ACUTE ASTHMA MANAGEMENT: WHAT’S NEW IN 2015
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FACULTY/DISCLOSURES

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Advisor: Spirometrix, Teva
Speaker: AAN, NJH, AstraZeneca, Meda, Teva
Research Grants: NIH, JPB Foundation

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NOW 26 MILLION AMERICANS WITH ASTHMA
From 2000 to 2010...

- Overall prevalence has increased by 12.3% to 8.4%
  - Children — 9.4%
  - Poor children — 13.5%
  - African-American male children — 17.0%
  - Adults — 8.2%
  - Women — 9.3%
  - Poor adults — 13.5%

Asthma in Michigan

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Currently have asthma</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Ever diagnosed with asthma</td>
<td>17%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Michigan’s adult lifetime prevalence has been higher than the U.S. prevalence for 10 years.

Asthma Insight and Management Survey: Asthma Control in the Last 4 Weeks

Patient Perspective

- Well Controlled: 40%
- Somewhat Controlled: 24%
- Not Controlled (2%)
- Poorly Controlled (4%)
- Completely Controlled: 31%

2007 NAEPP EPR-3 Control Classification

- Not Well Controlled: 29%
- Very Poorly Controlled: 47%
- Not Controlled: 24%
- Well Controlled: 24%


Asthma Insight and Management Survey. Executive Summary. SRBI; 2009. This survey was sponsored by Schering-Plough.
Acute Asthma Issues: Today’s Discussion

- Airway physiology and pathophysiology
- Oxygenation vs Ventilation: our (not so) old friend
- Peak Flow or No?
- Nebulization versus MDIs
- Medication dosing and aerosols
- Albuterol versus Levalbuterol
- Other stuff...
Asthma Pathophysiology

- Genetic predisposition
- Innate vulnerability
- Atopy/allergy
- Environmental triggers

AHR=airway hyperresponsiveness

Inflammation underlies disease processes
- Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time

INDIVIDUAL

IMPACT

AIRWAY INFLAMMATION

Symptoms
- Airway Obstruction
- AHR/Bronchospasm
- Airway Remodeling

Asthma: A Chronic **Inflammatory** Disease of Mostly Small Airways

**Large Airways:**
- Trachea
- Bronchi
- Bronchioles

**Small Airways:**
- Terminal bronchioles
- Respiratory Bronchioles
What are small airways?

- < 2mm in diameter (8th generation)
- Collectively huge surface area
- Laminar airflow or diffusion
- Traditionally contribute very little to total airway resistance (<10%)
- Small airways = “silent zone”
- Role of small airway obstruction in asthma underestimated
Structural Alterations in Small Airways Associated with Severe Asthma

Bronchiole (small airway) (200X magnification H&E stain) from a 9 years old child with severe persistent asthma demonstrating airway inflammation, smooth muscle hyperplasia and epithelial sloughing characteristic of significant small airway involvement.

Classifying Asthma Severity as a Basis to Initiate Asthma Therapy
## Classifying Asthma Severity and Initiating Treatment in Youths ≥ 12 years and Adults

