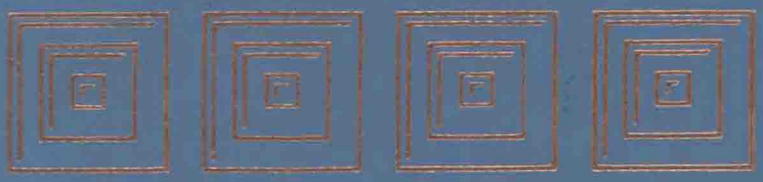
The Practical Management of ASTHMA



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The Practical Management of Asthma

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Introduction

From England it is reported that 10% of the patients enrolled in a general practice medical program will at some time require treatment for symptoms of asthma. The number of asthmatics in the United States is estimated at 8.9 million; this number probably represents only a fraction of the patients who have requested medical help because of symptoms due to reversible bronchial obstruction. Fifteen or twenty million might be a closer approximation of the whole asthmatic population if these "occasional asthmatics" are included. Clearly, asthma is one of the most common medical problems encountered by the primary care physician.

This book is based on our experience in teaching the practical management of asthma to practicing physicians. Our program appealed equally to family practitioners, internists, allergists, and chest physicians, and we concluded that there was a real need for a publication covering the practical aspects of managing bronchospastic patients. The number of these patients is so great that most will be seen by primary care physicians and will not be referred to specialists. Judging from the patients we see at Scripps Clinic—who, no doubt, represent a subset of "problem asthmatics"—there must be tens of thousands of Americans who suffer a great deal of unnecessary distress and disability because the nature of their disease is not appreciated or their treatment is not optimal. It is our belief that the great majority of asthmatics can be kept free of symptoms most of the time on a simple and safe outpatient regimen.

In the last few years there have been several important developments in the treatment of asthma. Not only have new therapeutic methods appeared, but better use is being made of some of the older medications such as theophylline and prednisone. Paradoxically, these advances have made it more difficult for the nonspecialist to treat asthma. With the greater number of effective drugs available, more experience and judgment are required to decide what combination to use and when to use it. With the greater range and sophistication of diagnostic tests, it is more difficult to strike an appropriate balance between making a thorough evaluation and squandering the patient's money.

Many exciting discoveries have also been made in the last decade in the fundamental pathophysiology of bronchospasm. If we have little to say about them in this handbook, it is not because we belittle their importance to practicing physicians. We do believe that many publications and teaching programs intended for clinicians tend to give disproportionate emphasis to the biochemical mechanisms of bronchospasm and to deal in a perfunctory way with those details of diagnosis and treatment that are so essential to successful management of the patient. The interested reader will find basic science aspects of asthma well discussed in a number of excellent texts and review articles. This manual brings together a discussion of many details of treatment that may not be found easily in the standard sources. Various aspects of diagnosis and management of asthma are covered in the standard textbook style, and the final section consists of a series of illustrative case reports. These patients' reports were not selected

because they represent uncommon or unusually difficult problems, but because they help to flesh out the preceding chapters by showing some of the approaches of physicians who treat asthmatic patients on an everyday basis.

The bulk of this book was written by the staff of Scripps Clinic, but we have been ably assisted by our colleagues in San Diego—Dr. Stephen I. Wasserman of the University of California, and Doctors Michael Schatz and Robert S. Zeiger of the Kaiser Permanente Medical Care Program. For the important and specialized topic of occupational asthma, we have drawn upon the expert knowledge of Dr. Jordan N. Fink of the University of Wisconsin. Our intention in making relatively limited use of outside authorities was to present a coherent approach to the treatment of asthma representing the thinking of a group of specialists working together who often consult on the same patients, and who were able to discuss each others' separate chapters informally as the book went through the months of gestation. By including approximately equal contributions from allergists and chest physicians, we have tried to present a balance between their somewhat different approaches to the management of asthma.

It is our hope that this book will help readers to recognize and treat successfully the majority of their asthmatic patients.

