

ALLERGY TO CHYMOTRYPSIN

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THIS report presents a case of allergic sensitivity to chymotrypsin (bovine) in a laboratory worker. The sensitivity apparently was induced by inhalation of the powdered material.

With the increasing use of purified enzyme preparations, the hazard of sensitization should be recognized. A larger number of scientific workers are being exposed to inhalation of the dried materials. Injectable chymotrypsin is being used to reduce tissue swelling following trauma and infection.¹ The other pancreatic proteolytic enzyme, trypsin, is used medically, both by injection in inflammatory disorders^{2, 3} and in the form of an aerosol to liquefy mucus in cases of asthma, bronchitis, and bronchiectasis.^{4, 5}

Chymotrypsin is produced by the action of trypsin on chymotrypsinogen. It acts on the peptide link in the carboxylic side of aromatic amino acids. Because of the proteolytic action, the enzymes have been used to dissolve mucus or fibrin.

During tests for specific skin sensitivity, the proteolytic activity of trypsin and chymotrypsin, with its resulting irritative wheal and flare, introduces the factor of nonspecific reactions, and this must be evaluated in each individual test. To reduce this source of error, we used the nonproteolytic precursor of chymotrypsin (chymotrypsinogen) in the passive transfer tests reported below.

Chymotrypsinogen and chymotrypsin have been reported to be distinguishable by means of the Schultz-Dale reaction in the guinea pig;⁶ however, they are very closely related immunologically. Their cross reactivity is sufficiently strong to have permitted the use of chymotrypsinogen to test for chymotrypsin sensitivity in the case reported here.

CASE HISTORY

A 28-year-old white male graduate student noted sneezing and itching eyes in the fall of 1955 whenever he was engaged in weighing out chymotrypsin powder. He had been working regularly with the material, mainly in solution, for about three years. A scratch test with chymotrypsin in 1/100 dilution (1.0 per cent) was said to have been positive one day but negative when the test was repeated the following day. He was given a dust mask to wear while weighing the powdered material.

The patient did not know of any close relatives with symptoms of allergic disease. As a child he had suffered frequent colds, and in late childhood and the early teens had severe nasal allergy from exposure to hay and feed on a farm in northern Washington.

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After coming to Southern California, the patient became sensitive to olive pollen, exposure to which resulted in swollen eyes, nasal congestion, and sneezing and coughing at night. Intracutaneous tests gave positive reactions to several grass and weed pollens, and some antigen injections were tried with moderate success. He was not sensitive to beef protein, either clinically or by skin test.

In December, 1955, he was tested intracutaneously with 0.25 per cent chymotrypsin solution. Approximately 0.01 ml. of solution or 0.025 mg. of the enzyme was injected. Within fifteen minutes he complained of itching of the nose and throat, and showed a 4 plus local reaction. He was seen fifteen minutes later with swollen eyes and uncontrollable sneezing; he was dyspneic, slightly cyanotic, sweating, and feeling weak and faint.

He was judged to be having a "constitutional reaction" to the injected chymotrypsin and was given slowly 10 mg. Benadryl by vein and 0.2 ml. of epinephrine 1/1,000 subcutaneously. The epinephrine was repeated in a few minutes and his condition began to improve gradually. After resting for an hour, he was back to normal, except for a sense of fatigue.

Skin Testing.—Serum was drawn from the patient four hours after the reaction and again seven days later. These sera were stored in the frozen state and tested three weeks later by passive transfer for the presence of skin-sensitizing antibody.

Skin sites on three nonallergic young adults were injected with 0.1 ml. of both the four-hour and seven-day sera. Twenty-four hours later these sites were challenged with 0.05 per cent chymotrypsinogen of bovine origin.

Two donors reacted with 3 plus wheal and erythema at the sites of the four-hour serum, and with 4 plus wheal and erythema at the seven-day-serum sites. Controls were negative in these two subjects. In the third subject both sera and the antigen control sites gave equal but slight reactions.

The patient was not tested directly with chymotrypsinogen. No precipitating antibody against chymotrypsinogen was detectable in either serum. Neither could passive anaphylaxis to chymotrypsinogen in the guinea pig be demonstrated, using either serum.

Our results show that exposure to bovine chymotrypsin can produce strong allergic sensitization, with transferable skin-sensitizing antibodies against the enzyme. It is logical to suppose that related enzymes, such as trypsin, can have the same effect in susceptible persons. We suggest that when proteolytic enzymes are to be used in treatment, particularly by injection, a sensitivity test be performed first. This would be an important precaution to take if the enzyme had been used before in the same patient. For the reason already discussed, the nonproteolytic enzyme precursor should be used first in skin testing for allergic sensitivity.

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