	SMG
					Melena	
4.	B.W.	F	8 Wks.	Vitamin Drops	Dermatitis	SMG
5.	D.J.D.	F	9 yrs.	Toothpaste	Dermatitis; Stomatitis;	GLW
					Gastro-intestinal	
6.	C.P.	F	14 mos.	Vitamin Drops	Gastro-intestinal;	GLW
					Salivary; Gland Swelling;	
					Allergic Nasal Disease	
7.	L.W.	F	6 yrs.	Vitamin Drops	Gastro-intestinal;	GLW
					Melena; Headaches; Fever	

flora.

After changing to a non-fluoride toothpaste the oral lesions, as well as an accompanying submaxillary lymphadenitis and the abdominal pains, subsided completely. On December 3, 1986, this child had a recurrence of the stomatitis. It began within 15 minutes after brushing her teeth and was again followed by severe abdominal pain. She had inadvertently used a fluoridated toothpaste.

*Case 6: C.P.*, female age 14 months, had been taking Tri-Vi-Flor drops regularly since 3 weeks of age. Shortly thereafter she started having a persistent diarrhea. At 8 weeks of age she developed what \*appeared to be pylorospasm, but a pylorotomy failed to relieve the gastric symptoms. At the age of 10 months she suffered from rhinorrhea, dyspnea, intermittent swelling of the salivary glands and submaxillary lymphadenopathy. These symptoms failed to respond to antihistamines and antibiotics. On December 5, 1965, the mother discontinued the drops. Within three days there was a marked improvement. The child has remained symptomfree since eliminating the drops.

*Case 7: L.W.*, a 6-year-old girl, consulted one of us (GLW) on December 26, 1963, for an allergic survey because of what appeared to be gastro-intestinal allergy. She had been taking

Poly-Vi-Flor, three to four drops daily, since early infancy. Her complaints were frequent nausea, vomiting, pains in the hypogastrium and episodes of abdominal cramps, diarrhea, headaches, and occasional bloody stools followed by fever, up to 104 degrees. These attacks occurred on an average of every ten days. The child failed to gain weight. At first the diagnosis of food allergy and/or chronic appendicitis was considered but neither diagnosis was corroborated by x-rays and an allergic work-up. Since the gastro-intestinal episodes usually occurred within one-half hour of the ingestion of the fluoride drops, the medication was discontinued. Improvement began immediately and was followed by complete recovery.

Table I presents a tabulation of the essential data on the above cases.

### Comment

In two of the above cases (1 and 5) the etiological role of fluoride was confirmed by a double-blind test and by a patch test respectively. In the other five cases, permission was not granted to carry out confirmatory tests. Nevertheless, the fact that three physicians, independent of each other, considered in independent fluoride responsible for the disease should

alert the profession to the danger of serious untoward reactions from fluoride in toothpaste and vitamin preparations.

With regard to tests which may be employed to establish the etiological role of fluoride, patch tests can be expected to be conclusive only in lesions of contact dermatitis. Dermal and intradermal skin tests are generally recognized to be of little value in allergic reactions due to simple chemicals. Fluoride determinations of the urine are of little avail because in infants and young children only a small, highly variable fraction of ingested fluoride is excreted in the urines [6] Data on blood fluoride levels are not sufficient

consistent [7] to be a reliable criterion of ill-effects from fluoride. Blind and double-blind studies in infants and young children would be valuable diagnostically but these are not without danger, especially after the drug has been discontinued for short periods. Therefore, the principal manner in which reactions to fluoride can be related to their cause is careful clinical assessment of the patient's symptoms in relation to administration of, or contact with the drug.

Of special interest are the gastro-intestinal manifestations in five of the seven children, particularly the presence of blood in stool in three of the cases. Gastric hemorrhages are a major feature in acute fluoride intoxications and gastro-intestinal disturbances such as gastritis and spastic bowels, have been reported by Frada' and Mentesanag in about one half of their 62 cases of hydrofluorosis. Gastric symptoms must be anticipated especially in subjects who have hyperacidity of the stomach. When inorganic fluoride compounds combine with gastric HCl, hydrofluoric acid (HF) is formed which exerts an irritating

action upon the mucosa of the stomach and the upper gastro-intestinal tract [10].

### Summary

Six children and one adult exhibited various allergic reactions after the use of toothpaste and vitamin preparations containing fluoride. The following conditions were encountered: Urticaria, exfoliative dermatitis, atopic dermatitis, stomatitis, gastro-intestinal and respiratory allergy.

The etiological relationship with fluoride was confirmed in one case by a double-blind test, in another by a positive patch-test. Five of six children, in whom other measures had been to no avail, improved promptly and the disease was controlled in all by discontinuing the fluoride drops or fluoride toothpaste.

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