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Part 1

Background

1

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Bronchospastic Disorders: An Overview

Asthma has been defined as "a disease characterized by an increased responsiveness of the airways to various stimuli and manifested by slowing of forced expiration, which changes in severity either spontaneously or with treatment." In contrast to some earlier definitions, this one, adopted by the American Thoracic Society and the American College of Chest Physicians, makes no reference to the etiology or to immune mechanisms, recognizing that variable obstruction of the airways can occur in response to a number of stimuli.

In addition, this definition of asthma represents a relaxation of older and stricter ideas of the disease in stating only that the obstruction of the airways changes in severity either spontaneously or with treatment. Therefore, we could describe as asthmatic all patients with chronic obstructive lung disease who show a significant variable component to their airways obstruction, even if most of the obstruction is due to permanent anatomical changes. Obviously, it would be very confusing if we used the same diagnosis of asthma to describe the range of patients from children who experience an occasional attack of wheezing to the older people with chronic obstructive pulmonary disease (COPD) who derive some benefit from their bronchodilator inhalers. From the therapeutic point of view however these patients have something in common. Since therapy is the focus of this book, we shall include their various disorders in this chapter on the bronchospastic disorders.

COMPONENTS OF THE BRONCHOSPASTIC REACTION

The bronchospastic reaction consists not only of bronchial smooth muscle constriction, but also increased bronchial mucus secretion and cough. This combination of reactions, when it occurs in appropriate circumstances, presumably serves the useful function of protecting the lower respiratory tract from aspiration of foreign materials and infectious agents. In the bronchospastic patient, these protective reactions occur in inappropriate circumstances or their intensity and duration are much greater than is necessary for the protective function.

The characteristic feature of asthma, therefore, is abnormally increased responsiveness of the airways to various stimuli. The cause of this hyperreactivity is unknown, but in individual patients it probably represents a mixture of genetic predisposition with humoral, neurogenic, and enivronmental factors interacting in varying degrees. Bronchial hyperreactivity is more than a theoretical concept. Abnormal bronchoconstriction in

response to aerosols of histamine or methacholine can be demonstrated not only in those with a history of asthma, but also in many of their asymptomatic relatives.

MECHANISMS OF BRONCHIAL OBSTRUCTION

In the majority of patients suffering from the bronchospastic disorders, bronchial obstruction results not only from constriction of the bronchial smooth muscle, but also from anatomic changes that cause narrowing of the bronchial lumen. These changes occur in the conducting airways themselves (chronic bronchitis). Airways obstruction can also result from destruction of the lung parenchyma (emphysema). Unfortunately, the terms "chronic bronchitis" and "emphysema" have been used so variously by clinicians, pathologists, and respiratory physiologists that they have become very confusing. Therefore, the expressions "mural obstruction" and "extramural obstruction" will be used here to distinguish two important mechanisms of chronic obstructive disease of the airways.

Mural Obstruction

This condition results from several different processes that can combine to cause narrowing of the bronchial lumen. These include mucosal edema, thickening of the mucosa and submucosa resulting from mucus gland hypertrophy and inflammatory cell infiltration, hypertrophy of the bronchial muscle layers, and postinflammatory fibrosis of the bronchial and peribronchial tissues. Some of these pathologic changes are at least potentially reversible, but eventually there is more or less permanent anatomic change in the bronchial wall.

Extramural Obstruction

In extramural obstruction there is bronchial narrowing through destruction of the elastic elements in the lung parenchyma that normally maintain the patency of the collapsible intrathoracic airways. The recoil pressure of the lung exerts an outward force from the lumen at each point of attachment of the parenchymal structures. As the elastic elements are destroyed, the recoil force diminishes and the airways tend to collapse.

