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Food and Drug Allergy Causation and Characteristics

*Richard R. Evans, M.D.**

IT SEEMS STRANGE INDEED that common and useful foods at times can do harm and even threaten life rather than sustain it. This is true of both advertised food products and of common, unadvertised foods.

A 16-year old boy, within minutes after eating a doughnut, had a severe constriction of the throat, wheezing and shortness of breath. He fell to the ground, head bent forward, elbows on knees, heaving and gasping for breath. An injection of epinephrine promptly relieved the symptoms, indicating that they were reversible and without lasting harm.

Peanuts had always made this boy sick. When it was discovered later that the doughnuts were fried in peanut oil, the explanation of the attack became evident: the peanut oil in the doughnuts had caused an allergic reaction. This is an unusually severe reaction, of course, but it illustrates some of the principles of food allergy.

The boy's mother has hay fever, and her father had asthma. There is a family history of allergic disease indicating the role of heredity. The boy has had asthma since the age of four years, which at first developed with colds in the winter, and later occurred during the ragweed pollen season of mid-August to late September. After eating peanuts or peanut butter, he has always immediately had burning of the tongue, tingling, itching and swelling of the lips, and itching welts over the skin. Although he learned early to avoid this food, only a trace of peanuts, such as a single bite of a chocolate nut bar, produces this reaction. The reaction takes place every time he eats peanuts, and develops at the same time interval after eating. Thus, he has more than one type of allergic disease, and unusual sensitivity to several common substances in the environment.

When watery solutions of regional pollen and of peanut protein are placed on a superficial scratch through the outer layers of his skin, not deep enough to draw blood, a small raised pale central wheal surrounded by an area of redness develops—a hive perhaps an inch in diameter. If similar dilute solutions are injected into the skin, similar but larger hives develop at the

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test site. He has positive skin tests to the substances which experience shows cause allergic reaction. The tests demonstrate the presence of specific substances in the skin, called antibodies, which play a part in producing symptoms when combined with the specific offending agent called an antigen. Antibodies to the specific antigen can be demonstrated in the blood serum by other techniques. A true allergic reaction depends upon an antigen-antibody reaction in the involved tissues, and the reaction is specific.

When skin tests are applied to many other common food and dust substances, hives indicating positive reactions develop to several of them, while experience shows that they do not produce any symptoms. The presence of positive skin tests to substances which are not clinically significant is a characteristic feature of such "allergic individuals," and adds to the difficulty in the interpretation of these tests.

This boy, then, may be said to be an "allergic individual" who has a constitutional susceptibility to develop allergic symptoms upon exposure to common, ordinarily harmless substances, and to show positive skin tests to the specific substances. The susceptibility is probably determined by heredity.

Symptoms

Food allergy may produce a variety of symptoms, including reactions involving the skin, the gastrointestinal tract, and the respiratory system; rarely, even severe constitutional shock-like reactions occur.

Infantile eczema, the red, scaling, thickening and oozing eruption on the skin chiefly localized to the folds, the bends of the elbows and knees, the neck, and the cheeks, but all too frequently involving a great portion of the skin surface, may depend at least partly upon food allergy. The substitution of goat's milk or a soy bean preparation for cows' milk, or the elimination of eggs from the diet may cause the eczema to disappear. Traditionally, hives are blamed on food allergy. To be sure, a great number of acute episodes do depend upon food allergy, such as to strawberries or to lobster. However, food allergy is only one of the causes of hives, and only rarely produces the chronic variety which tends to persist for weeks and months.

Nausea and vomiting may result from food allergy, and perhaps represent an attempt to get rid of specifically harmful foods. Hives often follow the ingestion of such an "antigenic" food if vomiting is not severe, or if more than a small amount

of the food is eaten. Diarrhea is another gastrointestinal symptom of allergy. For example, a man in his forties has had diarrhea since childhood, which regularly and only occurs eight hours after drinking milk or eating milk products. As long as he omits milk in any form from his diet, he does not have diarrhea.

