

Allergic contact sensitization to iron

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A case is reported of allergic contact dermatitis due to iron in a toolmaker. This is only the second case of iron contact allergy published in the literature. The possible reasons for the rarity of contact allergy due to iron are considered, among them the development of tolerance due to exposure to iron-containing compounds during fetal life.

Certain metals, such as chromates and nickel, according to several published series of results of patch tests,^{1, 3} are among the most common causes of allergic contact dermatitis. There are other metals, such as cobalt, gold, and platinum, that, although not among the most common causes, have been reported to have caused allergic contact dermatitis. It is the more remarkable that there is only one report of iron in the form of ferric ions having been the cause of allergic contact dermatitis.⁴ We present here the case of a toolmaker who developed an occupational contact dermatitis due to iron.

CASE REPORT

A 66-year-old white man was first seen by us in March, 1972. He was in good general health and stated that in 1967 he had developed an itchy eruption on the ankles and legs. This subsequently spread to the upper parts of the legs, hands, arms, and trunk. He described the eruption, which was usually worse during the winter months, as occurring in patches and consisting of small water blisters. The eruption had not cleared completely at any time during this period, even though he had been treated with various topical medications and with systemic corticosteroids.

Examination showed a widespread eruption, consisting of moderately erythematous papular and papulovesicular lesions. Many of these occurred in ill-defined patches, and some were crusted. In healing areas slight scaling was noted. The lesions were distributed over the upper and lower extremities and the trunk. On the upper extremities, the dorsa of the hands, the radial aspects of the forearms, and the anterior aspects of the arms were principally involved. There was no involvement of the scalp, face, neck, axillae, palms, soles, and anogenital region.

The patient stated that he was a toolmaker who used the lathe and did bench work, such as machining, shaping, and cutting. He did no welding. In the course of these activities metal dust came off, which settled in his shoes and socks. The cutting oil used also became heavily contaminated with metal dust. In addition to cast iron, he used brass, aluminum, copper, and steel. He changed into his work clothes, which were washed only once a week, in the morning and back into other clothing in the afternoon.

On the basis of the clinical findings and the history, a preliminary diagnosis of allergic contact dermatitis was made. Nummular eczema was considered in differential diagnosis. Patch tests were performed with 11 different metals in appropriate dilutions. At the time of the 24 hour reading all tests were negative (Table I), but at the 72 hour reading a strongly positive reaction to ferric chloride 2 per cent aqueous solution was seen. The morphologic

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TABLE I

Substances applied (3/6/72)	Date of first reading (3/7/72)	Date of second reading (3/9/72)
1. Nickel sulfate 2% aqueous solution	0	0
2. Cobalt sulfate 2% aqueous solution (nickel free)	0	0
3. Chromium chloride 2% aqueous solution	0	0
4. Ferric chloride 2% aqueous solution	0	3+
5. Silver nitrate 2% aqueous solution	0	0
6. Zinc chloride 2% aqueous solution	0	0
7. Gold chloride 0.5% aqueous solution	0	?
8. Copper sulfate 5% aqueous solution	0	0
9. Manganese chloride 2% aqueous solution	0	0
10. Nickel sulfate 5% aqueous solution	0	0
11. Potassium dichromate 0.5% aqueous solution	0	0
12. Aluminum chloride 5% aqueous solution	0	0

changes at this positive patch test site were identical with the lesions of the widespread clinical eruption.

Because of the history, clinical changes, and patch test results, the diagnosis of allergic contact dermatitis due to iron was considered established. Treatment with betamethasone valerate cream and tar baths topically and promethazine 25 mg. by mouth was instituted. A nonalkaline skin cleanser was prescribed. The patient was asked to have his work clothes laundered daily instead of weekly. Two weeks later there was almost complete clearing of the eruption. After 3 months, during which he continued his usual work, the patient reported that his skin had stayed clear with the exception of occasional mild localized eruptions.

