

The 1997 Asthma Guidelines and an Asthma Clinical Update

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Abstract

Asthma, a chronic disease with a histopathology profile that often does not correlate with perceived symptoms, is often treated as an episodic disease. Many patients and their physicians underestimate the severity of this disease. The recent guidelines recommend inhaled corticosteroids as first-line therapy for persistent asthma at all levels—mild, moderate, and severe. The guidelines focus on 4 aspects of asthma care: assessment and monitoring; identifying asthma triggers; pharmacotherapy; and patient education. Incorporating these 4 aspects, especially patient education, allows for optimal, cost-effective asthma care and improved patient outcomes.

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Asthma is becoming an ever-increasing health concern in the United States. The prevalence of self-reported asthma has increased by 75% from 1980 to 1994 and is now thought to occur in 6.4% of the US population.^{1,2} This translates

into 17.2 million cases of perceived asthma.¹ Although asthma is becoming more common, its natural history is not well documented, which affects the way it is managed by the patient and the healthcare provider. A recent study illustrated the effect of asthma on the natural history of lung function in adults. In both smokers and non-smokers, people with self-reported asthma had significantly greater decline in lung function than those who did not have asthma, as measured by height-adjusted forced expiratory volume in 1 second (FEV₁) measurements, over a 15-year follow-up period (22-mL decline in people without asthma versus a 38-mL decline in those with asthma).³

New guidelines were published in 1997 by the National Heart, Lung, and Blood Institute as a means to improve the detection and treatment of asthma; the previous guidelines were published in 1991.⁴ The new guidelines offer recommendations based on the most current knowledge and represent a broad consensus of opinion based on a review of the scientific literature. The guidelines were formed to assist physicians in changing their treatment of asthma, but awareness of guidelines and recommendations and changing the day-to-day office practices can be 2 very different challenges.⁵

Primary care physicians are responsible for learning and implementing an average of 2000 guidelines on various diseases, although the guidelines by themselves may not be enough to change physicians' behavior.⁵ In fact, clinical practice guide-

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lines have been particularly unsuccessful in influencing physicians.^{6,7} Physicians' practice behavior can change under certain conditions (Table 1). The challenge for those seeking to do this is to identify and address the concerns and needs of physicians.

The biggest change in the 1997 guidelines is the evolution of the definition of asthma. For more than 35 years, asthma was considered to be an episodic, reversible airway constriction. Since 1997, advances in medical research have shown that asthma needs to be considered as a chronic

airway inflammatory disease characterized by at least partially reversible airway constriction. This, in theory, would affect the way it is managed. However, when today's physicians are asked what asthma is, their response is that it is an airway inflammatory disease, but they treat the disease episodically in their practice.

Histopathology reveals many changes taking place in the airway lumen of asthma patients that are unrelated to how the patient feels. The symptoms do not correlate with objective findings, which are common in inflammatory diseases. The consequences of this silent inflammation include lower airway symptoms, air-flow limitation, and the potential progression to end-stage lung disease. This has implications, in particular, for children who are identified as asthmatic at a young age (eg, 3 to 5 years) and are not treated effectively.

Table 1. Reasons Physicians Will Change Their Practice Behavior

Physicians will modify their practice behavior if:
■ They recognize that the current practice needs improvement.
■ A feedback system is in place where information about the practice or patient outcomes can be compared with other physicians' findings or an external standard, such as a guideline.
■ Physicians can receive feedback on the practice and can act on it immediately.
■ The new practice will provide physicians a role in setting the standards by which their practices will be judged.

Source: Reference 5.

Treatment Goals and the 1997 Guidelines

Regarding pharmacologic therapy, the 1997 guidelines state that inhaled corticosteroids (ICSs) are the most potent and effective agent for long-term management of persistent asthma at all levels: mild, moderate, and severe. They are well tolerated and safe at the recommended doses. Corticosteroids affect almost all of the cells involved in the asthma inflammation process, and they affect multiple pathways within those cells. The consequences of delaying or not using corticosteroid therapy for persistent asthma are decreased control of asthma, increased risk for hospitalization and/or emergency department visits, and no alteration of the natural course of the disease.

