

The Journal of **Allergy**

VOL. 41, NO. 5

MAY, 1968

Presidential address

Allergy: Current crisis*

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Members of the American Academy of Allergy: The field of allergy is a fascinating one. Allergy, as originally defined by VonPirquet, is altered host responsiveness, and it depends upon the immunologic system. The normal function of the immunologic system is to maintain a pristine status quo in respect to foreign molecules or cells. Borrowing from Walter Cannon's greatest contribution to biology, one might view this function as "macromolecular," or "configurational homeostasis."

This homeostatic mechanism serves to protect us, contributing to our resistance to infection. In some cases it appears to inhibit the establishment and spread of neoplastic disease. On the other hand, it may serve to damage us, as in the allergic diseases. It also serves to obstruct man's meddling, as in organ transplantation; and it plays a modifying role in maternal-fetal relationships. It is thus a fascinating system with broad biologic meaning.

Again by definition, all that is clinical allergy is not immunologic. Clinicians have diverged from VonPirquet's original intent in the word "allergy" and have applied the word to certain illnesses with altered reactivity in which immunologic factors may not play a role. Some of the physical allergies or some of the abnormal neurohumoral phenomena, such as cholinergic urticaria, are obvious examples. Undoubtedly, the clinical states of asthma, rhinitis, and urticaria are enormously contributed to by nonimmunologic as well as immunologic factors, and we can expect to hear in the future of more

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Received for publication Feb. 20, 1968.

*Presented at the American Academy of Allergy, Feb. 6, 1968, Boston, Mass.

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effective clinical classifications and subclassifications of these three syndromes. In some of these subclassifications the illness may turn out to be entirely non-immunologic.

Clinical allergy is therefore a vast and complicated field. It needs all the attention it can get from all possible directions. It needs physiologists, immunologists, microbiologists, biochemists, geneticists, epidemiologists, statisticians, pharmacologists, pathologists, *and clinicians*, if we are to improve our understanding of it. It needs clinicians alone, if we wish *only* to continue to offer patients the best that today's understanding of allergy allows.

Why do I start my message this way? I do so because I want to discuss with you some of the stresses and strains that plague today the field of clinical allergy. It is hardly a secret that there are many *in* allergy who are dissatisfied with the way things have gone or are going in the field. There are even more *outside* the field of allergy, however, who are equally dissatisfied. But these two groups are dissatisfied generally from opposite points of view.

Dr. Jerome Glaser¹ has recently put forward what might be viewed as the case for the dissatisfied allergist in an article written in *Review of Allergy*. The title of his article is "The Menace of Immunology in the Clinical Practice of Allergy." While bowing to the fact that the ultimate bases for many problems in clinical allergy are probably immunologic, he asks "whether, at present, a thorough knowledge of immunology has great relevance in clinical practice." He then goes on to lament that portion of the Allergy Board examination that asks immunologic questions, and comments that he rarely if ever has obtained any help from immunologists in his private practice of allergy. Dr. Glaser formulated a list of what he regarded as the major contributions that have been made to clinical allergy over the years. This list has been put in brief form in Table I. It can be seen at a glance that this list mostly included contributions to differential diagnosis or therapy of atopic diseases—that is, skin test and treatment methodology, and the recognition of certain allergens clinically important in atopy. Only one contribution is included since the introduction of corticosteroid therapy in 1949. That was the delineation of the mechanism of hereditary angioedema. Immunology, in Dr. Glaser's opinion, is still so irrelevant to the clinical allergy he sees that he believes his and other clinical practices of allergy should be organized along lines quite independent of immunology, much as the usual practice of psychiatry is organized independently of more basic neuro-sciences. For this reason, Dr. Glaser finds

Table I. *Major contributions to clinical allergy (from Glaser)*

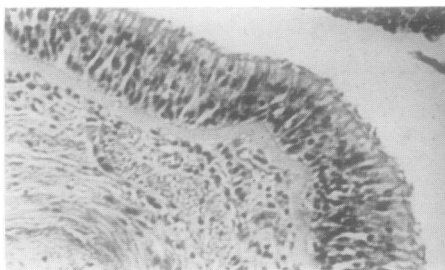
<i>Year</i>	<i>Contribution</i>	<i>Year</i>	<i>Contribution</i>
1903	Epinephrine	1927	Nasal eosinophilia
1906	The term "allergy"		Allergic purpura
1911	Hyposensitization	1929	Soy bean milk
1912	Scratch tests	1931	Meat base milk
1915	Intradermal tests	1935	Theophylline
1921	Passive transfer tests	1942	Antihistamines
1922	House dust antigen	1949	Corticoid therapy
1924	Ephedrine	1962	Hereditary angioedema

the content of the board examinations in allergy and, I suppose, these meetings of the Academy of Allergy correspondingly bothersome.

The dissatisfaction of the nonallergist was put forth by Dr. Emmett Holt² in the *New England Journal of Medicine* in an article entitled "A Non-allergist Looks at Allergy." Dr. Holt charges that "the limited acceptance of allergy by its conferees is in part due to a tendency to cling to dogmas unconvincingly demonstrated to others." He attacks particularly skin testing and hyposensitization as techniques of unproved reliability or usefulness. Although there are few here who will agree that the data Dr. Holt presented are incontestable, there are many who recognize some validity in his charges. Allergists have been prone to center especially on skin testing and hyposensitization; skin testing as a diagnostic aid can be abused and has been by at least some of our profession; and hyposensitization is widely used despite many demonstrations that its effectiveness, as indicated by a number of large group studies, has been of marginal benefit.

