Asthma: A Breathless Update

COL Douglas Maurer, DO, MPH, FAAFP

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COL Douglas Maurer, DO, MPH, FAAFP

Deputy Director, Army Graduate Medical Education, Office of the Surgeon General; Associate Professor, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Clinical Associate Professor, University of Washington School of Medicine, Seattle

Dr. Maurer is a graduate of the Ohio University Heritage College of Osteopathic Medicine, Athens. He completed his family medicine residency at Tripler Army Medical Center, Honolulu, Hawaii, and completed faculty development fellowships at the Madigan Army Medical Center in Waco, Texas, and Tacoma, Washington. Dr. Maurer served five years as Program Director of the Carl R. Darnall Army Medical Center Family Medicine Residency at Fort Hood, Texas. Subsequently, he spent five years as Program Director of the Madigan Faculty Development Fellowship at Joint Base Lewis-McChord (JBLM), Washington. He currently practices full-service family medicine with a diverse patient population at Fort Belvoir Community Hospital in Virginia. Having taught medicine for nearly 20 years, Dr. Maurer has won multiple teaching awards, including the 2015 Teacher of the Year award at Madigan Army Medical Center. His research interests include graduate medical education, medical simulation, medical applications, prevention of obesity and tobacco use, and evidence-based medicine.

Learning Objectives

1. Use evidence-based criteria to order and interpret appropriate tests for asthma.

2. Analyze environmental triggers for asthma with patients and select factors to reasonably avoid or control them.

3. Develop system-wide interventions that promote patient adherence to long-term management of chronic asthma.

4. Collaborate with asthma patients to develop an asthma action plan that encourages adherence.
Abbreviations

- **SABA**: short-acting beta agonist  
  - i.e.: albuterol
- **LABA**: long-acting beta agonist  
  - i.e.: salmeterol, formoterol
- **ICS**: inhaled corticosteroid  
  - i.e.: fluticasone, budesonide
- **LABA/ICS**: salmeterol/fluticasone (Advair), formoterol/budesonide (Symbicort)
- **LTRA**: leukotriene receptor antagonist  
  - i.e.: montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo)
- **LAMA**: long-acting muscarinic antagonist  
  - i.e.: tiotropium bromide (Spiriva)
Practice Recommendations

• ICS are best first line maintenance therapy
• LABAS are safe and can be used second line
• Consider novel treatments: SMART, tiotropium
• MDIs are as effective as nebulizers
• Consider 2 days of dexamethasone for AEA

The Burden
The Burden

Reducing the Burden
Postnatal

Current Guideline Review
Initial Evaluation of Asthma

1. Diagnose asthma
2. Assess asthma severity
3. Initiate medication & demonstrate use
4. Develop written asthma action plan
5. Schedule follow-up appointment

Diagnosis

1. Diagnose asthma
2. Assess asthma severity
3. Initiate medication & demonstrate use
4. Develop written asthma action plan
5. Schedule follow-up appointment
Poll Question 1

A 6-year old male presents with frequent episodes of wheezing. His mother reports that he has been having coughing spells at night every 2-3 weeks and will have wheezing approximately 2-3 times a week.

Which of the following is diagnostic of asthma:
   A. 3 episodes of wheezing per year and allergic rhinitis
   B. Reversibility of at least 12% in baseline FEV1
   C. Reversibility of at least 5% in baseline FEV1
   D. Non-reversible obstruction of at least 20% FEV1

Asthma Diagnosis

- Reversibility: FEV1 increases by > 200ml and 12% in baseline or 12% predicted FEV1
- Methacholine challenge most sensitive test
- Positive: decrease in FEV1 > 20% at 8 mg/ml
- Decreased FEV1/FVC suggestive of disease
- Normal spirometry does not exclude asthma!
Asthma Predictive Index
Children < 3 years of age with 3 or more episodes of wheezing in a year AND

• 1 Major Criteria
  - Eczema
  - Evidence of allergen sensitivity
  - Parent with asthma

OR

• 2 Minor Criteria
  - Evidence of food allergies
  - Eosinophilia >4%
  - Wheezing apart from colds

+ Test=76% of children diagnosed with asthma at age 6

Got Asthma? (Really?!)