The smaller the airways and the thinner their walls, the more they depend on the recoil pressure of the lung to maintain their normal patency (Fig. 1-1). Therefore, the principal site of extramural obstruction (emphysema) is the terminal airways. Bronchoconstriction, by contrast, is most prominent in larger airways that are abundantly supplied with smooth muscle. Mural obstruction due to various mechanisms probably can affect conducting airways of all sizes down to the terminal level. Presumably this accounts for the rather disappointing results of trying to classify patients as having large airways or small airways obstruction in order to predict their response to treatment. However, the concept of mural and extramural obstruction is helpful as an aid to understanding the interplay between potentially treatable and nontreatable components in chronic airways obstruction.

Mucus Plugging

When bronchial obstruction has persisted for a period of hours or days, there is a tendency for secretions to accumulate in the lumen. With severe bronchospasm, the secretions become more viscous as the cough becomes less effective as a result of fatigue, dehydration, and certain medications. In extreme cases, "bronchial casts" may form,

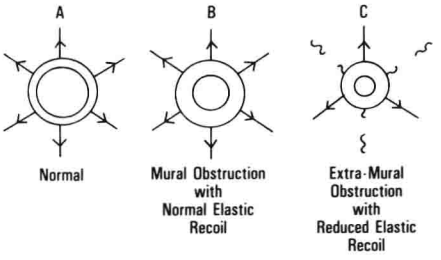

Fig. 1-1. Mural Obstruction Diagram. Normal; Mural obstruction with normal elastic recoil; Extra-mural obstruction with reduced elastic recoil.

extending to occlude segmental, lobar, and even mainstem bronchi, and at this stage the usual pharmacologic agents are ineffective even if they can increase the size of the lumen. When mucus plugging reaches this degree, the diagnosis "mucus impaction syndrome" becomes appropriate, but lesser degrees of mucus impaction probably are important in delaying recovery from many episodes of acute bronchospasm.

BRONCHOSPASTIC COPD

The chest physician sees relatively few patients with simple spasmodic or episodic asthma. Most older patients suffering from the bronchospastic disorders have chronic and nonreversible airways obstruction with more or less of a superimposed bronchospastic component. It is essential to recognize this reversible element of their disease because even a small improvement in their bronchial obstruction can have a major beneficial effect on their life-style. It is important to include discussion of bronchospastic COPD in this book because these patients respond to the same medications and other therapeutic interventions that are used so successfully in uncomplicated asthma. Often they have been inappropriately told by friends, or even unfortunately by a physician, that they have emphysema and that "nothing can be done for it." It is a great help in approaching these patients to tell them that they have "a form of asthma"—and, as explained earlier, they certainly do have a form of asthma according to the currently accepted definition. Treatment of such patients can be a very gratifying experience because the modest reversal of the airways obstruction that can be achieved may seem almost miraculous to them, especially if they have had severely obstructed airways for years.

A PHYSIOLOGIC CLASSIFICATION OF THE BRONCHOSPASTIC DISORDERS

Probably any person would develop bronchospasm in response to a sufficiently intense stimulus. Bronchoconstriction can be triggered in an asthmatic by stimuli that do not cause this reaction in most normal individuals, however. The bronchospastic disorders can be classified according to the nature of the stimulus, an etiologic classification, or according to the disturbance of function of the airways, a physiologic classification.

Bronchial hyperreactivity. Increased responsiveness of the airways to a variety of stimuli is a characteristic and perhaps invariable feature of the bronchospastic disorders. Here the term is used to refer to that large reservoir of potential asthmatics who have no bronchial obstruction at the time of testing and who sometimes give no history of asthma. They can be identified only by an abnormal response to inhalation challenge testing with drugs such as histamine or methacholine.[1] It is believed that this population of potential asthmatics is a reservoir of adult-onset clinical asthma cases. Until long-term follow-up studies have been done on otherwise normal subjects with bronchial hyperreactivity, however, this is only speculation.

Acute episodic asthma. This term has been used for those patients who experience attacks of bronchospasm but whose lung function is normal, or nearly so, between attacks.

Chronic asthmatic bronchitis. In these patients bronchospasm is perennial, although it is periodically exacerbated with acute attacks.

