

Managing Outpatient Asthma Exacerbations

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Abstract Asthma is a chronic inflammatory disease that renders individuals vulnerable to acute exacerbations. A wide variety of allergic and nonallergic triggers can incite an asthma exacerbation. The goals of managing an asthma exacerbation are prompt recognition, rapid reversal of airflow obstruction, avoidance of relapses, and prevention of future episodes. A written asthma home management plan is essential to minimize the severity of exacerbations. Short-acting β -agonists, oxygen, and corticosteroids remain fundamental to early intervention in acute asthma exacerbations. Anticholinergics and magnesium sulfate can help nonresponders. Combination inhalers of the long-acting β -agonist formoterol and inhaled steroid budesonide have been effective in flexible dosing in treating early acute exacerbations and as a daily controller medication outside the United States. Initiation or intensification of long-term controller therapy, treatment of comorbid conditions, trigger avoidance, and prompt follow-up can help prevent relapses. Listening to patient preferences and concerns enhances adherence, and regular follow-up care can help prevent future episodes.

Keywords Asthma · Exacerbation · Status asthmaticus · Acute asthma

Introduction

Asthma is a chronic disease affecting millions of people worldwide. In the United States alone, there were about 22.9 million individuals with asthma in 2007, conferring an estimated financial burden of 19.7 billion dollars in annual health care costs [1]. All asthmatics are at risk of having exacerbations characterized by worsening symptoms, airflow obstruction, and increased rescue bronchodilator need. In 2007, 12.3 million Americans (3.8 million <18 years of age) had an asthma attack. In 2005, 3884 deaths were attributed to asthma. In 2006, 444,000 discharges and 1.7 million emergency department (ED) visits were attributed to asthma. In 2003, asthma accounted for an estimated 10.1 million lost work days among adults. Regrettably, there is a high rate of patient and physician nonadherence to national guidelines for prevention and home management of asthma exacerbation [2, 3]. In this article, we discuss pharmacologic agents available to treat asthma exacerbations, home-based and ED management of asthma exacerbations, recognition and treatment of comorbid conditions, and strategies to prevent exacerbations.

Clinicopathologic Features of Acute Asthma

Asthma is a chronic inflammatory disease of the airways. The airways of an individual with asthma are hyperresponsive to a variety of allergic and nonallergic triggers. Alone or more often in various combinations [4], these triggers can initiate inflammatory cascades activating resident cells (ie, mast cells and airway epithelium) and recruiting a variety of immune cells, including eosinophils and neutrophils. Histamine, leukotrienes, prostaglandins, kinins, cytokines, and granular proteins are among a myriad of substances released that lead

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to epithelial damage, increased mucus production, impaired mucus clearance, vasodilatation, mucosal edema, smooth muscle contraction, and bronchial hyperresponsiveness. The final outcome is narrowed airways and airflow obstruction [5]. This inflammatory process and symptoms may progress gradually over days or suddenly over a few hours. The increased work of breathing through narrowed airways can manifest itself as an elevated respiratory rate; intercostal, subcostal, and suprasternal retractions; and nasal flaring. Tachycardia and pulsus paradoxus may be present. A ventilation–perfusion mismatch may lead to hypoxemia. Air trapping causes hyperinflation of the lungs. Complications of an acute asthma exacerbation may include atelectasis, lobar collapse, pneumonia, pneumothorax, pneumomediastinum, subcutaneous emphysema, hypoxic seizures, and worsening of comorbid cardiopulmonary diseases. With worsening episodes, fatigue, slowing of respirations, a silent chest, cyanosis, altered sensorium, and drowsiness develop; all may portend impending respiratory failure. Delays in instituting appropriate therapy for an asthma exacerbation lead to slower recovery and greater risk of preventable fatalities.

Clinical Assessment

A patient presenting with acute asthma should undergo a rapid focused assessment in conjunction with initiation of specific therapy to reverse airflow obstruction. The history elicited should include duration of symptoms, possible triggers (including occupational exposures and aspirin ingestion), progression of symptoms, nocturnal symptoms, treatments received for the exacerbation, and daily medications. Relevant points in the past history are timing of last exacerbation or prednisone burst, recent ED visits or hospitalizations for asthma, seasonal pattern of exacerbation, viral infections, and comorbid conditions. Vital signs should be taken at baseline and at regular intervals in stable patients or continuously monitored in severe cases. Pulse oximetry to check arterial oxygen saturation is critical to optimal management. Oxygen saturation of less than 92% on room air 1 h after initial treatment is a reliable predictor of the need for hospitalization in children. The physical examination should note overall degree of respiratory distress and condition of the patient, with specific note of accessory muscle use; nasal flaring; signs of dehydration, cyanosis, wheezing, rhonchi, or rales; and air exchange in all lung zones. Level of activity, feeding, and behavior can give clues about an infant or young child's respiratory status. Laryngeal wheeze on auscultation of the neck, with minimal or absent lung findings in any patient complaining of sudden onset of throat tightness and dyspnea, should raise the possibility of vocal cord dysfunction (VCD), which often coexists and sometimes mimics asthma [6].

Objective measures to confirm and assess airflow obstruction include peak expiratory flow rate (PEFR) and forced expiratory volume in 1 s (FEV₁). In a proportion of asthmatics, PEFRs do not correlate with symptoms of airflow obstruction. Hence, the new asthma guidelines encourage the use of FEV₁ for objective measurement in most settings. PEFR or FEV₁ less than 40% of predicted or personal best indicates severe airflow obstruction. Forced expiratory maneuvers can aggravate the bronchoconstriction in some cases. Classification of the severity of an asthma exacerbation has been developed by national and international guidelines [7, 8]. Serial measurements of lung function are very useful to monitor response to therapy.

