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ALIMENTARY ALLERGY

ALLERGY TO FISH

By

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Alimentary allergy is a frequently occurring pathological complex with manifestations in the skin, mucous membrane, gastrointestinal tract and joints. It occurs in all sections of society, depending on the eating habits of the population, and not only in highly industrialized districts, though it does seem to be found more frequently there than in other types of district, owing to the greater variety of foods encountered by the inhabitants.

In remote mountain villages where fish is seldom eaten, the existence of allergy to fish does not seem to have been proved. On the other hand, allergy to milk, eggs and honey has been proved to exist there, and indeed allergic subjects are found even among people with the simplest way of life.

There are two distinct types of allergic reaction to food. One is characterized by the rapid appearance of symptoms, often within a few minutes of eating the offending food. Some patients begin to react even before the food has been swallowed. On the other hand some foods are prone to cause a delayed type of allergic reaction. In such cases a number of hours or even a day may elapse between the ingestion of the allergenic food and the appearance of symptoms. It is often very difficult or impossible for patients who have the delayed type of reaction to associate their symptoms with food allergy. The foods which are apt to produce

this type of reaction are commonly eaten almost every day, and this tends to obscure a correct diagnosis. On the other hand, in the case of the immediate type of food sensitivity it may soon become quite obvious to the patient which food is causing his difficulties. Often he may not even bother to consult a physician, when the reaction is due to strawberries or lobster and sometimes to fish. It has been suggested that the actual allergen in the case of the immediate type of reaction to foods is the whole food protein. With delayed reactions, however, the allergen may be some protein breakdown product such as a proteose, peptone or polypeptides formed during the process of digestion of the protein.

Since skin tests are usually done with extracts of the whole food protein, the skin tests are usually positive in persons with immediate symptoms from foods, while the results of tests are often unreliable in cases of delayed food allergy.

In the first group are found patients with hypersensitivity to fish, berries, nuts, white, and sometimes yolk, of egg. In the other group we find the cereals (especially wheat and oats), milk, eggs, chocolate and vegetables.

There are several reasons for variability in clinical response. First, there is a *quantitative factor*, which allows small amounts to be tolerated without difficulty. Larger quantities will precipitate symptoms.

Secondly, the *degree of cooking* will affect the allergic response. Usually, foods in their raw condition are more allergenic than those which have been cooked thoroughly. Some people, for example, who have no difficulty in eating hard-boiled egg, cannot tolerate soft-boiled egg or egg nog.

The *cumulative factor* is also important. Patients who have no symptoms following occasional ingestion of a food may react if it is eaten on successive days.

Immediately after an allergic reaction caused by food there may be a brief *refractory period* during which further ingestion of the allergen will not provoke symptoms. Following this there may be a period of heightened sensitivity which is gradually replaced over a longer period of time by a state of diminished or subclinical sensitivity. During this time a troublesome food may be taken at least temporarily without symptoms.

Food allergies are frequently *multiple*, and sensitivity to several different kinds of food may be relatively mild in the case of each individual kind. A patient might have no clinical symptoms after eating separately small amounts of two or three foods to which he is mildly

sensitive. However, if he should happen to eat all three foods at the same meal, symptoms might result. Furthermore, patients with sensitivity both to inhalants and foods may have an allergic reaction to certain foods only after their ingestion during the pollen season but not at other times of the year.

Alcohol tends to cause capillary dilatation just as the allergic reaction itself does. Because of the capillary dilatation it induces in the intestinal tract, absorption from the intestines is accelerated. A mildly allergenic food to which the individual does not usually respond with symptoms may cause trouble in the presence of alcohol. Under these circumstances the food is so rapidly absorbed that it is tantamount to an overdose.

This situation is typified by the young woman who knew from experience that she could eat a moderate amount of lobster without trouble. If she ate a large quantity, however, she would suffer from giant hives. At one fateful meal she had two Martinis. She also had a small lobster cocktail. Within twenty-five minutes her tongue began to swell and breathing became difficult. She was rushed to the hospital, where only heroic emergency measures saved her. But it was a week before all of the giant hives left her. In this case the alcohol had the effect of permitting unusually rapid absorption of the lobster, which was therefore tantamount to eating a large quantity of it.

