Acute exacerbations of asthma in adults: Emergency department and inpatient management

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INTRODUCTION

The best strategy for management of acute exacerbations of asthma is early recognition and intervention, before attacks become severe and potentially life threatening. Detailed investigations into the circumstances surrounding fatal asthma have frequently revealed failures on the part of both patients and clinicians to recognize the severity of the disease and to intensify treatment appropriately [1].

The emergency department and inpatient management of acute asthma exacerbations will be presented here. An overview of asthma management, the management of acute exacerbations of asthma at home and in the office, identification of risk factors for fatal asthma, and use of mechanical ventilation in severe exacerbations of asthma are discussed separately.

- (See "An overview of asthma management".)
- (See "Acute exacerbations of asthma in adults: Home and office management".)
- (See "Identifying patients at risk for fatal asthma".)
- (See "Invasive mechanical ventilation in adults with acute exacerbations of asthma".)

ASSESSMENT OF EXACERBATION SEVERITY

A number of clinical findings and objective tests can assist the clinician in confirming the diagnosis of an exacerbation of asthma, assessing the severity of an asthma attack, and excluding complicating factors (eg, pneumonia, atelectasis, pneumothorax, pneumomediastinum) (algorithm 1). The diagnosis of asthma and the differential diagnosis of nonasthmatic wheezing are discussed separately. (See "Asthma in adolescents and adults: Evaluation and diagnosis" and "Evaluation of wheezing illnesses other than asthma in adults".)

Clinical findings — A focused history and physical examination are obtained concurrently with the initiation of therapy in order to confirm the diagnosis and assess the severity. A severe asthma exacerbation is potentially life-threatening and needs prompt and intense care.

- **Signs of a severe exacerbation** – The presence of certain clinical findings may help to identify patients experiencing severe asthma attacks. Tachypnea (>30 breaths/min), tachycardia >120 beats/min, use of accessory muscles of inspiration (eg, sternocleidomastoid muscles), diaphoresis, inability to speak in full sentences or phrases, inability to lie supine due to breathlessness, and pulsus paradoxus (ie, a fall in systolic blood pressure of more than 12 mmHg during inspiration) are all indicative of severe airflow obstruction [2,3].

  Unfortunately, these findings are not sensitive indicators of severe attacks. Up to 50 percent of patients with severe airflow obstruction will not manifest any of these abnormalities [4], whereas measurement of lung function, as discussed below, can detect severe airflow obstruction in the absence of suggestive symptoms and/or physical findings. Risk factors for fatal asthma are discussed separately. (See "Acute exacerbations of asthma in adults: Home and office management", section on 'Risk factors for fatal asthma' and "Identifying patients at risk for fatal asthma", section on 'Identifying high-risk patients' and "Examination of the arterial pulse", section on 'Pulsus paradoxus'.)

- **Features suggesting an alternate or comorbid condition** – Concomitant symptoms such as fever, purulent sputum production, urticaria, or pleuritic chest pain should raise the possibility of an alternative diagnosis such as pneumonia, flare of bronchiectasis, anaphylaxis, or pneumothorax.

Peak flow measurement — Measurement of maximal expiratory airflow with a peak flow meter (or spirometer) is the best method for objective assessment of the severity of an asthma attack in patients who are able to perform testing. Patients with signs of impending respiratory failure should not be asked to perform this testing. (See "Peak expiratory flow monitoring in asthma".)

Normal values differ with sex, height, and age (table 1A-B) (calculator 1 and calculator 2), but in general, a peak flow rate below 200 L/min indicates severe obstruction for most adults except those who are very short or over the age of 65 [5]. In terms of percent of predicted or percent of personal best, an exacerbation is considered severe when the peak expiratory flow (PEF) is ≤50 percent predicted; an exacerbation is considered moderate when the PEF is >50 but <70 percent [3].

Peak flow or spirometric measurements can also be used to monitor a patient's response to treatment and as a predictive marker for the possibility of hypercapnia, as discussed below. (See 'Hypercapnia' below.)

Guidelines advise including PEF measurement as part of a combined assessment of severity and response to treatment, although studies are conflicting regarding the benefit of PEF monitoring in terms of improved outcomes or reliable prediction of the need for admission [6-8]. In our opinion, a major advantage of checking peak flow in patients presenting with asthmatic symptoms is detection of unsuspected severe airflow obstruction in persons who may not manifest respiratory distress or intense wheezing despite the serious nature of their attack.

Oxygenation — The ready availability of pulse oxygen saturation testing by transcutaneous oximetry allows noninvasive screening for hypoxemia among patients suffering an exacerbation of asthma. Current guidelines recommend the use of transcutaneous pulse oximetry monitoring particularly among patients who are in severe distress, have a forced expiratory volume in one second (FEV_1) or PEF less than 50 percent of baseline, or are unable to perform lung function measurements [5]. However, the correlation between PEF and oxygen saturation is poor. In our practice, we use continuous transcutaneous oximetry during the emergency department treatment of almost all asthmatic exacerbations.

Marked hypoxemia (arterial partial pressure of oxygen [PaO_2] <60 mmHg [8 kPa], pulse oxygen saturation [SpO_2] <90 percent) is infrequent during uncomplicated asthma attacks; its presence suggests life-threatening asthma and possible complicating conditions, such as pneumonia or atelectasis due to mucus plugging. Severe hypoxemia poses the risk for severe cardiovascular or neurologic complications and death.

Hypercapnia — On the other hand, peak flow measurements provide a useful screening tool for hypercapnia (eg, arterial tension of carbon dioxide [$PaCO_2$] >45 mmHg or >6 kPa), making routine assessment of arterial blood gases (ABG) unnecessary in the majority of patients. In the absence of respiratory depressant medications, such as narcotics or sedatives, hypercapnia is rarely present when the PEF is ≥25 percent of normal or ≥150 L/min [9-11]. Thus, arterial blood gas measurements in acute asthma are indicated in the following settings:

- Patients with persistent dyspnea whose PEF is below 25 percent of normal or below 150 L/min despite initial bronchodilator therapy (low initial PEF should lead to prompt bronchodilator treatment and reevaluation rather than an immediate blood gas)
- Patients whose respiratory status is deteriorating despite intensive therapy
- Patients who are too ill to perform a peak flow measurement
- Patients who demonstrate signs or symptoms of hypercapnia, such as depressed consciousness, inappropriately slow respiratory rate, bradycardia, or myoclonus

Respiratory drive is almost invariably increased in acute asthma, resulting in hyperventilation and a correspondingly decreased $PaCO_2$. Thus, a normal $PaCO_2$ (eucapnia) during an asthma exacerbation indicates that airway narrowing and dynamic hyperinflation are so severe that tidal volume and alveolar ventilation are starting to decrease, despite persistent intense central respiratory drive. Hypercapnia and respiratory failure can then develop rapidly with any further airway obstruction or with respiratory muscle fatigue. Progressive hypercapnia during an exacerbation of asthma is generally an indication for mechanical ventilation.

Asthmatic exacerbations, with an associated sense of suffocation, are often associated with anxiety and at times with a counterproductive breathing pattern of rapid, shallow breaths. It is tempting to treat this manifestation of the exacerbation with anxiolytics such as benzodiazepines, but such treatment comes with the risk of central respiratory depression and potential precipitation of hypercapnic respiratory failure. A preferable strategy in most cases is effective bronchodilation to relieve the sense of dyspnea and on-going reassurance, with encouragement to take slow-deep breaths (to minimize dead space ventilation and breath-stacking with excessive hyperinflation).

Measurement of the tension of carbon dioxide in peripheral venous blood ($PvCO_2$) is becoming a more common practice in emergency departments. A normal or low venous blood $PvCO_2$ (that is, $PvCO_2$ <45 mm Hg) reliably predicts a normal or low $PaCO_2$ and can be used to exclude hypercapnia. However, the overall correlation between $PvCO_2$ and $PaCO_2$ is poor [12]. (See "Venous blood gases and other alternatives to arterial blood gases", section on 'Venous blood gases'.)

Chest radiograph — Chest radiographs are generally unrevealing in acute asthma attacks and are not routinely required in the urgent care setting [3,13]. However, a chest radiograph should be obtained when a complicating cardiopulmonary process is suspected (eg, temperature >38.3˚C, unexplained chest pain, leukocytosis, or hypoxemia), when a patient requires hospitalization, and when the diagnosis is uncertain [3]. The most common abnormality is

pulmonary hyperinflation. Other abnormal findings (eg, pneumothorax, pneumomediastinum, pneumonia, or atelectasis) are infrequent, occurring in only approximately 2 percent of chest radiographs obtained among patients presenting to emergency departments for the treatment of acute asthma [14,15].

Chest radiographs are also useful for patients at high risk for comorbidities (eg, a history of intravenous drug abuse, immunosuppression, granulomatous disease, recent seizures, cancer, chest surgery, or heart failure) [13,16].

EMERGENCY DEPARTMENT MANAGEMENT

The primary goals of therapy for acute severe asthma are the rapid reversal of airflow limitation and the correction, if necessary, of hypercapnia or hypoxemia. Airflow limitation is most rapidly alleviated by the combination of repeated administration of inhaled bronchodilators and early institution of systemic glucocorticoids. A table and an algorithm outlining the emergency management of severe asthma exacerbations in adults are provided (table 2 and algorithm 1).

Until their respiratory distress has abated, patients should receive close monitoring, including serial measurements of vital signs, pulse oximetry, and lung function (eg, peak expiratory flow [PEF]), to assess the response to treatment.

The advent of monoclonal antibodies ("biologics") to treat uncontrolled severe persistent asthma has introduced a personalized approach to severe asthma in the ambulatory setting, including distinction between allergic/eosinophilic ("type 2") asthma and nonallergic/eosinophilic ("type 1" or "type 2-low") asthma. However, the assessment and treatment of acute asthma exacerbations remains monolithic, with the same approach applicable to all patients regardless of type 2 or type 1 endotype and regardless of the known or supposed triggering stimulus.

Oxygen — Supplemental oxygen should be administered to all patients with hypoxemia (pulse oxygen saturation [SpO_2] <90 percent) and to those with a moderate or severe asthma exacerbation for whom continuous oxygen saturation monitoring is not available. The specific target for SpO_2 varies among guidelines [3,5,17], but we aim for an SpO_2 above 92 percent in adults (>95 percent in pregnancy) [3]. Usually, oxygenation is easily maintained with nasal cannula, but occasionally face mask delivery is needed.

For patients with severe exacerbations and risk for hypercapnia, there is some evidence that titrating oxygen supplementation to an oxygen saturation of 93 to 95 percent is preferable to

targeting an oxygen saturation close to 100% with high inspired oxygen concentrations [3]. In a trial that randomly assigned 106 patients with severe asthma exacerbations to mask oxygen at 8 L/min or titrated oxygen to achieve 93 to 95 percent saturation for 60 minutes, the transcutaneous carbon dioxide tension increased ≥4 mmHg in 44 percent of the high oxygen concentration group compared with 19 percent of the titrated oxygen group (relative risk [RR] 2.3, 95% CI 1.2-4.4) [18].