Patients showing fatigue, hypoxia, and PEFR or FEV₁ less than 40% of predicted or personal best should have arterial blood gas checked. Most patients with acute asthma have low PCO₂ and respiratory alkalosis due to high respiratory rates, but with worsening, they may have normal and then high PCO₂ levels and respiratory acidosis, reflecting progressive carbon dioxide retention. Patients in impending respiratory failure can have PCO₂ levels greater than 100 mm Hg. Any patient with a PCO₂ greater than 42 mm Hg should be considered to have severe airflow limitation. Chest x-ray may be required to check for several possible complications of asthma if prompted by examination findings and a lack of improvement despite treatment. Older patients with severe respiratory distress should have an electrocardiogram.

Pharmacologic Treatment of Asthma Exacerbations

β-Adrenergic Agonists

Short-acting, inhaled, selective β₂-adrenergic agonists remain the mainstay of acute asthma therapy. Their main action is to mediate airway smooth muscle relaxation by binding the β₂-adrenergic receptors. The most commonly used agents in this class of drugs are albuterol and pirbuterol. The onset of action for albuterol is within 5 min, and the duration is typically 4 to 6 h.

The established treatment for reversing airflow obstruction has been a short-acting β₂-agonist given by a small-volume jet nebulizer, but several recent studies reported the equivalent efficacy of a metered-dose inhaler (MDI) using a volume holding chamber or spacer [9, 10]. A systematic review concluded that these delivery devices produce similar outcomes [11]. Using the MDI and spacer may be faster, may result in fewer β-mediated side effects, and may be more cost-effective, but one has to keep track of how many doses have been delivered to avoid using an empty inhaler if it does not have a dose counter. Cleaning of the spacer is required, as dysfunctional valves and static charges in some spacers can markedly drop the dose delivered. Using the

MDI and spacer with a mouthpiece is more effective than using an MDI with a facemask alone.

Only 6 to 8 puffs (540–720 µg) of albuterol from the MDI may be sufficient to achieve an effect equivalent to that of 2.5 mg of nebulized albuterol. Such practice has become widespread in emergency care settings. Because excessive β_2 -agonist use has been implicated in masking the progression of asthma attacks, causing delays in seeking medical care, reducing bronchoprotection, and increasing airway reactivity—all leading to a risk for fatal or near-fatal asthma attacks—we must be cautious [12]. We must be particular about instructing our patients or parents of children with asthma to refrain from using “many” puffs of albuterol at home unless instructed to do so during an acute episode by their physician. Done correctly, the use of albuterol with an MDI and spacer during an asthma exacerbation can curb unnecessary ED visits, but excessive albuterol use, especially with inadequate provision of corticosteroids (CS), may lead to prolonged morbidity and avoidable mortality.

Racemic albuterol is a 50:50 mixture of the S-isomer and R-isomer of albuterol. All the activity of racemic albuterol resides in its R-isomer. S-albuterol has a much higher systemic absorption and a longer half-life than R-albuterol. This results in higher systemic levels and accumulation in the lungs, leading to the possibility that in the course of administration of high doses of racemic albuterol, some of the reduced effectiveness of β_2 -agonists might be due to the accumulation of the S-isomer [13]. However, continuous nebulization with levalbuterol showed no advantages over racemic albuterol with regard to adverse effects or total time of treatment in the inpatient setting for pediatric *status asthmaticus* [14].

Long-acting β -agonists (LABAs) such as salmeterol and formoterol are currently recommended as add-on therapy with inhaled CS (ICS) for moderate to severe asthma in the National Asthma Guidelines [7]. Salmeterol has a slower onset of action compared with formoterol, which causes bronchodilation within minutes. The systemic activity of formoterol is comparable to that of salbutamol or terbutaline, whereas that for salmeterol is long-lasting; hence, repetitive dosing of salmeterol is not advisable. The duration of action for both is 12 h. Concerns have been raised that if LABAs are used as needed in the acute setting, they might mask severe or progressive asthma episodes, thus delaying appropriate medical care and resulting in more fatal outcomes than past experience with fenoterol and isoproterenol might suggest. The use of formoterol with budesonide in a single device, as a daily controller therapy (1 or 2 puffs twice daily) with as-needed doubling or quadrupling of dosage (to a maximum of 8 puffs/d) during acute asthma exacerbations in adults has been shown to be efficacious, leading to its inclusion in the Global Initiative for Asthma summary guidelines [8]. The flexibility of a single combination as both a daily controller

and for early management of outpatient asthma exacerbations can lead to lower total burden of CS exposure and provide prompt escalation of anti-inflammatory and bronchodilatory therapies during acute exacerbations. In the United States, however, the currently available LABA plus inhaled CS combinations are not indicated for use during asthma exacerbations at higher-than-recommended maintenance doses.

Oxygen

Humidified oxygen helps relieve dyspnea, aids in bronchodilation, and supports the myocardium in acute asthma. Mild hypoxemia usually can be corrected by 2 to 4 L/min of oxygen via a nasal cannula. One pediatric study found that infants and young children with an oxygen saturation of less than 92% on room air were at increased risk for hospitalization during an asthma exacerbation [15]. Oxygen should be used to nebulize medications in acute asthma. Some patients who have normal pulse oximetry on first presentation develop hypoxemia following bronchodilator therapy due to ventilation–perfusion mismatch. Oxygen therapy helps correct this problem. One study raised the concern that 100% oxygen administered to acutely ill patients with severe airflow limitation may contribute to hypercapnia [16]. Controlled oxygen administration titrated with continuous pulse oximetry is invaluable in acute asthma care.