Saltwater fish acts as an allergen far more frequently than freshwater fish.

Among the foods most frequently found to be allergenic are strawberries, melons, nuts, tomatoes, shellfish, fish, eggs, milk and spices.

Fish is one of the most dangerous antigens in existence, capable of causing explosive and often universal symptoms of shock and a severe state of shock. There has not yet been any adequate investigation of the effects of the different kinds of fish. Thus for the present this type of allergy will have to be regarded as being produced by a whole category of allergens, although a number of patients have reported that they are only susceptible to one particular kind of fish, and on occasion the method of preparation may also be significant.

In fish allergy of nutritive origin even the smell of raw or boiled fish not infrequently causes asthma, and there are asthmatics who are subject to attacks on account of their work at places where fish is handled commercially. Some are susceptible when fish is being cooked, and others when they are in actual contact with it, with hives and Quincke's edema as a consequence.

Up to 1921 frequent attempts had been made to identify the elusive

antibodies known to exist in the blood of allergic subjects, and finally Prausnitz and Küstner succeeded in 1921, at the same time as de Besche, in demonstrating the existence of antibodies biologically. Küstner was sensitive to boiled fish, and showed a positive skin reaction on being tested. As we know, serum from Küstner was injected into the skin of a non-allergic subject. Several days later fish extract was injected into the same place, resulting in a violent skin reaction, and thus proving that the skin of the non-allergic subject had been passively sensitized to fish by means of fish-antibodies present in Küstner's blood. This reaction (also known as the Prausnitz-Küstner-de Besche test) is called passive transference, and this method of examination is particularly suitable for patients who are known to be allergic to fish, in order to avoid the risk of shock. Even the minimum amount of fish extract may be effective, and the greatest care in testing is essential if anamnesis arouses the slightest suspicion that the patient is allergic to fish. In some cases it may be advisable to apply fish allergen extract by means of a scratch test before trying intracutaneous testing, in which case it is possible to use a diluted extract which is 100 times stronger than the liquid used for intracutaneous injection.

The classic method of bringing about the Prausnitz-Küstner-de Besche reaction is to inject the allergen into the implantation area containing the antibodies. More recently an attempt was made to bring about the reaction indirectly by inhalation and ingestion, but this was only successful in the latter case in persons with achylia, in whom a reaction may start after an interval of anything between only 3/4 and 20/30 minutes. Persons with normal acidity do not show this reaction. This may be due to destruction of the allergen by gastric juice. In patients with anacidity the allergen is not destroyed; it passes into the duodenum, where it may be reabsorbed.

Patients who are allergic to fish must be cautious as regards the use of cod-liver oil and ointment, which may affect the mucous membrane. They must beware of touching fish or anything that has been in contact with fish. Glues containing fish products must also be avoided.

In Norway fish meal was often used as an addition to pig and chicken feed, with the result that the end product of pork and eggs contain fish antigen. In people who are hypersensitive to fish this causes an allergic reaction whose cause may be difficult to establish.

In France fish albumen is sometimes used to clear wine, and the symptoms of fish allergy may arise as a result of drinking this wine.

Persons who are allergic to fish often react positively to an intra-

cutaneous test, but a negative reaction has been found even in patients who have shown symptoms of primary shock after eating fish.

Inhalation allergy caused by various types of polish manufactured from octopus (*os sepiæ*) has been observed in furniture polishers, jewelers and dentists.

The patient I wish to describe this evening is a boy, born in 1942, with a family history of severe allergy. On his father's side, his grandfather suffers from allergic hoarseness, two uncles are allergic to apples and strawberries, one aunt had infantile eczema, and the father has had hay fever and gets a headache as a result of eating apples.

On the mother's side, the great-great grandfather had severe asthma, the great grandmother protracted fits of sneezing, the grandmother fits of sneezing, and an aunt gets a headache when she is in the neighbourhood of stocks, while the headache disappears when the stocks are removed. Two aunts had infantile eczema, and the patient's mother had infantile eczema, was allergic to fish, had a tendency to be affected by wool, and got a rash from contact with nickel.

