

Implementing Key Concepts from the 2007 NHLBI/NAEPP Guidelines for the Diagnosis and Management of Asthma

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Therapeutic Interventions for Asthma: Rationale for Guidelines Recommendations

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The “Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma” was published in August 2007. These new asthma guidelines were developed by an expert panel commissioned by the National Asthma Education and Prevention Program (NAEPP) Coordinating Committee, coordinated by the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH).

The EPR-3 guidelines are an updated version of the 1997 EPR-2 guidelines and the 2002 update. Three major changes in the new guidelines relate to pharmacologic therapy. First, three age categories are now delineated (0-4 years, 5-11 years, and ≥ 12 years). Second, equal weight is now given to medium-dose inhaled corticosteroids (ICS) and the combination of ICS and

long-acting beta-agonist (LABA) therapy for patients not controlled on low-dose ICS. Third, consideration of omalizumab for patients with severe persistent asthma has been added.

Three Age Groups

The rationale for delineating three age groups is based on both Food and Drug Administration (FDA) regulations and practical considerations. To gain FDA approval, most drugs are first evaluated in adults and adolescents (≥ 12 years of age). To test for pediatric use, most asthma drugs are then assessed in children aged 5 to 11, although this age range is not set by the FDA. Instead, it is largely due to the difficulty of assessing lung function and administering aerosols in children younger than 5 years old. In addition, children younger than age 5 with viral-induced wheezing may represent a different phenotype that responds differently to medication.

The basic therapy for children from birth to 4 years old is ICS, primarily because most of the evidence for drug efficacy in this age group comes from studies of ICS. Very little data on dose response in this age group exist, largely because dose response data is derived primarily from parallel design trials, which do not show a significant dose response. However, a few trials have suggested that there is a dose response relationship in infants up to age 4. For example, a study by Bisgaard compared placebo to fluticasone (50 μg bid and 100 μg bid) delivered via a spacer and face mask in infants aged 12 to 47 months.¹ The only comparison showing a statistically significant difference was between the 200 μg per day dose and placebo. However, there was a statistically significant trend analysis that has been interpreted as

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*A*ta symposium conducted in conjunction with the 2007 Annual Scientific Meeting of the American College of Allergy, Asthma and Immunology (ACAAI), chaired by Michael B. Foggs, MD, an expert panel discussed key concepts contained in the new NHLBI/NAEPP guidelines for the diagnosis and management of asthma. In addition to Dr. Foggs, the panel consisted of H. William Kelly, PharmD, from Albuquerque, New Mexico (“Therapeutic Interventions for Asthma: Rationale for Guidelines Recommendations”); Carlos Camargo, from Boston, Massachusetts (“Management of Asthma Exacerbations”); and Harold S. Nelson, MD, from Denver, Colorado (“Asthma Risk Factors and the Role of Immunotherapy in Asthma Management”).

Learning Objectives

Upon completion, participants should be able to:

- Identify three major changes in the new guidelines that relate to pharmacologic therapy;
- describe the major changes in the EPR-3 treatment recommendations for asthma exacerbations;
- understand the importance of considering inhaled corticosteroid initiation at discharge from the emergency department or hospital;
- be familiar with the data supporting the newly recognized risk factors for the development of asthma;
- understand the placement of immunotherapy in the guidelines;
- describe the new paradigm for asthma management;
- assess current asthma management with regard to current or recent impairment and future or long-term risk;
- apply guideline-based interventions to establish and maintain asthma control.

Target Audience

Practicing allergists/immunologists; fellows in accredited allergy/immunology training programs; primary care physicians who treat asthma patients; physician assistants, nurse practitioners; and other allied health professionals in the field of asthma, allergy and immunology.

Needs Assessment

Improvement in asthma outcomes has been limited with adherence to guidelines suboptimal as reflected in the literature. Use of guidelines can contribute to the improvement in quality of care rendered, help decrease unnecessary and

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inappropriate practice variations, help control healthcare costs, foster evidence-based decision making, and accelerate the application and translation of advances in medical science to everyday clinical practice. Careful analysis of therapeutic options for the treatment of asthma in an acute and non-acute setting, appreciation of the role that the environment may play in heightening asthma's expression, and the understanding of the impact of co-morbid conditions that may mimic or aggravate asthma is a productive exercise conducive to improving asthma outcomes.

