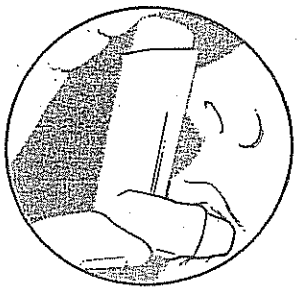
MAY 1991

ASTHMA BULLETIN



A Special Report

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DIAGNOSIS AND MANAGEMENT OF ASTHMA

Highlights of the recently released Expert Panel Report on the Management of Asthma, convened by the National Asthma Education Program of the National Heart, Lung, and Blood Institute, with additional insights provided by Panel members.

Editor: Richard N. Podell, M.D.

Asthma on Rise

Claude Lenfant, M.D., Director, National Heart, Lung, and Blood Institute, and Chairman, National Asthma Education Program Coordinating Committee, emphasized that the following facts make it critical to improve treatment approaches to asthma:

- The prevalence of asthma increased 29 percent between 1980 and 1987.
- The death rate from asthma increased 31 percent during this period.
- Asthma-related health care costs exceeded $4 billion in 1988.

Dr. Lenfant indicated that this Report is historic because it brings together in one comprehensive document the specialists' perspectives in the form of guidelines to serve primary care physicians in detecting, treating and controlling asthma. The NHLBI Director predicted that the Expert Panel Report will have a profound effect on how asthma will be treated. It reflects the current state of knowledge about causes of asthma and presents detailed recommendations to guide diagnosis and treatment. However, he stressed, treatment must be tailored to each patient's needs.

The full published report will be available free of charge in late spring from the National Heart, Lung and Blood Institute. Photocopies of the complete report are available now for $10. For either, write to National Asthma Education Program, 4733 Bethesda Ave., Suite 530, Bethesda, MD 20814

Airway inflammation is a key element of all cases of asthma, with moderate and severe cases requiring chronic anti-inflammatory treatment in the form of cromolyn sodium or inhaled corticosteroids.

Treatment Components

Albert L. Sheffer, M.D., Chairman of the Expert Panel and Clinical Professor of Medicine at Harvard Medical School, stated that asthma is a chronic disease, requiring ongoing medical care. However, with appropriate therapy, patients can prevent most asthma "episodes" (acute asthma exacerbations) and maintain the activity levels they desire. The essential components of treatment are:

- Educating the patient and family members.
- Controlling the patient's environment to avoid or control factors that trigger asthma exacerbations.

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- Instituting drug therapy to both treat acute episodes and prevent them. Inhaled beta$_2$-agonists are the therapy of choice for initial treatment of acute episodes, but for those patients who fail to respond appropriately, oral corticosteroids will help speed recovery. Preventive, or maintenance, anti-inflammatory therapy is required on a daily basis for patients with moderate to severe asthma. Anti-inflammatory therapy is in the form of cromolyn sodium (which the report describes as the best nonsteroidal anti-inflammatory drug for asthma since it is virtually without side effects) or inhaled corticosteroids.
- Patients and physicians regularly using objective measures to assess the severity of asthma and to monitor the course of therapy.

Diagnostic Clarification

Because various specialists–immunologists, pathologists, physiologists and physicians–each have their own perspectives of the entity called asthma, the Expert Panel agreed on a working definition. "Asthma is a lung disease with the following characteristics:

(1) airway obstruction that is reversible (but not completely so in some patients) either spontaneously or with treatment;

(2) airway inflammation; and

(3) increased airway responsiveness to a variety of stimuli."

Underdiagnosis

An estimated 10 million persons in the United States have asthma. The sharpest rise in cases is among people under age 20. The Report states that underdiagnosis is prevalent, especially among young children. Children who wheeze when they have respiratory infections are often thought to have bronchitis or pneumonia. In fact, the symptoms may be compatible with a diagnosis of asthma. A disproportionate number of hospitalizations and deaths occur among poor African-American people. The asthma death rate for all ages was almost three times higher among African Americans than Caucasians during 1987; in younger age groups (15 to 44 years old), death rates from asthma were at least five times higher. This is thought to reflect lack of access to regular medical care, the seeking of treatment only in emergency situations, or an underestimation of the severity of the disease. The development of airway obstruction — induced by allergens, viruses, exercise or other factors — is responsible for the clinical manifestations of asthma. As stated, monitoring (including self-monitoring) of the patient's respiratory capacity plus pharmacologic control of the inflammatory processes and hyperresponsive reactions can eliminate or greatly reduce acute exacerbations.