Titrated low-flow supplemental oxygen is particularly appropriate for patients at risk for chronic hypercapnia, such as those with asthma-chronic obstructive pulmonary disease (COPD) overlap and chronic hypoxemia, in whom a target SpO_2 of 90 to 94 percent is reasonable. (See "Asthma and COPD overlap (ACO)" and "COPD exacerbations: Management", section on 'Oxygen therapy'.)

These recommendations for careful titration of pulse oximetry are complicated by the observation that current pulse oximeters may overestimate the true arterial blood oxygen concentration in a significant percentage of the population, with larger errors for those with dark-toned skin and when true oxygen saturation is 80 to 90 percent [19]. There is no simple solution given the large variation in inaccuracy based on device type and skin color; future regulation may improve device characteristics. In the meantime, recognition of this problem favors somewhat more liberal oxygen saturation targeting in persons with darker skin tones.

Inhaled beta-agonists — The mainstay of bronchodilator treatment is inhalation of short-acting beta-2-selective adrenergic agonists (SABA), such as albuterol or levalbuterol [3,5,17,20]. (See "Beta agonists in asthma: Acute administration and prophylactic use".)

Dosing and delivery method — The standard therapy for initial care in the emergency department is inhaled albuterol (or an equivalent) (table 3). Typically, three treatments are administered within the first hour. The delivery method varies with the setting, suspected or known COVID-19 infection, and severity of the attack (table 3) [5]: High-dose inhaled SABA therapy can be associated with hypokalemia and lactic acidosis.

- **Standard nebulization** – Albuterol 2.5 to 5 mg by jet (also called "hand-held" or "updraft") nebulization every 20 minutes for three doses, then 2.5 mg to 5 mg every one to four hours as needed. Of note, the higher doses are associated with more frequent and severe sympathomimetic side effects and are generally reserved for very severe, refractory attacks. (See "Delivery of inhaled medication in adults", section on 'Nebulizers'.)

- **Metered dose inhaler (MDI)** – Albuterol by MDI with a spacer or valved-holding chamber (VHC; eg, Aerochamber, Optichamber, Vortex, and others) 4 to 8 puffs every 20 minutes, for the first hour. While guidelines include the possibility of up to 10 puffs [3], we generally

start with 4 puffs via VHC, emphasizing proper technique, and increase the number of puffs to 6 or 8, if no response. The higher number of puffs is associated with a greater likelihood of tremor and tachycardia. Most patients can then transition to dosing every one to four hours, and rarely require dosing at more frequent intervals.

- **Continuous nebulization** – The practice of administering "stacked" nebulizer treatments refers to delivering one nebulizer treatment immediately after the other without pause between treatments. In the intensive care unit, some clinicians use a special apparatus to achieve continuous nebulization, administering 10 to 15 mg over one hour (figure 1). The technique of continuous nebulization is discussed separately. (See "Delivery of inhaled medication in adults", section on 'Continuous nebulization'.)

Nebulizer versus MDI — The relatively large particle size generated by jet nebulizers and the loss of medication from the expiratory port of many nebulizer systems make this method of delivery relatively inefficient compared with an MDI. Comparisons of MDI plus valved-holding chamber with nebulizer delivery, using the same beta agonist but in much reduced doses when given by MDI, have demonstrated comparable improvements in lung function and risk of hospitalization [21-26]. (See "Delivery of inhaled medication in adults" and "The use of inhaler devices in adults", section on 'pMDI technique with spacer/chamber'.)

In a systematic review that included 13 trials (five open-label) with a total of 729 adults, the outcomes of delivery of beta-agonist via MDI with chamber/spacer versus nebulizer were examined [25]. The risk ratio of admission after emergency department administration of beta-agonist via spacer versus nebulizer was 0.94 (95% CI 0.61-1.43). Peak flow and forced expiratory volume in one second (FEV_1) responses and the duration of emergency department stay were similar between groups. The baseline severity of asthma varied from moderate to severe.

Four to six carefully administered inhalations from an MDI with chamber/spacer have generally been found to equal one nebulizer treatment, although the equivalent dose has not been precisely defined. In comparative trials, administration of beta agonist by MDI with chamber/spacer was directly supervised to ensure the patient's proper coordination and inhalational technique.

Many emergency departments (including our own) continue to rely on nebulized administration of beta agonists for acutely ill asthmatic patients, taking advantage of the simplicity of delivery during the patient's tidal breathing. This approach assumes ready availability of medication and nebulizer equipment to be administered by emergency department staff, without reliance on or potential delay while awaiting the services of a respiratory therapist. As patients recover in the hospital from acute, severe attacks, the transition can be made from nebulized beta-agonists to

a SABA by MDI with a valved holding chamber ("spacer") or dry powder inhaler (DPI) without loss of efficacy and with the opportunity for patient education in proper inhaler technique [27]. (See "The use of inhaler devices in adults", section on 'Spacers and holding chambers'.)

Inhaled muscarinic antagonists — In accordance with current guidelines for asthma exacerbations, we recommend addition of inhaled ipratropium, a short-acting muscarinic antagonist (SAMA; also called an anticholinergic agent), to inhaled SABA for patients who present to the emergency department with a severe exacerbation of asthma [3,5]. As differentiating moderate and severe exacerbations is imprecise, it is reasonable to extend ipratropium treatment to patients with moderate exacerbations based on clinical judgment.

- **Dosing** − The dose of ipratropium is 500 mcg by nebulization or four to eight puffs by MDI, every 20 minutes for three doses, and then hourly as needed for up to three hours [5]. Albuterol and ipratropium can be delivered simultaneously by nebulizer or soft-mist inhaler.

- **Duration** − We typically advise stopping inhaled SAMA therapy once the patient is admitted to the hospital, except in patients with refractory asthma who require treatment in the intensive care unit, are on monoamine oxidase inhibitor therapy (who may have increased toxicity from sympathomimetic therapy due to impaired drug metabolism), have COPD with an asthmatic component, and those whose asthma has been triggered by beta-blocker therapy. Discontinuation of SAMA therapy in hospitalized patients is based on studies in children that found no benefit from continuation of inhaled SAMA bronchodilators in hospitalized patients [28,29] and is supported by current guidelines [3,5].

- **Efficacy** − The efficacy of using both a SAMA and a SABA to treat asthma exacerbations has been examined in a number of trials and systematic reviews [30-36]. A systematic review found that patients presenting with an asthma exacerbation who were treated with both a SABA and a SAMA were less likely to be admitted to the hospital than those treated with a SABA alone (RR 0.72, 95% CI 0.59-0.87; 2120 participants; 16 studies; moderate quality), but the benefit pertained only to those with severe exacerbations, not those with mild or moderate exacerbations [33]. Combination therapy was associated with improved FEV_1 and PEF, but results were variable among studies. The rates of adverse effects such as tremor, palpitations, and agitation were greater with combination therapy than SABA alone.

Systemic glucocorticoids — Systemic glucocorticoid therapy is essential for the resolution of asthma exacerbations that are refractory to intensive bronchodilator therapy because the

persistent airflow obstruction is likely due to airway inflammation and intraluminal mucus plugging [37,38]. Glucocorticoids additionally increase airway smooth muscle expression of beta-adrenergic receptors [39]. Consistent with current guidelines, we recommend early administration of systemic glucocorticoids for patients with the following [3,5]:

- An asthma exacerbation that does not have a sustained improvement of symptoms and PEF with initial SABA treatment.
- An asthma exacerbation that occurs despite ongoing daily or alternate-day oral glucocorticoid therapy. Such patients require supplemental glucocorticoids above their baseline dose.
- The patient has a recurrent exacerbation after recent discontinuation of systemic glucocorticoids for a previous exacerbation.

Among patients with significant airflow obstruction despite intensive treatment with bronchodilators, systemic glucocorticoids speed the rate of improvement [40]. However, the onset of action of systemic glucocorticoids is not clinically apparent until as long as six hours after administration. Early administration helps to minimize the delay in improvement anticipated with systemic glucocorticoids [41,42].

Dose and route of administration

- **Dosing** – The optimal dose for systemic glucocorticoids in asthmatic exacerbations remains unknown [43]. The equivalent of prednisone 40 to 60 mg (methylprednisolone 32 to 48 mg) per day is typical for most asthma exacerbations (table 4 and table 5) [5].

  A higher dose is sometimes given for life-threatening asthma exacerbations, based on expert opinion and concern that a lower dose might be insufficient in a critically ill patient, rather than being evidence-based [44]. As an example, an initial dose of methylprednisolone 60 to 80 mg every 6 to 12 hours is often chosen for patients who are admitted to the intensive care unit, while a lower initial dose of 40 to 60 mg every 12 to 24 hours is considered adequate for patients who are admitted to the hospital, but do not require intensive care.

  A massive initial dose (eg, methylprednisolone 500 mg intravenous bolus) is no more effective than a large initial dose (125 mg) and is not advised [45].

- **Route of administration** – When comparable doses are administered, the effects of oral and intravenous routes of glucocorticoid administration are identical. Oral prednisone and methylprednisolone are rapidly absorbed (peak serum levels achieved at one hour after

ingestion) with virtually complete bioavailability, and their efficacy is comparable to intravenous methylprednisolone. Prednisone is rapidly converted to prednisolone in the liver.

Intravenous glucocorticoids should be given to patients who present with impending or actual respiratory arrest or are intolerant of oral glucocorticoids [5]. Transition from parenteral to oral administration of glucocorticoids can occur when the patient can tolerate and absorb oral medication.

Glucocorticoids can be given intramuscularly if intravenous and oral access are not available, although the onset of action of intramuscular glucocorticoids is delayed for up to 24 hours.

- **Efficacy** – Oral and intravenous glucocorticoids increase the rate of improvement during an asthma exacerbation [37,40]. The benefit of early administration (within one hour) was demonstrated in a systematic review (12 studies; 863 participants) that found a decrease in hospitalization (OR 0.40, 95% CI 0.21-0.78) with glucocorticoid initiation within one hour compared with later administration [37].

  A brief course of systemic glucocorticoids also reduces the rate of relapse and need for subsequent hospitalization following an asthma exacerbation, as described below. (See 'Oral glucocorticoids' below.)

High-dose inhaled glucocorticoids — While increasing the dose of inhaled glucocorticoids is recommended for patients with gradually deteriorating control of asthma, high-dose inhaled glucocorticoids are **not** recommended as an alternative to oral glucocorticoids for patients who present to the emergency department with a discrete asthma exacerbation. A few reports suggested that high-dose inhaled glucocorticoids might have an effect comparable to oral or intravenous glucocorticoids in patients with mild to moderate asthma following initial stabilization in the emergency department [46-49]. However, several larger controlled trials and meta-analyses have drawn the opposite conclusion [50-53]. In the emergency department, adding inhaled glucocorticoids to systemic glucocorticoids does not appear to confer any additive benefit [54].