CME Credits

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Off-label Uses of Products

This review contains no discussion of off-label use of products except for clinical trial data pertaining to potential uses of new and emerging treatment modalities.

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somewhat of a dose response, but this question requires further study.

A study by Guilbert and colleagues examined whether early introduction of ICS would prevent the onset of persistent asthma in children at high risk for asthma. In this randomized, double-blind, placebo-controlled trial, 285 children (2-3 years old) with high risk for asthma were treated for 2 years with fluticasone (88 µg bid) or placebo followed by a 1-year observation period.² The primary outcome was episode-free days during the observation period. Use of ICS did not prevent the onset of asthma; however, during the treatment period the ICS provided symptom relief compared to placebo. It did not change the natural course of the disease.

Several issues in pharmacotherapy for children younger than 5 years old remain unresolved. No comparison studies between long-term controllers for patients in this age group have been conducted, and very little safety and efficacy data exist. Few drugs have FDA approval based on efficacy; budesonide and cromolyn nebulizer preparations are exceptions. No adjunctive therapy studies in this age group have been conducted.

For children aged 5 to 11, the preferred therapy is an ICS. Alternatives include leukotriene receptor antagonists, theophylline, nedocromil, and cromolyn. For this age group, most new drugs gained FDA approval with primarily safety and pharmacokinetic data and limited efficacy data. Most efficacy data were extrapolated from studies of older children and adults. There are few adjunctive therapy studies and no comparative studies of adjunctive therapies.

The Pediatric Asthma Controller Trial (PACT) was one of the few studies that looked at adjunctive therapy in children.³ A total of 285 children (6-14 years old) with mild to moderate persistent asthma were randomized to an ICS (fluticasone), fluticasone at half dose plus the LABA salmeterol, or a leukotriene receptor antagonist (montelukast). No difference was reported between combination therapy and fluticasone alone in terms of percent of asthma-controlled days. Fluticasone was superior to montelukast. For certain aspects of the disease, fluticasone alone was more effective than the combination, but not by much.

In general, very little evidence exists to guide the use of adjunctive therapy in children aged 5 to 11. Adding a LABA to an ICS improves lung function and reduces symptoms and as-needed SABA use. However, a significant effect on reduction in exacerbations, as is seen in adults, has not been observed.

Change to Step 3 Therapy

The second major change in the EPR-3 asthma guidelines elevates use of medium-dose inhaled corticosteroids, giving it equal weight to combination therapy in patients who require Step 3 therapy. The rationale for changing Step 3 therapy to "preferred" only for medium-dose ICS and the combination of a low-dose ICS plus a LABA relates to potential risks with use of LABAs. In addition, recent large trials have demonstrated comparable efficacy of medium-dose ICS and low-dose ICS plus a LABA for reducing exacerbations.

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Severe asthma exacerbations resulting in death can occur with use of LABAs. For example, the Salmeterol Multicenter Asthma Research Trial (SMART) study found that there was increased risk of asthma-related deaths in both Caucasian and African-Americans given salmeterol plus usual care.⁴ A study of formoterol plus usual care also showed an increase in the number of serious asthma exacerbations in the group receiving the LABA.⁵ Based on these data, the FDA formulated an opinion that the potential for serious adverse asthma exacerbations from LABAs is a class effect.

This effect does not appear to be significant with ICS and LABA combination therapy, although very little data exist. A meta-analysis by Sin and coworkers showed that LABAs tend to reduce overall risk of significant asthma exacerbations.⁶ It has been suggested that the increased exacerbations noted with LABAs result from beta-agonist tolerance. However, while tolerance is a phenomenon of beta-agonist use, it does not appear to be clinically significant. Genotype has also been suggested as a possible explanation for increased exacerbations with LABAs. Patients with the Arg/Arg genotype do not fare as well on chronic SABAs as those with the Gly/Gly genotype.⁷ However, no data support an increased risk of exacerbations with LABAs associated with the Arg/Arg genotype. A study by Taylor and colleagues looking at the Arg/Arg genotype showed

an increase in exacerbations in patients on SABAs, but not on LABAs.⁸

Neither a physiologic nor a genetic mechanism for increased risk of death and serious asthma exacerbations from use of LABAs has been identified. This effect appears to occur only when monotherapy is added to usual therapy. Studies with combination therapy have not supported an effect. However, they have not been sufficiently powered to assess risk. Ultimately, the experts who wrote the guidelines felt that the benefit derived by the vast majority of patients outweighed a potential risk of uncommon severe reactions to LABAs that has not been clearly attributed to combination therapy.