THE ROLE OF ALLERGY IN ASTHMA

National Asthma Education Program Coordinating Committee member Allan T. Luskin, M.D., of the American College of Allergy and Immunology, stated that asthma is usually worsened by exposure to allergic factors. "These must be eliminated as much as possible to decrease the chronic inflammation associated with asthma." The Report cites studies that find 75% to 85% of patients with asthma have positive immediate skin test reactions to common inhalant allergens. Although these figures are believed to exceed the number of patients with asthma in whom allergic factors are important, they do suggest that allergy must be considered. Continued exposure to elements that people are allergic to will worsen the asthma, causing more symptoms, increasing the medication requirement, and diminishing the quality of life. In addition to allergens, there are indoor irritants, such as tobacco and wood smoke and strong odors and sprays, that can act as triggers of clinical asthma.

Environmental Control

Smoking

Dr. Luskin said one of the most important steps is "to completely eliminate cigarette smoking — both personal smoking and second-hand smoke."

Pets

Animals should not be in the home of an asthma patient with animal allergies. "This includes all furred or feathered animals." He added, "There is no such thing as an allergy-free dog, and the length of the hair makes no difference." The flakes of the animals' skin contain allergens, as does a cat's saliva–cats' frequent licking of their coat increases its allergenic potential.

The delayed response can involve airway hyperresponsiveness to a variety of stimuli, in addition to the allergen, and may persist for weeks. Persistent bronchial responsiveness is thought to be caused by inflammation.

He advises that, if it isn't possible to eliminate an animal from a home, it should be banned from the bedroom and washed frequently. Bathing cats may reduce the amount of dander and dried saliva deposited on furnishings. Patients also should consider undergoing specific allergy therapy.

Dust

An important factor to control is dust, which harbors the highly allergenic dust mite. The mite lives in bedding, carpeting, upholstered furniture and drapes. It thrives in warm, moist climates. The principal allergen of the house-dust mite is found in its feces. Vacuuming does little to control the mite. In fact, the Report indicates that vacuuming stirs up fine respirable allergen particles.

The Report advises that simple measures can help greatly. These include covering bedding with airtight plasticized covers; replacing feather pillows with polyester ones, and washing or changing these frequently. Bedding should be laundered in hot water in order to kill mites. Carpeting should be removed. If this is unfeasible, carpeting should be treated periodically with commercially available mite-eradicating preparations. Humidity should be kept low to decrease dust mite activity as well as mold growth (the Panel Report recommends humidity below 50% and above 25%).

Cockroaches

These, too, are an important source of allergenic substances — a fact few appreciate and which represents a major problem for people in urban areas. Efforts should be made to eradicate roaches.

School

School pets should be limited to insects, reptiles and fish. Mats used for small children at break time should be cleaned frequently.

Air filtration and other measures

Air conditioning with closed windows will help keep out pollens and other allergens as well as reduce indoor humidity. Filters placed within the ducts of a central forced air heating and cooling system, or as free-standing units within a room, can clean some allergens from indoor air. Certain allergen components of indoor air are more likely to remain airborne than others (pollen and animal dander are less likely). Therefore, it is important to consider whether a patient's specific allergens are present in the home air in quantities sufficient to make the investment in filter systems worthwhile.

Immediate and Late Reactions/ Different Age Groups

The Panel Report indicates that reaction to an allergen may be immediate bronchial obstruction, as well as one that is delayed several hours after initial exposure. The delayed response can involve airway hyperresponsiveness to a variety of stimuli, in addition to the allergen, and may persist for weeks. Persistent bronchial responsiveness is thought to be caused by inflammation.