• Patients (N = 701) underwent spirometry and symptom monitoring
• Patients without asthma per spirometry underwent medication weaning over 4 visits
• Repeat testing ruled out asthma in 203 (33%)
• After 1 year, 6 (2.9%) resumed treatment
• 12 with serious alternative diagnoses
Assessing Severity

A 6-year old asthmatic male presents with frequent episodes of wheezing. His mother reports that he has been having coughing spells at night every 2-3 weeks and will have wheezing approximately 2-3 times a week.

How is the severity of this patient’s asthma characterized?

A. Intermittent  
B. Mild persistent  
C. Moderate persistent  
D. Severe persistent  

Poll Question 2
### Components of Severity

<table>
<thead>
<tr>
<th>Intermittent</th>
<th>Mild</th>
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<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>Ages 0-4 years</td>
<td>≤2 days/week</td>
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<td>Ages 5-11 years</td>
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<table>
<thead>
<tr>
<th><strong>Nighttime awakenings</strong></th>
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<tbody>
<tr>
<td>Ages 0-4 years</td>
<td>0</td>
</tr>
<tr>
<td>Ages 5-11 years</td>
<td>≤2x/month</td>
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<td>1-2x/month</td>
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<td>Ages 0-4 years</td>
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<td><strong>FEV₁ (%) predicted</strong></td>
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<tr>
<td>Ages 0-4 years</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Ages 5-11 years</td>
<td>&gt;80%</td>
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<table>
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<tr>
<th>Asthma exacerbations requiring oral systemic corticosteroids</th>
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<tbody>
<tr>
<td>Ages 0-4 years</td>
<td>0-1/year</td>
</tr>
<tr>
<td>Ages 5-11 years</td>
<td>≥2/year</td>
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<td>≥2/year</td>
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*Generally, more frequent and intense events indicate greater severity.

Consider severity and interval since last asthma exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV₁.
A 6-year old asthmatic male presents with frequent episodes of wheezing. His mother reports that he has been having coughing spells at night every 2-3 weeks and will have wheezing approximately 2-3 times a week.

Which of the following is first line therapy for control medication for this patient?

A. Long-acting beta agonist (LABA)
B. Leukotriene receptor antagonist (LTRA)
C. Inhaled corticosteroid (ICS)
D. Theophylline
###Table for Treatment Options

<table>
<thead>
<tr>
<th><strong>STEP 1</strong></th>
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<th><strong>STEP 3</strong></th>
<th><strong>STEP 4</strong></th>
<th><strong>STEP 5</strong></th>
<th><strong>STEP 6</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0-4 years of age</strong></td>
<td><strong>Persistent Asthma: Daily Medication</strong></td>
<td>Consult with asthma specialist if step 1 care or higher is required. Consider consultation at step 2.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Preferred Treatment</strong></td>
<td>SABA* as needed</td>
<td>low-dose ICS*</td>
<td>medium-dose ICS*</td>
<td>medium-dose ICS* + either LABA* or montelukast</td>
<td>high-dose ICS* + either LABA* or montelukast + oral corticosteroids</td>
</tr>
<tr>
<td><strong>Alternative Treatment</strong></td>
<td>cromolyn or montelukast</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5-11 years of age</strong></td>
<td><strong>Persistent Asthma: Daily Medication</strong></td>
<td>Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.</td>
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<td>low-dose ICS*</td>
<td>low-dose ICS* + either LABA* or theophylline(a) OR medium-dose ICS</td>
<td>medium-dose ICS + LABA*</td>
<td>high-dose ICS* + LABA* + oral corticosteroids</td>
</tr>
<tr>
<td><strong>Alternative Treatment</strong></td>
<td>cromolyn, LTRA* or theophylline(b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>12+ years of age</strong></td>
<td><strong>Persistent Asthma: Daily Medication</strong></td>
<td>Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Preferred Treatment</strong></td>
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<td>low-dose ICS* + LABA* OR medium-dose ICS</td>
<td>medium-dose ICS + LABA*</td>
<td>high-dose ICS* + LABA* AND consider omalizumab for patients who have allergies</td>
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<tr>
<td><strong>Alternative Treatment</strong></td>
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<td>medium-dose ICS* + either LTRA* or theophylline OR zafirlukast</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Notes:**
(a) LTRA: leukotriene receptor antagonist
(b) LABA: long-acting beta2-agonist
(c) ICS: inhaled corticosteroid