Corticosteroids

CS are essential to the treatment of asthma exacerbations. Their role as controller therapy in asthma is very well recognized. In addition to wide-ranging anti-inflammatory effects, systemic CS can help overcome β_2 -receptor subsensitivity and upregulate β_2 -receptor expression on airway smooth muscle. They need at least several hours to show an effect in acute asthma. Given within the first hour of arrival to the ED, systemic CS can significantly reduce hospitalizations [17]. Several studies in adults and children have demonstrated equivalent effectiveness of oral and intravenous (IV) CS in treating acute asthma [18]. Some indications for IV CS use are severe respiratory distress, impending respiratory failure, severe hypoxemia, and inability to tolerate oral CS. In such situations, methylprednisolone can be used at an initial loading dose of 2 mg/kg (maximum, 120 mg) followed by 0.5 to 1 mg/kg every 6 h for the first 48 h, and then replaced by oral CS. The oral CS doses recommended are 2 mg/kg per day in two divided doses, with a maximum dose of 60 mg/d for most children and 80 mg/d for adults. Most 3- to 10-day steroid bursts do not need to be tapered [19]. The exceptions are when the patient is on chronic daily or every other day oral steroid therapy or has recently completed another prednisone burst.

This short course of oral CS significantly reduces the number of relapses to additional care in the weeks following discharge from the ED and decreases β -agonist use without an apparent increase in side effects [20]. Intramuscular corticosteroids (IMCS) such as dexamethasone, methylprednisolone, or betamethasone may be given as a one-time dose in patients who are likely to have difficulty obtaining oral CS after ED discharge. The increased risk of local pain and bruising should be explained to patients receiving IMCS [21••].

ICS are best used for long-term control of asthma wherein their effect can usually be seen in 3 to 4 weeks. Several pediatric and adult studies have examined the role of high-dose ICS in ED treatment of acute asthma [22, 23]. One randomized, double-blind study that treated severe asthmatics experiencing an acute exacerbation with oral CS or ICS found oral CS to be superior in reducing hospital admissions [24]. A systematic review concluded that ICS can reduce hospital admission rates in patients with acute asthma, but there is no clear benefit when they are used in addition to systemic steroids. There is insufficient evidence to indicate that ICS alone are as effective as systemic CS [25]. Although very high doses of ICS may be an option for managing mild asthma exacerbations, they are probably best used as an adjunct to an oral CS burst for more severe exacerbations and prevention of relapses [22, 26]. Cheaper and easily administered, short bursts of oral CS remain the cornerstone of anti-inflammatory therapy for acute asthma.

Anticholinergics

Cholinergic innervation is a major controller of the bronchomotor tone. Cholinergic muscarinic receptors can mediate bronchoconstriction (M_3) and antagonize the bronchoconstrictive effect via M_2 receptors. The quaternary ammonium derivative of atropine, ipratropium bromide, is a nonspecific muscarinic receptor-blocking agent that has been used to treat bronchospasm in acute asthma. It has marginal effectiveness in acute asthma when used as monotherapy. Combining ipratropium bromide with a short-acting β -agonist in several pediatric and adult studies has reduced hospitalization rates and led to improved lung function compared with albuterol alone [27, 28]. A recent meta-analysis found modest benefit from the addition of ipratropium bromide to β -agonists in the treatment of acute asthma in adults [29]. The recommended nebulized dose is 250 μ g in children and 500 μ g in adolescents and adults, used up to every 20 min for the first hour of treatment with albuterol. Its onset of action is 20 to 30 min and duration of action is 4 h. Less than 1% of patients may experience paradoxical bronchoconstriction with the use of ipratropium, and they need to be taken off it. Nebulized anticholinergics are

most valuable as add-on therapy for severe asthma exacerbations not responding to β_2 -agonists alone. Magnesium sulfate given intravenously in the ED for severe acute asthma exacerbation can have a role in certain cases [30].

Parenteral Bronchodilators

The use of parenteral aminophylline, terbutaline, and epinephrine in acute asthma has fallen out of favor due to the greater risk of side effects such as tachyarrhythmias, tremors, anxiety, vomiting, and myocardial ischemia compared with inhaled β_2 -adrenergic agonists. Despite its anti-inflammatory properties and a different mechanism of action, a recent systematic review found no further bronchodilation when IV aminophylline was used in addition to β -agonists in adults [31]. Another systematic review found no added benefits to the use of IV β_2 -agonists over standard inhaled bronchodilator therapy [32]. However, an uncooperative patient or one who cannot use aerosolized delivery devices and who has severe airflow obstruction might benefit from a subcutaneous injection of epinephrine or terbutaline. This may provide sufficient bronchodilation for subsequent inhaled bronchodilator treatments to take effect and prevent intubation.

Leukotriene Receptor Antagonists

The value of zafirlukast and montelukast in chronic asthma therapy is recognized. Additional studies are needed to evaluate the efficacy and safety of leukotriene modifiers in adults with acute asthma after ED discharge [21••]. We recommend using them as daily controller asthma therapy per current US Food and Drug Administration recommendations.

Heliox

Heliox is a mixture of helium and oxygen (60:40, 70:30, or 80:20) that is lighter and less dense than oxygen. It is believed that breathing this lighter gas mixture can reduce the work of breathing, as it creates less turbulence in narrowed asthmatic airways. Studies have yielded varying results with regard to its utility in acute asthma, with a systematic review concluding that heliox treatment does not have a role in the initial treatment of patients with moderate or severe acute asthma [33]. Heliox used to administer nebulized β -agonists instead of oxygen has been reported to result in greater increases in FEV₁, probably due to better drug delivery to the distal airways; this strategy deserves a closer look [34]. The current asthma guidelines reserve heliox for severe exacerbations unresponsive to the usual therapies listed previously [7]. Heliox (70:30) has been helpful in the treatment of exacerbations of VCD with or without asthma.

