

THE PRESENT STATUS OF ALLERGY IN CLINICAL MEDICINE

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Allergy in its various forms has been known for ages, but in recent years it has taken on a new importance. A knowledge of its management is even more important now that we know so much more about the condition. Moreover, industrialization and the consequent centralization of 85 per cent of our population seems to have made all allergic manifestations more prevalent. Our attempts to control our climate by means of air conditioning machines are still crude. They merely add to the wide variations in temperature and humidity to which we are already subjected. These variations in our environment produced by modern living put a great strain upon our autonomic nervous systems. As the years go by more and more of us develop imbalances of the nervous system which increase our disposition to develop allergy.

I make mention of this important fact because the students of the new school of psycho-somatic medicine regard the whole field of Allergy with a possessive eye. They point to the fact that a great percentage of psycho-neurotics are also allergic. To support this conception the age-old story is told over and over again of the woman who was allergic to roses and who on one occasion was seized with sneezing when a vase of paper roses was brought into the room. We all recognize that our mental reactions are the function of our brains. Emotional upsets are likely to bring on an allergic attack or to make it more severe than it otherwise would be only to the extent that they disturb the physiology of the individual. Stoic Indians, cows, and dogs are victims of Allergy just as are psycho-neurotics. So it would not seem wise to turn the field of Allergy over to Psychosomatic Medicine.

While Allergy has come to be a great joke in the radio world, we in the medical world do not take it so lightly. It has been found to be a cause of asthma, hay fever, sinus disease, hives, ango-neurotic edema, eczema, dermatitis, migraine headaches, colitis, epileptiform seizures, high blood pressure, and various disorders of the heart and other organs.

The commonest manifestations of Allergy is, of course, hay fever—properly called timothy allergy in its May and June phase and ragweed Allergy in late August and early September.

In reading the modern literature on Allergy one is thrown into great confusion. The reason for this is that there is a strange misuse of terms. To understand clearly even the popular literature on the subject one must realize that there are several types of Allergy. In the presence of all available knowledge we should recognize the following different types: (1) atopic; (2) non-atopic. Under this last we put: non-reagenic familial Allergy; the Allergy of infection; Allergy to chemicals, including contact Allergy; Allergy to serums; Allergy to physical agents.

The name atopy (literally a "strange malady") was given by Coca to the common Allergy of the ordinary case of hay fever, asthma, hives, and eczema to distinguish it from reactions to serums, ivy and primrose poisoning, and the hyper-sensitive reactions of tissues to the tubercle bacillus. Coca emphasized that it was a disease limited to human beings, that it was apparently inherited, and finally that it was characterized by the presence in the blood and tissues of its victims of a special kind of antibodies which he called *reagins*. It was later shown that these reagins were transferable to normal individuals. Strangely enough what literally thousands of farm people knew, namely, that dogs, horses and cows can and do suffer from atopic manifestations did not get into medical literature for a good many years.

The idea that atopy is inherited along Mendelian lines may be true. The familial appearance, on the other hand, may mean only that the genes have been

affected in some way by weather, nutrition, or other environmental factors. At any rate the concept of inheritance breeds despair when exhibited in our consultation rooms. Those among us physicians who are of an academic turn of mind cause much needless worry by invoking eugenics. As the late Logan Clendenning rightly observed: "Men are not going to embrace eugenics, they are going to embrace the first likely trim-figured girl with limpid eyes and flashing teeth who comes along in spite of the fact that her germ plasm is probably reeking with hay fever."

It is the third remaining characteristic of atopy named by Coca that constitutes the backbone of the modern treatment of Allergy. This characteristic is the presence of antibodies which may be detected by skin testing and which can be transferred in the serum of the patient to the skin of another individual. This characteristic is generally recognized now and made use of in the search for the cause of the particular allergic manifestation under investigation.

In recent years, Coca has described cases of familial migraine, urticaria, coryza, and asthma in which no reagins could be demonstrated. And which apparently did not fall into the regular types of non-atopic Allergy. In those suffering from this disorder Coca has found disturbances of autonomic nervous system in which the offending allergens could be detected by the marked increase in pulse rate which their presence induced. He reported that severance of the sympathetic nerves gives complete and permanent relief.