Let me make myself clear. I do not advocate abandoning skin testing or hyposensitization. Skin testing properly used, as was rightly pointed out in some of the vigorous responses to Dr. Holt's article in a subsequent issue of the *New England Journal of Medicine*,³ has a very proper place in diagnosis. Hyposensitization, to the extent that it offers even marginal benefit,⁴ is important to continue as one facet of the usual multipronged therapeutic attack that good allergists launch on patients with allergic disease.

But to return again to Dr. Glaser's list, it is evident that his list is composed of just these facets of clinical allergy which Dr. Holt attacked most strongly as constituting approaches which have captured and paralyzed the field of clinical allergy—skin testing, hyposensitization, and allergen avoidance. Left off Dr. Glaser's list are many contributions made in the past 15 years that I would regard as very substantial additions to our *understanding* of clinical allergy and contributions that Dr. Holt and others would surely include in their list of highly exciting or promising new developments for the field. A few of the immunologic contributions would be: the delineation of some of the mechanisms involved in sensitization to drugs, including new approaches in diagnosis of drug allergies and delineation of previously unrecognized drug-related syndromes; an improved understanding of the mechanism of induction of serum sickness, together with laboratory procedures that can be useful in predicting the likelihood of development of this complication; an appreciation of the expanding array of inflammatory diseases of the lung due to precipitating antibodies to inhaled microorganisms, such as in farmer's lung, aspergillosis, pigeon breeders' disease, maple bark disease, and others; a better understanding of contact sensitization and cellular hypersensitivity, whether induced by such common allergens as the pentadecyl catechol of poison ivy, by penicillin, by metallic nickel, by the sulfhydryl hardeners used in commercial rubbers, or by the commonly used investigative chemicals, dinitrochlorobenzene and picryl chloride; the series of fundamental observations on the role of complement in mediating the inflammation the clinician sees in allergic angiopathies, and the specific relationships between

Fig. 1*Fig. 2***Fig. 1**

Bronchial mucosa in a patient with asthma showing a thickened appearance to the basement membrane from deposits at and beneath the membrane (from the collection of Dr. Milton Bohrod).

Fig. 2

Immunofluorescent staining in the area of the basement membrane. Anti γ -G globulin serum. The very bright fibers in the lower part of the figure are autofluorescent elastic fibers.

complement components and anaphylatoxins and chemotactic activities; demonstration of quantifiable histamine release from peripheral blood leukocytes; the description of differential relationships between the allergic mediators SRS-A and histamine, and antibodies of different immunoglobulin classes; delineation of the γ E class of immunoglobulins; and the list could go on. I will not even attempt another list, that could be equally as long or longer, of physiologic advances that are important to allergy—but surely, by way of example, the considerable attention paid in our current meeting to autonomic factors in asthma will not have missed your attention.

Some of you may scoff at these areas of study, as they do not yet affect the day-by-day mechanics of the usual care of patients with atopic disease. To many of the younger men in our academy, however, these newer findings bring great excitement and seem to hold promise for new clinical approaches. Such excitement and hope also each year bring new and energetic blood into the field of allergy. It is upon this new blood that we will depend for continued forward motion.

These newer findings also offer a logical scaffolding upon which the allergist should be broadening his capabilities and responsibilities in patient care, reaching out to encompass more than atopy alone. Again, do not misunderstand me. I would not relegate atopy to a secondary place in an allergist's practice. Asthma is today better managed by allergists than by any other group of practitioners—assuming, of course, that we mean allergists who are reasonably complete physicians. The allergist, without any doubt, should continue to devote himself primarily to patients with asthma and those other diseases that have by tradition been in his domain, but there is an opportunity for him today to take on more, if he wishes it.

Is immunology irrelevant to the clinical practice of allergy? Hardly so! To the extent that its target is clinical allergy, immunologic investigation is

relevant, no matter whether the investigator has as yet hit his target. Many of you heard earlier today Dr. Connell's description of basement membrane disruption in the experimentally challenged nasal mucous membrane. Many others are familiar with the characteristic, though not unique, thickening that has been recognized by Dr. Milton Bohrod and others in the basement membrane in the bronchi of asthmatic patients (Fig. 1). Whether this thickening is an expression of the chronic effects of such damage as Dr. Connell has shown us cannot yet be known, but it has been of interest to us in Rochester to learn through Dr. John Condemi that this membrane may sometimes be packed with gamma globulin (Fig. 2). Drs. Vasquez and McCarter⁵ at Duke have published pictures similar to this. Obviously, this is one of a number of places where immunology should help us.

I do advocate, therefore, that dissatisfied clinical allergists divest themselves of their feelings of antagonism towards immunology and other basic sciences pertinent to clinical allergy. Allergy is, as Dr. Holt observes, "a fascinating subject with no end of intriguing problems to study and to solve. Its surface has only been scratched."

So let us get on with the job. Let practicing allergists take on those broader clinical responsibilities that are logically theirs. Let all of us in the Academy who have differing talents, aims, and interests get together. Let us keep the curtains raised and communicate in mutual respect. Let those of us who are older talk with our younger new blood in every way possible, or else we will never be able to show them where we see needs or hear from them their fresh viewpoints. Let those who are investigationally directed and those who are purely clinicians talk together, as each has much to give the other. With *good* clinical observation and *good* basic research the resultant benefits to allergy should answer both groups of complainants. From the laboratories and clinics alike will come our future. We should not imperil it with useless quarreling.

Finally, I want to thank Dr. Glaser for bringing this issue to the surface. We all recognize that Dr. Glaser has a long list of significant contributions to the general field of allergy. I trust that this exchange which he has initiated will represent yet another.

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