Other Supportive Care

Hydration during acute asthma exacerbation usually can be maintained by encouraging oral intake of fluids. Patients who have been sick for days with increased insensible losses due to fast respiratory rates, poor oral intake, and vomiting might be dehydrated. Fluid replacement should be at or just below maintenance. Overzealous rehydration could lead to pulmonary edema in the face of excessive antidiuretic hormone release that is sometimes seen with *status asthmaticus*. There is no compelling evidence to support the routine use of methylxanthines, mucolytics, chest percussion therapy, or sedation during an acute asthma exacerbation.

Home Management of Asthma Exacerbation

The key to successful management of an asthma exacerbation is early recognition with prompt initiation of medical therapy. All patients diagnosed with asthma should have a written asthma action plan to guide them. Education of patients or their caregivers to recognize common triggers such as viral upper respiratory infections and/or allergens is necessary. If exposed, patients should remove themselves or the asthmatic child from the environment with possible triggers and start daily and as-needed PEFr monitoring to identify a downward trend or wide diurnal fluctuations (>20%), which may precede frank symptoms. Persistent cough, chest tightness, wheeze, shortness of breath, and PEFr of less than 80% of predicted or personal best should prompt treatment with 2 to 6 puffs of their short-acting rescue bronchodilator MDI with a spacer or a single nebulized bronchodilator treatment. If symptoms persist 20 min after the treatment or worsen, or if PEFr remains less than 80% of personal best, patients should repeat the treatment and call their physician. Patients should be provided with a 24-hour telephone number and encouraged to contact their physician. If symptoms improve and do not recur, no further action is needed. A few indications for initiating a 3- to 10-day oral CS burst at home for symptomatic patients with PEFr greater than 50% but less than 80% of predicted or personal best include recurrent symptoms requiring every 4- to 6-hourly bronchodilator treatments, nocturnal awakening with asthma symptoms, and prolonged symptoms or limitation of activities. Telephone follow-up in 24 to 48 h can reassure the patient and the physician that the situation is improving after initiation of a CS burst. If that is not the case, the patient should be brought to the office/ED for evaluation. Patients with PEFr of less than 50% predicted or personal best, marked wheezing, or shortness of breath should continue to take nebulized bronchodilator therapy, initiate oral CS, and proceed to the ED.

A common empiric practice in the home management of mild asthma exacerbations has been to double the dose of

inhaled steroids. One study evaluated this practice and found it of no value and found that it can delay proper care [35]. In the future, doubling or quadrupling the dose of the combination formoterol plus budesonide inhaler may be an option for early intervention in asthma exacerbations. A 3-day burst of oral prednisone/prednisolone may be more appropriate in other situations.

Physician's Office or ED Management of Asthma Exacerbation

Treatment of asthma in the ED has not been standardized. The therapeutic benefits and cost-saving potential of an interactive care plan using decision algorithms based on serial measures of patient progress have been demonstrated [36]. The Expert Panel Report 3 has provided an algorithm for the management of asthma exacerbations in the ED or hospital-based setting (Fig. 1). Patients who do not respond to initial treatments or who are in severe respiratory distress in an office setting should be transported to the ED. The first and most crucial step is to differentiate patients with impending respiratory failure from all others. The management of such seriously ill patients requiring ventilatory support is beyond the scope of this article. All other patients must be aggressively treated with bronchodilators, oxygen, and oral CS during the first hour to help judge their disposition. Patients who have not shown improvement after initial albuterol treatment should receive albuterol plus ipratropium. Oral CS should be administered within the first hour. Patients who do not show improvement after three bronchodilator treatments are unlikely to improve with more treatments in the ED and should be considered for hospitalization. Higher doses (5–10 mg) and preferably continuous albuterol nebulization (7.5–15 mg/h) seem to be more effective in severe asthmatic exacerbations [37, 38]. Side effects such as tachycardia, tremors, and hypokalemia tend to be more frequent with higher dosing schedules, necessitating closer monitoring.

Patients who show slow but steady improvement can be treated further in the ED for up to 1 to 3 h. Patients who get worse in the course of therapy need an arterial blood gas. The decision to intubate a patient should be based on clinical signs and symptoms of impending respiratory failure. The indications for hospitalization for acute asthma exacerbation have been summarized in Table 1.

It is important to combine serially assessed clinical and objective criteria when making the decision to discharge a patient home. Resolution of symptoms per patient (eg, no shortness of breath or chest tightness), absence of accessory muscle use, normal oxygen saturation on room air, and PEFr or FEV₁ ≥70% of predicted or personal best all taken together are good indicators of readiness for discharge for