Omalizumab for Severe Persistent Asthma

The third major change in the EPR-3 guidelines adds consideration of omalizumab for patients with severe persistent asthma. Omalizumab is approved for the treatment of moderate to severe asthma. Evidence for the efficacy of omalizumab for severe asthma in atopic adults is primarily provided by the INNOVATE trial, a 28-week, double-blind, placebo-controlled, multicenter, parallel trial of 419 patients (12-75 years old) with severe persistent asthma receiving Step 4 therapy.⁹ All of the patients were receiving a high-dose ICS plus a LABA; 35% were also receiving a leukotriene modifier; 28% were receiving theophylline; and 21% were on oral corticosteroids. Study participants had a history of at least one hospitalization or two severe exacerbations requiring oral corticosteroids in the last year. Compared to placebo, there was a significant reduction in clinically significant and severe exacerbations and in emergency department visits in patients who received omalizumab.

Due to possible adverse effects with omalizumab, the guidelines recommend it only for severe asthmatics. For example, there is a black box warning based on post-marketing surveillance reports that have estimated anaphylactic reactions occur within 2 and up to 24 hours following omalizumab injection in 0.1% of the patient population. Other issues with omalizumab are the following: one study in children did not show sufficient efficacy to gain FDA approval for use in children; studies in adults were primarily in patients with moderate asthma uncontrolled on ICS; and no comparative studies with other adjunctive therapies (LABAs or leukotriene receptor antagonists) have been conducted in this population of patients.

Management of Asthma Exacerbations

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The EPR-3 guidelines contain a new chapter on management of asthma exacerbations, a topic that was previously incorporated into the chapter on pharmacotherapy. This new chapter includes several major changes from the 1997/2002 guidelines. For example, the new guidelines simplify classification of acute asthma exacerbation severity. They also reinstate the 1991 cut points for what represents a mild (FEV_1 or peak expiratory flow [PEF] $\geq 70\%$ of predicted), moderate (40-69% predicted), or severe ($<40\%$ predicted) exacerbation.

EPR-3 reverted to these earlier cut points because the goal for discharge from acute care is FEV_1 or PEF $\geq 70\%$ of predicted and the exacerbation severity level where adjunct therapies are helpful, and therefore may be considered, is FEV_1 or PEF $<40\%$ of predicted. These cut points differ from those used to determine long-term asthma control and treatments, thus underscoring the distinction between acute and chronic asthma management. The new guidelines also explicitly acknowledge the limited value of pulmonary function measures in the initial management of very severe exacerbations.

For home management, the guidelines no longer recommend doubling the dose of ICS at the first sign of an exacerbation.

Several changes in treatment recommendations for asthma exacerbations were also made, including adding levalbuterol as a SABA treatment. For home management, the guidelines no longer recommend doubling the dose of ICS at the first sign of an exacerbation. Instead, they recommend systemic steroids. For people who can't take systemic steroids, the recommendation is to at least quadruple the ICS dose. According to the revised algorithm for home management of asthma exacerbations, the patient should try to measure PEF. The guidelines state that "values of 50% to 79% predicted or personal best

indicate the need for quick-relief medication. Depending on the response to treatment, contact with a clinician may also be indicated. Values below 50% indicate the need for immediate medical care."

For prehospital management, the guidelines encourage standing orders for albuterol, and for prolonged transport they recommend repeated treatments and protocols to allow consideration of ipratropium and oral corticosteroids.