The role of increasing the dose of inhaled glucocorticoids early in the course of an asthma exacerbation is discussed separately. (See "Acute exacerbations of asthma in adults: Home and office management", section on 'Quadrupling the dose of inhaled glucocorticoid'.)

Magnesium sulfate — Intravenous administration of a single dose of magnesium sulfate (2 g infused over 20 min) is suggested for patients who present with a life-threatening exacerbation

or have a severe exacerbation that is not responding to initial therapy [3,5,55], although its additive benefit remains debated. Some society guidelines have recommended against routine administration of magnesium sulfate to patients with severe asthma exacerbations [56].

Intravenous magnesium sulfate has bronchodilator activity in acute asthma, possibly due to inhibition of calcium influx into airway smooth muscle cells [57]. The best evidence for benefit in acute asthma exacerbations comes from an early systematic review (14 studies, 2313 participants) that found a decrease in hospitalizations with intravenous magnesium compared with placebo (odds ratio [OR] 0.75, 95% CI 0.60-0.92) and some improvement in lung function [55]. No difference was noted in duration of emergency department treatment or admission to the intensive care unit. Although the routine use of this agent does not seem to confer significant benefit beyond that achieved with the conventional use of beta agonists and systemic glucocorticoids, intravenous magnesium may be helpful in the subgroup of patients with severe attacks [3,55,58-60].

However, a large, randomized trial of more than 1000 patients with severe asthma exacerbations that compared intravenous magnesium, inhaled magnesium, and placebo found no significant differences in any beneficial outcome, including lung function, patients' sense of breathlessness, need for hospitalization, duration of hospitalization, or admission to an intensive care unit. It should be noted that this trial excluded patients with features suggesting a possible life-threatening exacerbation [61].

Intravenous magnesium has an excellent safety profile; however, it is contraindicated in the presence of renal insufficiency, and hypermagnesemia can result in muscle weakness. (See "Hypermagnesemia: Causes, symptoms, and treatment", section on 'Symptoms of hypermagnesemia'.)

Inhaled magnesium, in contrast, is of marginal benefit in acute asthma exacerbations, when added to inhaled albuterol or the combination of inhaled albuterol and ipratropium. A systematic review found a borderline benefit to adding inhaled magnesium to inhaled albuterol plus ipratropium in reducing hospital admissions (RR 0.95, 95% CI 0.91 to 1.00) and no significant improvement in peak expiratory flow when inhaled magnesium was added to inhaled albuterol plus ipratropium or inhaled albuterol alone [62]. A subsequent trial found no benefit to addition of inhaled magnesium in children with refractory acute asthma treated in the emergency department [63].

Assessment after initial treatment — Identifying patients who should be kept for overnight observation or hospital admission versus discharged to home remains largely a matter of clinical judgment guided by the patient's response to therapy, severity of respiratory symptoms,

degree of airflow limitation (as assessed by PEF), living situation, and support services available following discharge. National and international guidelines are available to help guide decision making (algorithm 1) [3,5].

- After the first hour of intensive treatment, patients whose symptoms have resolved and PEF is >80 percent predicted can be discharged, to continue treatment for their asthma exacerbation at home. Those who have an incomplete response and PEF is 60 to 80 percent of predicted should continue intensive and closely observed treatment for approximately another one to three hours. Those who have worsening symptoms and a declining PEF or pulse oxygen saturation will need hospital admission and may need intensive care.

- Patients who continue treatment in the emergency department and have worsened, or not improved after an additional one to three hours of frequent inhaled beta-agonist bronchodilator treatments and systemic glucocorticoids, should continue care in an observation unit or be hospitalized. For those with partial improvement in symptoms and a PEF 60 to 80 percent predicted, an individualized assessment is needed. Among the factors favoring continued observation in this group are: new onset asthma, multiple prior hospitalizations or emergency department visits for asthma, use of oral glucocorticoids at the time of presentation with the acute deterioration, and complicating psychosocial difficulties. Patients who demonstrate improving lung function and have good asthma self-care skills and a supportive home environment may be candidates for discharge to home [3].

- Severe symptoms of coughing, wheezing, and shortness of breath that preclude self-care are additional indications for in-hospital care.

- PEF measurements provide objective data and are useful for determining which patients are "at risk" for poor outcomes if discharged home and which are generally safe for transition to home management [3,7,64]. As noted above, the major advantage of checking PEF is detection of airflow obstruction that is more severe than symptoms or physical examination would indicate. (See 'Peak flow measurement' above.)

- A home environment that does not allow for adherence to the medical regimen, ongoing self-monitoring, and rapid return to the emergency department for worsening symptoms may be a reason for the patient to stay in a monitored setting pending resolution of asthma symptoms and further asthma education.

Treatment during pregnancy — Medical therapy for asthma exacerbations in pregnant patients is essentially the same as for nonpregnant patients. Concerns about fetal harm or

premature labor caused by medications (eg, increased risk of cleft lip and palate from systemic glucocorticoids administered during first trimester) are outweighed by the risks to fetus and mother from hypoxemia, respiratory alkalosis (with consequent uterine arterial vasoconstriction), and other poor outcomes such as respiratory failure. In the pregnant patient, we are particularly attentive to maintaining adequate oxygenation (target SaO_2 ≥95 percent) and involving obstetrical consultation when exacerbations require prolonged emergency department care or hospitalization. (See "Management of asthma during pregnancy", section on 'Acute exacerbations'.)

LIFE-THREATENING ASTHMA EXACERBATIONS

For patients who present to the emergency department with impending or actual respiratory arrest, in addition to the treatments outlined above, options for ventilatory support must be assessed and implemented promptly, if needed.

Mechanical ventilation and noninvasive positive pressure ventilation — The decision to intubate and initiate mechanical ventilation during a severe asthma attack is clinical. Slowing of the respiratory rate, depressed mental status, inability to maintain respiratory effort or to cooperate with administration of inhaled medications, worsening hypercapnia and associated respiratory acidosis, or inability to maintain an oxygen saturation >92 percent despite face mask supplemental oxygen suggest that the patient requires intubation. In the absence of anticipated intubation difficulty, rapid sequence intubation is preferred. Nasal intubation is not recommended. (See "Airway management in acute severe asthma for emergency medicine and critical care" and "Invasive mechanical ventilation in adults with acute exacerbations of asthma", section on 'General approach'.)

Noninvasive ventilation (NIV) is increasingly used in patients with severe asthma exacerbations in hopes of avoiding invasive mechanical ventilation, although its role in asthma is not as well studied as in chronic obstructive pulmonary disease (COPD) and heart failure. A short trial of NIV may be appropriate in cooperative patients not responding to medical therapy who do not require immediate intubation. (See "Noninvasive ventilation in adults with acute respiratory failure: Benefits and contraindications", section on 'Asthma exacerbation'.)

Nonstandard therapies — Modalities, such as anesthetic agents (eg, ketamine, isoflurane), enoximone (available in Europe), helium-oxygen mixtures, extracorporeal membrane oxygenation (ECMO), and rarely parenteral beta-agonists, may be helpful in individual patients, but cannot be recommended for routine use due to insufficient evidence of efficacy. (See "Investigational agents for asthma".)

Anesthetic agents — Some anesthetic agents (eg, intravenous ketamine, inhaled halothane, isoflurane, and sevoflurane) have bronchodilating effects, and case reports have described favorable responses in patients with refractory status asthmaticus. The mechanism by which bronchodilation is produced remains unclear; a direct relaxant effect on airway smooth muscle and attenuation of cholinergic tone have been proposed [65,66]. None of these agents has been evaluated in a randomized trial and some adverse outcomes have been reported [67].

Inhalational agents — Experience is greatest with halothane for severe, life-threatening exacerbations requiring mechanical ventilation, but isoflurane and sevoflurane have also shown effectiveness in case reports [68-73]. Idiosyncratic reactions to these anesthetics have been described, and a given patient may respond better to one than to another. The dose of inhalational anesthetic is titrated to the clinical response (eg, improvement in airway resistance) and avoidance of intolerable side effects. Hypotension is often the limiting factor in the administration of these agents, and myocardial depression and increased ventricular irritability have been observed with halothane, particularly when used in the presence of acidosis, beta-agonists, and theophylline.

The use of inhalational anesthetics for treatment of asthma exacerbations complicated by respiratory failure is limited by their expense, the need for a full-time anesthesiologist at the bedside, adaptation of equipment for prolonged provision of anesthetics, and the abrupt return of bronchoconstriction upon discontinuation. There is also the issue of scavenging anesthetic gases released into the immediate environment to avoid second-hand inhalation of aerosolized anesthetic gases by health care personnel or other patients.

Intravenous ketamine — Several case reports have described successful treatment of children and adults with severe, treatment-refractory asthma exacerbations with intravenous ketamine [74-78]. Although experience with this therapy is limited, case reports describe infusion of an intravenous bolus of 0.5 to 1 mg/kg over two to four minutes, followed by a continuous infusion of 0.5 to 2 mg/kg per hour [77,78]. In one report, improvement followed increasing the infusion rate to 3 mg/kg per hour [77]. Beneficial results are reported within 30 minutes to several hours. Depending on the setting, ketamine infusions in this dose range may fall under the category of moderate sedation or anesthesia and require appropriate monitoring. In general, though, ketamine can be administered in the intensive care unit, rather than the operating room, making it preferable to general anesthesia. (See "Induction agents for rapid sequence intubation in adults for emergency medicine and critical care", section on 'Ketamine'.)

Enoximone — Enoximone, a selective phosphodiesterase III inhibitor available in Europe, was administered intravenously to eight patients with severe asthma exacerbations, six of whom had a respiratory arrest or hypercapnia [79]. The dose of enoximone varied, ranging from two

doses of 25 mg to two doses of 100 mg. Three patients were given enoximone by continuous infusion after the initial boluses. Response to enoximone is described as rapid, within one to twenty minutes. The amount of standard medications (eg, inhaled beta-adrenergic agonist, inhaled ipratropium, systemic glucocorticoid) given prior to enoximone was unclear from the report.

Phosphodiesterase inhibitors are associated with ventricular and atrial arrhythmias, hypotension, and hepatotoxicity. Further study is needed to evaluate the safety and efficacy of intravenous enoximone in patients with acute exacerbations of asthma that are refractory to standard measures.

Parenteral beta-agonists (epinephrine and terbutaline) — Intravenous, intramuscular, and subcutaneous beta-agonists (eg, epinephrine, terbutaline) are generally avoided when treating asthma exacerbations in adults, because inhaled short-acting selective beta agonists have equal or greater efficacy and a lower incidence of adverse effects (eg, tachycardia, arrhythmias, myocardial injury) compared with parenteral beta-agonists [3].

Systematic reviews have found no significant benefit to parenteral beta-agonists compared with inhaled beta-2-agonists in adults with acute severe asthma [80,81], and parenteral beta-agonists are not recommended for adults by current guidelines [3].

