Asthma

DISCUSSIONS IN PATIENT MANAGEMENT

by

M. HENRY WILLIAMS, JR., M.D.

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M. HENRY WILLIAMS, JR., M.D.
Professor of Medicine
Albert Einstein College of Medicine
Director, Chest Service
Bronx Municipal Hospital Center
New York, New York

CHANG SHIM, M.D.
Assistant Professor of Medicine
Albert Einstein College of Medicine
New York, New York

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INTRODUCTION

Asthma represents an extraordinarily fascinating and unusually rewarding challenge to the physician. An extremely common disorder, it may be manifest in many different ways among different patients and within a given patient. It varies from an asymptomatic sound in the chest to fatal obstruction of the airways and its course is often unpredictable. Treatment represents a unique blend of the science and the art of medicine. There is a great deal of information available about the different kinds of obstruction of the airways, how they may be detected and how they are caused. There is also a great deal of information available about different drugs that can reduce the airway obstruction, particularly through smooth muscle relaxation. There is even scientific evidence of the mind-body interaction in asthma in that suggestion has been shown to cause bronchoconstriction and bronchodilation. The physician must utilize this knowledge in the treatment of each patient, but he must go further in injecting his own personality into the therapeutic process by providing emotional support through availability and reassurance, by reinforcing the pharmacological action of drugs with his own enthusiasm and by having a compassionate interest in the patient which may have direct or indirect effects on the therapeutic process.

Each patient represents a unique diagnostic problem and there are more differences than similarities between patients. In taking a history, the physician must seek to elicit any possible environmental agents that may be causing asthma and seek clues as to the settings in which asthma occurs so as to assess the psychological component. The history taking also represents the beginning of psychotherapy.

The physician must also be alert to the variation that he will encounter in each individual patient ranging from mild to severe symptomatology, from good response to nonresponsiveness to therapy. He must seek the mechanism

for these differences which may relate to changes in the nature of the obstruction or to improper use of medication. A major principle of therapy is gradually to escalate treatment to induce maximal improvement and, then, to become sensitive to remission of the pathophysiological process so that the amounts of medication can gradually be reduced but at a tempo sufficient to maintain the patient free of symptoms. Therapy can become extremely frustrating for both the patient and physician when severe illness persists despite maximal treatment with all known drugs, but an optimistic attitude is warranted since, as will be seen, the most severely obstructed patients may experience a remission. The physician's attitude should be one of continuous probing and seeking out of mechanisms and new approaches to therapy, including both drugs and psychiatric intervention.

The objective assessment of asthma with a simple test of ventilatory function adds to the fascination of the condition and provides each physician with the opportunity for documenting the results of treatment and for learning more about the disease, its variation and its response to different types of therapy in different patients. The patient who makes his own measurement of ventilatory function assists the physician in the therapeutic process. The patient should be taught as much about his disease and the drugs available for his treatment as he can possibly understand and, with the guidance of his physician, develop sufficient understanding as to regulate therapy most of the time. In many cases, the patient will know a good deal more about his own illness than will his physician, and this is proper and good.

The frustrations and problems of treating difficult asthma are partially alleviated by the opportunity to learn more about the disease. Why is it that a patient will respond well on one occasion and not on another? Why does remission develop for no apparent reason in a desperately ill patient? Do patients actually become refractory to treatment with corticosteroids or isoproterenol, or do they develop a type of airway obstruction which is not responsive to these drugs? Is mucous obstruction of the airways a consequence of sustained bronchoconstriction

or does it develop for other reasons? How can it be reversed? The answers to these and to other important questions may be learned by the interested, observant practicing physician or by his patient.

In the pages that follow, we shall discuss asthma in its many forms, with emphasis on therapy. Because our experience is limited to the treatment of adults, we shall not discuss the particular problems encountered in children, but many of the principles apply to the pediatric population.