For emergency department management of exacerbations, the new guidelines reduce the dose and frequency of administration of oral corticosteroids recommended for severe exacerbations. They also add consideration of magnesium sulfate or heliox for severe exacerbations and consideration of initiating an ICS upon discharge. For hospital management, the guidelines no longer recommend ipratropium bromide due to evidence suggesting it has no benefit beyond the initial hours of emergency management. New information on the algorithm covering management of asthma exacerbations in the emergency department and hospital includes the addition of consideration of adjunct therapies (magnesium and heliox) for patients in impending or actual respiratory arrest and also for patients with a severe exacerbation who aren't responding to initial treatment.

A meta-analysis looking at patients with a high hospital admission rate for acute asthma showed a consistent reduction in admission rate with use of intravenous magnesium added to standard care compared to placebo.¹⁰ Therefore, magnesium is recommended as adjunctive therapy for the sickest patients, including those who are somewhat refractory to beta-agonist therapy. The evidence does not support its use in less severe cases.

Heliox is a combination of helium, which is about 25% as dense as room air, and oxygen. In a study by Kass and Terregino, of 23 patients randomized to receive heliox or oxygen the patients receiving heliox had a more rapid improvement in pulmonary function.¹¹ However, by 360 minutes after initiation of treatment the two groups were even. The authors concluded that heliox rapidly improves airflow obstruction dyspnea in patients with acute severe asthma. Unfortunately, a few smaller studies have produced conflicting findings. Ultimately, to determine the role of heliox, a large well-designed, randomized trial is needed.

The new algorithm on management of asthma exacerbations in the emergency department and hospital calls for considering initiation of an ICS upon discharge.

While the patient's primary care physician can write this prescription, there often is a lag time between discharge home and seeing the primary physician. Therefore, the guidelines encourage emergency department physicians to write this prescription when discharging patients who have had an exacerbation. This is in keeping with the emphasis in the guidelines on promoting prevention at every clinical encounter.

For patients who present to the emergency department with an asthma exacerbation, the guidelines also encourage emergency department staff, whenever possible, to schedule a follow-up appointment with their primary care physician or specialist.

Asthma Risk Factors and the Role of Immunotherapy in Asthma Management

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Three newly recognized risk factors for asthma are incorporated into the EPR-3 asthma guidelines. These are exposure to formaldehyde and volatile organic chemicals, use of acetaminophen, and obesity.

Evidence for increased risk from exposure to volatile organic compounds comes from several studies. In a case-control study, levels of volatile organic compounds were measured in the homes of children aged 6 months to 3 years who presented to the emergency department with acute asthma, as well as matching controls.¹² Children who presented with asthma symptoms had significantly higher levels of volatile organic compounds in their homes than controls. Sources of the compounds included recent painting, new carpets, new furniture, and indoor smoking. Children exposed to the median level or above of volatile organic compounds had a 4-fold increased risk of having asthma.

A study of 5,951 Russian children aged 8 to 12, which assessed them for recent exposure to new surface materials and respiratory symptoms, found that risk for current asthma, wheezing, and rhinitis increased with exposure to new linoleum flooring, synthetic carpeting, particle board, wall coverings, new furniture, and recent painting.¹³ Similar findings have also been found with adults. In a study of 4,521 women aged 30 to 65 who were exposed to cleaning compounds in an occupational setting (i.e., domestic cleaning work), 25%

of the asthma in this population was attributable to exposure to volatile cleaning agents.¹⁴

Use of acetaminophen may increase risk for asthma because it decreases glutathione levels in the lung, which may predispose to oxidant injury. In the Nurse Health Study, women who used acetaminophen for more than 14 days per month had an odds ratio of 1.63 for newly diagnosed asthma, compared to nonusers.¹⁵ A large European database showed that there was a positive correlation, by country, between acetaminophen use and asthma prevalence.¹⁶

In a study by Shaheen, there was a dose-related association between acetaminophen use during pregnancy and asthma and total IgE in the offspring.¹⁷ If this was a causal relationship, it could account for 7% of childhood asthma. The NHANES III data confirmed a dose-response association of acetaminophen use and asthma, chronic obstructive pulmonary disease (COPD), and decreased lung function.¹⁸ A study of 7,649 Ethiopian adults and children showed that symptoms of wheeze, shortness of breath, and eczema increased with acetaminophen use.¹⁹

Obesity as an asthma risk factor is supported by several studies. In a meta-analysis of seven studies with a total of 333,102 subjects, people who were overweight or obese had an odds ratio of 1.51 for development of asthma, compared to people who were of normal weight.²⁰ This was seen more consistently in women than in men.