The 1991 guidelines recommended that all patients with moderate to severe asthma receive anti-inflammatory medication. The reality as of 1997 was that these agents were still underused in patients with persistent asthma. So, in constructing the 1997

Table 2. Goals of Asthma Therapy

■ Prevent chronic and troublesome symptoms
■ Maintain near-normal pulmonary function
■ Maintain normal activities, including physical exercise
■ Prevent recurrent exacerbations and minimize the need for emergency department visits or hospitalizations
■ Provide optimal pharmacotherapy with minimal or no adverse effects
■ Meet the expectations of the patients and families and ensure they are satisfied with their asthma care

Source: Reference 4.

guidelines, the expert panel re-examined and redefined the goals of therapy (Table 2). In particular, physicians should be telling their patients to expect nothing less than normal activities, including all athletic activities. This prognosis is a major change for most patients in the way they perceive their illness and their care. Reaching these treatment goals can only take place with ongoing monitoring and periodic assessment by the physician of all aspects of patient health, including pulmonary function, quality of life, history of exacerbations, pharmacotherapy, patient-provider communication, and patient satisfaction, as well as a bigger role played by patients in monitoring their asthma, taking medications, and avoiding exposure to asthma triggers.

The new guidelines have 4 components: assessment and monitoring, factors contributing to asthma severity (triggers), pharmacologic therapy, and education for a partnership in asthma care. In reality, education should take place at each step. The defined goals of asthma therapy affect each of these components.

Assessment and Monitoring

Asthma symptoms alone—coughing, wheezing, chest tightness, shortness of breath—are not diagnostic because many patients will report good health unless the physician asks the appropriate questions. Numerous studies have shown that patients underestimate the severity of their disease and may not perceive their symptoms at all.⁸⁻¹¹ As histopathology demonstrates, patient history and physical examination do not always reflect disease severity.

The guidelines in both 1991 and 1997 called for measuring pulmonary function using a spirometer, yet few physicians use or know how to interpret the results in terms of diagnosing and assessing asthma.¹² Current recommendations indicate that spirometric measurements should take

place at the time of diagnosis, when the patient is stabilized, and at least every 1 to 2 years. Pulmonary function testing should be viewed as standard measurements for monitoring patients with asthma, as is glucose monitoring for patients with diabetes or blood pressure reading for patients with hypertension. This testing is more objective than peak flow assessment and is not difficult to perform. Peak flow assessment performed by the patient can be used to identify their best score, evaluate the effect of exposures to asthma triggers, and assess the response to changes in chronic therapy.

Assessment also requires classifying asthma severity. Asthma is defined as intermittent or persistent, depending on whether the patient has up to 2 or more than 2 asthma symptoms per week, respectively (Table 3). Persistent asthma is further subclassified as mild, moderate, or severe based on day and night symptoms and lung function results. The presence of any one of the features of severity is sufficient for that classification, and patients should be classified into the most severe category in which any

Table 3. Classification of Asthma Severity

	Mild Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Frequency of symptoms	< 2/wk	> 2/wk < 1/day	Daily	Continual
Exacerbations	Brief/mild	May affect activity	Affects activity	Frequent/severe
Nighttime asthma symptoms	< 2/mo	> 2/mo	> 1/wk	Frequent
Lung function FEV ₁ or FEF	> 80%	> 80%	> 60 < 80%	< 60%
% PEF variability	< 20%	20%-30%	> 30%	> 30%

FEV₁ = forced expiratory volume in 1 second; FEF = forced expiratory flow; PEF = peak expiratory flow.

Source: Reference 4.

feature occurs. Classifying the patient at the time of the diagnosis is important because medications and other efforts are determined based on the severity of the disease.