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**Additional Information:**
- If clear benefit is not observed in 4-6 weeks, medication technique and adherence are satisfactory, consider adjusting therapy or alternate diagnosis.
- Consider subcutaneous allergen immunotherapy for patients who have persistent, allergic asthma.

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**Diagram for Treatment Options**

- **STEP 1:** Intermittent Asthma
  - SABA* as needed
- **STEP 2:** Persistent Asthma: Daily Medication
  - low-dose ICS*
  - low-dose ICS* + either LABA* or theophylline(b)
  - low-dose ICS* + either LABA* or theophylline(b) OR medium-dose ICS
  - medium-dose ICS + LABA*
  - medium-dose ICS + either LTRA* or theophylline
- **STEP 3:** Persistent Asthma: Daily Medication
  - low-dose ICS* + either LABA* or theophylline(b)
  - low-dose ICS* + either LTRA* or theophylline
  - low-dose ICS* + either LABA* or theophylline(b) OR medium-dose ICS
  - medium-dose ICS + LABA*
  - medium-dose ICS + either LTRA* or theophylline
  - high-dose ICS* + either LABA* or theophylline(b)
  - high-dose ICS* + either LTRA* or theophylline
  - high-dose ICS* + either LABA* or theophylline(b) OR medium-dose ICS
  - high-dose ICS* + either LTRA* or theophylline
  - high-dose ICS* + either LABA* or theophylline(b) AND consider omalizumab for patients who have allergies
  - high-dose ICS* + either LTRA* or theophylline AND consider omalizumab for patients who have allergies

---

**Consider subcutaneous allergen immunotherapy for patients who have persistent, allergic asthma.**
**Box 3-5B**

**Children 6-11 years**

**Personalized asthma management:**
Assess, Adjust, Review response

**Asthma medication options:**
Adjust treatment up and down for individual child’s needs

**PREFERRED CONTROLLER** to prevent exacerbations and control symptoms

**RELIEVER**

<table>
<thead>
<tr>
<th>STEP 1</th>
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<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>As-needed low dose ICS-formoterol *</td>
<td>Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)</td>
<td>Low dose ICS-LABA, or medium dose ICS</td>
<td>Medium dose ICS-LABA</td>
<td>High dose ICS-LABA or add-on tiotropium, or add-on LTRA</td>
</tr>
</tbody>
</table>

* Off-label; separate or combination ICS and SABA inhalers; only one study in children

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**Box 3-5A**

**Adults & adolescents 12+ years**

**Personalized asthma management:**
Assess, Adjust, Review response

**Asthma medication options:**
Adjust treatment up and down for individual patient needs

**PREFERRED CONTROLLER** to prevent exacerbations and control symptoms

**PREFERRED RELIEVER**

<table>
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<td>As-needed low dose ICS-formoterol *</td>
<td>Daily low dose inhaled corticosteroid (ICS), or as-needed low dose ICS-formoterol *</td>
<td>Low dose ICS-LABA</td>
<td>Medium dose ICS-LABA</td>
<td>High dose ICS-LABA, or add-on tiotropium, or add-on LTRA</td>
</tr>
</tbody>
</table>

* Off-label; data only with budesonide-formoterol (bud-form) or BDP-form maintenance and reliever therapy

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© Global Initiative for Asthma, www.ginasthma.org
ICS for Everyone?