Three newly recognized risk factors for asthma are incorporated into the EPR-3 asthma guidelines. These are exposure to formaldehyde and volatile organic chemicals, use of acetaminophen, and obesity.

In a study of the effect of weight reduction on asthma, 38 subjects (18-60 years old) with asthma and a body mass index of 30 to 42 kg/m² were randomized to restrictive caloric intake for 8 weeks or a control group.²¹ Patients on the diet achieved substantial weight loss (14.5% weight loss), which persisted (11.3% weight loss) at the end of 1 year. The weight loss group had an improvement in both FEV₁ and forced vital capacity (FVC) of over 7%. They also had fewer symptoms

of asthma and fewer asthma exacerbations than the control group.

One theory about the underlying mechanism linking obesity and asthma proposed that adipose tissue may generate proinflammatory substances that could contribute to airway inflammation. However, the data do not support an inflammatory relationship between obesity and asthma. The relationship appears to be based on unidentified factors.

Role of Immunotherapy in Asthma Management

One difference in the EPR-3 guidelines from the previous version relates to the role of immunotherapy in asthma management. The step therapy charts now contain reminders to consider environmental controls at each step and to consider subcutaneous immunotherapy at Steps 2 through 4.

The recommendation for allergen immunotherapy is considered Category B evidence. It is largely based on a systematic review by Abramson of 75 randomized clinical trials, 56 of which were double blind and 5 single blind.²² All but five of the trials involved single allergens. Of the five multiple allergen studies, one was quality rated as a 5 (the best) and one was rated 4. The other three had small numbers of subjects; one of these was partially blinded, one had an outcome of bronchial hyperresponsiveness, and one involved only two intradermal injections.

The multiple allergen study that was rated 5 evaluated the value of hyposensitization therapy for bronchial asthma in children.²³ Every child with perennial bronchial asthma and positive skin tests referred to the pediatric allergy clinic of Strong Memorial Hospital between August 1953 and January 1955 was randomly assigned to receive injections of saline, an extremely low dose of allergen extract, or a moderate or the highest tolerated dose. The parents did not know their children were enrolled in a study. Those evaluating the patients did not have knowledge of each child's group assignment. Of 230 children enrolled, 173 were still in the study after 4 years and 130 completed the study upon reaching age 16. After 4 years, 18% of those on placebo or the lowest dose were free of asthma, while 58% of those on the moderate dose and 81% of those on the highest dose were free of asthma. At the end of the study (age 16), 22% of those on placebo or the lowest dose were free of asthma, which was true for 66% of the moderate-dose group and 78% of the high-dose group. The conclusion of this study was that allergen immunotherapy is clinically effective in children with asthma when

administered as a multiple allergen mix to multiply sensitized patients. It is dose dependent, with the highest tolerated dose resulting in maximum efficacy.

The multiple allergen study that was rated 4 is a more recent controlled trial of 121 children (5-14 years old) with moderate-to-severe perennial asthma.²⁴ Half of them were African-American children from inner cities and the other half were Caucasian children living in the suburbs. Children with pets in the home were excluded and medications were optimized prior to randomization. The subjects were randomized to immunotherapy with up to 7 allergens at doses of major allergen ranging from 4.3 to 30 µg. Treatment continued at least 18 months. This study found no difference between the active and placebo groups in daily medication use before and after immunotherapy. The authors concluded that immunotherapy with injections of allergens for over 2 years was of no discernible benefit in allergic children with perennial asthma who were receiving appropriate medical treatment.

Of the two highly rated studies looking at multiple allergen immunotherapy, one was supportive and the other was not. Therefore, the guidelines considered recommendations for immunotherapy as evidence level B rather than level A.

