Clinical Guidelines And Primary Care

Guidelines For The Diagnosis And Management Of Asthma

Alfred O. Berg, M.D., M.P.H., and Julie Graves Moy, M.D.

Guidelines for the Diagnosis and Management of Asthma were produced by the Expert Panel on the Management of Asthma convened by the National Asthma Education Program under the auspices of the National Heart, Lung, and Blood Institute of the National Institutes of Health. The full report (PHS publication no. 91-3042) and executive summary (PHS publication no. 91-3042A) were released in August and June of 1991, respectively, and mailed directly to family physicians and other practitioners under sponsorship of several pharmaceutical firms whose products are often used in treatment of asthma. Additionally, special issues of the *Journal of Allergy and Clinical Immunology* and *Pediatric Allergy* reprinted the entire report for their subscribers.

In the Foreword to the report, Claude Lenfant, M.D., Director of the National Heart, Lung, and Blood Institute, presents the charge of the panel: "To develop guidelines to improve the detection and treatment of asthma." He goes on to state that the guidelines ". . . are likely to have a profound effect on the way asthma is treated." Dr. Albert Sheffer, chair of the expert panel, states in the Preface his hope that with use of these guidelines, "Patients with asthma can expect to control their symptoms, prevent most acute asthma exacerbations, maintain the activity levels they desire, and attain near normal lung function."

Clinicians caring for patients with asthma are the intended audience for the guidelines. Dr. Lenfant comments in the Foreword that the report is designed to provide clinicians with new insights into asthma management, but whether the report is principally for primary care physicians or other specialists is not clear.

Sources of information used in preparing our review included the report itself and interviews with members of the panel and coordinating committee and staff. In addition, approximately 100 of the cited references were examined directly.

It is important to emphasize that the goal of our review is not specific clinical "take homes," but rather an assessment of the guidelines themselves. If the process of developing a guideline is of high quality, one can trust the clinical recommendations. If the process is of poor or unknown quality, one cannot trust the recommendations. Unfortunately, *Guidelines for the Diagnosis and Management of Asthma* falls into the latter category.

Importance of the Problem

The burden of suffering associated with asthma provides the justification for developing guidelines. The report notes that there are an estimated 10 million persons in the United States with asthma, with a 29 percent increase in prevalence from 1980 to 1987. The death rate attributed to asthma has climbed 31 percent in the same period, to 4360 persons each year, ending the 1980s with a death rate of approximately 30 per 10,000 persons per year.[1]

Medical care for asthma now requires approximately 6.5 million office visits (1 percent of all office visits) and 450,000 hospitalizations each year.[2]

The report presents no data suggesting that medical care currently provided to patients with asthma is in need of clinical policy development and dissemination. Such justification might include uncertainty in current practice, recent important research findings, and documented deficits in medical outcome related to inadequate care, among other factors.

Submitted, revised, 20 July 1992.

From the Department of Family Medicine, University of Washington, Seattle, and the Center for Health Policy Studies, University of Texas Health Sciences Center, Houston. Address reprint requests to Alfred O. Berg, M.D., M.P.H., Department of Family Medicine, SA-01, University of Washington, Seattle, WA 98195.

Process for Developing the Guidelines

Selection of the Panel

The expert panel comprised 10 physicians — all specialists in pulmonary disease, allergy, or immunology — a nurse, and a researcher. No family physicians were included on the panel. A 29-member coordinating committee of organizational representatives included a family physician, Dr. Marc Rivo, currently director of the Division of Medicine, Health Resources and Services Administration, officially representing the American Academy of Family Physicians. The charge of the coordinating committee was one of oversight; nominations for membership on the expert panel, problem definition, and comments on drafts of the report were among their activities.

