Background:

Asthma is a chronic inflammatory condition of the airways affecting nearly 23 million Americans (17 million adults and 6 million children).\(^1\) Asthma exacerbations result in approximately 440,000 hospitalizations, 1.8 million ED visits and 14.2 million office visits annually.\(^1\) The aim of this guideline is to review the diagnosis, treatment and prevention of acute asthma exacerbations in the outpatient setting.

Various sources are cited, but the majority of this guideline is based on National Heart, Lung and Blood Institute’s National Asthma Education and Prevention Program, Expert Panel 3: Guidelines for the Diagnosis and Management of Asthma.

Definitions/Clarifications:

- Asthma Action Plan: A written treatment plan for home use, based on symptoms and PEF
- FEV\(_1\): Forced expiratory volume in 1 second
- PEF: Peak expiratory flow
- SABA: Short-acting beta agonist
- LABA: Long-acting beta agonist
- ICS: Inhaled corticosteroid
- MDI: Metered-dose inhaler (“puffer”)
- An asthma exacerbation is an acute or subacute episodes of progressively worsening asthma symptoms, namely shortness of breath, cough, wheeze, chest tightness or a combination thereof that corresponds with an objectively measurable decrease in expiratory airflow (FEV\(_1\) or PEF).\(^2\)
- All recommendations in this guideline presume that patients have an existing diagnosis of asthma.
- This guideline applies to the outpatient office or urgent care setting.
- As with all facets of medicine, guidelines should inform and guide clinical judgment, but all patients and cases must be considered on an individual basis.
- Specific dosages of medications will be provided in table format near the end of the guideline

Pathogenesis:
Asthma is a complex pathogenic process that is a combination of chronic inflammation of the airways and bronchial smooth muscle constriction leading to airway obstruction. Histologically, various cell types (neutrophils, eosinophils, lymphocytes, macrophages) are responsible for the inflammatory changes depending on the chronicity, provoking factors, age and individual genetic differences. In some patients, the chronic inflammation leads to airway remodeling over time. Generally speaking, exacerbations are thought to involve similar pathophysiology as chronic asthma. It was historically thought of as a simple worsening or loss of control. Some more recent evidence suggests that the pathophysiology of acute exacerbations may not be identical. This is based on specific histologic patterns. It is also suggested by the fact that PEF values are often markedly different during acute exacerbations compared to chronically very poorly-controlled asthma, suggesting a possible difference in how the beta2-adrenoreceptor functions during acute exacerbation.

**Diagnosis:**

- As stated above, this presumes that patients already have a known diagnosis of asthma.

The diagnosis of acute asthma exacerbation is a clinical diagnosis made in the setting of acutely worsening asthma symptoms (SOB, chest tightness, wheezing, cough). Objective measurements such as hypoxemia, hypercapnea, decreased FEV1, decreased PEF and specific physical exam findings can help to confirm the diagnosis and qualify the severity of the exacerbation.

As always, a differential diagnosis of other possible conditions must be considered; the following are a few examples but should not be considered an exhaustive differential:
- Foreign body aspiration / upper airway obstruction
- Chemical exposure / pneumonitis
- Bacterial pneumonia (does not exclude concomitant asthma)
- Vocal cord dysfunction
- Tracheomalacia
- Pulmonary embolism
- Congestive heart failure
Assessment of severity / Triage:

- Once the diagnosis can be made, the first question to ask is “can I safely manage this patient in the current setting?” If not, transfer to a higher level of care (ED) is indicated.

Table 1.2.3: Assessing the Severity of Exacerbations — table taken directly from NHLBI EPR3.
## Treatment:

Treatment goals as defined by the 2007 NHLBI expert panel²

- **Correction of significant hypoxemia** with supplemental oxygen; this is especially important in moderate to severe exacerbations.
- **Rapid reversal of airflow obstruction**

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Initial PEF (or FEV₁)</th>
<th>Clinical Course</th>
</tr>
</thead>
</table>
| **Mild**           | Dyspnea only with activity (assess tachypnea in young children) | PEF/FEV₁ ≥ 70 percent predicted or personal best | - Usually cared for at home  
- Prompt relief with inhaled SABA  
- Possible short course of oral systemic corticosteroids |
| **Moderate**       | Dyspnea interferes with or limits usual activity | PEF/FEV₁ 40–60 percent predicted or personal best | - Usually requires office or ED visit  
- Relief from frequent inhaled SABA  
- Oral systemic corticosteroids; some symptoms last for 1–2 days after treatment is begun |
| **Severe**         | Dyspnea at rest; interferes with conversation | PEF/FEV₁ < 40 percent predicted or personal best | - Usually requires ED visit and likely hospitalization  
- Partial relief from frequent use of inhaled SABA  
- Oral systemic corticosteroids; some symptoms last for >3 days after treatment is begun  
- Adjunctive therapies are helpful |
| Subset: Life threatening | Too dyspneic to speak; perspiring | PEF/FEV₁ < 25 percent predicted or personal best | - Requires ED/hospitalization; possible ICU  
- Minimal or no relief from frequent inhaled SABA  
- Intravenous corticosteroids  
- Adjunctive therapies are helpful |