Periodic Long-Term Management of Asthma: Practical Applications of the Guidelines

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Asthma is a heterogeneous disorder, and the inherent variability of the disease can result in unpredictable exacerbations. Following the new paradigm for asthma management as outlined in the EPR-3 guidelines, particularly as it pertains to patient education, determining asthma severity, and maintaining asthma control, can lead to successful periodic long-term management of asthma.

The goals of clinical practice guidelines, including the EPR-3 guidelines, are to improve quality of care (and thereby improve outcomes), decrease practice variation (especially if unnecessary and inappropriate), control healthcare costs, foster evidence-based decision making, and accelerate the application and translation of advances in medical science to everyday clinical practice. While these are desirable

goals, clinical practice guidelines are not always followed. Nonadherence to guidelines can result from lack of familiarity or lack of agreement on the part of the physician or lack of an appropriate institutional infrastructure to facilitate implementation.

Education for Partnership

The EPR-3 guidelines encourage physicians to provide asthma self-management education so patients have the necessary skills to control their asthma and improve outcomes. The physician should teach and reinforce the following: basic facts about asthma, definition of well-controlled asthma and the patient's current level of control, roles of medications, skills (inhaler/spacer/holding chamber use, self monitoring), when and how to seek quick relief, when and where to seek care, and environmental exposure and control measures. Asthma education should begin at the time of diagnosis and continue through follow-up care as an integral part of asthma management. The Expert Panel recommends self monitoring with peak flow monitoring, symptom monitoring, or both.

Asthma interventions should be tailored to an individual patient's underlying knowledge and beliefs about the disease, and the needs of patients with limited literacy must be considered. Patients will be more willing to adhere to recommendations that are based on a fundamental understanding of the disease reached in partnership with the clinician.

Classifying Asthma Severity

A new paradigm introduced in the guidelines delineates two domains common to both classifying asthma severity and assessing asthma control. These are impairment and risk.

Classifying asthma severity as intermittent or chronic persistent (mild, moderate, or severe) is based on assessment of symptomatology and an objective assessment of lung function. In patients not on controller medications, severity is based primarily on domains of current or recent impairment and future risk. The level of severity is also based on the most severe category in which any feature appears. In

The EPR-3 guidelines encourage physicians to provide asthma self-management education so patients have the necessary skills to control their asthma and improve outcomes.

patients on controller therapies, severity is based on the lowest step required to maintain clinical control, but control of asthma is also based on the domains of current or recent impairment and future risk. For patients who have controlled asthma, severity can be defined, in part, as the minimum amount of medicine necessary to maintain established control. Objective assessment of lung function with FEV₁ and FEV₁ to FVC ratio is also critically important.

In the guidelines, use of oral or systemic corticosteroids is used to define an exacerbation of asthma. In addition to asthma exacerbation, other risks include the risk of progressive decline in lung function and the risk of reduced lung growth in children, as well as the risk of adverse events associated with the use of asthma medications. For purposes of treatment, the Expert Panel decided that any person who had two or more asthma exacerbations within the past 12 months fit into the category of chronic persistent asthma.

The objective in classifying asthma severity is to couple a therapeutic intervention that is appropriate for that level of asthma severity. Patients with intermittent asthma do not require anti-inflammatory controller therapy. However, all patients with chronic persistent asthma do require anti-inflammatory therapy, with ICS being the treatment of choice. Some of these patients will require combination therapy with a LABA. The preferred medications provide the best balance of efficacy and safety for patients at a given level of asthma severity. Therapy must also be tailored to individual patients' needs, circumstances, and responsiveness.

Assessing Asthma Control

Because asthma severity can fluctuate over time, it is important to continuously assess asthma control. Like classifying asthma severity, assessment of asthma control is based on current or recent impairment and future risk. Impairment is assessed with symptomatology, objective assessment of lung function, and validated questionnaires (i.e., ATAQ/ACQ/ACT) to classify asthma as well controlled, not well controlled, or very poorly controlled. Assessment of future risk includes risk of exacerbation, progressive loss of lung function, reduction in lung growth rate in children, and medication-related adverse events. In all patients, it is important to determine whether there are environmental triggers or co-morbid conditions that need to be addressed. Subcutaneous immunotherapy should be considered for all patients with allergic asthma.