Infants

Viral respiratory infections are the principal trigger of asthma in infants. Allergens play a less significant role, since it takes time for allergic sensitivity to develop. Foods are not comon triggers of asthma in infants.

Children

Children with asthma tend to have allergies. The severity and frequency of asthma correlates with the number of positive skin tests, suggesting the allergies cause a chronic inflammatory process in the airways. Inhalants appear to be the most important allergens.

Adults

Aeroallergens are also important for patients whose illness began before age 30 (although some patients do experience allergy for the first time over age 30) or who are exposed to occupational allergens.

More than 200 sensitizing agents have been identified in a great variety of workplace settings. These range from small bakeries where an estimated 44 percent of workers are allergic to flour, to those exposed to laboratory animals where an estimated 4% to 10% react to dander and urine proteins.

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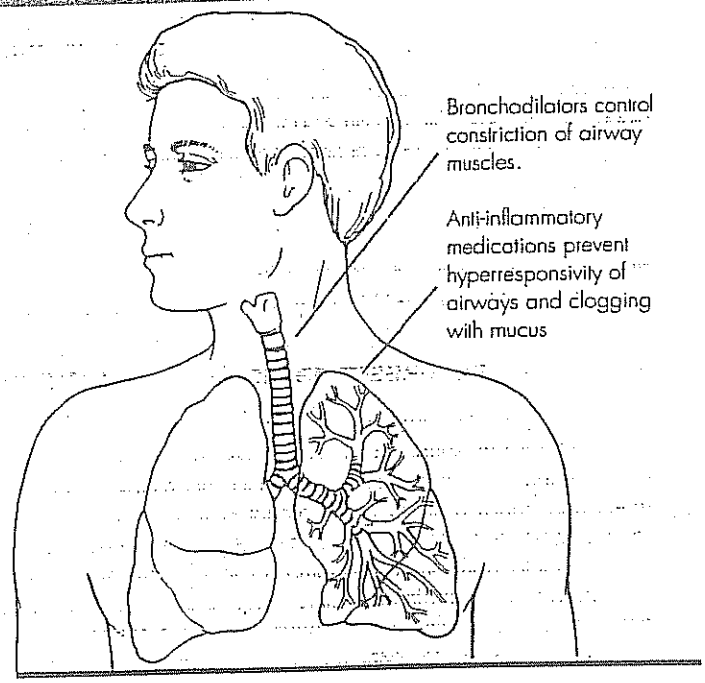

PATIENT INTERVIEW CHECKLIST TO ASSESS ROLE OF ALLERGY

Is asthma worse in certain months? If so, are there symptoms at the same time of allergic rhinitis — sneezing, itching, nose both runny and obstructed? (May indicate pollens and outdoor molds. In general, tree pollen may be present from February through May, grasses from May to June, weeds from August to October, and outdoor molds throughout the warm months.)

Do symptoms appear when visiting a house where there are indoor pets? (animal dander)

If there are pets in the patient's home, do symptoms improve when the patient is away from home for a week or longer? Do nasal, eye, and chest symptoms improve? Do the symptoms become worse in the first 24 hours after returning home? (animal dander)

Do eyes itch and become red after handling the pet? If the pet licks the patient, does a red, itchy welt develop? (animal dander)

Do symptoms appear in a room where carpets are being vacuumed? (animal dander or mites)

Does making a bed cause symptoms? (mites from dispersed dust)

Do symptoms develop around hay or in a barn or stable? (molds and miles)

Do symptoms develop when the patient goes into a damp basement or a vacation cottage that has been closed up for a period of time? (molds)

Do symptoms develop related to certain job activities, either at work or after leaving work?

If symptoms develop at work, do they improve when away from work for a few days?

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Farmers are exposed to storage and poultry mites, plastics workers and automobile painters may be affected by numerous agents, hospital workers may react to disinfectants and anesthetists to enflurane (to cite just a few examples).

