Allergic Diseases of Infancy, Childhood and Ado

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Edited by

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PREFACE

Allergy is one of the most common causes of acute and chronic childhood disease. It is the leading cause of school absenteeism for chronic conditions of the respiratory tract and is responsible for a wide range of problems for the child and family. It may cause physical disability, may interfere with the normal psychosocial development of the child and often creates severe social and economic difficulties for the family as well. Unfortunately, allergy is a misunderstood and mysterious area of medicine for many physicians. On the one hand, it commonly is invoked as the basis for numerous types of symptoms for which no other explanation is apparent. On the other hand, allergic disease often is not recognized and, even when recognized, is managed inappropriately. This book was conceived and developed for physicians who provide primary patient care and addresses itself to diagnosis and treatment of those disorders, symptoms, complexes, and signs in the pediatric age range in which the question of "allergy" may arise.

The terminology of allergy suffers from divergent and often vague usage, in itself obstructing recognition and treatment of allergic disease. The term "allergy" was coined in 1906 by von Pirquet following his recognition with Bela Schick that antibodies could cause as well as ameliorate disease. The term, taken from the Greek *allos* ("change in the original state") referred to the concept that encounter with a foreign substance induced an alteration in specific responsiveness, so that subsequent contact with that substance was heightened (hypersensitivity) or decreased (hyposensitivity or immunity). Eventually, an association was recognized between immune factors and various clinical syndromes, leading to the idea that these disorders had an immune basis; in this context "allergy" came to refer only to the hypersensitive (adverse) manifestations of the immune response, and the terms "allergic disease" and "allergic disorder" came into use. Current understanding of the pathogenesis of many of these disorders, however, differs from earlier concepts on which the terms were based, and the terms "allergy" or "allergic" often are more confusing than helpful.

Accordingly, we have adopted the following definitions for "allergy" in this book:

An *allergic reaction* is the adverse consequence of a specific immune event, that is, of the interaction between antigen and antibody or sensitized lymphocytes.

An *allergic disorder (disease)* is a complex of symptoms and signs in which immune events are thought frequently to play a major role. It should be recognized that in some individuals with an allergic disease, immune events may not be of major importance or may not participate in the disease at all and, further, that even when "allergy" is an important factor in the disease, it may not be

the underlying basis of the disease (see Chapter 14 and chapters that deal with individual disorders).

Atopy (from the Greek, *atopos*, or "strangeness"), another term that requires definition, was first used by Coca and Cooke over 50 years ago with reference to a group of diseases (seasonal rhinitis, perennial rhinitis, asthma) that shared certain clinical features, suggesting a common basis for these disorders. Sulzberger later argued for the inclusion of infantile eczema ("atopic dermatitis") as well. The occurrence of a specific skin-sensitizing substance ("atopic reagin"), now considered to be principally IgE antibody, was recognized in a high proportion of individuals with atopic disorders and was believed to contribute to the pathogenesis of the disorder in such individuals. Though frequently associated, there is considerable evidence that atopic disease can be independent of IgE antibody.

We have chosen, therefore, to consider *atopy* in terms of a constellation of complexes of symptoms and signs that exhibit certain features in common: a familial (and presumably hereditary) basis, an end-organ hypersensitivity to a variety of chemical mediators of inflammation, and precipitation or aggravation of the complex by various mechanisms, only one of which may involve IgE antibody. Thus, involvement of IgE antibody is not a required characteristic of an atopic disorder. Conversely, the capacity to produce IgE antibody, known to be present in many individuals without any other feature of atopy, does not in itself warrant the designation "atopic." Thus, atopic disorders are considered to represent a subgroup of allergic disorders, which include perennial and seasonal allergic rhinitis, asthma, and atopic dermatitis.

This book is for the practicing physician, and its orientation, therefore, is practical. Some sections may appear at first glance to be academic considerations of physiology, biochemistry, and immunology, but they provide background information necessary for a rational approach to diagnosis and treatment of allergic disease. Also included is consideration of various nonallergic conditions that exhibit features sometimes confused with "allergy" and a consideration of disorders in which a *deficiency* in immune mechanisms may result in disease. In addition, an attempt has been made to reference individual chapters broadly, including review articles and in some cases additional general references on the subject matter covered. We hope that the information and the manner in which it is provided not only will foster more intelligent diagnosis and therapy of allergy but, in so doing, also will encourage the physician to deal more effectively with allergic diseases of infancy, childhood, and adolescence.

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INTRODUCTION

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The recorded history of allergic disorders is almost as old as the recorded history of man. Asthma was known to the ancients, as well as the concept that one man's food may be another's poison. The modern perspective with regard to allergy began to be formed early in the 19th century, when Bostock (1819) gave the first modern description of hay fever; a few years later Blackley proved hay fever to be a pollenosis and reported the first confirmatory diagnostic tests, including (in 1873) the first skin test. The recognition that asthma and hay fever and certain other clinical syndromes were related to an altered reactivity of the body, often excited by environmental particles, foods, or other conditions, led to a long and exciting period during which the practice of the clinical allergist was dominated by the quest for the identity of those inciting factors.