DISCUSSION

Nater⁴ published the only previous case of allergic contact dermatitis due to iron. His patient was a 44-year-old man with a background of atopic dermatitis, who had a severe vesicular dermatitis on the soles and medial aspects of the legs. The patient was a steel welder by occupation and reacted to patch tests with ferric chloride and ferric sulfate. He did not react to ferrous tartrate and ferrous sulfate, nor to other metals found in iron ore, such as manganese, cobalt, nickel, and chrome. In our patient the eruption also began on the ankles and the adjoining parts of the legs. It then gradually spread to involve many other parts of the body. It was noteworthy that the morphology of the positive patch test reaction to ferric chloride was identical to that of the clinical changes. As in Nater's case, there was no allergic contact sensitivity to other metals tested.

From the clinical viewpoint, the question arises why neither in our nor in Nater's case there was involvement of the face and in particular of the eyelids, which are so commonly involved in allergic contact dermatitis. This may well be due to the weight of iron filings and iron dust, which makes these particles rapidly sink to the floor and thus cause eruptions on the distal parts of the lower extremities. Apparently these particles do not become "airborne," as occurs with so many other contact allergens.

The fact that Nater's and our case are the only reported instances of contact allergy to iron raises the question why iron is such an infrequent cause of allergic contact sensitization. There is no biochemical characteristic that would make one assume that iron behaves differently from chromate or nickel with

TABLE II*

<i>Iron</i>
As porphyrins: Hemoglobin, myoglobin, cytochrome oxidase
As nonporphyrins: Transferrin, ferritin, hemosiderin, catalase, tryptophane oxidase, homogentisicase
<i>Copper</i>
Tyrosinase, phenolase, ascorbic acid oxidase, cytochrome, cytochrome oxidase, monoamine oxidase, also needed for hemoglobin synthesis
<i>Molybdenum</i>
Xanthine oxidase, nitrate reductase, liver aldehyde oxidase
<i>Zinc</i>
Carbonic anhydrase, lactic dehydrogenase, carboxypeptidase, insulin, white blood cells
<i>Magnesium</i>
Peptidases, phosphatases, ATP-enzymes such as hexokinases
<i>Manganese</i>
Arginase, phosphoglucomutase, dipeptidases, cholinesterase, carboxylase
<i>Cobalt</i>
Peptidases, vitamin B ₁₂ †

*Based on References 7 and 8.

†The enzymes either contain the metal or are activated by it.

respect to combining with proteins to form complete antigens. Iron is thought to be the first metal worked by the human race. Since iron is probably the most widely used metal in consumer items, there is no reason to assume that the population at large has any less exposure to iron than to chromates and nickel, two of the most common contact allergens. Iron is usually combined with other metals, such as chrome, manganese, copper, and molybdenum. Also many consumer products, containing iron, are plated with other metals. This could be a factor in the rarity of allergic contact sensitization to iron. Another possibility is that western man is genetically not susceptible to allergic sensitization to iron-protein conjugates.

Still another possible, but at this time speculative, explanation for the extreme rarity of allergic contact sensitization to iron is that all human beings become tolerant to iron-containing contact antigens because they have exposure to iron and iron-containing compounds during fetal life since it is a basic constituent of the body. Ever since the fundamental work of Burnet⁶ and Medawar,⁵ it has been known that exposure to certain antigenic materials during fetal life leads to recognition of these materials as "self" and consequently to tolerance for them. The existence of contact allergy to iron in Nater's and our case then would have to be interpreted either as a failure to develop tolerance in fetal life or as a loss of tolerance in adult life, for whatever reason.

Table II shows the role of some metals as essential constituents of human tissues. Perhaps this data explains why chromate, nickel, mercury, and certain other metals, which are not essential constituents of human tissues, may be causes of allergic sensitization, while other metals, e.g., iron, magnesium, zinc, and copper, which are essential constituents, are among the rarest causes of allergic sensitization. Cobalt, however, does not fit in with this hypothesis, since

it occurs in essential factors for human tissues but is known to cause allergic contact sensitization.

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