- 2016 industry-funded RCT (N=7100, ages 4-66) mild asthma
  - Randomized to budesonide or placebo daily x 3 years
  - ICS group with 50% fewer severe asthma-related events vs placebo regardless of symptom frequency at baseline
  - ICS group with 8 fewer adverse events per 1000 patient-years
  - Absolute difference: small; could consider ICS in patients with infrequent symptoms (2 days/week or less)
- NHLBI/NAEPP guidelines still rec ICS only for patients with symptoms on 3 or more days/week

Adult Height and ICS

- 2012 RCT: 1000 children ages 5-13
  - Treated with ICS, nedocromil or placebo for 4 yrs
  - Height measured in adulthood (mean age 25)
  - ICS caused modest height reduction of 1.2 cm
  - Most pronounced in girls
- 2014 Cochrane Review
  - 0.48 cm/yr in growth velocity
  - 0.61 cm change in baseline height at 1yr
What About Other Therapies?

Cromolyn and Theophylline

- **2011 Cochrane Review (23 studies, N=1026)** evaluated efficacy of cromolyn
  - Cromolyn no better than placebo in symptom free days
  - Small decrease in bronchodilator use

- **2009 Cochrane Review (36 studies, N=2838)** evaluated efficacy of theophylline
  - Theophylline better than placebo
  - ICS better than theophylline alone in alleviating symptoms
LTRAs

• Leukotriene receptor antagonists (LTRA) single agent for control in mild persistent

• 2012 Cochrane Review (19 studies, N=3333) examining LTRA vs. ICS
  - Increase in exacerbations (NNH=28)
  - Increase in hospitalizations
  - Increase need for rescue treatments
  - Decreased quality of life
  - Increase in nighttime symptoms

Develop Asthma Action Plan

1. Diagnose asthma
2. Assess asthma severity
3. Initiate medication & demonstrate use
4. Develop written asthma action plan
5. Schedule follow-up appointment
Asthma Action Plans (AAP)

• 2017 CR of 15 RCTs, N=3062 (AAP vs no AAP: N=2602; AAP plus education vs education alone: N=460)

• Ages 22-49, most studies 6 months long

• No benefit or harm with AAPs on ED visits or admissions (OR 0.75; 95% CI, 0.45-1.24; N=1385)

• No benefit or harm with AAP + education on ED visits or hospitalizations (OR 1.1; 95% CI, 0.27-4.32; N=70)

• Similar results with AAP on steroids, symptoms, function

• Overall evidence rated “low/very low”
Asthma Action Plans (AAP)

- 2006 Cochrane: 3 RCTs, (N=355), children, symptom-based vs. peak-flow AAP
  - Less acute visits with symptom-based AAP
  - Children preferred symptom vs. peak flow
  - No difference in need of oral steroids, admissions, quality of life

AAPs and Steroids

- 2012 RCT (N=230, 5-12 years), Australia
  - Oral prednisolone 1mg/kg vs. placebo
  - May reduce symptoms and healthcare use
  - May be useful with experienced parents
  - Not recommended for preschool children

- 2016 Cochrane (3 RCTs, N=422)
  - Increasing ICS does NOT help reduce ER visits, oral steroids, hospitalizations

- 2018 RCT’s quadruple-dose ICS for symptoms
  - Completely ineffective in children; minimal benefit in adults
Assess Control

Assess & monitor asthma control

Schedule next follow-up appointment

Review medication technique & adherence; assess side effects; review environmental control

Review asthma action plan, revise as needed

Maintain, step up, or step down medication
Review Inhaler Technique

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?
   - All of the time [1]
   - Most of the time [2]
   - Some of the time [3]
   - A little of the time [4]
   - None of the time [5]

2. During the past 4 weeks, how often have you had shortness of breath?
   - More than once a day [1]
   - Once a day [2]
   - 3 to 6 times a week [3]
   - Once or twice a week [4]
   - Not at all [5]