Although Coca's concept and its interpretation have not been investigated as thoroughly by others as they deserve, they do illustrate that neuroses, organ neurosis, and shock are matters of degree, and that the clinical manifestation represents Nature's attempt to prevent the break-down of a personality.

An Allergy to chemicals accounts for many cases. It consumes a large portion of the workmen's compensation funds earmarked for occupational diseases. Not much has been said in the literature about the possibility of contact other than in plant dermatitis and occupational dermatoses, but certainly most allergists are familiar with cases of coryza and asthma which have been induced through a specific hyper-sensitiveness to oils, fumes and gases. Some years ago I expressed the opinion that these were due to a contact Allergy—an opinion which others more recently confirmed. Many drugs, especially the organic ones, act as allergens. For years aspirin has been the worst offender and the most difficult to manage. But now it is being shoved aside by sulfa-drugs and penicillin. The mechanism has been quite clearly defined by Landsteiner, who has shown that the chemical unites with the serum of the victim to form a conjugate that can then act as a protein allergen. From this point on, the story of each case is exactly like that of serum sickness.

The most common reaction to penicillin is urticaria. This occurs in 5 per cent or more individuals who are undergoing systemic treatment. Vesicular eruptions occasionally occur and they resemble dermatophytids. Penicillin has provoked exfoliative dermatitis.

The allergy of infection is important. Some authorities question its existence. This again is pretty much a matter of terms. The usual definition of Allergy is that it is an abnormal and harmful response to a substance which is not harmful to normal individuals. This is a perfectly good definition of atopen, but it cannot be made to apply to the hypersensitiveness that develops in our bodies toward bacteria with which we have had an encounter. In fact, the severity of our illness during the course of an infection is an expression of this form of Allergy. Upon this fact depends the use of skin testing for the recognition of tuberculosis and undulant fever. There can be no doubt that hypersensitiveness or Allergy, if you will, to bacteria, is a very real thing.

Then there are people who will develop all of the signs and symptoms of one of the allergic manifestations when they are exposed to cold, or heat, or light, as the case may be. These conditions have been named by Duke as physical Allergy.

Compared with them, however, are other members of which heat, light and cold only serve as precipitating factors on account of the nervous imbalance. These and many other accessory factors predisposing at times to an attack of Allergy have at some time been brought forward as the cause of the condition. Among such secondary factors are: barometric changes; temperature changes, especially cold; light; emotional upsets and worries; fatigue; focal infection; acute and chronic infections; constipation, especially with food allergy; deficiency states such as malnutrition, hypochlorhydria; vitamin deficiencies, and particularly thyroid and liver disfunction; and mechanical and chemical irritations, especially dust, dirt, gases, fumes, or fogs.

Skin testing is a convenience when properly performed, and often saves time for the patient. It must be remembered that skin tests do not indicate for certain that the test substance is or is not the cause of his trouble. They are merely clues, the significance of which depends upon the knowledge and skill of the physician and above all upon his familiarity with the properties of his own testing material. For this reason every allergist wants to do his own skin tests in his own way with his own materials. It cannot therefore be emphasized too strongly that skin tests with atopens are only clues to aid and facilitate the search for the real offenders. Good medicine can be practiced without them if necessary.

Like certain other biological phenomena used in medical diagnosis, skin tests require interpretation, because positive reactions may be persisted from previous allergic disturbances, even in other parts of the body. These reactions—for example, pyloric stenosis, infantile eczema, or cyclic vomiting in children—may or may not have been recognized as allergic manifestations at the time of their occurrence. The most common of such reactions is a positive reaction to ragweed or timothy pollen after one season before the initial onset of hay fever in the next season. Finally, at times certain testing materials may be irritating in themselves and so give false positive tests on everyone, or they may become irritating if not properly kept. Extract of house dust, silk, tobacco and certain foods such as rhubarb and cranberries have to be watched closely in this respect.