Identifying Asthma Triggers

Common factors that contribute to asthma severity include perennial indoor allergens from pets, dust mites, mold, and cockroaches, as well as seasonal allergies, depending on the geographic location. Occupational exposure to an allergen and environmental irritants such as tobacco smoke and indoor/outdoor pollution may also cause asthma symptoms. Other factors can include rhinitis/sinusitis, gastroesophageal reflux, aspirin or sulfite sensitivity, use of β -blockers, and infections.

Opportunities of exposure to asthma triggers need to be identified with information from the patient. After the triggers are identified and documented, a plan to reduce exposure

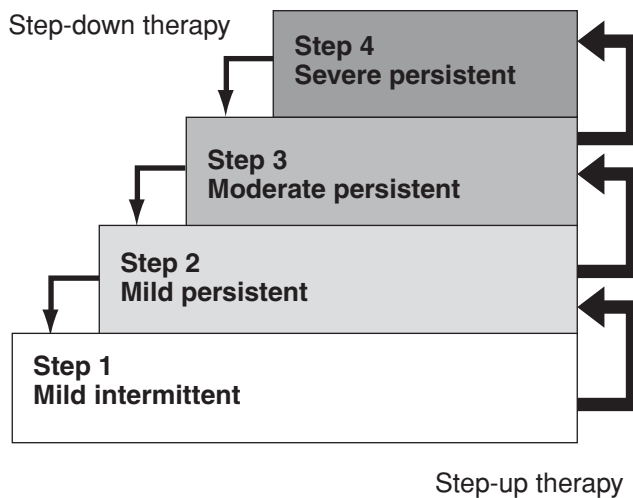
should be constructed through discussion with the patient. In developing the plan, consideration needs to be given to the patient's lifestyle. Determining which environmental controls the patient can live with is in the best interests of both the patient and the physician. For example, replacing all carpeting and getting rid of pets may not be a feasible first step and may alienate the patient from seeking further treatment. A practical, staged approach will yield much more effective results over the long term. Discussions with patients on the length of time necessary to see an improvement (eg, 6 months or longer may pass before the patient notices symptom improvement after removing a pet from the home) will also help to prevent discouragement.

Pharmacotherapy

Pharmacotherapy for asthma falls into 2 categories: quick relief and long-term control medications. Quick-relief medications should be used infrequently, only for exacerbations. They include β_2 -agonists, anticholinergics, and systemic corticosteroids. If a patient has persistent asthma, physicians should encourage their patients to take long-term control medications every day, regardless of whether they feel symptoms. Long-term medications include ICSs, cromolyn sodium and nedocromil, long-acting β_2 -agonists, methylxanthines, leukotriene modifiers, and systemic corticosteroids. Because asthma is largely asymptomatic, convincing patients to take medications long term while they are not experiencing exacerbations is often the most difficult part of asthma care.

As part of the paradigm shift to viewing asthma as a chronic disease, pharmacotherapy must also be viewed as a continuum. Physicians need to reinforce the message that although a patient may be initially diagnosed with severe, persistent asthma based on the history and lung

Figure 1. Step-Up/Step-Down Therapy



Source: Reference 4.

function results, the ultimate goal is to have mild asthma, or even mild intermittent asthma. As control is gained over the disease, the medication profile must be modified. This is known as step-up and step-down therapy (Figure 1).

With mild persistent asthma, ICSs are the preferred therapy, although other drugs may be considered, especially nonsteroidal anti-inflammatory therapy in the pediatric age group (Figure 2). At this point, the amount of medication needed to control the disease is given at the time of diagnosis and, approximately every 2 to 3 months, the physician can consider step-down therapy based on symptom control and lung function testing. Step-up therapy may be required at certain times. This step-up/step-down process originated from the European guidelines published in 1995.¹³