Key: ED, emergency department; FEV₁, forced expiratory volume in 1 second; ICU, intensive care unit; PEF, peak expiratory flow; SABA, short-acting beta₂-agonist.
Treating Acute Asthma Exacerbations in Adults and Children in the Primary Care or Urgent Care Settings

Clinical Practice Guideline

January 2016

- Repetitive or continuous administration of SABA
- Early administration of systemic corticosteroids to patients who do not respond quickly and completely to SABA administration

- Reducing the likelihood of future exacerbations by **intensifying therapy**
  - Short course of systemic corticosteroid, typically 5-10 days depending on severity
  - Consideration of increasing controller medications (typically ICA and/or LABA)
  - Identifying triggers, risk factors

NHLBI recommends serial measurements and reassessments to determine response to treatment, to help guide care and to determine if transfer to a higher level of care is needed.

- Serial measurements of lung function (FEV₁ and PEF)
  - These will be less helpful / impossible in younger children and infants
    - Pulse oximetry is a reasonable alternative for patients in whom measurements of lung function are not feasible
    - There are a variety of signs and symptoms scores that have been shown to be somewhat helpful in predicting outcomes and guiding care

**Home management of exacerbations:**
• The cornerstone of treatment of asthma exacerbations is early recognition and early treatment initiation; this can often most efficaciously be initiated by the patient or parents at home.
• It is imperative to have a written Asthma Action Plan which is reviewed with the patient at least annually by a physician or nurse\(^2\)\(^3\).
  ○ This plan should be based on PEF measurements.

- PEF should be checked by patient or parent when asthma symptoms are present and also occasionally when symptoms are not, especially in patients who have difficulty recognizing symptoms.

Symptomatic, but PEF > 80% predicted

PEF 50-79% predicted

PEF < 50% predicted

Seek immediate medical care.

Inhaled SABA, one nebulized treatment or 2-6 inhaler puffs every 20 minutes x 2 total initial doses

 Improvement:
Resolution of symptoms; PEF ≥ 80% predicted.
  • Call PCP for follow up instructions
  • Continue SABA q 3-4 hours
  • Continue to monitor symptoms and PEF

 No or Minimal Improvement:
Continued symptoms; PEF remains <80% predicted
  • Arrange for urgent appointment (same day)
  • Continue SABA as needed
  • Add oral corticosteroid (either at home or in MD office)
  • Continue to monitor

 Worsening:
Worsening symptoms; PEF < 50% predicted
  • Add oral corticosteroid
  • Continue repeating SABA
  • Call physician and
  • Go to ED (consider 911 call and ambulance transport)
Note: Patients with the following risk factors for death from asthma should seek immediate medical attention after initial treatment (regardless of response to treatment):²,³

- History of exacerbation requiring ICU or intubation
- Two or more hospitalizations for asthma in the past year
- Three or more ED visit for asthma in the past year
- Hospitalization or ED visit in the past month for asthma
- Using > 2 canisters of SABA per month
- Difficulty perceiving asthma symptoms or severity of exacerbations
- Those with significant cardiac or pulmonary comorbidities

Treatment of acute asthma exacerbation in the outpatient setting:

- SABA treatment is recommended for all patients.²
  - Initially, up to three (3) treatments spaced every 20-30 minutes is safe
  - In mild to moderate exacerbations, high dose MDI is equally effective as nebulization.
    - Nebulized SABA is preferable for patients unable to cooperate with MDI administration and in severe exacerbations.