The Panel Report includes a sample questionnaire that physicians may utilize to discover possible environmental allergens. *(See previous page.)*

MEASURING LUNG FUNCTION: ESSENTIAL TO TREATMENT AND SELF-CARE

The Expert Panel Report underscores the need for objective measures of lung function because patients' reports of symptoms and findings on physical examination often do not correspond to the severity of airflow obstruction. Patients may feel free of symptoms even when peak expiratory flow rate (the greatest flow rate during a forced expiration starting with fully inflated lungs) and forced expiratory volume (the volume of air expired in one second from maximum inspiration) are markedly abnormal on testing.

It is recommended that all patients undergo office spirometry to determine lung volumes and flow rates in the initial assessment for asthma, and periodically thereafter, as appropriate. While more sophisticated techniques exist for measuring lung volume, spirometry is the most practical in the setting of general medicine. When findings on office spirometry suggest a pathologic condition, a complete set of pulmonary function tests can be performed in a specialized facility.

Patients may feel free of symptoms even when peak expiratory flow rate is markedly abnormal on testing.

Abnormalities of lung function are categorized as restrictive and obstructive. Restrictive defects involve reduced lung volume with no apparent airflow obstruction. Restrictive defects are often associated with parenchymal lung disease or limitations of chest wall movement. Obstructive defects involve impaired airflow through the trachea and bronchi leading from the alveolar sacs. Obstructive impairment may be associated with bronchial secretions, bronchospasm, loss of supporting structure, or edema of the bronchial wall. Making this distinction in individual patients does not identify the specific condition, but in many cases clinical decisions can be made with the use of spirometry alone.

To determine whether the problem is restrictive or obstructive, spirometry measures the following timed volumes:

Peak expiratory flow rate (PEFR)

The maximum flow rate that can be generated during a forced expiration; measured in liters per second, the measurement requires maximum effort for accuracy.

Forced vital capacity (FVC)

Total volume of air expired as rapidly as possible.

Forced expiratory volume 1 second (FEV1)

The volume of air expired in one second from maximum inspiration.

Maximum midexpiratory flow rate (MMEF)

The slope of line between 25% and 75% of the forced expiratory volume.

Spirometers measure the volume of expired air in liters and the time in seconds during which the air is expired. Electronic spirometers provide readings as a percentage of normal for patients of a given age, height and other characteristics. The following guidelines help to interpret findings.

Interpreting Results of Spirometry

Parameter	Restrictive Defect	Obstructive Defect
FVC	Low	Normal or low
FEV_1	Normal or low	Low
FEV_1/FVC	Normal or high	Low
MMEF (FEF_{25-75})	Normal, high or low	Low

- Using the above guide, a reduced forced vital capacity and a normal flow rate are consistent with a restrictive defect.
- A normal forced vital capacity with either impaired FEV1 or impaired MMEF indicates pure obstruction. When the FEV1 is severely reduced with clear evidence of obstruction (FEV1/FVC ratio of less than 75%), the vital capacity can also be reduced due to severe obstruction alone.
- When the maximum midexpiratory flow rate is the only abnormal finding, mild airflow obstruction is present, indicating small airway disease.

Familiarity with the spirometer and instruction in interpretation of findings can enable the physician to draw tentative conclusions, as well as guide the clinician to refer for further measures when mixed restrictive and obstructive defects appear to exist.

However, the Expert Panel advised that, because asthma patients often find it necessary to make frequent objective assessments of flow rates (more than once daily), the office spirometer may be too inconvenient. It is more practical to accept the peak expiratory flow rate (PEFR) as the parameter to follow, obtained with a less sophisticated instrument. While PEFR may not be adequate to make a diagnosis or to fully evaluate the impairment associated with asthma, it can monitor status and help make therapeutic recommendations. Most important, it is a simple measure of airway obstruction that can be obtained using inexpensive, portable peak flow meters.