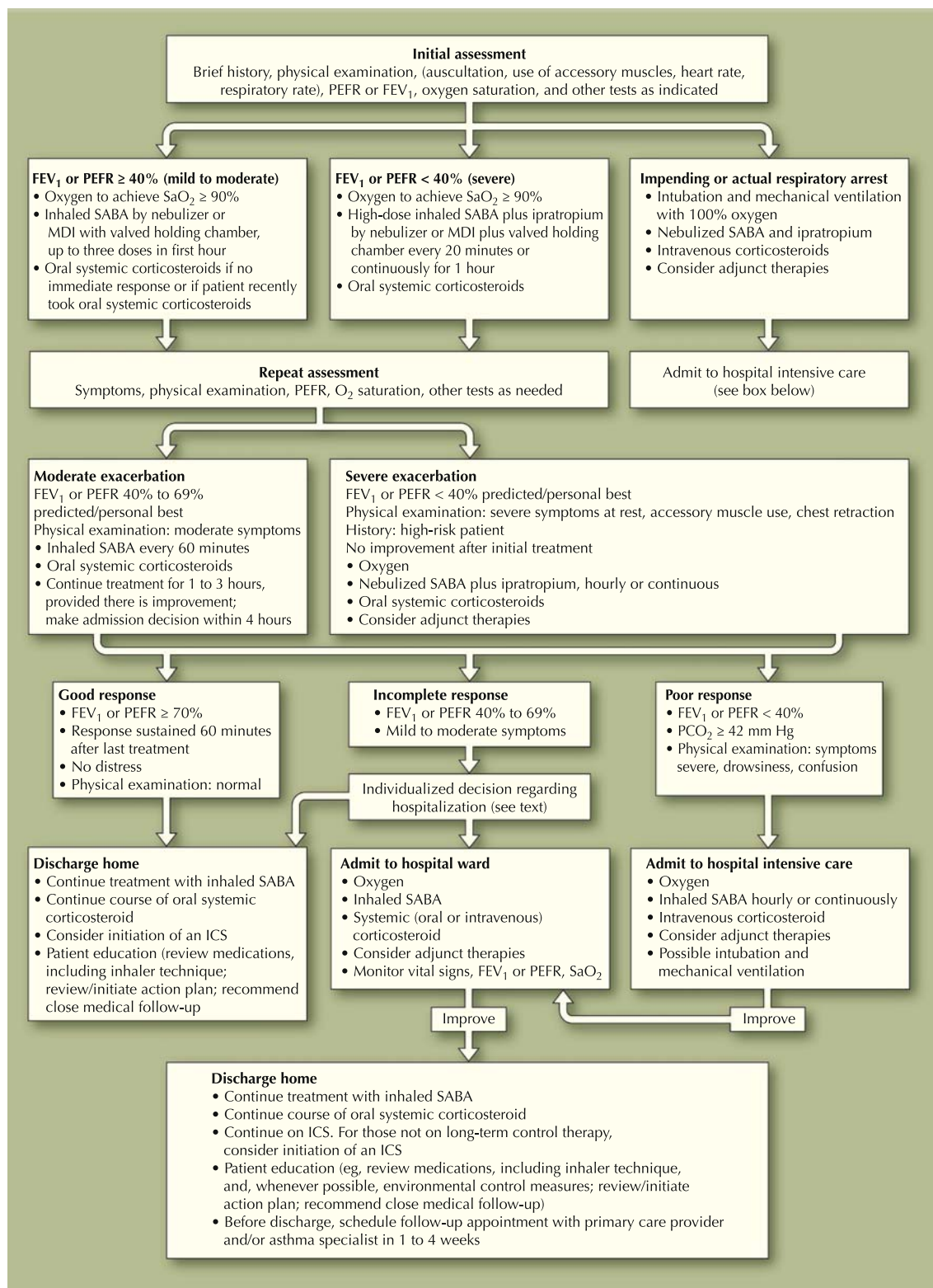


Fig. 1 Management of asthma exacerbations: emergency department- and hospital-based care. FEV₁ forced expiratory volume in 1 s, ICS inhaled corticosteroid, MDI metered-dose inhaler, PEFR peak expira-

tory flow rate, SABA short-acting β -agonist. (From National Asthma Education and Prevention Program Expert Panel Report 3 [7]; with permission.)

Table 1 Indications for hospitalization for an acute asthma exacerbation^a

FEV₁ forced expiratory volume in 1 s, *ICU* intensive care unit, *PEFR* peak expiratory flow rate

^a Using objective criteria such as *PEFR/FEV₁* with symptoms and clinical assessment rather than relying on subjective judgement alone can reduce relapses of discharged patients and unnecessary hospitalizations

^b Indication for admission to the ICU

<i>FEV₁/PEFR</i> <60% of predicted or personal best with ongoing symptoms despite aggressive treatment
<i>FEV₁</i> <30% with marked respiratory distress ^b
Worsening symptoms despite aggressive treatment ^b
Oxygen saturation <90% on room air for adults and <92% for children
<i>PaCO₂</i> >42 mm Hg and/or <i>PaO₂</i> <60 mm Hg ^b
Impending respiratory failure ^b
Multiple recent asthma-related visits to the emergency department or physician's office
Recent hospitalization for asthma
History of ICU admission or intubation with mechanical ventilation for asthma
Prolonged duration of symptoms
Multiple triggers
Poor access to medications and medical follow-up
Lack of understanding of the disease and its management
Psychiatric or psychosocial conditions that may interfere with medical adherence
High-risk status or history of near-fatal asthma ^b

most patients. Some patients may still have some wheezing, but as long as they meet the above criteria, they can be discharged home. It seems prudent to observe a patient who has received more than three bronchodilator treatments in the ED for at least 1 h and sometimes longer to confirm sustained improvement before discharge. A written ED asthma discharge plan and a review of inhaler techniques and medication prescriptions, including ICS, should be provided to prevent relapses (Fig. 2). The Joint Task Force Report for Management and Follow-up of Asthma Exacerbations recommends initiating daily ICS (in patients not currently taking one) or continuing daily ICS (in patients already taking one) on ED discharge (in addition to short oral CS burst) for patients with a history compatible with persistent asthma [22]. One study reported relapses or “bounce backs” in 17% of all ED discharges for acute asthma in the 2 weeks following discharge [39]. Many emergency or urgent care visits for asthma in the past year, availability of a home nebulizer, and longer duration of symptoms (1–7 days) were some of the risk factors for relapses in these adults [40]. A 24- to 48-hour telephone follow-up might enhance adherence to therapy and identify poor responders. A follow-up in person within 1 week of discharge with the primary care physician or asthma specialist is essential. Follow-up with an asthma specialist or a specialized asthma clinic seems more likely to reduce subsequent emergency hospital care than follow-up with a primary care provider.

