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SYMPOSIUM: IATROGENIC DISEASE

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IATROGENIC DISEASE IN ALLERGY

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THE MOST obvious physician-caused trouble in the field of allergy is the immediate constitutional reaction caused by the injection of an overdose of antigen during the course of desensitization treatment. Such a reaction can take several forms, including itching of the palms of the hands and soles of the feet, urticaria, angioedema, as well as asthma or hay fever—especially if the latter were the patient's clinical complaints. Shock can also occur and, in addition, there may be flushing of the face, headache, or vomiting and diarrhea. These symptoms, or any combination of them, are usually associated with a large local redness and swelling at the site of injection.

The more sensitive the patient and the greater the overdose, the more severe the reaction is likely to be, and the sooner it will occur after injection. Under these circumstances it may resemble anaphylactic shock and, like it, may be fatal. The number of such fatalities is certainly few; I personally can recall only one instance in

which such a serious outcome was even in question. However, the patient who experiences a full-blown constitutional reaction is not in a position to take much comfort from statistics and would much prefer that his physician avail himself of all the means at his disposal to anticipate such an occurrence and thereby avoid it. These precautions include observance of the size of the local reaction 10 or 15 minutes after each injection so long as increases in dosage are being made, informing the patient and his parent that malaise, or occurrence of minor symptoms within an hour or two after treatment should be reported, and recognition of the patient initially as being very sensitive from the large size of the skin tests and the degree of severity of symptoms. Such a patient should start treatment with a less than usual concentration of antigen, and the greatest dose should be much below that of the less-sensitive, average patient.

Besides the prompt systemic reactions to which we have referred, overtreatment may

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result in more delayed and less spectacular symptoms, or consist simply in an aggravation of the patient's complaint. It is not rare for patients with asthma to be made worse rather than better by uncritically administered injections of antigen. The trouble in such cases lies not with the basic theory of desensitization or failure of production of helpful antibodies by the patient, but rather in failure on our part as physicians to appreciate the wide variation which exists in tolerance and sensitivity. Where continued overtreatment with an antigen, such as house dust, is associated with our failure to stress the importance of removing it, insofar as possible, from the patient's immediate environment, we are guilty of a double oversight, and iatrogenically-sponsored failures in therapy are only too understandable.

Systemic reactions can also occur from skin testing. These are practically confined to intradermal tests; if scratch tests are done first, as should be the case, the danger can be avoided. An antigen to which there is exquisite sensitivity will then not be tested intradermally, since a positive reaction will have occurred with the scratch test.

Before leaving the subject of difficulties caused by injection of antigen, the occasional aggravation of a coexisting eczema by desensitization given in proper dosage for respiratory allergy should be mentioned. Exactly why an occasional patient's skin should be so intolerant of a dose of antigen, which in all other respects is well tolerated, is not clear. This state of affairs is reflected also in a need to employ a much smaller dose of antigen in those cases of primary eczema where desensitization is attempted. We do not advise such attempts, feeling that the chances of making the eczema worse, rather than better, are greater—even when greatly reduced dosage is used.

One well known additional danger, in cases of infantile eczema, is that of the child who acquired generalized vaccinia from a recently vaccinated sibling. This has been seen to occur more than once. It is especially likely to happen in clinic situations where the physician who gives the

vaccination does not know of the presence in the home of an infant with open eczema. The resultant illness can be very severe and disfiguring.

Another iatrogenic difficulty in the field of allergy is the tension-state an occasional parent feels when told his child is allergic, or that he has asthma or eczema. Such parents have an exaggerated idea of the implications of such a statement—and may visualize a lifetime of illness, injections, or dieting for their child. The mother may be worried because she knows of a chronic invalid whose asthma is uncontrolled and whom she considers to be the prototype of allergic disease. The very word "asthma" is abhorrent to many parents. Such parents and, indeed, all parents of allergic children should receive a proper orientation on what allergy is and is not—and have a chance to talk through some of their worries, misconceptions, and concern. We, as pediatricians, should be prepared to tell our parents something of the natural history of allergy, including the wide variation in its degree of severity, and what type of help is available. The extent to which such help is called upon can then depend on a better informed, less emotional mother working more comfortably with her physician.

As is true with many diseases, drugs may add to the patient's problems instead of subtracting from them. Antihistamines, used continually, may be responsible for change in disposition and personality of the child. This occurs much more frequently than is generally recognized. Irritability, onerousness, weeping and loss of appetite have been reported frequently. They disappear promptly upon stopping the antihistamine administration. Ephedrine or epinephrine by injection, adrenalin or epinephrine-like drugs by vaporizer, and aminophylline are frequently overprescribed or overused by the asthmatic. Where two or three doses of these drugs have failed to give relief, it is not likely that seven or eight will do so. With their continued overuse, they lose what benefit they had, and only cause unpleasant side reactions. Rest, fluids, iodides and oxygen may be what the patient needs,

besides the possible removal of a feather pillow, cat or dog from the environment.

Aminophyllin is a valuable drug frequently employed in the treatment of asthma, whose use particularly should be carefully controlled. Many instances of severe toxicity from overdosage, as well as deaths, have been reported. All the leading American pediatric journals have had recent full-length articles on this subject. Overdosage, rather than idiosyncrasy, has been the problem. The large doses present in most suppositories are a particular hazard—especially where small children or infants are concerned. Signs of early toxicity are restlessness, excitement, vomiting, muscle twitching, and pallor.