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>CLASSIFICATION OF ASTHMA SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>INTERMITTENT</td>
</tr>
<tr>
<td></td>
<td>PERSISTENT</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
</tr>
<tr>
<td>Impairment</td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC</td>
<td></td>
</tr>
<tr>
<td>8-19 yr 85%</td>
<td></td>
</tr>
<tr>
<td>20-39 yr 80%</td>
<td></td>
</tr>
<tr>
<td>40-59 yr 75%</td>
<td></td>
</tr>
<tr>
<td>60-80 yr 70%</td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>≥2 days/week not daily</td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td></td>
</tr>
<tr>
<td>Continuous</td>
<td></td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2x/month</td>
</tr>
<tr>
<td>3-4x/month</td>
<td></td>
</tr>
<tr>
<td>&gt;1x/week not nightly</td>
<td></td>
</tr>
<tr>
<td>Often nightly</td>
<td></td>
</tr>
<tr>
<td>SABA use for sx control (not for EIB)</td>
<td>≤2 days/week</td>
</tr>
<tr>
<td>&gt;2 days/week not daily</td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td></td>
</tr>
<tr>
<td>Several times daily</td>
<td></td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Minor limitation</td>
<td></td>
</tr>
<tr>
<td>Some limitation</td>
<td></td>
</tr>
<tr>
<td>Extremely limited</td>
<td></td>
</tr>
<tr>
<td>Lung Function</td>
<td>• Normal FEV₁ between exacerbations</td>
</tr>
<tr>
<td>• FEV₁ &gt; 80%</td>
<td></td>
</tr>
<tr>
<td>• FEV₁/FVC normal</td>
<td></td>
</tr>
<tr>
<td>• FEV₁ &gt;80%</td>
<td></td>
</tr>
<tr>
<td>• FEV₁/FVC normal</td>
<td></td>
</tr>
<tr>
<td>• FEV₁ &gt;60% but &lt;80%</td>
<td></td>
</tr>
<tr>
<td>• FEV₁/FVC reduced 5%</td>
<td></td>
</tr>
<tr>
<td>• FEV₁ &lt;60%</td>
<td></td>
</tr>
<tr>
<td>• FEV₁/FVC reduced &gt;5%</td>
<td></td>
</tr>
<tr>
<td>Exacerbations requiring oral corticosteroids</td>
<td>0-2/year</td>
</tr>
<tr>
<td>Frequency and severity may vary over time for patients in any category</td>
<td></td>
</tr>
<tr>
<td>Relative annual risk of exacerbation may be related to FEV₁</td>
<td></td>
</tr>
<tr>
<td>Recommended Step for Initiating Treatment</td>
<td>STEP 1</td>
</tr>
<tr>
<td>STEP 2</td>
<td></td>
</tr>
<tr>
<td>STEP 3</td>
<td></td>
</tr>
<tr>
<td>STEP 4 or 5</td>
<td></td>
</tr>
<tr>
<td>Consider short course of oral steroids</td>
<td></td>
</tr>
<tr>
<td>In 2-6 weeks, evaluate asthma control that is achieved and adjust therapy accordingly</td>
<td></td>
</tr>
</tbody>
</table>

Let’s Get to the Bottom Line:
Determine if your patient has intermittent vs. persistent asthma

- **INTERMITTENT**
  - Mild, infrequent (< twice weekly) symptoms or use of albuterol
  - Infrequent (< twice monthly) night awakenings
  - Normal exercise tolerance

  **RX:** prn Albuterol

- **PERSISTENT**
  - Moderate and more frequent (> twice weekly symptoms or use of albuterol
  - More frequent sleep disruption
  - Altered exercise tolerance

  **RX:** Controller Therapy + prn Albuterol
<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Impending respiratory failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental status</td>
<td>Normal</td>
<td>Might look agitated</td>
<td>Usually agitated</td>
<td>Drowsy or confused</td>
</tr>
<tr>
<td>Activity</td>
<td>Normal activity and exertional dyspnea</td>
<td>Decreased activity or feeding (infant)</td>
<td>Decreased activity infant, stops feeding</td>
<td>Unable to eat</td>
</tr>
<tr>
<td>Speech</td>
<td>Normal</td>
<td>Speaks in phrases</td>
<td>Speaks in words</td>
<td>Unable to speak</td>
</tr>
<tr>
<td>Work of breathing</td>
<td>Minimal intercostal retractions</td>
<td>Intercostal and substernal retractions</td>
<td>Significant respiratory distress. Usually all accessory muscles involved, and may display nasal flaring and paradoxical thoraco-abdominal movement</td>
<td>Marked respiratory distress at rest. All accessory muscles involved, including nasal flaring and paradoxical thoraco-abdominal movement</td>
</tr>
<tr>
<td>Chest auscultation</td>
<td>Moderate wheeze</td>
<td>Loud pan-expiratory and inspiratory wheeze</td>
<td>Wheezes might be audible without stethoscope</td>
<td>The chest is silent (absence of wheeze)</td>
</tr>
<tr>
<td>SpO2 on room air</td>
<td>&gt;94%</td>
<td>91-94%</td>
<td>&lt;90%</td>
<td>Unable to perform the task</td>
</tr>
<tr>
<td>Peak flow versus personal best</td>
<td>&gt;80%</td>
<td>60-80%</td>
<td>best &lt;60%</td>
<td>Unable to perform the task</td>
</tr>
</tbody>
</table>