Conduct of the Panel

The panel was convened in August 1989 and met five times, approving the final report in February 1991. The scope of the report was established by staff and consultants before the first session. During the first session, topics were divided among individuals and small subgroups on the panel. Between meetings, panel members took responsibility for selecting and reviewing the literature and preparing drafts of reports, which were then examined at subsequent meetings. According to several panel members, there was remarkable agreement among members on most issues. Meetings themselves were characterized as collegial, with few disputes. The final draft was prepared and edited by agency staff, based upon panel member's drafts, discussion, and comment from members of the coordinating committee. Several outside consultants reviewed parts or all of the report at various stages. According to panel staff, neither the report itself nor supporting background papers have been subjected to standard peer review with publication in peer-reviewed journals, although the entire report has been reprinted as a supplement to two specialty journals, as noted.

Review of Evidence

The panel's principal mode of operation was that of global subjective judgment. Not included in the process were specification of causal pathways, evidence tables, grading the quality of individual research reports, identification of specific health outcomes, and preparation of balance sheets listing benefits and harms.

The report provides no information regarding the method of literature retrieval and the critical assessment of literature collected. The process depended upon having panel experts locate and summarize relevant information, with only occasional direct review of evidence by the full panel.

The bibliographies provided in the report are incomplete. Many of the references are review articles or research studies of poor quality with limited numbers of subjects and poor internal and external validity. Some of the literature citations are inaccurate in either the citation itself or in overstating what the original study actually showed.

Gaps in the available evidence are not mentioned; no areas requiring further research are noted.

Content of the Report

General

In the aggregate, the final report includes hundreds of individual recommendations appearing in the narrative, in tables, and in extensive flow diagrams. Readers are not informed which of the many recommendations are based on good evidence, which are based on expert opinion, and which are educated guesses. Particularly problematic are the recommendations for consultation and referral of various types of problems commonly seen in patients with asthma, but without providing evidence suggesting that better outcomes result.

It is not possible to examine critically all of the published recommendations. Below each of the 10 sections is briefly reviewed.

Section 1: Definition and Diagnosis

Asthma is defined as a lung disease characterized by airway obstruction that is reversible either spontaneously or with treatment, by airway inflammation, and by increased airway responsiveness to a variety of stimuli. The definition of asthma is adapted from other consensus panels; the process used to develop this definition is not described.

The report presents asthma as a fairly uniform condition with a known, defined etiology and pathophysiology. It is possible, alternatively, that asthma is a heterogeneous disease with several

mechanisms that lead to bronchospasm and airway narrowing. Some patients react when allergens are inhaled, others when they are exposed to irritants and pollutants, and some have innately reactive airways; combinations of these mechanisms are possible. The cited references do not provide adequate support for the central importance of inflammation as a uniform feature of airway reactivity. A small number of actual research reports are cited, many with remarkably few study subjects.

The recommendations for diagnosis include a guide for a thorough history, but workplace sidestream smoke is not mentioned, and little attention is given to indoor air pollutants that can be found in many homes. The notes on laboratory studies recommend referral to an allergy specialist for skin testing, when in actual practice many other primary care physicians offer indicated allergy testing.

Theories concerning pathophysiology are put forward with special emphasis on the newer theory that inflammation and epithelial injury are the primary pathologic processes. Inflammation is specified as the primary mechanism associated with airway obstruction; many of the references cited are review articles, and those that report original research data have a limited number of subjects. In one of the cited reviews on inflammation, Djukanovic, et al.[3] noted that most of the evidence for inflammation comes from autopsy studies and that postmortem changes can interfere with this assessment. Many of the research reports employed bronchoalveolar lavage, a process that itself can stimulate inflammatory mediators through mechanical and irritant effects.