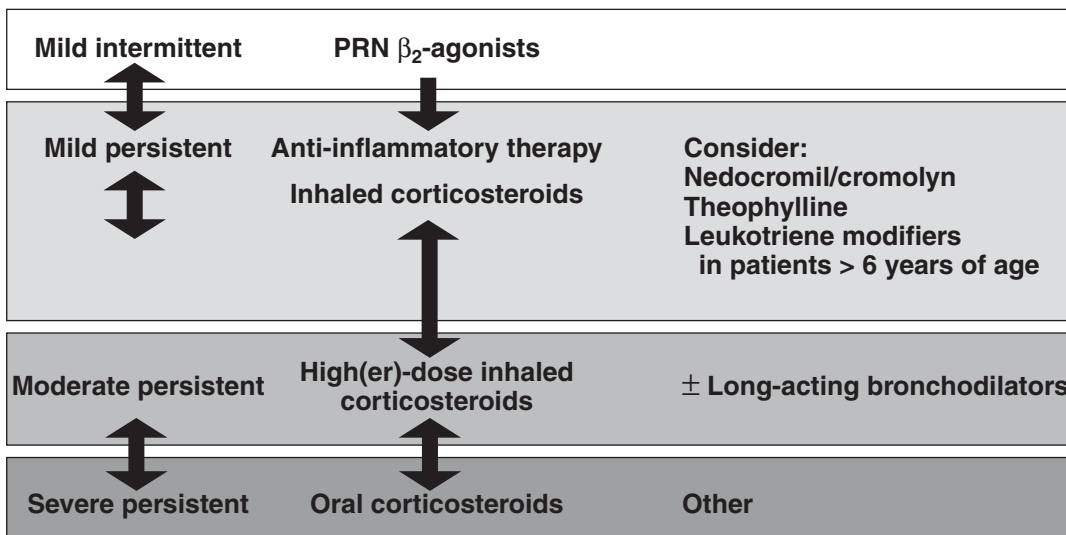
Educating Patients on Pharmacotherapy

Asthma therapies have 2 routes of administration—systemic and inhaled.

Systemic medications can be taken via oral or parenteral routes. Inhaled medications are delivered by metered-dose inhalers, dry powder inhalers, or nebulizers. Inhaled medications have several pharmacokinetic advantages including drug delivery directly to the lungs, avoidance of or minimal systemic side effects, and a more rapid onset of action. In fact, all of the rescue, quick-relief medication is in the inhaled form, so patients need to be educated on the proper use of an inhaler. If patients are given an inhaler with no information or training, the probability of them using it properly is extremely low. Review of proper inhaler technique is necessary at each office visit.

Healthcare providers must also understand the multiple factors in inhaled medication pharmacokinetics. One puff of Drug A does not equal one puff of Drug B (Table 4). When physicians consider a drug dose for any given patient, they must also consider the probability of adherence or compliance by that patient if 10 to 20

Figure 2. Progression of Pharmacologic Therapy in Asthma



puffs a day must be taken. Clinical efficacy will vary based on the patient population and the drug delivery device. In addition, a risk:benefit ratio range for each ICS must be considered. The range is considered favorable when the desired effects on lung function increase steeply with the dose and the unwanted effects increase gradually. At higher doses, outside of the favorable range, the unwanted side effects begin to outweigh the benefits.^{14,15} The favorable range varies for each ICS; for more potent drugs, lower doses offer greater overall clinical efficacy.

Several studies have shown that, in both pediatric and adult populations, the low-dose range of 100 to 400 µg, up to a maximum of about 800 µg per day, of ICS offers the best benefit with the lowest incidence of systemic side effects.^{15,16} When the dose is doubled from 800 µg to 1600 µg, the dose-response curve flattens out in most

people, whereas the systemic side effects increase.

Other recent studies have done direct comparisons between medium-dose fluticasone versus triamcinolone and low- and medium-dose fluticasone versus beclomethasone. In both of the studies reviewed, the lower doses of fluticasone showed greater efficacy in lung function.^{17,18} In fact, the relative dose needed to achieve comparable clinical efficacy (on a per-µg basis) is as follows: fluticasone, 1X; beclomethasone, 2X; and triamcinolone, 4X. These doses depend on the delivery device and patient's age.