Home Use of Peak Flow Meter

Shirley A. Murphy, M.D., Professor of Pediatrics at the University of New Mexico School of Medicine, and a member of the Expert Panel, reinforced the Panel's recommendation for office and home use of peak flow meters. At the conference announcing the Panel Report, she demonstrated their ease of use for patients at home. By placing the mouth around the instrument, taking the biggest breath possible, then blowing out as hard and fast as one can, the patient achieves a number on the dial that can be compared with normal values for a person of his or her age and height. The best of three successive measurements is taken as the peak expiratory flow rate. However, since many patients' PEFR values are consistently higher or lower than average, it is helpful to establish an individual's "personal best" score at a time when aggressive anti-inflammatory and bronchodilator therapy have maximized that person's capacity.

Restrictive defects are often associated with parenchymal lung disease or limitations of chest wall movement. Obstructive defects involve impaired airflow through the trachea and bronchi leading to the alveolar sacs.

In general, when a person is in the zone of 80% to 100% of their personal best score, the asthma is under control and current treatment can be maintained or even reduced on a trial basis. A reading that is 50% to 80% of personal best may signal that an acute episode is about to occur or maintenance medication may need to be increased. A reading of below 50% indicates a medical alert. A bronchodilator should be taken immediately and the physician notified if the PEFR does not immediately improve to safer ranges. Patients can keep diaries of their scores, which can be taken to the physician during visits to assess status. The peak flow meter and diaries can be used to discover the effects of exercise at school and to determine if medication is needed before sports participation. The meter can be used at home or the workplace to measure reactions to environmental triggers. The peak flow meter is patients' "early warning system," said Dr. Murphy, which enables them to control their asthma more effectively, and thus lead normal lives, participating in all desired activities.

MEDICAL MANAGEMENT OF ASTHMA

The National Asthma Education Program's Expert Panel Report underscored that management of asthma requires a continuous care approach. The objective is not merely to treat acute symptoms when these occur, but to treat the underlying pathology so as to:

- Control symptoms
- Maintain normal activity
- Maintain normal or near-normal pulmonary function
- Prevent acute exacerbations
- Avoid adverse effects of asthma medications

The first steps are the previously outlined measures to avoid or minimize exposure to allergens and irritants; eventually, selected patients may utilize immunotherapy-a series of injections of specific allergens to develop tolerance and decrease bronchial responsiveness and allergic inflammation to that allergen.

The mainstays of pharmacologic therapy are: anti-inflammatory agents to treat and prevent bronchial inflammation, in order to eliminate or minimize bronchial hyperresponsiveness to allergens or irritants; and, bronchodilators to dilate the airways by relaxing bronchial smooth muscle.

Therapy will be dictated by severity of the disease, medication tolerance, and sensitivity to environmental triggers.

Anti-inflammatory agents currently indicated for asthma management include:

Cromolyn sodium

Corticosteroids

Bronchodilators include:

Beta-adrenergic agonists

Methylxanthines (theophylline)

Anticholinergics

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Anti-Inflammatory Agents

Cromolyn Sodium

The Panel Report states that "cromolyn sodium is currently the best nonsteroidal anti-inflammatory drug for asthma." Administered prophylactically, it inhibits allergen- and exercise-induced airway narrowing. A 4–6 week trial of cromolyn sodium therapy may be required to determine its efficacy in individual patients. It is virtually free of significant side effects. Thus, the Report says, "cromolyn sodium is an important therapeutic approach to the treatment of airway inflammation in asthma."

Additional drugs are cited as being investigated as future anti-inflammatory treatments in asthma. Nedocromil sodium appears to inhibit asthmatic reactions to exercise, hyperventilation, allergens and sulfur dioxide, without significant adverse effects. Antihistamines also are being reevaluated for asthma, as is ketotifen.

Corticosteroids

These anti-inflammatory agents may be administered parenterally, orally, or as aerosols. Early treatment of acute exacerbations prevents progression of the exacerbation, and decreases the need for emergency treatment and hospitalization. The Report states that "during the past decade, there has been less fear of using short courses of oral (or parenteral) corticosteroids to treat severe acute exacerbations of asthma." Acute short-term corticosteroid therapy for adult outpatients is begun with high dosages of 40–60 mg oral prednisone daily in divided doses, tapered over several days; and 1-2 mg/kg/day in children, in single or divided doses. Children may need only three days of treatment; if treatment is longer than three days, it should be tapered. For emergency department and hospital treament, doses are higher.