Patients with a history of severe asthma, a near-fatal asthma episode, or risk factors for near-fatal or fatal asthma need more stringent improvement criteria, such as *PEFR/FEV₁* greater than 70% predicted and longer observation in the ED, before they can be discharged (Table 2). We must remember that any patient with a history of near-fatal asthma is at high risk for a repeat episode, which

could be fatal and hence should be managed aggressively [41].

Recognizing and Treating Comorbid Conditions

Certain conditions can make acute asthma difficult to manage, mimic it, and increase relapses. One condition that has been frequently mistaken for asthma in the acute setting and more commonly coexists with acute asthma is VCD [42]. VCD causes acute upper airway obstruction due to paradoxical vocal cord adduction on inspiration. VCD has been classically described in young women and elite athletes. VCD episodes tend to be triggered by strong emotions, exercise, and inhaled irritants. Typically, they have a sudden and rapid onset, sometimes followed by progression to severe respiratory distress within minutes. This scenario commonly prompts a paramedic or ED physician to intubate the patient, resulting in rapid resolution of symptoms. Such patients are often mistakenly labeled as severe, high-risk asthmatics and are treated ill-advisedly. Others with less dramatic presentations complain of shortness of breath, chest tightness, cough, wheeze, and dysphonia. Patients with only VCD have normal oxygen saturations. Spirometry during an episode reveals a low to normal *FEV₁*, with a normal *FEV₁/forced vital capacity* ratio and irregularities of the inspiratory loops. Patients suffering from asthma and VCD demonstrate airflow obstruction in addition to irregular inspiratory loops. A diagnosis of VCD can be confirmed by visualization of the narrowed glottic opening with a characteristic posterior diamond-shaped chink during an acute episode using a fiberoptic laryngoscope. Empiric treatment involves calming the patient; slow, relaxed abdominal breathing exercises; and heliox. Referral to a speech therapist knowledgeable in VCD and its treatment is very beneficial [43].

Fig. 2 Emergency department asthma discharge plan
(From National Asthma Education and Prevention Program Expert Panel Report 3 [7]; with permission.)

EMERGENCY DEPARTMENT ASTHMA DISCHARGE PLAN

Name: _____ was seen by **Dr.** _____ on ____/____/____

- Take your prescribed medications as directed—do not delay!
- Asthma attacks like this one can be prevented with a long-term treatment plan.
- Even when you feel well, you may need daily medicine to keep your asthma in good control and prevent attacks.
- Visit your doctor or other health care provider as soon as you can to discuss how to control your asthma and to develop your own action plan.

Your follow-up appointment with _____ is on ____/____/____ **Telephone:** _____

YOUR MEDICINE FOR THIS ASTHMA ATTACK IS:

Medication	Amount	Doses/d, for # days
Prednisone/prednisolone (oral corticosteroid)		____ a day for ____ days. Take the entire prescription, even when you start to feel better.
Inhaled albuterol		____ puffs every 4 to 6 hours if you have symptoms, for ____ days

YOUR DAILY MEDICINE FOR LONG-TERM CONTROL AND PREVENTING ATTACKS IS:

Medication	Amount	Doses/d, for # days
Inhaled corticosteroids		

YOUR QUICK-RELIEF MEDICINE WHEN YOU HAVE SYMPTOMS IS:

Medication	Amount	Doses/d, for # days
Inhaled albuterol		

ASK YOURSELF 2 OR 3 TIMES PER DAY, EVERY DAY, FOR AT LEAST 1 WEEK:
“How good is my asthma compared with when I left the hospital?”

If you feel much better: • Take your daily long-term control medicine	If you feel better but still need your quick-relief inhaler often: • Take your daily long-term control medicine • See your doctor as soon as possible	If you feel about the same: • Use your quick-relief inhaler • Take your daily long-term control medicine • See your doctor as soon as possible—do not delay!	If you feel worse: • Use your quick-relief inhaler • Take your daily long-term control medicine • Immediately go to the emergency department or call 9-1-1
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YOUR ASTHMA IS UNDER CONTROL WHEN YOU:

1 Can be active daily and sleep through the night	2 Need fewer than four doses of quick-relief medicine in a week	3 Are free of shortness of breath, wheeze, and cough	4 Achieve an acceptable “peak flow” (discuss with your health care provider)
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Table 2 Risk factors for fatal and near-fatal asthma^a

Previous episode of the following:
Near-fatal asthma requiring intubation and mechanical ventilation [47]
Asthma with hypoxic seizure and loss of consciousness
Sudden, severe asthma attacks with rapid deterioration
History of anaphylaxis due to food, insect sting, or medications in an asthmatic patient
Blunted perception of dyspnea [48]
Decreased chemosensitivity to hypoxia
Denial of severity of illness
Hospitalization or emergency department visit for asthma in past month
3 or more emergency department visits in the past year
2 or more hospitalizations in the past year
Lack of a written asthma action plan and sensitivity to <i>Alternaria</i> spp mold
Advanced age
Poor compliance with or lack of anti-inflammatory controller therapy
Use of >1 canister of β -agonist/mo [42]
Escalating β -agonist use [42]
Comorbid depression or other psychiatric diagnosis
History of alcoholism or illicit drug use
Comorbid cardiac disease
Dysfunctional family unit
Low socioeconomic status and inner-city residence
Poor access to medical care
Nonwhite ethnic background (African American, Hispanic, or Asian)

^a Mild, moderate, and severe asthmatics are all at risk of fatal asthma episodes. Recognizing some of the indicators that predispose a patient to have serious asthma exacerbations is the first step in intervening to prevent bad outcomes

Prevention: The Best Cure

The best way to manage an acute asthma exacerbation is to prevent it. Careful avoidance of allergens, reducing or eliminating environmental tobacco smoke exposure, and smoking cessation are most beneficial.