Asthma and hay-fever-like symptoms may result from food allergy. There is much controversy among allergists as to the importance of food allergy in respiratory tract symptoms. Many, including the writer, do not find food allergy to be a frequent cause of those symptoms in adults.

Constitutional reactions due to food are as frightening as the severe asthma attack, but are rare, fortunately. A fifty year old man ate a particular type of cookie, and at once had violent itching and bright redness of the skin: then he became pale and broke out in a cold sweat, his pulse was rapid and weak, his blood pressure dropped abruptly, and he became unconscious. The reaction evidently depended upon a small amount of some substance used in the preparation of this particular type of cookie to which he was allergic, since other types of cookies had caused no trouble before. Cotton-seed flour was the ingredient suspected of being the antigen.

Antigens

Any food may act as an antigen. When statistics or frequency of reactions are compiled, milk, eggs, wheat and fish usually lead the list. These figures are of no value however in any particular case. Seeds and nuts seem prone to produce some of the most violent reactions. Skin tests are often helpful in diagnosis, but true food allergy may exist in the absence of a positive test. The best test is the demonstration that symptoms are absent when the food is withheld, and invariably recur following the ingestion of the food, and at the same time interval. It must be emphasized that true food allergy is a specific reaction. The diagnosis is easy when the allergy is as clear cut as in the examples above. However, when food allergy plays a lesser part in more persistent allergic conditions, the identification of the specific offender becomes much more difficult.

Food allergy of infancy and childhood is frequently lost, so that foods initially harmful can be eaten without any trouble later in life. Once the pattern of food allergy is established in adult life, however, it usually persists indefinitely. Fortunately, such food allergy does not often include more than one or a few

foods. The treatment is avoidance. Hyposensitization methods have not proved effective.

Drug Allergy

There are three chief types of harmful reactions from drugs: toxic, idiosyncratic, and allergic.

Almost every drug has toxic properties in addition to useful properties, and its safety depends upon the difference between the effective therapeutic dose and the toxic dose. Toxic reactions range from mildly unpleasant symptoms to lethal effects, and they are an inherent property of the drug. Quinine, for example, is a drug useful in the treatment of malaria, but in large doses, it is toxic; an early symptom of a toxic dose is ringing in the ears.

Some people are unusually susceptible to the toxic effects of drugs when they are taken in ordinarily safe or in even tiny doses. This increased susceptibility is called drug idiosyncrasy. The reaction depends upon both the inherent property of the drug and the unusual sensitiveness of the individual. The person who has an idiosyncrasy to quinine, for example, may have ringing in the ears from even the small amount of quinine in gin and tonic.

An allergic reaction to a drug is a reaction quite apart from its therapeutic or toxic effect. It depends to some extent upon the nature of the drug, but more importantly upon the ability of the individual to react in this specific and unusual manner. Any drug may cause an allergic reaction, although some are stronger potential allergens than others. Proteins, especially antitoxens prepared in horse serum, are particularly strong allergens. Antibiotics, which are complex substances, are moderately potent producers of allergic reactions. Even drugs that are simple chemicals, such as aspirin can also cause such reactions. Although "allergic individuals" possibly tend to develop drug allergy more frequently and severely than do others, anyone can be subject to these reactions. The type of reaction is not constant for any one drug; the same drug may cause various allergic manifestations in different individuals.

The manifestations of drug allergy are similar to those of any other type of allergy, such as those to foods mentioned above. Skin reactions are common, and hives and eczematous eruptions include types that mimic other diseases. Diffuse skin redness, similar to that caused by scarlet fever, may be caused by allergy to sulfa drugs. A pink-red blotchy rash suggestive of

measles may be due to phenobarbital allergy. Respiratory tract symptoms, similar to those of the peanut-sensitive boy, may develop from aspirin sensitivity. Shock-like constitutional reactions may occur after the administration of penicillin. Such severe reactions are much more likely to occur after injection than after ingestion of the drug.