Long-term oral corticosteroids are associated with significant adverse effects, including abnormal glucose metabolism, fluid retention, mood alteration, hypertension, peptic ulcer, and others. Other conditions such as osteoporosis, cataracts, myopathy, and Cushing's syndrome, among others, also may develop. Thus, the Report urges that patients requiring chronic therapy with oral corticosteroids should be given a trial of inhaled corticosteroids, which have minimal systemic effects, to determine if oral steroids can be reduced or eliminated. Prolonged use of oral forms is reserved for patients with severe asthma, using the lowest possible dose (a single early-morning dose every 48 hours), with regular pulmonary function tests to assess efficacy.

Beta-agonists block symptoms during exposure and may encourage the patient to spend long periods in the contaminated environment; this can lead to asthma symptoms occurring 4-6 hours later. However, cromolyn sodium taken before antigen exposure blocks this late reaction.

Inhaled corticosteroids in recommended doses do not have the systemic adverse effects associated with oral or parenteral steroids. Inhaled corticosteroids are excellent anti-inflammatory agents and their use as long-term primary therapy for chronic moderate and severe asthma is recommended. (Use of inhaled corticosteroids can lead to oropharyngeal candidiasis, dysphonia or coughing, but these may be prevented or reduced by using a spacer device with the inhaler or by rinsing the mouth with water after use.)

Bronchodilators

Beta-adrenergic Agonists

Beta$_2$-agonists are termed "the medication of choice for treatment of acute exacerbations of asthma and for the prevention of exercise-induced asthma." Aerosol or inhaled therapy is comparable to, or better than, oral therapy in producing bronchodilation and causes fewer systemic adverse effects (cardiovascular stimulation, anxiety, skeletal muscle tremor). Inhaled therapy has a more rapid onset of action. Because asthma is an airway disease, inhaled therapy, with beta$_2$-agonist delivered directly to the airways, is usually preferable.

These drugs can be used as needed to control episodic airway narrowing, or used chronically to control persistent airway narrowing; however, there is some question as to the efficacy of chronic use in all patients, and there can be cardiovascular complications such as arrhythmias and ischemia, particularly in elderly patients with preexisting cardiovascular disease. Currently available beta$_2$-agonists have limited duration of action (4-6 hours).

Methylxanthines (Theophylline)

Theophylline is the principal methylxanthine used in asthma therapy. It is a bronchodilator that may also increase respiratory muscle contractility as well as have some anti-inflammatory effect (a subject of debate). Physicians are advised to become familiar with the properties of the various theophylline products as well as how they are utilized by the bodies of individual patients (patterns of serum levels). Some patients pass sustained release forms from the gut too quickly to benefit from the full dose, and forms of the medication differ in response to food in the gut or the fat content.

Monitoring theophylline serum concentrations is an important part of management of asthma patients, since drug toxicities can occur in patients with reduced elimination rates, such as those with liver disease, congestive heart failure, febrile illness, and patients taking drugs such as cimetidine, antibiotics and others. Nausea and vomiting are the most common early symptoms of toxicity; seizures can occur, as well as heart rhythm disturbances and other adverse reactions.