The role of inflammation in airway hyperresponsiveness is supported by two review articles, one editorial, and one research study.[4-7] Other mechanisms mentioned for asthma are briefly discussed. Nonallergen environmental factors, while considered in the section on recommended history, are not mentioned in the discussion on pathophysiology. The theory that epithelial injury is associated with asthma is supported only by one review and one research study of 8 patients.[4,8]

The guidelines for referral to a specialist presume differences in outcomes of care that are not supported in the cited literature. The one study in the references that supports better outcomes when specialists care for patients was a 1979 British study of general practitioners,[9] likely of little relevance to the US environment of residency-trained generalists in family practice, pediatrics, and general internal medicine. In addition, specialists are recommended as a solution to problems with difficult family dynamics and problems with self-management. The assumption that an allergist or pulmonologist is more capable than a family physician in dealing with patient education and family issues ignores the training that family physicians have in these areas, while presuming that these specialists receive this training.

Section 2: Objective Measures of Lung Function

Section 2 summarizes the benefits and capabilities of spirometry and peak expiratory flow rate measurement and includes nomograms and charts of normal values. The section is generally well-organized and well-referenced, but the recommendation for frequent home monitoring with peak flow meters is not well-supported with outcome studies. Because peak flow meters are not found in some physicians' offices, a discussion of the cost, maintenance, ease of use, and other characteristics would have been helpful.

Section 3: Asthma Mortality

This section summarizes studies addressing factors associated with fatal asthma and notes that hospital admissions are increasing. Increased asthma death rates in African Americans are mentioned. Inadequate medical management and lack of access to medical care are mentioned briefly.

The panel acknowledges that asthma morbidity and mortality are higher among the poor. The panel lumps poverty and lack of money for medical care along with psychiatric illness and addiction as "psychosocial problems" that exacerbate asthma, but it does not make recommendations aimed at decreasing asthma mortality resulting from these factors.

Section 4: Overview of Approaches to Asthma Therapy

The goals for therapy are listed as follows: maintain normal activity levels, maintain "near normal pulmonary function," prevent chronic and troublesome symptoms, prevent recurrent exacerbations of asthma, and avoid adverse effects from asthma medications. Nonpharmacologic treat-

ment recommendations include patient and family education, avoidance of agents that induce or trigger asthma, and consideration for immunotherapy. Recommendations for pharmacologic therapy list anti-inflammatory agents first, then bronchodilators.

The overall goals of therapy are admirable, but it is unrealistic for patients with this chronic disease to expect "near normal pulmonary function," avoidance of adverse effects from asthma medications, and prevention of exacerbations. Asthma is a chronic disease, and management goals should reflect this reality. Recommendations for anti-inflammatory medications are supported only by review articles.[10-12] Safety of inhaled steroids is supported with two studies of short duration (4 months and 4 weeks) and on few subjects.[13,14] Focus on allergen avoidance ignores the role of ambient and indoor air pollutants; the role of cigarette smoking is noted but not emphasized. A warning is given that regular therapy with a β-agonist could lead to deterioration of control in some patients; the single article cited to support this contention reports a study of 64 patients receiving fenoterol dry powder for 24 weeks, some of whom were also taking oral steroids.[15] Several references in this section were cited incorrectly; many were reviews or editorials rather than sources of primary data.

Section 5: Patient Education

This section summarizes strategies for patient education and includes a patient information sheet for metered-dose inhalers and a sample letter from physician to teachers. The discussion focuses on prevention of exacerbation and planning for emergencies.

The content and tone of the general discussion of patient education in asthma are appropriate. Strategies for helping families to identify irritants and triggers in the home ignore indoor air quality (although covered briefly in section 6) and do not mention the home visit as a mechanism for investigating potential triggers and providing site-specific education about avoidance of these triggers. The heading Feelings About Asthma includes a recommendation that seriously depressed patients be referred to a psychologist for counseling, because depression is a risk factor for fatal asthma. This recommendation could jeopardize the life of a suicidal patient if appropriate psychiatric treatment is delayed. There is no warning to clinicians about the increased risk for child abuse that chronically ill children suffer.

Section 6: Managing Allergy in the Asthma Patient

This section summarizes environmental control measures and suggests strategies for reducing exposure to allergens. Immunotherapy is recommended for consideration.