- Oxygen is recommended for most patients.²,⁵
  - Goal is to maintain SpO² levels > 90% (greater than 95% for patients who are pregnant or have concomitant heart disease).
  - SpO² levels should be monitored until a clear response to SABA therapy is noted.
    - When SpO² monitoring is not available, give supplemental oxygen to patients who:
      - have FEV₁/PEF of less than 40% predicted
      - have coexisting heart disease
      - are pregnant
      - appear to be in significant distress

- Systemic corticosteroids are recommended for most patients.²,⁴
Give systemic corticosteroids to patients who have moderate and severe exacerbations (see table 1 above)
Give systemic corticosteroids to patients who do not completely improve with initial SABA therapy.
- Depot intramuscular corticosteroid therapy seems to be equally efficacious when compared to oral therapy; consider this option in patients who have a risk of non-adherence to oral therapy.\textsuperscript{2,6}

- The following therapies are generally \textbf{not} recommended:\textsuperscript{2}
  - Methylxanthines
  - Antibiotics (unless there is compelling clinical evidence of bacterial pneumonia)
  - Aggressive hydration
  - Chest physical therapy
  - Mucolytics
  - Sedation

- Repeat assessment of clinical status as well as objective measurement of lung function (FEV\textsubscript{1} or PEF) is needed to assess response to therapy.

\textbf{Indications against need for higher level of care:}\textsuperscript{2,5}

- Patients whose symptoms are minimal or absent and FEV\textsubscript{1}/PEF is \geq 70\% predicted with initial treatment
  - Patients should be observed 30-60 minutes after improvement to ensure continued stability
- Patients with mild symptoms and FEV\textsubscript{1}/PEF 50-69\% predicted can be considered on a case by case basis
  - Patients with risk factors for death from asthma (see above) likely require higher level of care even if initial improvement occurs
  - Individual clinical assessment is key
Indications for transfer to higher level of care:²

- FEV₁/PEF less than 50% predicted despite treatment
- Continued moderate or severe symptoms despite treatment
- Continued need for supplemental oxygen
- Inability to go longer than 30-60 minutes without SABA treatment
- Concerning physical exam findings (intercostal retractions, cyanosis, paradoxical breathing, significant tachypnea, signs of fatigue etc)
- Patients with significant comorbidities
- Patients with risk factors for death from asthma (see above)

Follow up care:

Prevention of recurrence is key:

- Regular follow up with PCP or asthma specialist²
  - Lack of PCP follow up has been shown to be a risk factor for death from asthma⁷
- The need for continued patient education cannot be overstressed
  - Reviewing medications individually; ensure adequate quantity and refills
  - Reviewing (updating if necessary) asthma action plans
  - Ensure that all necessary equipment is on hand and is working
    - Peak flow meter
    - Spacer for MDI use
    - Nebulizer
Pharmacotherapy: The following tables are imported directly from the NHLBI 2007 EPR-3 guidelines on asthma.²

Note, the initial tables included the drugs bitolterol and pirbuterol; these have been manually removed from the original table as they have been withdrawn from the market.

### Dosages of Drugs for Asthma Exacerbations

<table>
<thead>
<tr>
<th>How Supplied</th>
<th>Adult Dose</th>
<th>Pediatric Dose</th>
<th>Comments</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhaled Short-Acting Beta 2-Agonists (SABA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol (AccuNeb)</td>
<td>nebulizer solution (0.63 mg/3 ml, 1.25 mg/3 ml, 2.5 mg/3 ml, 5.0 mg/ml)</td>
<td>2.5 – 5 mg every 20 minutes for 3 doses, then 2.5 – 10 mg every 1-4 hours as needed, or 10-15 mg hour continuously</td>
<td>0.15 mg/kg (min dose 2.5 mg) every 20 minutes for 3 doses then 0.15-0.3 mg/kg up to 10 mg every 1-4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization</td>
<td>Only selective beta2 agonists are recommended. May mix with ipratropium nebulizer solution.</td>
</tr>
<tr>
<td>(generics available)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ProAir, Proventil, Ventolin)</td>
<td>HFA, MDI (90 mcg/puff)</td>
<td>4-8 puffs every 20 minutes up to 4 hours, then every 1-4 hours as needed.</td>
<td>4-8 puffs every 20 minutes for 3 doses, then every 1-4 hours inhalation, maneuver as needed. Use valved holding chamber (VHC); add mask in children &lt;4</td>
<td>In mild-to-moderate exacerbations, MDI plus VHC is as effective as nebulized therapy with appropriate administration technique and coaching by trained personnel.</td>
</tr>
</tbody>
</table>
### Levalbuterol
- **Xopenex**: Nebulizer solution (0.31 mg/3 ml, 0.63 mg/3 ml, 1.25 mg/0.5 ml, 1.25 mg/3 ml)
  - 1.25-2.5 mg every 20 minutes for 3 doses, then 1.25 -5 mg every 1-4 hours as needed
  - 0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075 – 0.15 mg/kg up to 5 mg every 1-4 hours as needed.
  - Levalbuterol administered in one-half the mg dose of albuterol provides comparable efficacy and safety. Has not been evaluated by continuous nebulization.
  - $6-$7 each (generic) ~$10 each brand