If asthma is controlled, the physician

should ensure that control is established for a minimum of 3 months before stepping down therapy. The guidelines recommend decreasing the ICS by 25% to 50% every 3 months to the lowest effective dose, with the understanding that some patients will relapse with total discontinuation of ICS. If asthma is not well controlled, consider environmental triggers, poor adherence to medical regimen, comorbidities, and inhaler technique problems before stepping up therapy. If asthma is very poorly controlled, consider increasing by two steps, prescribing oral corticosteroids, or both.

Monitoring and follow-up are essential for long-term care of patients with asthma. When initiating therapy, patients should be monitored at 2- to 6-week intervals to ensure that asthma control is achieved. Subsequently, patients should be followed up at 1- to 6-month intervals, depending on the level of control. At each follow-up visit, the physician should determine whether the asthma is controlled (i.e., whether the patient is impaired) and whether the patient is at risk for adverse outcomes.

The fluctuation of asthma control over time was demonstrated in a study by Stempel et al., in which more than 70% of patients met one or more criteria for uncontrolled asthma during the 3 years of the study.²⁵ During year 1, 27,229 patients (43%) met one or more of the following criteria for uncontrolled asthma: ≥ 4 SABA prescription claims, ≥ 1 oral corticosteroids prescription claim, and ≥ 1 asthma-related emergency department visit or asthma-related hospitalization. In each quarter during years 2 and 3, 19,431 of the control patients (53%) from year 1 met at least one criterion for uncontrolled asthma in a given quarter.

In summary, long-term management of asthma requires the following: 1) confirm the diagnosis; 2) identify and address relevant environmental factors, co-morbid conditions, and adherence; 3) assess severity or control (impairment and risk) and use step therapy to achieve and maintain control, stepping up therapy if necessary and stepping down therapy when possible; 4) provide asthma self-management education and written asthma action plan; and 5) follow the patient to be sure control is maintained at the lowest effective dose of medications.

Asthma severity, asthma control, and responsiveness to treatment are key elements of assessment and monitoring. The goal of asthma therapy is to achieve control, based on EPR-3 guidelines. ICS are the preferred monotherapy for controller

therapy in patients with persistent asthma, across all ages. LABAs are the preferred adjunctive agents in patients age 12 and over who cannot be controlled on ICS monotherapy. LABAs also may be used in patients under age 12 under special circumstances.

Infrastructure Changes to Facilitate Optimal Asthma Care

The guidelines are based on evidence-based medicine. But the challenge remains to translate these recommendations into real world situations in clinical practice.

The Expert Panel recommends that clinical pathways be considered for the inpatient setting for patients who are admitted to the hospital with asthma exacerbations. In addition, prompts that encourage guideline-based care should be integrated into system-based interventions, focused on improving overall quality of life rather than used as a single intervention strategy.

The guidelines also recommend the use of multifaceted clinician education programs to reinforce guideline-based asthma care. These education programs should be based on interactive learning strategies, such as interactive formats or practice-based case studies (also called problem-based learning).

In conclusion, effective asthma disease management can lead to improved health outcomes for patients and reduced health-care costs. Ultimately, there is a need for infrastructure change within the system.

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Implementing Key Concepts from the 2007 NHLBI/NAEPP Guidelines for the Diagnosis and Management of Asthma

If you wish to receive CME credit and confirmation of your participation, please complete the Self-Assessment Test and the Program Evaluation and mail a photocopy of the completed material to The American College of Allergy, Asthma and Immunology, 85 West Algonquin Road, Suite 550, Arlington Heights, IL 60005, or FAX your Self-Assessment Test to (847) 427-1294. If you attended the 2007 Annual Scientific Meeting and received CME credits for attending the live symposium, you are not eligible to receive credit from this monograph. Your answers will be graded, and you will be advised of passage (or failure). A minimum score of 80% must be achieved in order to earn a certificate of credit. Credits for this CME post-test are available until March 1, 2009.

Self-Assessment Test

For each question or incomplete statement, please select one answer that is correct and enter your choice on the answer sheet on the reverse.