A recommendation is made that special air-conditioning filters be used. Studies comparing the effectiveness of these special filters with clean, frequently changed standard filters are not cited. Particles greater than 10 microns in diameter are exonerated as causing exacerbations, although particles of this size can affect the nose and mouth and lead to delayed asthma reactions. Air conditioning is recommended. The utility of a home visit to assess allergens and indoor pollution is not mentioned. The panel notes that scientific data are lacking on the frequency and length of effective immunotherapy, but recommendations to consider this therapy are made nonetheless.

Section 7: Management of Asthma

This section presents the general principle that treatment should be aimed at the underlying pathologic conditions of asthma and that general guidelines should be tailored to individual patient needs. A stepped-care pharmacologic approach is presented with accompanying flow diagrams.

Many of the references that support the treatment recommendations in this section are review articles or reports of consensus panels. This report lacks a delineation and analysis of the available evidence for effectiveness of various treatments. Outcome studies are lacking, and clinical studies have small numbers of subjects (as few as 10). While a statement is made that asthma patients must not smoke or be exposed to passive smoke, no strategies for parental or patient smoking cessation are offered. The recommendation for influenza and pneumonia vaccine is not emphasized. Asthma specialists are said to be essential in the management of moderate and severe asthma. Also, a second warning about inhaled β-agonists is supported solely by the study of powdered fenoterol noted earlier.

Section 8: Management of Exacerbations of Asthma

Management of exacerbations of asthma in the home, office, and emergency department is summarized and illustrated in flow diagrams that are generally easy to follow. Strategies to recognize patients at risk for asthma-related death are designed to lead to earlier and more aggressive treatment in these patients.

This section includes a better match between the recommendation and the supporting evidence found in the references, although this evidence is not presented in the report.

Section 9: Exercise-Induced Asthma

Exercise-induced asthma refers to airway narrowing occurring minutes after the onset of exercise. It is thought to be caused by bronchial smooth-muscle constriction, not inflammation. A provocative test is described; management with inhaled β-agonists before exercise is recommended.

Again, a small number of research reports with few subjects is provided to document the assumptions made; although this section does note the paucity of available evidence.

Section 10: Special Considerations

Pregnancy, surgery, the older patient, occupational asthma, gastroesophageal reflux, rhinitis, sinusitis, nasal polyps, and sensitivity to aspirin, sulfite, and tartrazine are discussed in the context of patients with asthma.

These sections supply only a brief mention of issues involved in these special conditions and contain few recommendations. References are few.

Conclusions

Guidelines for the Diagnosis and Management of Asthma is a document produced by an expert panel and sponsored by a federal agency concerned with lung disease. The panel's goals were lofty and admirable. All physicians share the panelists' wish that patients with asthma could have resolution of their chronic condition; but that desire seems to have led to oversimplification of the current state of knowledge about etiology, pathophysiology, management, and outcome.

The individual recommendations are not formally graded, but it is clear that none are standards and few are guidelines. Most recommendations fall into the category of practice options based on the panel's global subjective judgment. Family physicians will find the report in places useful and interesting, but in other places provocative, and in a few places infuriating in its condescension toward primary care physicians.

The tendency in the report to support recommendations with published reviews rather than with primary research is scientifically problematic and an affront to the reader. Reviews cited are of variable (at times poor) quality. Some of the cited research is of extraordinarily poor quality and should not have been included.

More useful for researchers, clinicians, and patients alike would have been a critical examination of the basic and clinical science underlying asthma diagnosis and treatment, cataloguing along the way the many areas in desperate need of better quality data, especially in the important area of clinical outcome for many of the treatment interventions. As presented in the report, most such areas are obscured by well-intentioned guesses, which nonetheless are communicated with all the force of fact.

In the Foreword Dr. Lenfant, director of the National Heart, Lung, and Blood Institute promises to update the recommendations "as scientific research advances." In our view, the process should begin now using the more rigorous methodology of an expert evidence-based panel and with broader representation from the scientific and practice communities. At a minimum a reconvened panel should include generalists and research methodologists who do not come into the process with preconceived biases based on clinical specialty training and experience.