The patient was breastfed, and came out in a rash when eleven days old. At two months this was so extensive that he had to wear protective wristbands.

When he was five months old the mother had a mammary abscess, whereupon the patient became much worse, began to vomit, and was admitted to the dermatological department of the National Hospital, where he remained for six weeks. Vomiting took place 10/20 minutes after each meal, but when the meal was repeated, the food was kept down. Vomiting continued for about five months, until the summer when the patient was taken to the sea, and in the course of the 5/6 weeks there his symptoms practically disappeared and both the eczema and the vomiting ceased. Shortly after his return home, the eczema reappeared.

The patient was then given additional foods, including fish pudding, but his eczema became much more severe, and he was unable to take any more fish. He also showed signs of hypersensitivity when fish was brought into the kitchen, and if he touched it. Quincke's oedema resulted. During the autumn he had aggravations during colds and during two attacks of bronchopneumonia. The following autumn his doctor administered anticatarrh vaccine. This was a success in respect of the catarrh, but had no effect on the eczema.

In the autumn of 1945 and the beginning of January 1946, the patient was seen to react to margarine, liver, pork and pig's liver.

In 1951 he was again tested at the pediatric department of the National Hospital, and showed a positive reaction to fish, with +++ in the case of cod. Later he was proved to react positively to horses, dogs, domestic dust, feathers, wool and lilies of the valley.

A visit to the circus showed that horses brought on an asthmatic reaction.

On account of the violent reaction to fish and the risk involved, hyposensitizing treatment was tried in 1956. The patient was given drops of fish extract diluted 1:10 mill., but reacted to these, so that the dilution had to be altered to 1:100 mill. 1 drop was tolerated the first day, and 2 the second day, but 3 drops caused a return of the symptoms of hypersensitivity, so that we had to increase the dose more gradually, keeping the patient on 1 drop for 3/4 days, 2 drops for 3/4 days, and so on. By May 1960 he was on a dose of fish extract of 1:10.

From then onwards we were able to increase the dose more sharply than before, and fish extract was made by the patient's mother in the form of fish stock, which was frozen in cubes in the refrigerator, thus being both easily available and labour-saving.

The patient's ability to tolerate fish has gradually increased, and in August 1960 we put him on to fish meal tablets of 0.068 gr., corresponding to 2 ml. of fish extract 1:10, and we were then able to increase the dose by 3 drops per day, i.e. 1 tablet every 10 days, as 1 tablet corresponded to 30 drops. An attempt was then made with fish pudding, and on January 11th, 1961 the patient was able to eat 7 gr. of this, but had to eat it with potatoes, as otherwise it had an irritating effect on the mucous membrane.

The patient has now progressed to a dose of 18 gr. of fish pudding at breakfast, and 20 gr. at dinner, which corresponds to half a fish ball at each meal. Fish pudding contains 50 % fish.

The dose is being increased by 2 gr. of fish pudding per day now, which may be regarded as a large dose, considering the anamnesis and the fact that after eating a piece of bread cut with a knife that had been used to slice fish, the patient had an attack of Quincke's oedema and had to be brought home. Another time a fish ball had been placed in his tomato soup by mistake but immediately recovered. After eating a little of the soup, the patient had vomiting and dyspnea, and had to go outside for air.

The only inconvenience the patient suffers at present is that the taste

of whole fish balls is repulsive to him, while they are tolerable when mixed with potatoes and jam. There are then no symptoms such as itching or soreness of the throat or dyspnoea.

The only fish allergen the patient enjoys is caviare, but this is too expensive a form of hyposensitizing treatment for his father, who is dependent on a university salary.

Boiled fish is to be tried next, and it is thought that the patient will gradually be able to manage this without reaction, even in the usual quantity for normal people $2/3$ times a week.

No antihistamines or other tablets have been taken during the period of treatment.

This has been an extremely tiresome form of treatment for the patient's mother to carry out. She has shown great intelligence and interest, and says that the result is worth the great effort involved.

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