**Treating the Disease:
How much? How soon?**

As discussed, early intervention is key to prevent lung function decline. Studies of children with asthma have shown that if more than 5 years pass from symptom onset before ICS therapy is initiated, lung function (as mea-

Table 4. Estimated Comparative Daily Dosages for Inhaled Corticosteroids for Adults

Drug	Low dose	Medium dose	High dose
Beclomethasone 42 µg/puff 84 µg/puff	168-504 µg 4-12 puffs: 42 µg 2-6 puffs: 84 µg	504-840 µg 12-20 puffs: 42 µg 6-10 puffs: 84 µg	>840 µg >20 puffs: 42 µg >10 puffs: 84 µg
Budesonide Turbuhaler 200 µg/dose	200-400 µg 1-2 inhalations	400-600 µg 2-3 inhalations	>600 µg >3 inhalations
Flunisolide 250 µg/puff	500-1000 µg 2-4 puffs	1000-2000 µg 4-8 puffs	>2000 µg >8 puffs
Fluticasone MDI: 44, 110, 220 µg/puff DPI: 50, 100, 250 µg/dose	88-264 µg 2-6 puffs: 44 µg 2 puffs: 110 µg 2-6 inhalations: 50 µg	264-660 µg 2-6 puffs: 110 µg 3-6 inhalations: 100 µg	>660 µg >6 puffs: 110 µg >3 puffs: 220 µg >6 inhalations: 100 µg OR >2 inhalations: 250 µg
Triamcinolone acetonide 100 µg/puff	400-1000 µg 4-10 puffs	1000-2000 µg 10-20 puffs	>2000 µg >20 puffs

MDI = metered-dose inhaler; DPI = dry powder inhaler.
Source: Reference 4.

sured by FEV₁) is significantly lower after 3 years of ICS therapy compared with children who began ICS therapy within 2 years of asthma onset.¹⁶ In adult patients treated with budesonide for 2 years, a negative correlation was seen between the duration of symptoms and the maximal increases in peak expiratory flow rate (PEFR) and FEV₁ in response to ICS therapy. In patients with symptom duration of less than 2 years before ICS therapy, the mean FEV₁ and PEFR were higher at all time points.¹⁹ These data support the guideline recommendations of early treatment in asthma. Early ICS therapy appears to prevent patients from developing chronic, irreversible airway obstruction.

Questions regarding the recommended frequency of rescue medication use have also been raised. One study showed that using more than 5 refills of a short-acting rescue β_2 -agonist per year increased the risk for hospitalization for all age groups compared with those receiving no short-acting β_2 -agonist rescue therapy.²⁰ The risk for hospitalization rose dramatically in those using more than 8 refills per year. Those taking ICS had protection from this increased risk across all levels of β_2 -agonist use, including those using more than 8 refills. Patients using 5 to 8 refills per year are not considered to have their asthma under control, although this is not an uncommon amount of rescue therapy for many patients. These data also support the use of ICS for the long-term control of asthma.

Patients have their own needs and concerns regarding pharmacotherapy. Specifically, they would prefer taking no medication at all. If they have to take the drug, they want to take it only when needed and they want an immediate onset of action. A comparison of 8 studies on fluticasone used by 1600 patients showed that the onset of action (ie, change in baseline PEFR) occurred within the first week, and lung function improved by 50%

within 2 weeks and by 90% within 3 weeks.²¹ Rapid symptom improvement is also important. As is often seen with antibiotic use, patients can become frustrated if they do not see a

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noticeable improvement in their symptoms very shortly after therapy is initiated. The 8-study comparison also showed improvements in the asthma symptom score within the first week.