### Xopenex HFA
- **HFA, MDI (45 mcg/puff)**
  - 4-8 puffs every 20 minutes up to 4 hours, then every 1-4 hours as needed.
  - 4-8 puffs every 20 minutes for 3 doses, then every 1-4 hours inhalation, maneuver as needed. Use valved holding chamber; add mask in children <4 years.
  - 45 mcg/puff, 200 puffs/canister, $74.52

### Systemic (injected) Beta2 agonists

#### Epinephrine
- **Epinephrine (1 mg/ml)**
  - Injection solution 1 mg/ml
  - 0.3-0.5 mg every 20 minutes for 3 doses subcut
  - 0.01 mg/kg up to 0.3-0.5 mg every 20 minutes for 3 doses subcut
  - No proven advantage of systemic therapy over aerosol. Generally reserved
  - $3.42 per 1 ml vial
### Anticholinergics

**Ipratropium**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mg every 20 minutes for 3 doses then as needed</td>
<td></td>
<td>May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to SABA therapy for severe exacerbations. (The addition of ipratropium has not been shown to provide further benefit once the patient is hospitalized)</td>
</tr>
</tbody>
</table>

**Terbutaline**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/kg every 20 minutes for 3 doses subcut then every 2-6 hours as needed</td>
<td></td>
<td>No proven advantage of systemic therapy over aerosol. Generally reserved for cases where nebulized therapy is either unavailable or clinically ineffective.</td>
</tr>
</tbody>
</table>

**Ipratropium**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 – 0.5 mg every 20 minutes for 3 doses, then as needed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Terbutaline**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg every 20 minutes for 3 doses subcut</td>
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</table>

**Terbutaline Injection solution (1 mg/ml)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01 mg/kg every 20 minutes for 3 doses subcut then every 2-6 hours as needed</td>
<td></td>
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</table>

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## Atrovent HFA MDI (17 mcg/puff)

- 8 puffs every 20 minutes as needed up to 3 hours
- 4-8 puffs every 20 minutes as needed up to 3 hours
- Should use with valved holding chamber and face mask for children <4 years.
- 17 mcg/puff, 200 puffs/canister, $311.87

## Combination Products

### Ipratropium with albuterol

#### Nebulizer solution (each 3 ml contains 0.5 mg ipratropium bromide and 2.5 mg albuterol)

- 3 ml every 20 minutes for 3 doses, then as needed
- 1.5 – 3 ml every 20 minutes for 3 doses, then as needed
- May be used for up to 3 hours in the initial management of severe exacerbations.
- $2.29

### Ipratropium with albuterol (Combivent Respimat Inhaler)

#### MDI / respimat inhaler (each puff contains 20 mcg ipratropium bromide and 100 mcg of albuterol)

- 8 puffs every 20 minutes as needed up to 3 hours
- 4-8 puffs every 20 minutes as needed up to 3 hours
- Should be used with VHC and face mask for children <4 years
- 20-100 mcg/puff (ACT), 120 ACT, $355

### Systemic Corticosteroids

#### Prednisone

- Regular release tablets available in 1 mg, 2.5 mg, 5 mg, 10 mg, 20 mg, and 50 mg strengths.
- Oral solution available in 5mg/5ml concentration and 5 mg/ml concentrate
- (Applies to all 3 corticosteroids )
- 40-80 mg/day in 1 or 2 divided doses until PEF reached 70% of predicted or personal best
- 1-2 mg/kg in 2 divided doses (maximum = 60 mg/day) until PEF is 70% of predicted or personal best
- For outpatient “burst”, use 40-60 mg in single or 2 divided doses for total of 5-10 days in adults (children 1-2 mg/kg/day maximum 60 mg/day for 3-10 days)
- prednisone 5 mg = prednisolone 5 mg
- 40 mg dose as tablet ~$0.50
- Oral liquid 20 mg dose: $6

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**Next Scheduled Review Date:** January 2018 by Ambulatory Best Practice Committee
### Methylprednisolone
- Tablet available in 2 mg, 4 mg, 8 mg, 16 mg, 32 mg strengths.
- Injection solution as sodium succinate available in 40 mg, 125 mg (and other) strengths

### Prednisolone
- Available 5 mg tablet;
- 10 mg, 15 mg, 30 mg oral dispersible tablet;
- Oral solutions (varied concentrations); oral syrup 15 mg/5 ml

### Cost
- 40 mg dose $6.64

### References
References:

1. [http://www.cdc.gov/asthma/most_recent_data.htm](http://www.cdc.gov/asthma/most_recent_data.htm)
2. NHLBI ‘07
5. NHLBI EPR-2 1997