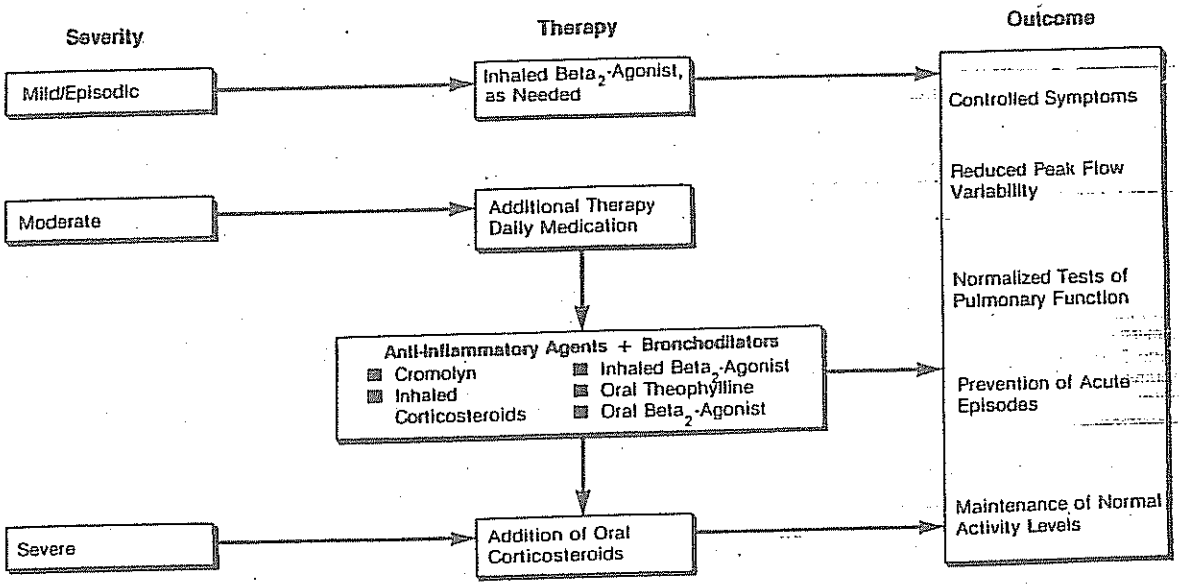
The Panel Report advises that a steady-state theophylline serum concentration of 10-20 mcg/ml gives optimal effect; a more conservative approach would be levels between 5 and 15 mcg/ml. The theophylline dose should be increased if a patient is at the lower end of the recommended serum concentration range and symptoms persist.

Sustained-release theophylline may be particularly useful for control of nocturnal asthma. Theophylline may have additive bronchodilator effects when used in conjunction with inhaled beta-agonists.

Anticholinergics

Anticholinergics are the oldest form of bronchodilator treatment for asthma, though they have lost favor because of slow onset of action and undesirable side effects. However, ipratropium may have benefits over older forms such as atropine; its low bioavailability when inhaled reduces side effects, and it has demonstrated bronchodilator action in children suffering acute exacerbations of asthma. However, it is not of proven usefulness in day-to-day management of asthma in children and adults. The regular use of anticholinergics as bronchodilators appears most effective in treating chronic obstructive pulmonary disease and partially reversible airflow obstruction.

Management of Asthma– Overview of Therapy*



** All therapy must include patient education about prevention (including environmental control where appropriate) as well as control of symptoms.*

Individualized Treatment

The Expert Panel emphasized the need for individualized, continuing care. Patients have different triggers and patterns of physiologic response, including varying levels of severity. However, there are common elements in all patients' therapy.

Prompt treatment of acute episodes

Medication should be taken within five minutes of the first symptoms. It is easier, and takes less medicine, to stop an episode in its earlier phase than later. Patients should know what early symptoms are — shortness of breath, wheezing, tightness in the chest, and/or recurrent cough persisting more than a week. Persistent cough alone may be the first symptom, particularly in children. Peak flow measurements 10-20% below personal best level can help detect early signs of asthma before symptoms appear.

Prevention

It is important to take preventive medicine regularly and consistently. Those who have infrequent, mild, episodic exacerbations should take 1-2 puffs of a beta$_2$-agonist and/or cromolyn in anticipation of an event, such as before exercise, to prevent bronchospasm. Those with moderate to severe asthma should have ongoing daily treatment with inhaled steroids or cromolyn sodium to prevent airway inflammation.

The other key element common to all good therapy is forming an alliance with the patient so that care will be ongoing and an informed patient will participate fully. To formulate a treatment approach for a particular patient, the physician will evaluate the extent to which activity is limited, nighttime symptoms, and pulmonary function (via spirometry and diaries of peak expiratory flow kept by the patient). Therapy will be dictated by severity of the disease, medication tolerance, and sensitivity to environmental triggers. Physicians must be ever-alert to special situations, such as many children's pattern of having their asthma deteriorate whenever they have a viral respiratory infection; physicians may institute a short course of oral corticosteroids at the first sign of such infection rather than waiting for acute symptoms to develop. Similarly, adults may have to increase anti-inflammatory asthma medications during upper respiratory infections. Bacterial otitis and sinusitis may be associated factors for asthma in all age groups, and should be treated with antibiotic therapy, which is adjuvant to primary antiasthma therapy.