1. THE NATURE OF ASTHMA

Asthma is generally defined as reversible airway obstruction. It is extremely common, effecting from 5-10% of the population at some time in their life. It is also extremely variable. It may occur as mild airway obstruction, manifest as wheeze and tightness in association with viral respiratory infections; it may occur as allergic bronchoconstriction after inhalation, or, more rarely, ingestion of an antigen to which the patient is sensitive; it may be manifest as long continued, relatively severe airway obstruction with some improvement with therapy or it may be a reversible component present in patients with chronic obstructive pulmonary disease. It also varies in severity in a given patient. A child who wheezes with colds may become free of symptoms at puberty and never have asthma again, or a youngster with allergic bronchoconstriction may lose his apparent sensitivity and symptoms in adult life. Likewise, asthma can appear for the first time late in adult life, remain severe for long periods of time and for unknown reasons undergo remission. A patient who has been severely obstructed despite intensive therapy for months or years may become well and require little or no therapy at all.

The physician must seek to indentify the mechanisms causing the airway obstruction in each patient, and apply appropriate and sufficient therapy to induce a maximum improvement. Therapy will vary from patient to patient and the intensity of therapy will vary with the severity of the illness. There are some features common to most patients which include an unusual reactivity of the airways to a whole host of agents which cause increased airway resistance and the need for emotional support. The general principles governing the use of potent pharmacological agents also apply to most patients. Other characteristics such as allergic bronchoconstriction, sensitivity to aspirin or a marked exacerbation of symptoms after exercise are only present in some patients. A constitutional factor, reflected in a strong family history is common in most forms of asthma. The spectrum of asthma is represented by the following three cases:

CASE 1: This is a 15-year-old girl who, at age of 7, noted uncomfortable chest tightness and, occasionally, audible wheeze 3 or 4 times a year in association with upper respiratory infections. On several occasions, she was treated with small doses of oral ephedrine and theophylline with disappearance of symptoms over a period of 5 to 7 days as the upper respiratory infection resolved. During the past year, with the onset of puberty, she has had no chest symptoms with respiratory infections.

COMMENT: This is a patient with childhood asthma, apparently nonallergic in origin but related to viral infections, only requiring oral bronchodilator therapy during such infections. It is likely that these symptoms will disappear in adult life but the long-term clinical course of such a patient is unpredictable.

CASE 2: This is a 43-year-old female who developed asthma at the age of 23. She was evaluated by an allergist at age 30, received injection therapy and was relatively free of symptoms for five years until, in 1971, she traveled in Europe and developed a persistent cough associated with wheeze. This persisted upon her return to New York City and she twice took corticosteroid therapy with some relief. She first appeared at the emergency room at this hospital cyanotic with an arterial P_{CO2} of 80 mm Hg. She was immediately intubated in the emergency room and admitted to hospital. Shortly thereafter she was able to breathe spontaneously without difficulty, the endotracheal tube was removed and she was discharged asymptomatic. For the last five years she has been followed in the outpatient department taking isoproterenol for wheeze, theophylline and oral prednisone, 20mg a day 3 or 4 times a year when asthma worsens. Steroids are generally tapered over a period of several days and discontinued. In 1973 she was placed on triamcinolone acetonide aerosol which she has continued to take in doses of 4 to 20 puffs a day (.02-1.0mg). Asthma has been controlled without the need for oral steroids.

COMMENT: This is a patient who appeared to respond to antiallergic therapy but then developed one attack of severe, nearly fatal asthma subsequent to which her symptoms have been controlled by the use of steroids, currently

steroid aerosols. Noteworthy is the spectrum that she represents from total freedom from symptoms on no therapy to near fatal asthma.

CASE 3: This is a 48-year-old male truck driver who noted the onset of wheeze and dyspnea at age 42. The symptoms were relatively mild until age 45 when they become severe and required hospitalization in 1972. He was started on prednisone therapy and continued to require large doses of steroids, 30 to 40 mg a day. When he reduced this dose to 15mg symptoms recurred and he had to increase it again. After about a year of steroid therapy, he developed back pain and was found to have three collapsed vertebrae, and he was started on a trial of steroid aerosol. Initially it appeared that he was able to taper his oral steroid but when prednisone was discontinued asthma worsened and required another hospitalization. He remained badly obstructed on large doses of prednisone and then went to Arizona for several months where, despite the addition of cromolyn, he again had worsening of his symptoms while taking 10mg of prednisone a day and was hospitalized. He finally improved on larger doses of steroids, returned to New York on 20 mg of prednisone a day and was asymptomatic though obviously Cushingnoid. His peak expiratory flow rate (PEFR) was 410 L/min. He was once again started on steroid aerosol and over the past several months has been gradually tapering his dose of prednisone. After three months of therapy, while he was maintained on the maximal dose of aerosol (2 mg per day), he had one exacerbation of asthma requiring hospitilization and increase from 7-1/2 mg to 30 mg of prednisone with prompt improvement. Since that time he has continued to taper the prednisone and is currently well on 2-1/2 mg. per day.