Another significant concern is the effect of ICSs on growth, the hypothalamic-pituitary-adrenal (HPA) axis, bone density, ophthalmic parameters (glaucoma and posterior subcapsular cataracts), and bruising. Patients need to know that ICSs will not build muscle; only their genetic propensity will determine muscle growth. In addition, ICSs do not impair growth rates in terms of attaining predicted adult height when they are used in the lowest effective dose and the step-down approach is used.^{16,22} Fluticasone has been shown to have no clinically relevant effects on the HPA axis, bone density, or ophthalmic parameters in adults with mild asthma.²³ The benefits of ICS therapy balance any potential small risk for adverse effects on growth. To minimize the risk, the patient’s height should be monitored regularly (ie, every 3 to 4 months), with careful attention paid to the seasonal differences in growth and the different height standards and growth charts used by the patient’s previous physicians.

Comparing Long-term Therapies in Patients With Chronic Asthma

A comparison of a leukotriene receptor antagonist (montelukast) and ICS therapy (beclomethasone) in chronic asthma revealed a greater clinical benefit with beclomethasone in terms of FEV₁ over 12 weeks; however, montelukast also showed clinical benefit (5% to 7% increase/improvement in FEV₁) and a faster onset of action.²⁴ However, in other studies, placebo can show an approximate 5% improvement. This may be associated with more consistent care and more assertive action in eliminating asthma triggers for those participating in clinical trials.

The guidelines recommend an increased dose of ICS for patients with uncontrolled asthma on low-dose ICS (step-up therapy). However, increasing the ICS dose may not be the most effective treatment strategy. A study comparing salmeterol as add-on therapy to low-dose beclomethasone versus doubling the dose of beclomethasone showed that add-on therapy with a long-acting β_2 -agonist led to much greater improvement in FEV₁ than the doubled dose of ICS.²⁵ No significant difference in adverse effects or exacerbations was seen between the 2 groups. Therefore, a flexible approach to asthma management is warranted. Comparing long-acting β_2 -agonists and leukotriene modifiers, both as add-on therapy, supports use of long-acting β_2 -agonists for patients with persistent asthma.²⁶

... CONCLUSION ...

The newest asthma guidelines focus on 4 aspects of asthma care: assessment and monitoring; identifying asthma triggers; pharmacotherapy; and patient education. Having patients need treatment in emergency departments or hospitals should be considered unacceptable. Asthma is an outpatient disease that should be treated on a frequent basis by health-

care providers and primary care physicians, with the assistance of specialists when needed.

Asthma management is an educational process that begins at diagnosis and should be integrated in every step of care. Physicians should see patients frequently to provide asthma therapy, which includes identifying fears and concerns of the patients as well as controlling symptoms and promoting normal lung function. Asthma management may be considered analogous to managing a patient with diabetes or hypertension or providing smoking intervention. If the clinician does not talk to the patient about the disease and its management, the health improvements do not occur.

Environmental controls for eliminating or reducing exposure to triggers should be changes that patients are willing to accept. The changes can be chosen based on discussions with the patient, documentation of allergens to which the patient is sensitive as well as suspected or known exposure to triggers, and practical considerations regarding the patient's lifestyle and quality of life. In this way, the patient-physician partnership is maintained. The role of ICS therapy is to reduce symptoms, frequency of severe exacerbations, use of quick-relief medications, and the risk for hospitalization. It may also help reduce airway remodeling and improve or prevent deterioration of lung function. These roles require a paradigm shift in asthma management.

Education should include a review of asthma in lay terms and basic information about how to use the inhalers properly. Patients need to demonstrate proficiency in using an inhaler, which should be repeated during each visit. When and how to take rescue actions should also be reviewed. Education also involves encouraging adherence, in part by jointly developing treatment goals with the patient. Identify what patients are seeking from the current visit and future vis-

its, their treatment goals, and their quality-of-life goals. Remind patients that asthma cannot be cured but can be treated effectively. This partnership, or alliance, results in providing cost-effective optimal asthma care and improved patient outcomes.

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