Two exceptions would be patients suspected of having an anaphylactic reaction and those unable to use inhaled bronchodilators for a severe asthma exacerbation.

- For suspected anaphylaxis manifest as an asthma exacerbation, give epinephrine 0.3 to 0.5 mg intramuscularly (eg, 0.3 to 0.5 mL of 1 mg/mL solution [also labeled 1:1000 in some countries]) into the mid-outer thigh (vastus lateralis muscle), every 20 minutes for up to three doses.

- For patients unable to use inhaled bronchodilators, epinephrine (0.3 mg, subcutaneously) or terbutaline (0.25 mg, subcutaneously) can be administered every 20 minutes for up to three doses.

Epinephrine and terbutaline should not be combined.

Helium-oxygen — Helium-oxygen (heliox) mixtures (eg, helium 70 to 80 percent mixed with oxygen 30 to 20 percent, respectively) are used at some centers for severe asthma exacerbations that are unresponsive to standard therapy or appear to have a component of upper airway obstruction. Routine use of heliox mixtures for asthma exacerbations alone cannot be recommended due to conflicting data about efficacy.

The rationale for using heliox is that the low density of helium decreases resistance to airflow under conditions of turbulent flow, such as in the central airways and at branch points, which would in turn decrease the work of breathing and improve ventilation. In patients with upper airway obstruction (such as epiglottitis, paradoxical vocal fold motion, a common comorbidity complicating asthma, or subglottic stenosis), heliox is effective temporizing therapy while the underlying problem is being addressed. Airflow in smaller airways, which are more likely narrowed by asthma, is typically laminar, dependent on gas viscosity rather than density, and not improved with heliox. The physiology and clinical application of heliox are reviewed separately. (See "Physiology and clinical use of heliox" and "Clinical presentation, diagnostic evaluation, and management of malignant central airway obstruction in adults".)

Despite the theoretical benefits of heliox, studies have reported conflicting results concerning its efficacy in asthma exacerbations. Two systematic reviews of the published literature found insufficient evidence, due to the small size and nonrandomized design of available studies, to recommend the use of helium-oxygen gas mixtures in the treatment of asthmatic attacks. These analyses are discussed separately. (See "Physiology and clinical use of heliox", section on 'Use in adults'.)

Nebulization of albuterol using a heliox gas mixture as the driving gas, instead of the usual compressed air or oxygen, results in a smaller particle size, which may in theory improve drug penetration to the small airways. However, clinical trials have failed to provide consistent evidence of benefit. The use of heliox for aerosol delivery is discussed separately. (See "Physiology and clinical use of heliox", section on 'Aerosol delivery'.)

Extracorporeal life support — Oxygenation and carbon dioxide removal through an artificial membrane may be beneficial as a temporizing measure in patients with severe asthma refractory to usual care and mechanical ventilation. Extracorporeal life support in asthma is discussed separately. (See "Invasive mechanical ventilation in adults with acute exacerbations of asthma", section on 'Extracorporeal life support' and "Extracorporeal life support in adults in the intensive care unit: Overview".)

INPATIENT CARE

The purpose of hospitalization during an acute exacerbation of asthma is close observation and availability of aggressive interventions in the event of worsening asthma. Hospitalization also serves to remove the patient from stimuli in the home environment that potentially aggravate asthma, ensure medication compliance, and permit inactivity during recovery from the illness.

In many cases, airway obstruction remains labile for days following an acute exacerbation, with wide swings in expiratory flow over minutes or hours. Nocturnal deteriorations are common.

Tobacco smoking cessation — For patients who are cigarette smokers prior to admission, hospitalization is an opportunity to discuss and initiate a plan for smoking cessation. (See "Overview of smoking cessation management in adults" and "Pharmacotherapy for smoking cessation in adults".)

Medications — In general, inpatient management of asthma exacerbations is a continuation of emergency department or intensive care unit treatment, followed by a transition to a regimen close to their discharge regimen.

- The majority of patients improve over the next 24 to 48 hours as inhaled short-acting beta-agonists (SABAs) are gradually tapered from hourly to every four to six hours and a transition is made to use of metered dose inhalers (MDIs) rather than nebulizer-delivered SABA.

- Systemic glucocorticoids are continued; if intravenous administration was given initially, a transition to oral therapy is generally made as soon as the patient is able to take medications orally.

- We typically begin (or resume, if previously taking) inhaled glucocorticoids as soon as patients are able to tolerate medication delivery from dry-powder inhalers (DPIs) or MDIs. We review the patient's technique carefully. Many patients have difficulty achieving good technique with MDIs and benefit from addition of a valved holding chamber ("spacer").

- The use of combination inhaled glucocorticoids plus long-acting beta-agonists (LABAs) during hospitalization has not been well studied. It seems reasonable to resume a combination inhaler if the patient was using one prior to admission. If the LABA is a new addition, it may be reasonable to delay starting a combination inhaler until administration of SABAs has decreased in frequency to fewer than four times per day.

- If a new inhaler device will be used after discharge, we find it helpful to start the new inhaler prior to discharge to ensure proper instruction on technique.

Failure to respond to therapy — Most patients hospitalized with asthma will show clear improvement over the course of 24 to 48 hours with resolving symptoms, less wheezing on examination, and improving lung function (peak flow values), but some will not. Prolonged wheezing and shortness of breath despite intensive anti-asthmatic therapy raise the possibility of alternative or coexistent diagnoses.

Clinical considerations in patients with seemingly refractory asthmatic attacks include the following:

- Viral bronchitis and bronchiolitis, such as with influenza or respiratory syncytial virus, and less commonly other infectious bronchitis (eg, *Mycoplasma pneumoniae, Chlamydia pneumoniae, Bordetella pertussis)* can provoke severe and prolonged airway inflammation. Nasal swab with polymerase chain reaction (PCR) testing for SARS-CoV-2, influenza, and other respiratory viruses can be helpful in evaluating this possibility. (See "Acute bronchitis in adults" and "Seasonal influenza in adults: Clinical manifestations and diagnosis".)

- Bronchiectasis (including allergic bronchopulmonary aspergillosis), rhinosinusitis, and pneumonia can intensify asthmatic symptoms and delay recovery. Depending on symptoms and physical examination, further evaluation may include chest or sinus imaging, sputum culture, total immunoglobulin E level, and blood procalcitonin. Leukocytosis typically becomes an unreliable indicator of bacterial infection in the context of therapy with high-dose systemic glucocorticoids, which can cause leukocytosis, and peripheral blood eosinophilia typically resolves quickly under the influence of systemic glucocorticoids. (See "Clinical manifestations and diagnosis of bronchiectasis in adults" and "Acute sinusitis and rhinosinusitis in adults: Clinical manifestations and diagnosis" and "Clinical evaluation and diagnostic testing for community-acquired pneumonia in adults".)

- Patients with underlying chronic airflow obstruction (asthma with irreversible airflow obstruction and asthma-chronic obstructive pulmonary disease [COPD] overlap) may clear airway secretions and inflammation more slowly due to structural airway abnormalities. Review of risk factors for COPD and previous results of spirometry before and after bronchodilator can help identify a component of COPD. (See "Asthma and COPD overlap (ACO)" and "Chronic obstructive pulmonary disease: Diagnosis and staging".)

- Gastroesophageal reflux (GER) may intensify asthmatic symptoms and delay recovery. In general, patients will report symptoms of GER, such as heartburn or regurgitation, although some patients will attribute chest tightness to asthma when it is actually caused by GER. (See "Gastroesophageal reflux and asthma".)

- In an older-aged population, cardiac dysfunction with volume overload, especially heart failure with a preserved ejection fraction, can mimic asthma and may be difficult to diagnose. Plasma brain natriuretic peptide (BNP) and echocardiography can be helpful in the evaluation. (See "Determining the etiology and severity of heart failure or cardiomyopathy".)

- Other processes such as disseminated strongyloidiasis, pulmonary thromboembolism, eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome), oropharyngeal aspiration, and tracheobronchomalacia are less common reasons for failure to improve. (See "Evaluation of severe asthma in adolescents and adults", section on 'Assessing conditions that mimic asthma'.)

It is at times difficult to judge the rate of improvement of an asthmatic attack based solely on patient-reported symptoms, the intensity of wheezes, or the loudness of breath sounds on inspiration. In the cooperative patient, measurement of lung function with peak flow meter or spirometer gives more objective and trackable information about the severity of airflow obstruction.

It is tempting to attribute lack of improvement during a severe asthmatic attack to inadequate steroid dosing. Persons failing to improve will often have their dose of systemic glucocorticoids increased two-fold or more. Although this is common practice, we find no scientific evidence to support it. Likewise, we do not find evidence to support the use of oral or intravenous theophylline in this setting. When other diagnoses and comorbidities have been excluded or treated and when the patient is not deteriorating, it may be that continuation of standard treatment (as outlined above) is appropriate, recognizing that some asthmatic attacks resolve with a time course longer than the typical 24 to 48 hours. (See 'Medications' above.)

Preparations for discharge — In general, an asthma exacerbation has not fully resolved even when symptoms have abated. Residual airflow obstruction due to airway inflammation may last for several days. Thus, in addition to short-acting beta agonists to be used as needed, the patient will need a brief course of systemic glucocorticoids and, in most cases, long-term inhaled glucocorticoids to treat the inflammation and prevent recurrent symptoms.

Oral glucocorticoids — Nearly all patients with a significant asthma exacerbation requiring emergency department management and/or hospitalization should receive a course of systemic glucocorticoids [3,5]. A short course of oral glucocorticoids significantly reduces the likelihood of a repeat severe exacerbation with emergency department bounce back ("relapse") within the succeeding two weeks and lessens the frequency of persistent severe symptoms evaluated at a two-week telephone follow-up [82-85].

Accumulated clinical experience favors a course of prednisone 40 to 60 mg/day for 5 to 7 days. In a systematic review, no difference was found between higher dose/longer course and lower dose/shorter course prednisone or prednisolone, although the quality of the evidence was rated as low [43].

- In a systematic review that included six trials and 374 participants with asthma exacerbations, systemic (oral or intramuscular) glucocorticoids decreased the rate of relapse in the first week after treatment compared with placebo (relative risk [RR] 0.38; 95% CI 0.2-0.74) and decreased subsequent hospitalizations (RR 0.35; 95% CI 0.13-0.95) [82].

- A separate systematic review (nine trials and 804 participants) compared a course of oral glucocorticoids with a single dose of intramuscular glucocorticoids and failed to find a difference in relapse requiring additional care or subsequent treatment with systemic glucocorticoids [83]. While no statistically significant difference was noted in adverse events, fewer patients receiving intramuscular administration reported adverse events (50 per 1000 fewer patients).