Emphasis on daily controller therapy is of utmost importance. Listening to patient preferences regarding choice of controller medication improves adherence to therapy. A significant proportion of patients presenting to the ED for acute asthma are not on any anti-inflammatory medications, have poorly controlled asthma, and will never see any physician outside the ED [44]. Initiating or intensifying ICS therapy and stressing daily, uninterrupted use can make a significant impact on emergent asthma care expenditure. Annual influenza immunization 4 to 6 weeks before “flu” season as well as H1N1 immunization can reduce acute asthma cases caused by these common triggers. Influenza vaccination can be safely given to asthmatics even during an acute exacerbation [45].

Identifying patients with risk factors for near-fatal or fatal asthma is paramount in preventing fatalities and exacerbations (Table 2). Addressing these issues (eg, by referring a depressed patient to a psychiatrist or teaching a patient with poor perception of dyspnea to regularly follow objective measures of airflow obstruction, such as PEFr) could save lives.

A written asthma action plan is crucial to reducing office or ED visits for acute asthma [46]. An action plan should include symptoms and objective measures such as PEFr to aid in early recognition of exacerbation and its severity. Simple and clear medication instructions, physician contact numbers, and emergency care steps must be included. Patients tend to forget when and how to use these treatment plans, so reiterate the asthma action plan at each office visit and review the various medications, inhaler techniques, and PEFr measurement with the patient. Most patients can be given a prescription for an oral CS to be kept at home and instructed on using it as per physician directions only.

Conclusions

Preventing asthma exacerbations is the most effective way to manage them. Those cases that end up in a physician’s office or ED must be promptly evaluated and aggressively treated using clinical and objective parameters to guide therapy.