COMMENT: This is a patient with very severe asthma despite massive doses of steroids producing Cushing's Syndrome and osteoporosis. Ultimately symptoms have become controlled with steroids but there has been marked variability of the severity of asthma such that he may be well on relatively small doses or sick on large doses. The mechanisms responsible for variable responsiveness to steroids are unknown but the occurrence of striking, dramatic remission is always possible in a patient with

severe asthma and one cannot anticipate when it will occur. In most patients, steroid aerosols eliminate the need for all but occasional supplementary doses of oral steroids. In this patient, the aerosol has seemed to have had some effect in reducing oral steroid requirements; but the variability of the asthma and need for steroids makes it impossible to assess the exact value of this therapeutic agent, a common problem in the evaluation of any therapy of asthma.

TYPES OF OBSTRUCTION

There are three causes of the airway obstruction present in patients with asthma. They are all present in patients with severe asthma but may occur independently and vary in their severity between patients and from time to time in a given patient.

BRONCHOCONSTRICTION: The aspect of the obstruction which has been most intensively studied and which is most responsive to therapy is bronchoconstriction. The smooth muscle in the airways may contract in response to a wide variety of stimuli. Enhanced sensitivity to bronchoconstricting agents including drugs, such as histamine, cold air, inert irritants and suggestion all characterizes most patients with asthma. An important determinant of the amount of bronchoconstriction is the level of CAMP in the airway smooth muscle. It is now believed that beta stimulating catecholamines cause increase of CAMP whereas alpha stimulators cause reduction. For this reason, beta stimulants and alpha blockers cause relief of bronchoconstriction whereas beta blockers and alpha stimulants increase bronchoconstriction. Cyclic AMP is broken down by phosphodiesterase and this enzyme is inhibited by theophylline, which is possibly an important mechanism of action of this bronchodilator.

Airway smooth muscle is also under important control by the parasympathetic nervous system. Vagal stimulation and acetylcholine cause severe bronchoconstriction, perhaps by way of increased GMP in the smooth muscle, and atropine is an effective bronchodilator. The airways are maintained in a chronic state of bronchoconstriction,

as evidenced by the fact that, in normal subjects, inhalation of atropine or isoproterenol causes a slight but prompt increase of expiratory flow rates. The normal bronchial tone, and its increase under various conditions of stress, may stabilize the airways so as to prevent closure during forced expiration or during cough. There is some evidence that bronchodilation is actually associated with reduction of expiratory flow rates at small lung volumes because of premature closure of more flaccid airways.

It is thought that allergic bronchoconstriction is related to release of mediators from sensitized mast cells in the airways which, when contacted by antigen, release a number of substances which affect the airways. These are probably modulated by the local concentration of CAMP. There is some evidence that atropine blocks this local allergic reaction, at least to some extent, and that it requires the integrity of the parasympathetic nervous system. Possibly the mediators of the allergic reaction act through the parasympathetic system via irritant receptors in the small airways. In any event, beta stimulators and parasympatholytic agents are potent bronchodilators, both by direct action on smooth muscle and by modulation of the allergic reaction in the airways.

Bronchoconstriction can be induced and reversed very rapidly with pharmacological agents. It may constitute the major cause of airway obstruction or, in severe asthma, it may be relatively unimportant. The degree to which bronchoconstriction is the cause of obstruction is an important determinant of the rapidity and completeness of pharmacological therapy.

PATHOLOGICAL CHANGES: The second cause of airway obstruction is anatomical change in the walls of the airways. Bronchial biopsies and postmortem studies have revealed that the basement membrane is thickened, apparently by edema fluid, and there are inflammatory changes in the airways marked by the presence of eosinophils. There is also evidence of increased amounts of smooth muscle in the airways of asthmatics. These abnormalities are reflected in thickening of the walls of the airways visible on careful examination of the x-ray film