As an alternative, preliminary evidence, mainly from studies done in children, suggests that one to two doses of dexamethasone may have comparable benefit in uncomplicated patients [43,86]. In one study of 200 adults with asthma exacerbations, the relapse rate for dexamethasone 16 mg/day for two days was not different from prednisone 50 mg/day for five days [87]. In a separate emergency department trial published after the systematic review, 376 adults with an acute asthma exacerbation not requiring hospitalization were randomly assigned to dexamethasone 12 mg for one dose or prednisone 60 mg a day for five days [88]. The 14-day relapse rates for dexamethasone and prednisone were 12.1 and 9.8 percent, respectively, difference 2.3 percent (95% CI -4.1-8.6).

For glucocorticoid courses lasting three weeks or less, there is no need to taper the dose if patients are also taking inhaled glucocorticoids. (See "Glucocorticoid withdrawal", section on 'HPA suppression unlikely'.)

Intramuscular glucocorticoids — Intramuscular injection of a long-acting glucocorticoid formulation at the time of discharge from the emergency department is occasionally used for patients without access to oral medication or at high risk of medical nonadherence. Intramuscular long-acting glucocorticoid formulations appear to be as effective as oral therapy in this setting [89-94]. In a randomized trial of 190 adult patients with acute asthma, intramuscular injection of long-acting methylprednisolone (160 mg) resulted in a similarly low rate of relapse as oral methylprednisolone given in a tapering schedule over eight days (total dose = 160 mg) [89].

A disadvantage of intramuscular glucocorticoids is that the duration of effect varies from one individual to another and cannot be predicted. Cutaneous atrophy and depigmentation at the injection site are also possible.

Inhaled glucocorticoids — Treatment with regular inhaled glucocorticoids constitutes an important method to prevent recurrent asthma attacks after discontinuation of oral glucocorticoids and to prevent the potential decline in lung function associated with any future severe asthma exacerbation [5,42]. Virtually every patient who has suffered an asthma attack severe enough to require urgent care should receive an inhaled glucocorticoid as part of his or her discharge medication plan (table 6). (See "An overview of asthma management".)

Upon discharge from the hospital or emergency department, some clinicians delay initiation (or reinitiation) of inhaled glucocorticoids until the oral glucocorticoid dose has been reduced to approximately 20 mg of prednisone or the equivalent. However, in our experience this approach more often leads to confusion and medication nonadherence than prescription of these inhaled medicines in parallel with oral glucocorticoids.

Asthma biologics — Biologics therapies approved as add-on treatment of moderate to severe and steroid-dependent asthma reduce asthma exacerbations. They are not recommended for the treatment of acute exacerbations. Biologic therapies are not routinely initiated at the time of discharge from an acute exacerbation, even in patients meeting criteria for their use, due to insurance prior approval requirements, high costs, and the need for ongoing outpatient specialist care.

Patient education — The recovery period following an asthma exacerbation often offers a "teachable moment," as the anxiety associated with the patient experience abates and the desire to avoid a recurrence becomes paramount. Patients should be provided with information about asthma, avoidance of asthma triggers, and a personalized action plan, such as the NHLBI Asthma Action Plan or the action plan in the graphic (form 1). Follow-up care with a primary provider or asthma specialist is essential to achieve adequate disease control and minimize asthma risk and medication side effects. (See "Asthma education and self-management" and "Trigger control to enhance asthma management" and "Acute exacerbations of asthma in adults: Home and office management", section on 'Information for patients'.)

INEFFECTIVE THERAPIES

Leukotriene receptor antagonists, intravenous methylxanthines and empiric antibiotic therapy are not recommended as treatments for acute asthma exacerbations [5]. Other ineffective therapies not recommended for treatment of acute exacerbations of asthma include hydration (in the absence of evidence of dehydration), expectorants (eg, guaifenesin), antihistamines, and chest physiotherapy.

- **Leukotriene receptor antagonists** – Leukotriene receptor antagonists are an established therapy for chronic asthma and are continued during an exacerbation (for those patients already on this therapy), but a systematic review did not find sufficient evidence to support acute initiation of these medications at the time of an exacerbation [95-99]. We do not administer leukotriene receptor antagonists as part of routine treatment of acute exacerbations, except in patients whose exacerbation was triggered by ingestion of aspirin or a nonsteroidal anti-inflammatory drug (NSAID), events associated with dramatic overproduction of leukotrienes. (See "Aspirin-exacerbated respiratory disease", section on 'Leukotriene-modifying agents'.)

- **Methylxanthines** – The use of intravenous methylxanthines (eg, theophylline, aminophylline), once the standard of care for severe asthmatic attacks, has been shown to be relatively ineffective and is no longer recommended in this setting [3,5,100]. These agents are not as potent as the beta agonists when used alone for the treatment of asthma and provide no further bronchodilation beyond that achieved with inhaled beta agonists alone when used in combination [101,102]. In addition, methylxanthines appear to increase the incidence of adverse effects when combined with beta-agonist bronchodilators [102].

  Studies extending over several hours of emergency department care have also failed to show a benefit of theophylline therapy in terms of need for or duration of subsequent hospitalization [103]. For patients who are taking oral theophylline at presentation, we typically continue maintenance oral therapy (and check a theophylline blood level) during hospitalization; but if continued oral intake is not possible, we would very rarely use intravenous therapy with aminophylline or theophylline.

- **Empiric antibiotics** – Clinical practice guidelines recommend against empiric antibiotic therapy for the treatment of an asthma exacerbation, because most respiratory infections that trigger an exacerbation of asthma are viral rather than bacterial [3]. Evidence against routine antibiotic therapy in this setting comes from a systematic review and large observational database studies [104-106]. In general, we reserve antibiotics for treatment of suspected bacterial sinusitis or pneumonia complicating an asthmatic attack even in patients hospitalized for an asthma exacerbation. (See "Uncomplicated acute sinusitis and rhinosinusitis in adults: Treatment" and "Treatment of community-acquired pneumonia in adults in the outpatient setting" and "Treatment of community-acquired pneumonia in adults who require hospitalization".)

  A systematic review (six trials, 681 adults and children), which included the AZALEA trial of azithromycin for acute asthma exacerbations [107], found insufficient evidence of benefit

in patient-important outcomes to support use of empiric antibiotics (macrolides or penicillins) in asthma exacerbations [104]. The methodologic quality of the trials (one open-label) was considered to be variable, ranging from very low to moderate. Limited evidence of a benefit of antibiotics in symptoms and peak expiratory flow was noted in two studies, but the finding was inconsistent across studies. Combining adverse events across three studies (502 participants) yielded no significant between group differences and no deaths.

A lack of benefit to the routine addition of antibiotics for asthma exacerbations is supported by an observational database study of 19,811 patients hospitalized for an asthma exacerbation in which 8788 patients (44 percent) received antibiotics during the first two hospital days [105]. Patients with a diagnosis of infection (eg, sinusitis, sepsis, pneumonia, urinary tract infection) were excluded. Antibiotic-treated patients had a longer median length of stay (ratio 1.29, 95% CI 1.27-1.31) than those not treated with an antibiotic, even after controlling for disease severity. No difference in the likelihood of treatment failure was found between antibiotic-treated and untreated patients (adjusted OR 0.96, 95% CI 0.85-1.10).

It is possible that measurement of serum procalcitonin levels will allow identification of a bacterial etiology among patients whose asthma exacerbations are triggered or complicated by a respiratory tract infection [108]. (See "Procalcitonin use in lower respiratory tract infections".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Asthma in adolescents and adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading

level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Asthma treatment in adolescents and adults (Beyond the Basics)" and "Patient education: Trigger avoidance in asthma (Beyond the Basics)" and "Patient education: How to use a peak flow meter (Beyond the Basics)" and "Patient education: Inhaler techniques in adults (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Assessment of exacerbation severity** – Early recognition and intervention are critical for successful management of asthma exacerbations. In the acute care setting, assessment of the severity of an asthma exacerbation is based upon symptoms, physical findings, peak expiratory flow (PEF), or less commonly forced expiratory volume in one second (FEV_1), measurements, pulse oxygen saturation (SpO_2), and in certain circumstances, arterial blood gas measurement. (See 'Assessment of exacerbation severity' above.)

- **Algorithm and rapid overview table for management** – An approach to the management of patients presenting to the emergency department with an asthma exacerbation is provided in the algorithm (algorithm 1). Focused treatment of severe asthma exacerbations is described in the rapid overview (table 2). (See 'Emergency department management' above.)

- **Supplemental oxygen** – Supplemental oxygen should be administered to all patients with hypoxemia (SpO_2 <90 percent) and to those with a moderate or severe asthma exacerbation for whom continuous oxygen saturation monitoring is not available. We titrate supplemental oxygen to maintain the SpO_2 >92 percent (>95 percent in pregnancy). (See 'Oxygen' above.)

- **Prompt administration of SABA** – For all patients presenting with an asthma exacerbation, we recommend prompt administration of an inhaled short-acting beta-agonist (SABA; albuterol, or an equivalent) (**Grade 1B**). The typical dose is 2.5 mg by jet nebulization every 20 minutes for three doses, then 2.5 mg every one to four hours as needed (table 3). Alternatively, albuterol can be given by metered dose inhaler (MDI) with a spacer, four to eight puffs every 20 minutes for three doses, then four to eight puffs

every one to four hours as needed. For critically ill patients, some clinicians prefer continuous nebulization, administering 10 to 15 mg over one hour. (See 'Oxygen' above and 'Inhaled beta-agonists' above and "Delivery of inhaled medication in adults", section on 'Continuous nebulization'.)

- **Early administration of systemic glucocorticoids** – For patients with a moderate or severe exacerbation, we recommend systemic glucocorticoids (**Grade 1A**). Evidence suggests that earlier administration (eg, within first hour) improves outcomes.

  - The equivalent of prednisone 40 to 60 mg (methylprednisolone 32 to 48 mg) once daily for five to seven days is the typical dose for patients who will be discharged home. (See 'Systemic glucocorticoids' above.)

  - Similarly, for patients admitted to the hospital, the equivalent of prednisone 40 to 60 mg per day is typical. Oral administration is comparable to intravenous unless the patient is unable to tolerate oral intake. Methylprednisolone 60 to 80 mg administered intravenously every 6 to 12 hours is sometimes used for patients in the intensive care unit, although supportive data are lacking. (See 'Systemic glucocorticoids' above.)

- **Adding inhaled** ipratropium – For patients with severe exacerbations of asthma, we recommend addition of inhaled ipratropium to inhaled SABA (**Grade 1B**). Because differentiating moderate and severe exacerbations is imprecise, ipratropium treatment may be extended to patients with moderate exacerbations based on clinical judgment. Adult dosing of ipratropium is 500 mcg by nebulization or four to eight puffs from an MDI, every 20 minutes for three doses and then hourly as needed for up to three hours. Ipratropium does not appear to provide additional benefit to frequent inhaled beta agonists during hospitalization. (See 'Inhaled muscarinic antagonists' above.)