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References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. American Lung Association: Asthma in adults fact sheet. Available at <http://www.lungusa.org/lung-disease/asthma/resources/facts-and-figures/asthma-in-adults.html>. Accessed October 25, 2009.
2. Scarfone RJ, Zorc JJ, Capraro GA: Patient self-management of acute asthma: adherence to National Guidelines a decade later. *Pediatrics* 2001, 108:1332–1338.
3. Warman KL, Silver EJ, McCourt MP, Stein REK: How does home management of asthma exacerbations by parents of inner-city children differ from NHLBI guideline recommendations. *Pediatrics* 1999, 103:422–427.
4. Green RM, Custovic A, Sanderson G, et al.: Synergism between allergens and viruses and risk of hospital admission with asthma: case-control study. *BMJ* 2002, 324:1–5.
5. McFadden ER Jr, Hejal RB: The pathobiology of acute asthma. *Clin Chest Med* 2000, 21:213–224.
6. Milgrom H, Wood RP II, Ingram D: Respiratory conditions that mimic asthma. *Immunol Allergy Clin North Am* 1998, 18:113–132.
7. National Asthma Education and Prevention Program: Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Treatment of Asthma—Summary Report 2007. *J Allergy Clin Immunol* 2007, 120(Suppl):S94–S138.
8. Bateman ED, Hurd SS, Barnes PJ, et al.: Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008, 31:143–178.
9. Idris AH, McDermott MF, Raucci JC, et al.: Emergency department treatment of severe asthma, metered dose inhaler is equivalent in effectiveness to nebulizer. *Chest* 1993, 103:665–672.
10. Closa RM, Ceballos JM, Fomez-Papi A, et al.: Efficacy of bronchodilators administered by nebulizers versus spacer devices in infants with acute wheezing. *Pediatr Pulmonol* 1998, 26:344–348.
11. Cates CJ, Rowe BH, Bara A: Holding chambers versus nebulizers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev* 2002, 2:CD000052.
12. Beasley R, Crane J, Buess C: Beta-agonists: what is the evidence that their use increases the risk of asthma morbidity and mortality. *J Allergy Clin Immunol* 1999, 103:S18–S30.
13. Ahrens R, Weinberger M: Levalbuterol and racemic albuterol: are there therapeutic differences? *J Allergy Clin Immunol* 2001, 108:681–684.
14. Andrews T, McGintee E, Mittal MK, et al.: High-dose continuous nebulized levalbuterol for pediatric status asthmaticus: a randomized trial. *J Pediatr* 2009, 155:205–210.
15. Geelhoed GC, Landau LI, LeSouef PN: Evaluation of SaO₂ as a predictor of outcome in 280 children presenting with acute asthma. *Ann Emerg Med* 1994, 23:1236–1241.
16. Chien JW, Ciuffo R, Novak R, et al.: Uncontrolled oxygen administration and respiratory failure in acute asthma. *Chest* 2000, 117:728–733.
17. Rowe BH, Spooner C, Ducharme FM, et al.: Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev* 2002, 2:CD002178.
18. Ratto D, Alfaro C, Sipsey J, et al.: Are intravenous corticosteroids required in status asthmaticus. *JAMA* 1988, 260:527–529.
19. O'Driscoll BR, Karla S, Wison M, et al.: Double blind trial of steroid tapering in acute asthma. *Lancet* 1993, 341:324–327.
20. Rowe BH, Spooner CH, Ducharme FM, et al.: Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database Syst Rev* 2000, 2:CD000195.
21. •• Schatz M, Kazzi AA, Brenner B, et al.: Joint Task Force Report: supplemental recommendations for the management and follow-up of asthma exacerbations. *J Allergy Clin Immunol* 2009, 124:S1–S4. *This is a state-of-the-art, in-depth review of literature with categorical recommendations related to asthma exacerbation management and follow-up. It is the first-ever official joint statement from the American Academy of Allergy, Asthma, and Immunology; the American Academy of Emergency Medicine; and the American Thoracic Society.*
22. Rodrigo G, Rodrigo C: Inhaled flunisolide for acute severe asthma. *Am J Respir Crit Care Med* 1998, 157:698–703.
23. Volvovitz B, Bentur L, Finkelstein Y, et al.: Effectiveness and safety of inhaled corticosteroids in controlling acute asthma attacks in children who were treated in the emergency department: a controlled comparative study with oral prednisolone. *J Allergy Clin Immunol* 1998, 102:605–609.
24. Schuh S, Reisman J, Alshehri M, et al.: A comparison of inhaled fluticasone and oral prednisone for children with severe acute asthma. *N Engl J Med* 2000, 343:689–694.
25. Edmonds ML, Camargo CA Jr, Pollack CV Jr, Rowe BH: Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database Syst Rev* 2003, 3:CD002308.
26. Rowe BH, Bota GW, Fabris L, et al.: Inhaled budesonide in addition to oral corticosteroids to prevent relapse following discharge from the emergency department: a randomized controlled trial. *JAMA* 1999, 281:2119–2126.
27. Qureshi F, Pestian J, Darius P, Zaritsky A: Effect of nebulized ipratropium on the hospitalization rates of children with asthma. *N Engl J Med* 1998, 339:1030–1035.
28. Rodrigo GJ, Rodrigo C: First-line therapy for adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. *Am J Respir Crit Care Med* 2000, 161:1862–1868.
29. Stoodley RG, Aaron SD, Dales RE: The role of ipratropium bromide in the emergency management of acute asthma exacerbation: meta-analysis of randomized clinical trials. *Ann Emerg Med* 1999, 34:8–18.
30. Rowe BH, Bretzlaff JA, Bourdon C, et al.: Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev* 2000, 2:CD001490.
31. Parameshwaran K, Belda J, Rowe BH: Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma. *Cochrane Database Syst Rev* 2000, 4:CD002742.
32. Travers A, Jones AP, Kelly K, et al.: Intravenous beta2-agonists for acute asthma in the emergency department. *Cochrane Database Syst Rev* 2001, 2:CD002988.
33. Rodrigo G, Rodrigo C, Pollack C, Rowe B: Helium-oxygen mixture for non-intubated acute asthma patients. *Cochrane Database Syst Rev* 2006, 4:CD002884.
34. Kress JP, Noth I, Gehlbach BK, et al.: The utility of albuterol nebulized with heliox during acute asthma exacerbations. *Am J Respir Crit Care Med* 2002, 165:1317–1321.
35. Garrett J, Williams S, Wong C, Holdaway D: Treatment of acute asthmatic exacerbations with an increased dose of inhaled steroid. *Arch Dis Child* 1998, 79:12–17.
36. McFadden ER Jr, Elsanadi N, Dixon L, et al.: Protocol therapy for acute asthma: therapeutic benefits and cost savings. *Am J Med* 1995, 99:651–661.
37. Shreshta M, Bidadi K, Gourlay S, Hayes J: Continuous vs intermittent albuterol at high and low doses, in the treatment of acute severe asthma in adults. *Chest* 1996, 110:42–47.

38. Schuh S, Parkin P, Rajan A, et al.: High versus low dose, frequently administered nebulized albuterol in children with severe acute asthma. *Pediatrics* 1989, 83:513–518.
39. Emerman CL, Cydulka RK: Factors associated with relapse after emergency department treatment of acute asthma. *Ann Emerg Med* 1995, 26:6–11.
40. Emerman CL, Woodruff PG, Cydulka RK, et al.: Prospective multicenter study of relapse following treatment for acute asthma among adults presenting to the emergency department. *Chest* 1999, 115:919–927.
41. Marquette CH, Saulnier F, Leroy O, et al.: Long term prognosis of near fatal asthma. A 6-year follow-up study of 145 asthmatic patients who underwent mechanical ventilation for a near-fatal attack of asthma. *Am Rev Respir Dis* 1992, 46:76–81.
42. Newman KB, Mason UG, Schmalzing KB: Clinical features of vocal cord dysfunction. *Am J Respir Crit Care Med* 1995, 152:1382–1386.
43. Wood RP 2nd, Milgrom H: Vocal cord dysfunction. *J Allergy Clin Immunol* 1996, 98:481–485.
44. Mak H, Johnston P, Abbey H, et al.: Prevalence of asthma and health service utilization of asthmatic children in an inner city. *J Allergy Clin Immunol* 1982, 70:367–372.
45. Park CL, Frank AL, Sullivan M, et al.: Influenza vaccination of children during acute asthma exacerbation and concurrent prednisone therapy. *Pediatrics* 1996, 98:196–200.
46. Lieu TA, Quesenberry CP, Capra M, et al.: Outpatient management practices associated with reduced risk of pediatric asthma hospitalization and emergency department visits. *Pediatrics* 1997, 100:334–341.
47. Magadle R, Berar-Yanay N, Weiner P: The risk of hospitalization and near-fatal and fatal asthma in relation to perception of dyspnea. *Chest* 2002, 121:329–333.
48. Suissa S, Blais L, Ernst P: Patterns of increasing beta-agonist use and the risk of fatal or near-fatal asthma. *Eur Respir J* 1994, 7:1602–1609.