Chronic obstructive lung disease with bronchospasm. This type of disease has already been mentioned (bronchospastic COPD). In many of these cases there will be no reported history of attacks of wheezing or exacerbations of dyspnea except, perhaps, at the time of an acute respiratory infection. These patients are recognized by their response to bronchodilator therapy. These patients constitute a large and important group, especially to the chest physician and the primary care internist.

NONBRONCHOSPASTIC CAUSES OF WHEEZING

The following list includes a wide variety of disorders that should be ruled out whenever a diagnosis of asthma is supspected but especially when the case and setting appear atypical or the response to treatment is poor:[2]

1. Congestive heart failure
2. Pulmonary embolism
3. Increased airway collapsability (tracheomalacia and bronchomalacia)
4. Chronic bronchitis with mucosal edema and secretions
5. Endobronchial disease: tumor, foreign body, granulomatous inflammation
6. External bronchial compression
7. Substernal thyroid

ETIOLOGIC CLASSIFICATION (PROVOKING FACTORS)

In 1918 Rackemann[3] recognized that not all asthma was caused by allergy to inhalants or ingestants (extrinsic), and he used the term "intrinsic asthma" for those cases where "the cause lies within the patient's body." In the years since Rackemann's report, this classification has proved useful and has gained widespread acceptance. However, there is so much heterogeneity among asthmatic patients that it is no longer sufficient to consider them simply as "extrinsic," "intrinsic," or "mixed." We believe that successful management of the asthmatic patient depends on a systematic search for potential

Table 1-1
Provoking Factors in Bronchial Asthma: 1-Year Prospective Study of 234 Patients

	Patients with Factor (%)		
Provoking Factor	Sole	Major	Contributing
Immediate hypersensitivity infection	5.1	25	45
Acute upper respiratory illness	2.6	7	19
Sinusitis	1.3	9	23
Acute bronchitis (purulent sputum)	1.3	3	12
Postviral onset	0.4	7	11
Aspirin intolerance	0.9	9	10
Asthmatic bronchitis (COPD)	0.9	17	20
Isoproterenol abuse	0.0	0.4	4
Irritant inhalation	0.0	3	24
Exercise	0.0	0.4	18
Atmospheric change	0.0	0.4	21
Emotional upset	0.0	1.7	9.8
Associated disease	0.0	0.4	1.7
Idiopathic	10.0		
Total	22.5	83.3	

mechanisms and settings that may aggravate the asthmatic state. Provoking factors in bronchial asthma that we look for are listed in Table 1-1.[4]

Allergies

In a prospective study of 234 adult patients presenting to the Allergy and Immunology Division at Scripps Clinic in the early 1970s, only 58 (25%) had asthma in which an allergic immunoglobulin E (IgE)-mediated immediate hypersensitivity mechanism was the major provoking factor. In an additional 47 patients, allergic mechanisms were judged to be minor provoking factors. Even with these two groups combined, only 45% of the patients had "allergic" asthma. Other studies have shown the frequency of allergic asthma to vary from 56% to 66%, depending on the patients' age (with an increased incidence in children), the population studied, and the criteria used to establish the diagnosis. In the Scripps Clinic study, to incriminate immediate hypersensitivity as contributing to the asthmatic state, we required documentation of skin-sensitizing antibodies (reagins) to allergens to which the patient is exposed, and evidence from the history or—even better—controlled inhalation challenges that these allergens indeed provoke asthmatic symptoms.[5] Although 66% of patients had positive wheal and flare skin tests to one or more antigen tested, 31 of the 234 had positive skin tests only to allergens not present in their environment.

Only about one-third of the patients who were challenged with inhaled extracts of the allergens to which they had shown positive skin tests developed a bronchospastic response. Therefore, when the 31 patients with irrelevant but positive skin test were combined with the 18 patients who had negative bronchial challenges to relevant positive skin tests, there was a total of 49 patients with reaginic antibodies that were not contributing to their asthma.