Definitions are not absolute and can overlap. The presence of several parameters indicates the classification of the exacerbation.
Stepwise Approach for Managing Asthma in Youths ≥ 12 Years and Adults

<table>
<thead>
<tr>
<th>Intermittent Asthma</th>
<th>Persistent Asthma: Daily Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consult with asthma specialist if step 4 or higher care is required</td>
<td></td>
</tr>
<tr>
<td>Consider consultation at step 3</td>
<td></td>
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**Step 1**
- **Preferred:** SABA prn

**Step 2**
- **Preferred:** Low-dose ICS (A)
- **Alternative:** LTRA (A), Cromolyn (A), Theophylline (B)

**Step 3**
- **Preferred:**
  - Medium-dose ICS (A)
  - OR
  - Low-dose ICS + LABA (A), or LTRA (A), Theophylline (B), or Zileutin (D)
- **Alternative:**
  - Medium-dose ICS + either LTRA (B), Theophylline (B), or Zileutin (D)

**Step 4**
- **Preferred:**
  - High dose ICS + LABA (B)
  - **AND**
  - Consider Omalizumab for patients with allergies (B)

**Step 5**
- **Preferred:**
  - High dose ICS + LABA (B)
  - **AND**
  - Consider Omalizumab for patients with allergies (B)

**Step 6**
- **Preferred:**
  - High-dose ICS + LABA + oral Corticosteroid
  - **AND**
  - Consider Omalizumab for patients with allergies (B)

**Assess Control**

**Patient Education and Environmental Control at Each Step**

Acute Asthma Issues: Today’s Discussion

- Airway physiology and pathophysicsology
- Oxygenation vs Ventilation: our (not so) old friend
- Peak Flow or No?
- Nebulization versus MDIs
- Medication dosing and aerosols
- Albuterol versus Levalbuterol
- Other stuff...
Characteristic Flow-Volume Loops due to Increasing Airflow Obstruction
Case Presentations
You meet a 43 year old woman of northern European heritage with a long history of recurrent bronchitis who was recently seen in urgent care due to a severe cough. She was given qid albuterol and oral steroids for 3 days and is improving, and is finishing a course of azithromycin as well. Today her chest is clear and she’s not in any distress. Her history is remarkable for several emergency room visits all of which resolve with “machine breathing treatments”. She only needs her albuterol puffer twice daily when healthy and smokes occasionally when well.

What is your diagnosis?

What management plan do you choose...and why?
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2015: Pharmacist’s Asthma Report

Pharmacist's Asthma Report

Provider's Name

Patient's Name

Patient's current asthma controller medications

I have noticed excessive refills of this quick-relief medication at a rate of refills per 90 days.

Patient's other relevant medications

Pharmacist's Recommendations:

When evaluated by a pharmacist, the patient demonstrated improper inhaler technique which may have contributed to excessive SABA use. After consultation, the patient demonstrated proper device technique. You may wish to re-evaluate at next visit.

Based on refill history, the patient’s adherence to prescribed controller therapy is suboptimal. The pharmacist discussed the importance of using controller medications daily and only using rescue medication when needed. You may wish to reinforce these messages at next visit.