All substances that are suspected should be put to clinical trial under controlled conditions, regardless of the results of the skin tests. Likewise, all positive tests must be proved before they are accepted. We see all too many patients who may or may not be allergic to certain substances but who think that they are because they have been told the skin tests to those substances were positive. Too frequently also we hear that the patient was tested and was allergic to nearly everything. It is the rule to be allergic to one or two inhalants and a food or two and possibly a pollen or two but seldom any more.

Treatment.—So far as the relief from the torments of allergy are concerned the greatest advance was made when we were given epinephrin for hypodermic injection. Then came ephedrine with like action but with the advantage that it could be given by mouth. In recent years, the sufferer from severe asthma has been blessed by the introduction of aminophyllin and more recently by its administration in rectal suppositories.

I, with certain others, began the use of histamine some 16 years ago. We found that by frequent injections of carefully graduated doses of very small amounts of histamine we could obtain relief in hives and certain forms of headache with surprising regularity. Then came attempts to tie histamine to some chemical so that it would be gradually released to the body for the purpose of stimulating the body of the allergic to produce enough of the anti-histamine enzyme to destroy at once the histamine released by the struggle between the allergen and its antibodies. In the meantime, the isolation of the enzyme, Histaminase, gave great promise but failed us when put to clinical trial. So the investigators went back to conjugating histamine with various chemicals. The first to be given extensive trial was Hepamine—a conjugate with an azoprotein from horse serum. The

Committee of Treatment of the American Academy of Allergy issued just yesterday its pronouncement that histaminase (Torantil) and Hepamine are of no value in the treatment of allergic diseases. Benadryl holds the stage at present.

Benadryl.—It is supposed that in anaphylactic shock in animals and in the allergic phenomena of human beings there is released a histamine-like substance which accounts for the clinical signs and symptoms. Various anti-histamine substances have been developed, some of them too toxic for general use, but one will hear a good deal of a recently developed benzhydryl compound which has been termed benadryl. When administered orally in doses of 50 to 100 mg. three to five times daily, it is highly efficient in controlling symptoms of acute and chronic urticaria and angioneurotic edema, although the relief is purely palliative. Side effects are not serious: drowsiness, dizziness, dryness of the mouth and dilated pupils may be noted. The drug is given by mouth or by the intravenous or intramuscular route. Preliminary investigations indicate that benadryl relieves pruritus in certain dermatologic conditions besides urticaria; therefore, extensive use of the drug may be anticipated. In my own experience it is a complete disappointment. It only confuses and delays the systematic investigation of hives.

One other drug needs to be mentioned to be condemned and that is ethylene disulphonate. As the Director-General and Editor of *The Letters* of the International Correspondence Club of Allergy, this has caused me no end of trouble. Appearing into respectable circles with a shadowy background, ethylene disulphonate was hailed by the daily press and *Time* magazine as "the one-shot cure" for allergy. It had a great run in Australia at 75 dollars an injection. It lived for awhile in scientific circles in England. In the United States some half a dozen honest men believed that they got good results with it. Careful trial at the University of Maryland and at the University of Minnesota have shown that it has all of the properties of triple distilled water. This left two questions: Are the chemicals which act as reduction enzymes in dilution so great as not to be detectable by ordinary chemical analytical methods, and secondly, what does happen when you give an intramuscular injection of distilled water? Is any histamine-like substance released? These questions appear to me as important, but are being used here as a defense to hold the line while many more vials of the one shot cure can be foisted upon the American physician anxious to give his allergic patient the benefit of the latest thing.

In conclusion, may I warn you against getting lost in the semantics of allergy. Remember that there are seven different kinds. Please be advised that none of the new remedies are much good but that the tedious treatment with pollen and other protein extracts brings about complete and permanent relief in better than 50 per cent of cases and relief in all but a few, that asthma can be controlled and that all forms of hives respond promptly to systematic management and investigation. We in allergy are proud of the clinical results that we get for they are much better than the average in clinical medicine.

We look forward with you to the day when the missing factor whose absence makes a Don Quixote of the tissues of the allergic so that they go off tilting at windmills will be found but in the meantime there is no reason for the allergic to be in any way discouraged.