Mention should also be made that iodides given over a long time may induce enlargement of the thyroid gland; that morphine sulfate is a respiratory depressant—dangerous to use in status asthmaticus; and that steroid therapy—welcome as it may be as a last resort for a few chronic cases—is increasingly dangerous with prolonged use and large dosage.

Overenthusiastic dieting is not an uncommon physician-error in handling an allergic patient. The trap is an insidious one. By taking out one food from the diet, the physician may imply that he is sure that food is the etiology of the trouble. Failing to obtain initial relief, other foods may be successively removed from the diet—some by the physician and some by the mother on her own. It is not unusual for what was intended as a simple short-term *test* diet to drift into a complicated long-term *treatment* diet, despite no convincing evidence that such a diet is necessary or, indeed, that any food allergy exists. Though fully aware of the difficulties one often has in unearthing the true facts of food allergy, we should all be wary of adding to the patient's problems, the mother's frustration, her guilt feelings at violations of directions, and her discomfort in being a policewoman day after day in the matter of diet, unless she has something to show for it.

The doctor may be led into the trap, as I was years ago, by numerous false-positive

intradermal tests to foods. One of my patients was the son of a nurse who followed my extensive elimination dietary directions to the letter. This 2½-year-old was not happy with the numerous restrictions I had imposed on him and, in addition, was not improving. One day he picked a small empty glass ampule out of the waste-paper basket where his mother had discarded it, and bit into it. I saw the light, resolved not to continue to make glass-eaters out of my patients, and have had a more skeptical view of food tests ever since. (Lest I give the wrong impression, I find skin tests to inhalant substances very helpful.)

Other errors into which we may fall, in the dietary management of our patients, include failure to prescribe calcium if milk is removed for any considerable length of time from the diet of the older child who is not using one of the standard milk substitutes, and failure to see that vitamins are added if their usual food sources are eliminated. The last case of xerophthalmia with partial blindness which I saw was in an infant on a soy-bean milk formula; this particular product now carries adequate vitamin A.

At present there is considerable interest in pediatric allergy circles in the question of whether we, as physicians, are taking part in a large scale iatrogenic disease movement when newborns from allergic families are fed cow's milk in one form or another in the months immediately after birth. Glaser is of the opinion that such is the case. He has found that simply by avoiding cow's milk and certain other allergenic foods for 6 months or more after birth and, instead, feeding soybean milk to babies with a clear-cut family history of allergy, he can reduce the incidence of infantile eczema from about 30% to 8%. Furthermore, he found, unexpectedly, that there was an equally impressive reduction in the incidence of subsequent major allergic disease such as asthma and hay fever in these children as he continued to follow them over a 10-year period.

Further work is needed to test the validity of Glaser's observations.

That the early feeding of egg white favors the development of sensitization is widely accepted. Some pediatricians—myself included—feel that the too early introduction of other solid foods also favors the development of allergy.

The matter of adenoid-tonsillectomy in the allergic child is one of frequent concern. Some physicians feel that this operation should not be done in allergic children, or in children of allergic parents, during the height of the pollen season, as pollen sensitization is then more likely to occur. This may be a valid precaution, especially in areas where the pollen count rises to great heights. Not valid, in my opinion, is the avoidance of needed adenoid-tonsillectomy simply because the child is allergic—on the theory the allergy may be flared up—or the performance of the operation routinely in allergic children. I believe the indications for operation are the same in allergic and non-allergic children; the retention of obstructing adenoid tissue is no more logical in an allergic child than in one who is nonallergic.

Finally, I would like to venture the view that just as the retention of obstructive adenoid tissue is not logical, retention of a pet to which a patient is sensitive is equally illogical. There is no question, in my mind, that by condoning such an arrangement we physicians have permitted a great deal of

asthma to persist in our patients. I have seen much more harm done in this way than is done psychologically by the removal of the dog or cat from the homes of asthmatic children. Our patients and their parents are like ourselves in wanting to have their cake and eat it, too. They would like to get rid of asthma, while keeping the cause of it. The attempt to do so is no more successful in this situation than it is in others like it. As physicians, it behooves us not to become party to this type of self-deception.

A discussion of this type would not be complete without mentioning the potential danger of giving horse serum or other serum to sensitized patients. Such sensitization may have been induced by previous administration of serum or may have occurred naturally, as in the case of a horse-sensitive asthmatic. It is, therefore, necessary to question the recipient about known sensitivity to horses, as well as previous administration of serum. Intradermal testing of such patients will reveal those in whom serum administration may be dangerous. Foremost among these is the horse-sensitive asthmatic whose skin test is markedly positive. Ordinary delayed serum sickness in a previously untreated patient following therapeutic doses of diphtheria or tetanus antitoxin is an example of justifiably induced iatrogenic disease.

ANTIBIOTICS AND IATROGENIC DISEASE

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THE ASSOCIATION of the term "iatrogenic disease" with the clinical use of antibiotics poses many problems.

Physicians generally are familiar with most of the untoward reactions that may follow the use of antibiotics, and many ex-

cellent reviews of the subject are to be found in the literature.¹⁻⁴

One cannot divorce the undesirable effects of antibiotics from the beneficial ones and, in this light, therapy becomes a calculated risk. If the probable discomforts or

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