Overall, the recommended approach to asthma is stepped-care pharmacologic therapy (of course, always accompanied by environmental control and patient education). The number of medications and frequency of administration are increased as necessary.

Mild Asthma

Patients with mild or episodic asthma usually have no baseline abnormalities in pulmonary function, but have hyperresponsive and mildly obstructed airways (<20% below usual) on certain occasions. As stated above, inhaled beta2-agonists or cromolyn sodium, or both, prior to exposure to a known trigger can prevent or diminish an asthmatic response. However, the Panel Report indicates, beta-agonists block symptoms during exposure and may encourage the patient to spend long periods in the contaminated environment; this can lead to asthma symptoms occurring 4-6 hours later. Cromolyn sodium taken before antigen exposure blocks this late reaction.

Inhaled beta$_2$-agonists are usually adequate to control asthma symptoms; but the need to use them more than 3 to 4 times a day usually indicates a need for therapy in addition to beta$_2$-agonist.

Moderate Asthma

Patients whose exacerbations are poorly controlled by inhaled beta-agonists or have exacerbations more than twice a week may require additional treatment. These patients tend to have pulmonary function (peak expiratory flow rate) in the 60%-80% of predicted range.

Inhaled beta$_2$-agonists have limited duration of action (4-6 hours), and may leave a patient unprotected at night. Sustained-release oral beta$_2$-agonist or sustained-release theophylline may help. If theophylline is the primary bronchodilator for a given patient, beta$_2$-agonist therapy can be used episodically.

Since airway inflammation is present in virtually all patients with asthma, anti-inflammatory therapy should be considered for patients with moderate asthma. Aggressive use of inhaled corticosteroids (e.g., 400-800 mcg/day beclamethasone) may provide protection with minimal side effects. Cromolyn sodium also may be used for anti-inflammatory activity. It is virtually devoid of side effects, but is not effective for all patients. Patients who use sustained-release theophylline or oral beta$_2$-agonist to control nocturnal symptoms and who also take anti-inflammatory medication may be able to discontinue bronchodilator usage after 4-6 weeks of anti-inflammatory therapy.

When asthma is exacerbated to the degree that it cannot be controlled by any combination of bronchodilators (beta-adrenergic agonists and/or theophylline), plus cromolyn sodium, or inhaled corticosteroids, a short burst of systemic corticosteroids is indicated. For example, 40 mg prednisone per day, in single or divided doses, for one week, followed by 7-14 days of tapering doses may be effective.

If asthma symptoms do not occur and pulmonary functions remain normal, no additional therapy (beyond the previous regimen) is necessary. But those who require frequent periods of oral corticosteroid therapy need further attention. Some patients may need even higher doses (1,000-1,600 mcg of inhaled corticosteroids per day). Suppression of symptoms and PEFR improvement may not be evident until 2-4 weeks of treatment.

Patients with "fragile" control of asthma often benefit greatly from inhaled cromolyn sodium or steroids, concludes the Report.

Severe Asthma

Patients who are not controlled on maximal doses of bronchodilator and cromolyn or inhaled corticosteroids are at risk for severe exacerbations, and care should be under the supervision of an asthma specialist. These patients may require systemic corticosteroids on a routine basis, using the lowest possible dose. Patients should be monitored for side effects, and regular attempts should be made to reduce prednisone by trying maximal doses of inhaled steroids (a spacer may help prevent oral candidiasis). For patients with severe disease, experimental anti-inflammatory drugs such as gold and methotrexate are being investigated. Use of these is limited to asthma specialists experienced in their use.

Further Guidelines

The Expert Panel Report also contains extensive outlines of treatment of children, management of acute exacerbations, and treatment of patients with asthma within the hospital.

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