Immunology is much younger conceptually than allergy. It had its birth in the late 19th century in studies of bacterial infection and resistance, in studies of resistance to snake venom, in the development of antisera against diphtheria and other scourges, and in the description of anaphylaxis. The link between allergy and immunology was forged early in the 20th century by a host of investigators too numerous to list but whose names include Arthus, Calmette, Cooke, Noon, Richet, Schick, Schloss, Theobald Smith, von Behring, and von Pirquet. Richet described *anaphylaxis* (1902) and became the father of modern experimental immunology; von Pirquet invented the word *allergy* (1906) to describe *altered reactivity*; Leonard Noon first (1911) injected an extract of allergen to treat hay fever by *desensitization* (hyposensitization). The next half century was dominated by a clinical orientation among allergists, based on the concepts developed in these early years. The fundamental notion of allergy was that altered reactivity was based upon prior exposure and that its management was to identify and avoid the inciting factors or to desensitize against those inciting factors when they cannot be avoided altogether and when an effective extract could be prepared.

The romance between allergy and immunology began almost a century ago, and the marriage at its diamond jubilee seems secure, but recent studies have both put the relationship on a more solid conceptual and experimental basis and revealed areas in which appeals to immunology for understanding of allergic problems have failed to find adequate responses. New techniques and new rigors in the scientific study of allergic diseases are changing our perceptions of their natures and are calling upon us to modify or abandon time-honored notions with respect to allergic and related immunologic problems.

The development of sophisticated immunologic tests and their correlation with traditional clinical observation and allergic testing have indicated that

some patients with clinical allergy by traditional definitions have no substantial evidence of an immunologic disorder nor any clear-cut sign that traditional measures are likely to be helpful. For such patients, traditional management is to be regarded as unacceptably costly, intrusive, and futile. For them, management with drug therapy may be the only effective present recourse; the same will be true for many other patients who have more traditional forms of allergy. The advances in pharmacologic therapy in the past quarter century have aided in this differentiation and management.

Hyposensitization began to be used in 1911 in the treatment of hay fever. The process was long known as "desensitization" and still may be for some allergists, though it is clear that when wheal and flare reactivity is part of the response to a skin test, this reactivity may not much abate as symptoms are controlled by the injection of extracts. Recent rigorous experimental studies have sharply revised our notions of the effectiveness of this time-honored procedure. The anecdotal evidence of nearly two generations of clinical allergists has supported the procedure with enthusiasm, but studies using modern criteria for statistical reliability and validity were not done until nearly 40 years after desensitization was first introduced. These studies and others that have followed have validated the procedure statistically but have also raised problems as to how the procedure should be properly used in the particular patient. For example, the results of an early study might be interpreted as suggesting that *all* the statistically significantly beneficial effects of desensitization in a study group might have represented major impact on the symptoms of a relatively small subgroup of those who were treated. We are left to wonder how to identify reliably those patients who will and those who will not benefit from or need this form of treatment.

It is clear that attitudes towards allergic diseases are in a state of rather rapid change. Our attitudes towards skin testing and immunization therapy (desensitization or hyposensitization) are more conservative than a decade ago, and with the refined chemical techniques that allow us to accurately measure the levels of drugs (and especially of theophylline) in the blood, we have entered a new era in management of asthma. Cromolyn and corticosteroids also have roles to play in this new development. All of these developments are discussed in detail in the pages that follow, and the contributors to this volume will indicate our present conceptualization of the relationship between the basic sciences and the clinical conundrum known as allergy and will show us where we are sometimes served best by immunology, sometimes best by pharmacology, and sometimes best by an empiric common sense rooted in decades of clinical practice.

Nothing in the foregoing comments should be construed as suggesting that the allergist or any other physician should abandon in any major respect the traditional plan of study of allergic children, which is to attempt through complete and creative history-taking to identify events or substances precipitating symptoms of allergic disorders. Skin tests have a place in the study of certain children. Some constraint on exposure to inciting agents is appropriate, and prophylactic constraints often may also be useful. But any of these processes may become cost-ineffective when pushed to the point where the frustration of physician, child, or parents outweighs relief of tolerable symptoms or to the point where guilt and depression are generated by the failure of intense efforts to abate symptoms that nothing can control. Even though for many years skillful conventional allergic management has brought comfort or relief to millions, we must be ready to test and retest our notions as to what best fits the individual patient

and must be ready as soon as possible to identify those patients for whom non-immunologic therapy is the only kind required or likely to be helpful.

When value systems are in rapid evolution, it is helpful to have substantial reviews such as this volume to bring us to the advancing edge of a changing field and show us where we are, what is going on, and what likely lies ahead. We may guess that what lies ahead for allergic children and their families is continued progress in clinical immunology, clinical physiology, clinical pharmacology, and clinical psychology of child development. This continuing progress will tell us with ever more confidence what allergic children need and how to provide it for them.

CONTENTS

PRINCIPLES OF IMMUNITY