- **Adding** magnesium sulfate – For patients who present with a life-threatening asthma exacerbation or a severe asthma exacerbation that is not responding to initial therapy, we suggest a one-time infusion of magnesium sulfate, based on modest evidence of benefit and low likelihood of harm (**Grade 2C**). The usual dose is 2 grams administered intravenously over 20 minutes. (See 'Magnesium sulfate' above.)

- **Assessing response to therapy and triage** – Patients should be reassessed frequently. After the first hour of therapy, some patients may be ready for discharge while others need hospitalization or further emergency department management (algorithm 1). (See 'Assessment after initial treatment' above.)

- We advise admitting patients to the hospital in a setting with a high level of patient monitoring and care if they do not respond well after an additional few hours of emergency department therapy; if they have symptoms of coughing, wheezing, and shortness of breath that preclude self-care; and/or have a PEF ≤60 percent of predicted or their personal best value.

- Patients with an incomplete symptomatic response and a PEF >60 to 80 percent of predicted may need hospitalization, especially if they have new onset asthma, are at high risk for fatal asthma, or presented during a course of oral glucocorticoids, but others may be sufficiently stable for discharge; this decision needs to be individualized.

- **Nonstandard therapies** – Therapies such as bronchodilating anesthetic agents, enoximone, helium-oxygen mixtures, and extracorporeal life support have limited evidence of benefit in severe asthma. We generally do not use parenteral beta-agonists, methylxanthines, or leukotriene receptor antagonists in the management of asthma exacerbations except in rare and selected circumstances. (See 'Life-threatening asthma exacerbations' above and 'Ineffective therapies' above.)

- **Discharge planning** – In addition to oral (or intramuscular) glucocorticoids, patients who are well enough to go home should be given a prescription for inhaled glucocorticoids, education about asthma and its management including a personalized asthma action plan (NHLBI Asthma Action Plan), and instructions to seek follow-up care (form 1). (See 'Patient education' above.)

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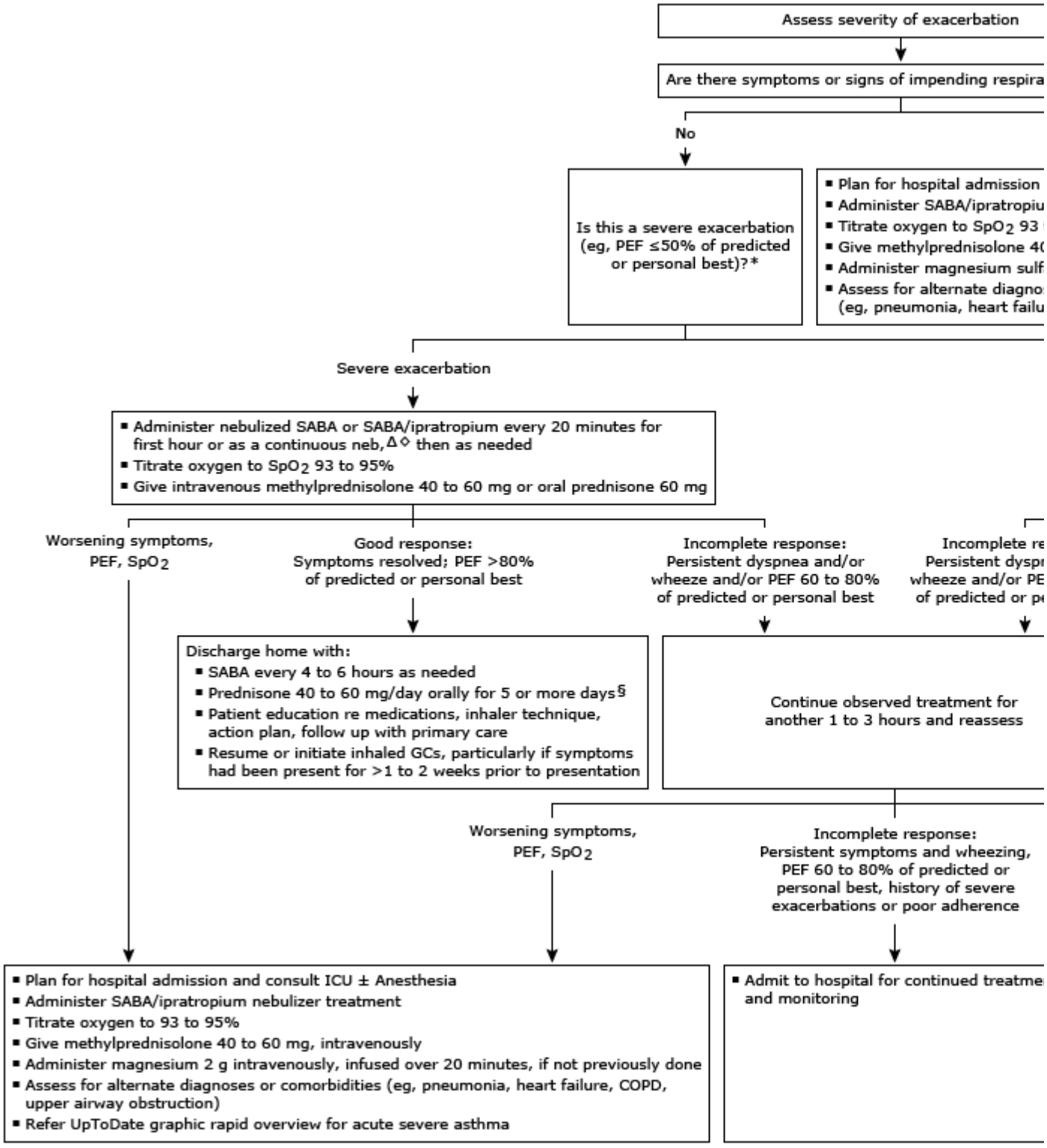
Topic 119093 Version 37.0

GRAPHICS

Management of asthma exacerbations in adults: Emergency department or urgent care



Features that help with assessment of severity (may or may not be present):

- Impending respiratory failure:

- Cyanosis, inability to maintain respiratory effort, depressed mental status, SpO_2 <90%
- $PaCO_2$ >40 mmHg

- Severe exacerbation:
  - Speaks in single words
  - Sits hunched forward
  - Agitated, diaphoretic
  - Respiratory rate >30 breaths/minute
  - Heart rate >120 beats/minute
  - SpO_2 (on air) <90%
  - PEF ≤50% predicted or personal best
- Mild to moderate exacerbation:
  - Talks in phrases or sentences
  - Prefers sitting to lying
  - Not agitated
  - Respiratory rate 16 to 30 breaths/minute
  - Heart rate 100 to 120 beats/minute
  - SpO_2 >90%
  - PEF >50% but <80% predicted or personal best

PEF: peak expiratory flow; ICU: intensive care unit; SABA: short-acting beta agonist (eg, albuterol); SpO_2: pulse oxygen saturation; COPD: chronic obstructive pulmonary disease; MDI: metered dose inhaler; GC: glucocorticoid; $PaCO_2$: carbon dioxide tension.

* Titrate oxygen to SpO_2 93 to 95% for patients with severe exacerbations, particularly if at risk for hypercapnia. Aim for SpO_2 >95% in pregnant patients. Titrate to SpO_2 88 to 92%, if asthma-COPD overlap.

¶ Magnesium sulfate is 4.06 mmol/g (2 g = 8.1 mmol).

Δ Please refer to the UpToDate topic on treatment of asthma exacerbations in adults.

◇ Adding ipratropium to albuterol nebulizer treatments is preferred for patients with severe exacerbations; alternatively, SABA/ipratropium can be given via MDI 4 to 8 inhalations every 20 minutes, as needed for up to 3 hours.

§ The dose and duration of therapy can be modified based on the patient's past history of response, severity of exacerbation, and response to current treatment.

Graphic 111835 Version 3.0

Predicted peak expiratory flow (PEF; liters/minute) for males age 20 to 70 years

Age (years)	Height				
	60 inches/152 cm	65 inches/165 cm	70 inches/178 cm	75 inches/191 cm	80 inches/203 cm
20	477	539	606	678	748
25	484	546	613	685	756
30	488	550	616	688	759
35	487	549	616	688	758
40	483	545	611	683	754
45	474	536	603	675	746
50	462	436	591	663	733
55	446	508	575	646	717
60	426	488	554	626	697
65	402	464	530	602	673
70	374	436	503	574	645

For patients who do not know their personal best PEF, this table can help estimate an expected "personal best." This table uses a prediction equation for White males, age 20 to 70 years. Refer to UpToDate calculator for values for additional age, height, and race/ethnicity parameters.

Reference:

1. *Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med. 1999; 159(1):179.*

Graphic 57257 Version 10.0

Predicted peak expiratory flow (PEF; liters/minute) for females age 20 to 70 years

Age (years)	Height				
	55 inches/140 cm	60 inches/152 cm	65 inches/165 cm	70 inches/178 cm	75 inches/190 cm
20	333	372	418	468	517
25	340	379	425	475	524
30	344	383	429	479	528
35	344	383	430	479	529
40	342	381	427	477	526
45	336	376	422	471	521
50	328	367	413	463	512
55	316	323	401	451	501
60	301	341	387	436	486
65	283	323	369	419	468
70	263	302	348	398	447

For patients who do not know their personal best PEF, this table can help estimate an expected "personal best." This table uses a prediction equation for White females age 20 to 70 years. Refer to UpToDate calculator for values for additional age, height, and race/ethnicity parameters.

Reference:

1. *Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med. 1999; 159(1):179.*

Graphic 62839 Version 10.0

Severe asthma exacerbation in adults: Rapid overview of emergency management

Clinical danger signs
Use of accessory muscles of respiration; brief, fragmented speech; inability to lie supine; profound diaphoresis; agitation; severe symptoms that fail to improve with initial emergency treatment
Life-threatening airway obstruction can still occur when these signs are **NOT** present
Signs of imminent respiratory arrest: cyanosis, inability to maintain respiratory effort, and depressed mental status
Assessment
Measurement of expiratory airflow (peak expiratory flow rate or PEFR) is the best measure of severity; PEFR <40% predicted (or <200 L/minute in most adults) indicates severe obstruction; patients in severe distress are often unable to perform peak flow tests
Severe hypoxemia (eg, SpO_2 ≤95% despite high flow O_2 treatment by nonrebreather mask) **portends imminent respiratory arrest** or possibly severe complication (eg, pneumothorax); continuous pulse oximetry monitoring should be performed
Patients in extremis should be managed clinically without waiting for arterial blood gases (ABGs). ABGs can aid assessment of hypercapnia or impending respiratory failure: hypercapnia usually does not occu unless PEF is <25% of normal (generally <100 to 150 L/min).
Chest radiograph is generally unhelpful; obtain if complications suspected (eg, pneumonia, pneumothorax), diagnosis is in doubt, or patient is high-risk (eg, IV drug abuser, immunosuppressed, chronic pulmonary disease, heart failure)
Standard treatments
Inhaled beta agonist: give **albuterol** 2.5 to 5 mg by nebulization every 20 minutes for three doses, then 2.5 to 5 mg every one to four hours as needed, or give 4 to 8 puffs by metered dose inhaler (MDI) with spacer every 20 minutes for three doses, then every one to four hours as needed. Alternatively, for severe exacerbations, 10 to 15 mg can be administered by continuous nebulization over one hour.
Oxygen: give sufficient oxygen to maintain SpO_2 ≥92% (>95% in pregnancy)
IV: establish intravenous access; give IV boluses of isotonic saline if patient is dehydrated due to reduced intake and prolonged episode
Ipratropium bromide: give 500 mcg by nebulization every 20 minutes for 3 doses OR 4 to 8 puffs by MDI with spacer every 20 minutes for 3 doses; then may administer additional doses hourly as needed for up to 3 hours
Systemic glucocorticoids: for patients with impending respiratory failure, give methylprednisolone 60 to 125 mg IV. For the majority of less severe asthma exacerbations, give prednisone 40 to 60 mg orally; alternatives include: dexamethasone 6 to 10 mg IV or hydrocortisone 150 to 200 mg IV; glucocorticoids may be given IM or orally if IV access is unavailable.