1. In the EPR-3 guidelines, what is the rationale for dividing children into two age groups for pharmacotherapy recommendations?
 - a. Most children younger than 5 years old grow out of asthma.
 - b. Children younger than 5 years old cannot take aerosol medications.
 - c. There has been inadequate assessment of efficacy for most therapies in children younger than 5 years old.
 - d. Most drugs have different toxicity profiles in children younger than 5 years old compared to older children.
2. Why is omalizumab not recommended for allergic patients with moderate persistent asthma?
 - a. It has not been compared to other adjunctive therapy such as LABAs and leukotriene modifiers.
 - b. It has been approved by the FDA only for the treatment of severe persistent asthma.
 - c. It is ineffective in the treatment of moderate persistent asthma.
 - d. It does not provide added benefit when added to high-dose ICS and LABA combination therapy.
3. Why are a low-dose ICS plus a LABA and a medium-dose ICS given equal weight for Step 3 therapy in adults with moderate persistent asthma?
 - a. Combination therapy is more expensive and more difficult to comply with.
 - b. Combination therapy results in an increased risk of asthma exacerbations.
 - c. Recent trials suggest comparable efficacy for both therapies.
 - d. LABAs only improve lung function but not symptoms and exacerbations.
4. What is the new FEV₁ or PEF cut off for a severe asthma exacerbation?
 - a. 20% of predicted
 - b. 25% of predicted
 - c. 40% of predicted
 - d. 50% of predicted
 - e. 60% of predicted
5. Clinicians are encouraged to consider adjunct treatments (such as intravenous magnesium sulfate or heliox) for:
 - a. all patients with asthma exacerbations.
 - b. patients with severe exacerbations.
 - c. patients with moderate-to-severe exacerbations.
 - d. no patients
6. Which of the following statements is false?
 - a. For home management, the guidelines recommend systemic steroids at the first sign of an asthma exacerbation.
 - b. For home management of asthma exacerbations, PEF values of 50% to 79% predicted or personal best indicate the need for quick-relief medication.
 - c. For prehospital management, the guidelines encourage standing orders for albuterol.
 - d. Several randomized trials have demonstrated the value of doubling the dose of ICS at the onset of an asthma exacerbation.
7. Which of the following statements is not true regarding acetaminophen and asthma?
 - a. Acetaminophen reduces lung levels of glutathione.
 - b. Adult women who used acetaminophen > 14 days per month had an increased incidence of asthma.
 - c. A dose relationship has been shown between acetaminophen use by pregnant women and wheezing in their offspring.
 - d. In NHANES III increased acetaminophen use was associated with lower lung function.
 - e. Acetaminophen use has been associated with the incidence of nasal polyps.
8. Which of the following statements is true regarding the relationship between obesity and asthma?
 - a. Overweight/obesity is associated with an increased risk for incident asthma.
 - b. There is an association between overweight/obesity and level of exhaled nitric oxide.
 - c. The association between overweight/obesity and asthma is seen only in women.
 - d. Weight loss in obese asthmatics has not been shown to improve asthma symptoms.
 - e. Obesity is associated with increased response to bronchial methacholine challenge.
9. Which statement is true for studies of immunotherapy in patients with asthma?
 - a. Include more than 10 studies employing multiple allergen mixes.
 - b. Have shown clinical improvement only with perennial allergens.
 - c. Have shown a clear-cut dose response.
 - d. Have been consistently positive.
 - e. Have not included as many as 7 non-cross reacting allergens.
10. If asthma is controlled for a minimum of 3 months and step down therapy is indicated, the guidelines recommend:
 - a. decreasing the ICS by 25% to 50% every 3 months to the lowest effective dose.
 - b. decreasing the ICS by 10% to 25% every month to the lowest effective dose.
 - c. maintaining the dose of ICS for at least 3 more months before decreasing it.
 - d. step down therapy is not recommended.

Continued on reverse.

Answer Sheet

Please place your answers to the test questions in the appropriate box.

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
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Program Evaluation

1. How well organized was this publication? (1 = poor; 2 = fair; 3 = good; 4 = excellent) _____

2. How would you rate the clarity of this publication? (1 = poor; 2 = fair; 3 = good; 4 = excellent) _____

3. Overall, how would you rate the importance of this publication? (4 = very; 3 = moderate; 2 = little; 1 = not at all) _____

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