In summary, the hundreds of policies that comprise this report are practice options that practitioners should treat as they would any recommendation from a consultant: as expert opinion and not as science-based policy. Readers hoping for specific clinical "take homes" from this review may be justly disappointed, but the blame rests with the process of the panel and the inclusion of recommendations not supported by evidence. The point of our review is to show that specific clinical advice based on these guidelines *is not possible*, because the process of developing and communicating the guidelines was critically flawed.

Dr. Lenfant's comment in the Foreword provides justification for family physicians to use this report with caution:

> In issuing these guidelines, the panel emphasizes that these are general guidelines developed to assist clinician and patient decisions about appropriate asthma care; specific therapeutic regimens must be tailored to individual needs and circumstances.

The guidelines offer clinicians a handy summary of a sample of current expert opinion but have not advanced the level or certainty of our diagnosis and care for this common and chronic condition.

References

1. Centers for Disease Control. Asthma—United States, 1980-1987. MMWR 1990; 39:493-7.
2. Bryant E, Shimizu I. Sample design, sampling variance, and estimation procedures for the National Ambulatory Medical Care Survey. Vital and Health Statistics, Series 2; no. 108. Washington, DC: US Government Printing Office, 1988. (DHHS publication no. (PHS) 88-1382.)
3. Djukanovic R, Roche WR, Wilson JW, Beasley CR, Twentyman OP, Howarth RH, et al. Mucosal inflammation in asthma. Am Rev Respir Dis 1990; 142:434-57.
4. Boushey HA, Holtzman MJ, Sheller JR, Nadel JA. Bronchial hyperreactivity. Am Rev Respir Dis 1980; 121:398-414.
5. Bleecker ER. Airways reactivity and asthma: significance and treatment. J Allergy Clin Immunol 1985; 75:21-4.
6. Cockcroft DW. Airway hyperresponsiveness: therapeutic implications. Ann Allergy 1987; 59: 405-14.
7. Ryan G, Latimer KM, Dolovich J, Hargreave FE. Bronchial responsiveness to histamine: relationship to diurnal variation of peak flow rate, improvement after bronchodilator, and airway caliber. Thorax 1982; 37:423-9.
8. Laitinen LA, Heino M, Laitinen A, Kava T, Haahtela T. Damage of the airway epithelium and bronchial reactivity in patients with asthma. Am Rev Respir Dis 1985; 131:599-606.
9. Crompton GK, Grant IW, Bloomfield P. Edinburgh Emergency Asthma Admission Service: report on 10 years' experience. Br Med J 1979; 2:1199-1201.
10. Barnes PJ. A new approach to the treatment of asthma. N Engl J Med 1989; 321:1517-27.
11. Reed CE. New therapeutic approaches in asthma J Allergy Clin Immunol 1986; 11:537-43.
12. Hargreave FE, Dolorich J, Newhouse MT. The assessment and treatment of asthma: a conference report. J Allergy Clin Immunol 1990; 85: 1098-111.
13. Bel EH, Timmers MC, Hermans J, Dijkman JH, Sterk PJ. The long-term effects of nedocromil sodium and beclomethasone dipropionate on bronchial responsiveness to methacholine in nonatopic asthmatic subjects. Am Rev Respir Dis 1990; 141:21-8.
14. Kraan J, Koeter GH, Mark W, Sluiter HJ, deVries K. Changes in bronchial hyperreactivity induced by 4 weeks of treatment with antiasthmatic drugs in patients with allergic asthma: a comparison between budesonide and terbutaline. J Allergy Clin Immunol 1985; 76:628-36.
15. Sears MR, Taylor DR, Print CG, Lake DC, Li QQ, Flannery EM, et al. Regular inhaled beta-agonist treatment in bronchial asthma. Lancet 1990; 336: 1391-6.