Magnesium sulfate: give 2 g (8 mmol) IV over 20 minutes for life-threatening exacerbations and severe exacerbations that are unimproved after one hour of intensive bronchodilator therapy
Additional treatments
Epinephrine: for patients suspected of having an anaphylactic reaction or unable to use inhaled bronchodilators for severe asthma exacerbation, give epinephrine 0.3 to 0.5 mg IM (eg, 0.3 to 0.5 mL of 1 mg/mL [may be labeled 1:1000] solution) into the mid-outer thigh (vastus lateralis muscle); if needed can repeat every 20 minutes for up to 3 doses; give epinephrine OR terbutaline but not both
Terbutaline: may give 0.25 mg by SC injection every 20 minutes times 3 doses for patients unable to use inhaled bronchodilators; give terbutaline OR epinephrine but not both
Endotracheal intubation and ventilation
The decision to intubate during the first few minutes of a severe asthma attack is clinical. Slowing of the respiratory rate, depressed mental status, inability to maintain respiratory effort, or severe hypoxemia suggests the patient requires intubation. In the absence of anticipated intubation difficulty, rapid sequence intubation is preferred. Nasal intubation is not recommended.
The goal of mechanical ventilation is to maintain adequate oxygenation and ventilation while minimizing elevations in airway pressures. This is accomplished by using low tidal volumes (6 to 8 mL/kg), and low respiratory rates (10 to 12/minute). In some patients, elevations in $PaCO_2$ must be tolerated to avoid barotrauma (ie, permissive hypercapnia).*

IM: intramuscular; IV: intravenous; MDI: metered dose inhaler; PEFR: peak expiratory flow rate; SC: subcutaneous; SpO_2: pulse oxygen saturation.

* Please refer to the UpToDate topics on mechanical ventilation in adults with acute severe asthma and permissive hypercapnia.

Graphic 54125 Version 9.0

Usual doses of short-acting bronchodilators for asthma in adolescents and adults*

Drug name(s)	Preparation(s)¶	Dose
Albuterol MDI[Δ]	MDI: 90 mcg/inhalation (United States) MDI: 100 mcg/inhalation (Canada)	▪ Usual dose: 2 inhalations every 4 to 6 hours as needed ▪ Acute exacerbation at home: 2 to 4 inhalations, can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses[§], then taper depending on response to therapy
Albuterol DPI	DPI[Δ]: 90 mcg/actuation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours, as needed ▪ Acute exacerbation at home: 2 to 4 inhalations, can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses[§], then taper depending on response to therapy
Albuterol DPI (Canada)	DPI: 200 mcg/actuation (Canada)	▪ Usual dose: 1 inhalation every 4 to 6 hours, as needed ▪ Exercise-induced bronchoconstriction: 1 inhalation 15 minutes prior to exercise
Albuterol solution for nebulization	Nebulizer solutions: ▪ 0.083% (2.5 mg/3 mL) ▪ 0.5% (2.5 mg/0.5 mL) concentrate; must be diluted in 2.5 mL saline	▪ Usual dose: 2.5 mg every 4 to 6 hours, as neede ▪ Acute exacerbation at home: Administer 2.5 mg, can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated[¥] ▪ Acute care setting: Administer 2.5 to 5 mg, can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated ▪ Acute care setting (critically ill): Continuous nebulizer treatment: Use a large volume nebulizer, 10 to 15 mg/hour in monitored settin
Albuterol-budesonide MDI	MDI: Albuterol 90 mcg and budesonide 80 mcg/actuation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours as needed ▪ Acute exacerbation at home: 2 inhalations, can be repeated every 20 minutes for a total of 3

		doses, then as directed[¥]
Levalbuterol MDI[Δ]	45 mcg/inhalation (United States)	▪ Usual dose: 2 inhalations every 4 to 6 hours, as needed ▪ Acute exacerbation at home: 2 to 4 inhalations; can be repeated every 20 minutes for a total of 3 doses, then as directed[◇] ▪ Acute care setting: 4 to 8 inhalations every 20 minutes for 3 doses, then taper depending on response to therapy[§]
Levalbuterol solution for nebulization	Nebulizer solution: ▪ 0.63 mg/3 mL ▪ 1.25 mg/3 mL ▪ 1.25 mg/0.5 mL concentrate; must be diluted in 2.5 mL saline	▪ Usual dose: Administer 0.63 to 1.25 mg (equivalent to 1.25 to 2.5 mg albuterol) every 6 to 8 hours, as needed (up to 3 doses per 24 hours) ▪ Acute exacerbation at home: Administer 1.25 mg; can be repeated every 20 minutes for a total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated[¥] ▪ Acute care setting: Administer 1.25 mg to 2.5 mg (equivalent to 2.5 to 5 mg of albuterol); can repeat every 20 minutes for total of 3 doses, then decrease frequency to every 1 to 4 hours, as tolerated
Terbutaline DPI	DPI: 0.5 mg/actuation (Canada)	▪ Usual dose: 1 inhalation every 4 hours, as needed ▪ If no effect after 5 minutes, can repeat dose
Ipratropium-albuterol SMI	SMI: Ipratropium 20 mcg and albuterol 100 mcg/inhalation (United States)	▪ Usual dose (off-label): 2 inhalations every 6 hours, as needed ▪ Acute exacerbation (off-label): 4 to 8 inhalations every 20 minutes for 3 doses, and then as needed for up to 3 hours
Ipratropium-albuterol solution for nebulization	Nebulizer solution: Ipratropium 0.5 mg and albuterol 2.5 mg per 3 mL/vial[‡]	▪ Usual dose (off-label): Administer 1 vial (3 mL) every 4 to 6 hours, as needed ▪ Acute exacerbation (off-label): Administer 1 vial (3 mL), every 20 minutes for 3 doses, and then as needed for up to 3 hours[¥]

MDI: metered-dose inhaler; DPI: dry-powder inhaler; SMI: soft mist inhaler.

* Oral formulations of albuterol and terbutaline are less effective than inhaled formulations and are not recommended in asthma. Inhaled epinephrine (MDI or nebulized) is not recommended for routine use.

¶ Doses shown and strengths (ie, mcg per puff or inhalation) are based upon product descriptions approved in the United States and Canada as noted, which may differ from how strengths are described

for products available in other countries. Consult local product information before use.

Δ Agent can also be used to prevent exercise-induced bronchoconstriction, 2 inhalations 5 to 20 minutes prior to exercise.

◇ Typically, two puffs are used for mild-to-moderate symptoms and four puffs for more severe symptoms; over the course of the first hour, the patient can determine (based on action plan or clinician guidance) whether to continue self-care at home or seek additional medical attention.

§ The number of inhalations is based on the severity of respiratory impairment, number of inhalations the patient has already used, and availability of monitoring. When administering an albuterol MDI for acute asthma exacerbation in an office or acute care setting, use of a valved holding chamber and careful attention to technique are recommended.

¥ Over the course of the first hour, the patient can determine (based on action plan or clinician guidance) whether to continue self-care at home or seek additional medical attention.

‡ Nebulizer solution in Canada is ipratropium 0.5 mg and albuterol 2.5 mg per 2.5 mL.

Graphic 72467 Version 27.0

Aeroneb Solo mesh nebulizer for intermittent or continuous nebulization

Nebulizers like the Aeroneb Solo mesh nebulizer can be used for intermittent or continuous nebulization. The Aeroneb Pro controller accommodates nebulization cycles of 15 to 30 minutes.

Graphic 61793 Version 4.0

Usual dosages for oral glucocorticoids in asthma

Medication	Oral preparations	Dose	Comments
Methylprednisolone	2, 4, 8, 16, and 32 mg tablets	Short-course "burst" for asthma exacerbation: 32 to 48 mg per day as a single dose in the morning for 3 to 10 days; typically 32 mg daily for 5 days.	Short course therapy: ▪ Short courses or "bursts" are effective for establishing control when initiating therapy, during an acute exacerbation or a period of deterioration. ▪ The burst should be continued until patient achieves substantial symptom improvement or resolution, which is usually associated with PEFR >70 to 80 percent of predicted or personal best. This usually requires 3 to 10 days, but may require longer treatment. ▪ In patients receiving inhaled glucocorticoids, there is no evidence that tapering the oral dose following improvement prevents relapse. Long-term control: ▪ Oral glucocorticoids are used only rarely as long-term control medications, eg, in patients with very poorly controlled symptoms despite an optimal treatment
Prednisolone*	5 mg tablets; 10, 15, and 30 mg orally disintegrating tablets (ODT)	Short-course "burst" for asthma exacerbation: 40 to 60 mg per day as single dose in the morning for 3 to 10 days; typically 40 mg daily for 5 days.	

Prednisone*	1, 2.5, 5, 10, 20, and 50 mg tablets		regimen and environmental controls. ▪ The lowest effective dose is given daily in the morning, or on alternate days to minimize adrenal suppression.
Dexamethasone*	0.5, 0.75, 1, 1.5, 2, 4, and 6 mg tablets	Short-course "burst" to achieve symptom control: 6 to 9 mg per day as a single dose in the morning for 3 to 10 days; typically 6 mg daily for 5 days.	

For specific recommendations about the use of oral glucocorticoids in asthma, refer to UpToDate reviews on the management of asthma exacerbations and severe asthma.

PEFR: peak expiratory flow rate.

* Oral liquids are available for use by patients who are unable to swallow pills.