There are other reactions which are less frequent but which may be more dangerous and less reversible. The small blood vessels of various organs may be involved in an inflammatory reaction—"allergic vasculitis"—which can seriously interfere with the function of the organs. Antibiotics and even simple chemicals such as potassium iodine have been demonstrated offenders.

The blood cells may be affected: the red blood cells may become clumped and broken up to produce anemia; the white blood cells may be destroyed with increased susceptibility to and poor defense against infection; the blood platelets may be destroyed to produce bleeding within the tissues and interference with the blood-clotting mechanism.

The allergic reaction to drugs probably is mediated by the same type of antigen-antibody mechanism as in other allergic reactions. However, with drugs, antibodies can be demonstrated only irregularly by means of skin tests and with many drugs cannot be demonstrated at all. Positive tests to penicillin occasionally appear after violent allergic reaction to the drug, but may not be demonstrable a few months later. The skin test often cannot be elicited at all, however, even after severe reactions. A positive skin test to aspirin has never been demonstrated even in persons exquisitely sensitive to it. The skin test, then, is quite unreliable as an indicator of drug allergy.

Clinical studies of the history of previous reactions and of the time relation between the reaction and the administration of various suspected drugs, are the only means available to diagnose most cases of drug allergy.

As a rule, allergic reactions to drugs do not occur upon first exposure to the drug. Time is necessary for allergy to develop, and it may range from ten days to several years. The size of the dose does not necessarily determine the speed or the severity of the allergic reaction, although in general the larger doses produce the more severe response. An ordinary drug, such as aspirin, taken without untoward reaction repeatedly over several years, can finally cause severe hives, even in doses of only one tablet. The point is that allergy has developed through the multiple exposures over a period of time; once developed, only

a small amount of the drug is necessary to produce the reaction, which subsequently occurs in a predictable manner.

As in all types of allergy, the reaction in drug allergy is specific for the particular drug involved. Specificity appears to depend upon the chemical configuration, for some drugs of similar chemical constitution can "cross-react." When allergy has developed to one, the initial exposure to the second will produce an identical reaction: the second is not a useful substitute. A drug of similar activity but with a different composition must be used. Procaine and Pontocaine, two local anesthetics, cross-react with each other; by Xylocaine, a third local anesthetic, does not cross-react with either Procaine or Pontocaine, and so can be safely used by the dentist or surgeon in patients allergic to Procaine. The major groups of antibiotics do not cross-react. When penicillin allergy has developed, tetracycline or erythromycin might be used to treat the infection without fear of producing an unpleasant reaction.

Treatment of allergic reaction to drugs includes stopping the administration of the drug and alleviation of the symptoms produced. The best treatment is prevention. Since drug allergy may have developed silently after initial or repeated exposure, prevention is not always possible. Such reactions are true accidents of disease, of treatment and even of living in an age where therapeutics have been developed to a high level. If there is to be any "blame," it must rest on the individual's tissues which have the ability to react in their peculiar manner.

When known drug allergy exists, however, it should be the responsibility of the patient to inform the physician whenever any medication is prescribed. In order to reduce the chance of development of allergy to important drugs and to drugs of a high allergenic potency, it is important that they not be used indiscriminately. Toothpaste containing small amounts of penicillin have no therapeutic value, but its use conceivably could lead to the development of penicillin allergy. When a physician believes a respiratory infection is a cold or a virus infection that will not respond to penicillin, and refuses to prescribe penicillin despite the pleadings of the patient, he is only trying to prevent needless potential harm.

Chemists and pharmacologists will continue to develop more drugs of greater complexity and of lesser toxicity. It is likely, however, that allergic drug reactions also will continue to occur, and even increase, since the problem of individual allergic reactivity is so difficult to control.