Based on SABA fills/apparent control level, you may wish to consider a step up in therapy based on the most recent national asthma guidelines: GetAsthmaHelp.org/guidelines

Patient was not available at the pharmacy to discuss proper asthma medication and device use. Please review with patient at next visit.

Comments

Patient’s Asthma Control Information: (If available)

<table>
<thead>
<tr>
<th>Well Controlled</th>
<th>Short-Acting Beta-Agonist Use</th>
<th>Asthma Control Test™ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 days per week or less</td>
<td>20 or more</td>
</tr>
<tr>
<td></td>
<td>More than 2 days per week</td>
<td>16-19</td>
</tr>
<tr>
<td></td>
<td>Several times per day</td>
<td>15 or less</td>
</tr>
</tbody>
</table>


Pharmacist’s signature:

Insert e-sign or print/sign

Permission to reproduce blank form
www.GetAsthmaHelp.org
Two months later...
Asthma 2015: Disease of Inflammation & Communication

PACE: Physician Asthma Care Education

http://www.nhlbi.nih.gov/health/prof/lung/asthma/pace/
Barriers To Effective Communication

**Studies show that patients often:**

- Feel they are wasting the clinician’s valuable time
- Omit details they deem unimportant
- Are embarrassed to mention things they think will make them look bad
- Don’t understand medical terms
- May believe the clinician has not really listened and therefore doesn’t have the information needed to make a good treatment decision
- Believe the clinician doesn’t understand their social and cultural experience
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- Other stuff...
Acute Asthma I

Mild exacerbation
- Keep O₂ sats ≥94%
- Salbutamol q20 min x 1-3 doses
- Consider inhaled corticosteroids (ICS)

Moderate exacerbation
- Keep O₂ sats ≥94%
- Salbutamol q20 min x 3 doses
- Oral steroids
- Consider ipratropium x 3 doses in 1 hr

Severe exacerbation
- Keep O₂ sats ≥94%, consider 100% O₂
- Salbutamol and ipratropium x 3 doses
- Give oral steroids
- Consider IV methylprednisolone
- Consider continuous aerosolized β₂-agonists
- Consider IV magnesium sulphate
- Keep patient NPO

Severe to impending respiratory failure
- Keep O₂ sats ≥94%, non-rebreather mask with 100% O₂
- Continuous aerosolized salbutamol and ipratropium x 3 doses
- Keep NPO and start IV access
- Continuous cardiac and O₂ sats monitor
- IV methylprednisolone
- Consider:
  - IV magnesium sulphate or IV aminophylline or IV salbutamol
  - Draw blood for gases and electrolytes
  - Consider SC epinephrine
  - If deteriorating consider Rapid sequence intubation

CALL PICU PHYSICIAN

### Acute Asthma II

<table>
<thead>
<tr>
<th>Asthma severity</th>
<th>Drug and route</th>
<th>Dose (maximum)</th>
<th>Risks</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>inhaled corticosteroids</td>
<td>See discharge plan and Table 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate*</td>
<td>salbutamol, MDI with spacer</td>
<td>&lt;20 kg = 5 puffs (0.1 mg/puff), &gt;20 kg = 10 puffs every 20 min during the first h</td>
<td>Preferable route</td>
<td></td>
</tr>
<tr>
<td></td>
<td>salbutamol, intermittent nebulization</td>
<td>5 mg in 2 ml of normal saline to be given every 20 min during the first h</td>
<td>Monitor potassium serum levels in patients requiring frequent doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>oral corticosteroids</td>
<td>prednisone or prednisolone 1 to 2 mg/kg/day (maximum 60 mg) OR dexamethasone 0.15–0.3 mg/kg/day (maximum 10 mg)</td>
<td>Prolonged course or frequently repeated doses can be associated with adrenal suppression</td>
<td>Start treatment early. Recommended as one single dose in the morning to decrease risk of adrenal suppression</td>
</tr>
<tr>
<td></td>
<td>ipratropium bromide, MDI/spacer</td>
<td>Puffs (20 µg) every 20 min x 3 doses &lt;20 kg = 3 puffs &gt;20 kg = 6 puffs</td>
<td>Use with caution in children with soy allergy</td>
<td></td>
</tr>
</tbody>
</table>
## Acute Asthma III