Data from:

1. *Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2017. Available from: www.ginaasthma.org (accessed February 17, 2017).*
2. *Lexicomp Online. Copyright © 1978-2024 Lexicomp, Inc. All Rights Reserved.*

Graphic 66549 Version 11.0

Comparison of systemic glucocorticoid preparations

	Equivalent doses (mg)	Antiinflammatory activity relative to hydrocortisone*	Duration of action (hours)
Glucocorticoids			
Short acting			
Hydrocortisone (cortisol)	20	1	8 to 12
Cortisone acetate	25	0.8	8 to 12
Intermediate acting			
Prednisone	5	4	12 to 36
Prednisolone	5	4	12 to 36
Methylprednisolone	4	5	12 to 36
Triamcinolone	4	5	12 to 36
Long acting			
Dexamethasone	0.75	30	36 to 72
Betamethasone	0.6	30	36 to 72
Mineralocorticoids			
Fludrocortisone	Not used for an antiinflammatory effect¶. The typical dose of fludrocortisone for mineralocorticoid replacement is 0.1 to 0.2 mg.		12 to 36

The mineralocorticoid effect of commonly administered glucocorticoids may be estimated as follows:

- When given at replacement doses, triamcinolone, dexamethasone, and betamethasone have no clinically important mineralocorticoid activity.
- 20 mg hydrocortisone and 25 mg of cortisone acetate each provide a mineralocorticoid effect that is approximately equivalent to 0.1 mg fludrocortisone.
- Prednisone or prednisolone given at antiinflammatory doses ≥50 mg per day provide a mineralocorticoid effect that is approximately equivalent to 0.1 mg of fludrocortisone.

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* Equivalent antiinflammatory dose shown is for oral or intravenous (IV) administration. Relative potency for intraarticular or intramuscular administration may vary considerably.

¶ The antiinflammatory potency is 10 to 15 times that of hydrocortisone; however, fludrocortisone is not used clinically as an antiinflammatory agent.

Data from:

1. *Schimmer BP, Funder JW. ACTH, adrenal steroids, and pharmacology of the adrenal cortex. In: Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 12th ed, Brunton LL, Chabner BA, Knollmann BC (Eds), McGraw-Hill Education 2011.*
2. *Liu D, Ahmet A, Ward L, et al. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy Asthma Clin Immunol 2013, 9:30.*

Graphic 64138 Version 23.0

Estimated comparative daily doses for inhaled glucocorticoids in adolescents ≥12 years and adults

Drug	Low dose (total daily dose)	Medium dose (total daily dose)	High dose (total daily dose)*
Beclomethasone HFA (Qvar RediHaler product available in United States) Administer as 2 divided doses	80 to 160 mcg	>160 to 320 mcg	>320 to 640 mcg
40 mcg per actuation	2 or 4 inhalations	¶	¶
80 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Beclomethasone HFA[Δ] (Qvar product available in Canada, Europe, and elsewhere) Administer as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPI (Pulmicort Flexhaler product available in United States) Administer as 2 divided doses	180 to 360 mcg	>360 to 720 mcg	>720 to 1440 mcg
90 mcg per actuation	2 or 4 inhalations	¶	¶
180 mcg per actuation	2 inhalations	4 inhalations	6 or 8 inhalations
Budesonide DPI[Δ] (Pulmicort Turbuhaler or Turbohaler product available in Canada, Europe, and elsewhere) Administer low doses (ie, ≤400 mcg/day) once daily; administer higher doses (ie, >400 mcg/day) as 2 to 4 divided doses	200 to 400 mcg	>400 to 800 mcg	>800 to 2400 mcg
100 mcg per actuation	2 to 4 inhalations	¶	¶
200 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
400 mcg per actuation	1 inhalation	2 inhalations	3 to 6 inhalations

Ciclesonide HFA (Alvesco product available in United States, Europe, and elsewhere) United States: Administer as 2 divided doses Australia, Europe, and elsewhere: Administer lower doses (ie, 160 to 320 mcg/day) once daily; administer 640 mcg dose as 2 divided doses	160 mcg	320 mcg	640 mcg
80 mcg per actuation	2 inhalations	4 inhalations	¶
160 mcg per actuation	◇	2 inhalations	4 inhalations
Ciclesonide HFA[Δ] (Alvesco product available in Canada) Administer lower doses (eg, 100 to 400 mcg) once daily; administer 800 mcg dose as 2 divided doses	100 to 200 mcg	>200 to 400 mcg	>400 to 800 mcg
100 mcg per actuation	1 to 2 inhalations	3 to 4 inhalations	¶
200 mcg per actuation	1 inhalation	2 inhalations	3 to 4 inhalations
Fluticasone propionate HFA (Flovent HFA product available in United States) Administer as 2 divided doses	176 to 220 mcg	>220 to 440 mcg	>440 to 1760 mcg
44 mcg per actuation	4 inhalations	¶	¶
110 mcg per actuation	2 inhalations	4 inhalations	¶
220 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate HFA[Δ] (Flovent HFA product available in Canada; Flixotide Evohaler product available in Europe and elsewhere) Administer as 2 divided doses	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg
50 mcg per actuation	2 to 4 inhalations	¶	¶
125 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
Fluticasone propionate DPI (Flovent Diskus product available in United States and Canada; Flixotide	100 to 250 mcg	>250 to 500 mcg	>500 to 2000 mcg

Accuhaler product available in Europe and elsewhere) Administer as 2 divided doses			
50 mcg per actuation	2 to 4 inhalations	¶	¶
100 mcg per actuation	2 inhalations	4 inhalations	¶
250 mcg per actuation	◇	2 inhalations	4 to 8 inhalations
500 mcg per actuation (strength not available in United States)	◇	◇	2 or 4 inhalations
Fluticasone propionate DPI (Armonair Digihaler product available in United States; Aermony Respiclick product available in Canada) Administer as 2 divided doses	110 mcg	226 mcg	464 mcg
55 mcg per actuation	2 inhalations	¶	¶
113 mcg per actuation	◇	2 inhalations	¶
232 mcg per actuation	◇	◇	2 inhalations
Fluticasone furoate DPI (Arnuity Ellipta product available in United States, Canada, Australia, and elsewhere, but not available in Europe or UK) Administer once daily **NOTE:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.	50 mcg (by use of pediatric DPI, which is off-label in adolescents and adults)	100 mcg	200 mcg
50 mcg per actuation	1 inhalation	¶	¶
100 mcg per actuation	◇	1 inhalation	2 inhalations
200 mcg per actuation	◇	◇	1 inhalation
Mometasone DPI (Asmanex Twisthaler product available in United States) May administer lower doses (ie, 220 to 440 mcg/day) once daily; administer 880 mcg dose as 2 divided doses	220 mcg	>220 to 440 mcg	>440 to 880 mcg

110 mcg per actuation	2 inhalations	¶	¶
220 mcg per actuation	1 inhalation	2 inhalations	4 inhalations
Mometasone HFA (Asmanex HFA product available in United States) Administer as 2 divided doses	200 mcg	>200 to 400 mcg	>400 to 800 mcg
100 mcg per actuation	2 inhalations	4 inhalations	¶
200 mcg per actuation	◇	2 inhalations	4 inhalations
Mometasone DPIΔ (Asmanex Twisthaler product available in Canada, Europe, and elsewhere) May administer lower doses (ie, 200 to 400 mcg/day) once daily; administer 800 mcg dose as 2 divided doses	200 mcg	>200 to 400 mcg	>400 to 800 mcg
200 mcg per actuation	1 inhalation	2 inhalations	¶
400 mcg per actuation	◇	1 inhalation	2 inhalations

- **The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effects.
- Suggested total daily doses for low, medium, and high dose inhaled glucocorticoid regimens are based on daily doses recommended by Global Initiative for Asthma (GINA), National Asthma Education and Prevention Program (NAEPP), and/or product labeling[1-5]. This is not a table of equivalence.
- Depending on the specific product, total daily doses are administered once or divided and given twice daily. Refer to local product information or a clinical drug reference (eg, Lexicomp).
- Some doses are outside the approved product information recommendations.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant metered dose inhaler.

* Evidence for additional improvement with dose increases >1000 mcg/day is limited.

¶ Select alternate preparation with higher mcg/actuation to improve convenience.

Δ Products shaded in light gray color are not available in the United States but are available widely elsewhere.

◇ Select preparation with fewer mcg/actuation.

Data from:

1. *Global Initiative for Asthma (GINA); Global Strategy for Asthma Management and Prevention; 2021. Available at www.ginasthma.org.*
2. *National Heart, Blood, and Lung Institute Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma; 2007. NIH Publication 08-4051 available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report and pro.*
3. *US Food & Drug Administration (FDA) approved product information. US National Library of Medicine. (Available online at www.dailymed.nlm.nih.gov/dailymed/index.cfm.)*
4. *Health Canada-approved product monograph. Health Canada. (Available online at https://health-products.canada.ca/dpd-bdpp/index-eng.jsp.)*
5. *European Medicines Agency (EMA) summary of product characteristics. European Medicines Agency. (Available online at www.ema.europa.eu/en/medicines.)*

Graphic 78011 Version 17.0

Asthma action plan

My Asthma Action Plan

Age ≥5 years

Patient Name: _____

Medical Record #: _____

Clinician's Name: _____ DOB: _____

Clinician's Phone #: _____ Completed by: _____ Date: _____

Long-Term Control Medicines	How Much To Take	How Often	Other Instructions
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
		_____ times per day EVERY DAY!	
Quick-Relief Medicines	**How Much To Take**	**How Often**	**Other Instructions**
		Take ONLY as needed	NOTE: If this medicine is needed frequently, call clinician to consider increasing long-term control medications.

Special instructions when I feel *good*, *not good*, and *awful*.

GREEN ZONE

I feel *good*.

{My peak flow is in the **GREEN** zone.}

My Personal Best Peak Flow

PREVENT asthma symptoms everyday:

- ☐ Take my long-term control medicines (above) every day.
- ☐ Before exercise, take _____ puffs of _____
- ☐ Avoid things that make my asthma worse like:

_____

YELLOW ZONE

I do *not* feel *good*.

{My peak flow is in the **YELLOW** zone.}

My symptoms may include one or more of the following:

- Wheeze
- Tight chest
- Cough
- Shortness of breath
- Waking up at night with asthma symptoms
- Decreased ability to do usual activities
- _____

80% Personal Best

CAUTION. I should continue taking my long-term control asthma medicines every day AND:

- ☐ Take _____

If I still do not feel good, or my peak flow is not back in the *Green Zone* within one hour, then I should:

- ☐ Increase _____
- ☐ Add _____
- ☐ Call _____

RED ZONE

I feel *awful*.

{My peak flow is in the **RED** zone.}

Warning signs may include one or more of the following:

- It is getting harder and harder to breathe
- Unable to sleep or do usual activities because of trouble breathing

50% Personal Best

Unable

Peak Flow Meter

MEDICAL ALERT! Get help!

- ☐ Take _____ until I get help immediately.
- ☐ Take _____
- ☐ Call _____

Danger! Get help immediately! **Call 9-1-1 if you have trouble walking or talking due to shortness of breath or lips or fingernails are gray or blue.**

Reproduced from: National Heart, Blood, and Lung Institute Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma. NIH Publication no. 08-4051, 2007.

Graphic 55900 Version 4.0