<table>
<thead>
<tr>
<th>Severe†</th>
<th>Salbutamol, continuous nebulization</th>
<th>Tachycardia, hypokalemia, hyperglycemia</th>
<th>Monitor heart rhythm and rate, glucose and electrolytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.3 mg/kg/hr 5 mg in 4 ml of normal saline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ipratropium, bromide nebulized</td>
<td>&lt;20 kg = 0.25 mg, &gt;20 kg = 0.5 mg every 20 min maximum 3 doses</td>
<td></td>
<td>Can be mixed with salbutamol aerosols</td>
</tr>
<tr>
<td>IV corticosteroids</td>
<td>methylprednisolone: 1–2 mg/kg/dose (maximum 60 mg q.6 h) hydrocortisone: 5–7 mg/kg (maximum 400 mg q.6 h)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe to impending respiratory failure</td>
<td>IV magnesium sulfate</td>
<td>Hypotension</td>
<td>Consider if patient is not improving</td>
</tr>
<tr>
<td></td>
<td>25–50 mg/kg IV bolus over 20 min (maximum 2 g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV salbutamol</td>
<td>Load: 7.5 mcg/kg over 2–5 min, followed by 1 mcg/kg/min. Titrate upwards with increments of 1 mcg/kg/min (maximum 5 mcg/kg/min)</td>
<td>Tachycardia, hypokalemia, hyperglycemia</td>
<td>Monitor heart rhythm and rate, glucose and electrolytes</td>
</tr>
</tbody>
</table>

The Heliox Story I

**CLASS**

- Heliox is a mixture of helium and oxygen
- Helium is an inert gas with a significantly lower density (and specific gravity) than room air (1.42g/L for O2 vs 0.17g/L for He)

**MECHANISM OF ACTION**

- by substituting helium for nitrogen -> reduction in density of the gas -> reduction in Reynolds number - > more laminar flow
- reduces airflow resistance, work of breathing and dynamic hyperinflation
**PHARMACEUTICS**

- gas administered via a mask with a reservoir bag or via endotracheal tube
- supplied at 137 bar as either Heliox (79% He, 21% O₂) in white cylinders with white/brown shoulders or as 100% helium in brown cylinders (size C, D, E and G cylinders (410, 1400, 3500 and 7300L nominal capacity respectively)
- can be used as the driving gas for nebulisation

**DOSE**

- helium:oxygen mix of 80:20 or 70:30, which are 1.8 and 1.6 times less dense than pure oxygen, respectively.
The Heliox Story III

INDICATIONS

- lower airways disorders – e.g. severe asthma, severe COPD, bronchiolitis, bronchiectasis, lung cancer
- extrathoracic or tracheal obstruction – e.g. croup, epiglottitis, foreign body, tumour, tracheal stenosis, tracheomalacia
- FRC assessment (helium dilution technique)
- decompression sickness

ADVERSE EFFECTS

- expensive (10x the cost of oxygen)
- lack of availability
- can’t use on those with a high FiO2 (>0.4)
- ventilators require recalibration for FiO2 and TV – interferes with valve function
- requires heated humidified circuits as helium conducts heat 6x faster than nitrogen
- alteration of vocal pitch
- may reduce the efficiency of coughing
The Heliox Story IV

PHARMACOKINETICS

- near instantaneous onset and offset
- eliminated within a few breaths

EVIDENCE

- anecdotal evidence of avoiding need for intubation in upper airway obstruction
- little evidence of benefit in lower airways obstructive lung disease – the common theme is that heliox is a temporising measure but is not a treatment

...not so fast, there’s more!
Recent Heliox Meta-Analysis

Rodrigo, G. Curr Opin Pulm Med. 2015. 21: 22-26
THANK YOU