3. During the past 4 weeks, how often did your asthma symptoms (wheeze, cough, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   - 4 or more nights a week [1]
   - 2 to 3 nights a week [2]
   - Once a week [3]
   - Twice a week [4]
   - Not at all [5]

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?
   - 3 or more times per day [1]
   - 1 to 2 times per day [2]
   - 2 or 3 times per week [3]
   - Once a week [4]
   - Or less [5]

5. How would you rate your asthma control during the past 4 weeks?
   - Not Controlled [1]
   - Poorly Controlled [2]
   - Somewhat Controlled [3]
   - Well Controlled [4]
   - Completely Controlled [5]

TOTAL:  

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**Review Inhaler Technique**

- **Assess & monitor asthma control**
- **Schedule next follow-up appointment**
- **Review medication technique & adherence, assess side effects; review environmental control**
- **Maintain, step up, or step down medication**

- **Review asthma action plan, revise as needed**
A 6-year old asthmatic male presents with frequent episodes of wheezing, despite ICS. His mother reports that his nighttime symptoms occur once a month but he continues to have wheezing approximately 2 times a week.

Which of the following is the best option for stepping up control therapy?

A. Adding tiotropium
B. Switching to montelukast
C. Adding theophylline
D. Adding LABA
Box 3-5B
Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review response

Asthma medication options:
Adjust treatment up and down for individual child’s needs

**PREFERRED CONTROLLER**
to prevent exacerbations and control symptoms

Other controller options

**RELEIVER**
As-needed short-acting β₂-agonist (SABA)

* Off-label, separate ICS and SABA inhalers; only one study in children
Risks of LABA’s

• Cochrane Reviews of LABA safety
  - 6 deaths in combo formoterol vs. 1 in ICS alone
  - No difference in non-fatal events
  - Salmeterol deaths all occurred with drug alone
  - No diff in head to head comparisons

• 2010 FDA black box warning placed on LABA’s

• FDA mandated surveillance studies...

• FDA dropped black box warning on ICS/LABA in Dec 2017 (still NEVER use LABA alone in asthma)
The Return of the LABAs

- **2016 RCT (N=11,693):** formoterol + budesonide (Symbicort) vs budesonide alone in patients > 12 yrs
  - Combo reduced exacerbations 16.5% (HR 0.84; 95% CI, 0.74-0.94)
  - No diff in asthma-related side effects (43 vs 40); 2 deaths in combo

- **2016 RCT (N=6028):** salmeterol + fluticasone (Advair) vs. fluticasone alone in children 4-11
  - Combo non-inferior to fluticasone alone; no diff in serious asthma related side effects (21 vs. 27); no deaths in either group
  - No benefit to add on LABA, but safety was primary endpoint

LABAS Are Safe!

- **2018 meta-analysis (4 RCTs, N=36,010)**
  - Compared safety of ICS alone vs. ICS/LABA
  - No difference in intubations, death at 26 wks
  - No difference in hospitalizations
  - Decreased exacerbations in ICS/LABA (9.8% vs. 11.7%)
ICS plus LABA…Right Away?

- 2013 Cochrane Review, 27 trials, N=8050
- RCT’s comparing ICS + LABA with ICS alone
- Combo ICS/LABA no better than ICS alone
- Higher dose ICS superior to add on LABA
- Children responded similarly to adults
- No difference in adverse events

Single Inhaler Therapy (SiT)

- Combo formoterol/budesonide (SiT)
- 2013 Cochrane Review: 13 studies of over 13,352 patients; no children < 12; all industry funded
- Key results:
  - Asthma exacerbations requiring oral steroids
  - ER visits and hospitalizations
  - Adverse events/discontinuation higher in SiT group
  - NNT 100 to prevent admission or ER visit
Most Recent SiT Evidence

• SYGMA 1 and SYGMA 2 trials NEJM 2018
  – Non-inferior for severe exacerbations vs ICS + SABA
  – 64% reduction in severe exacerbations vs SABA alone
  – Greater symptom reduction, better adherence
• 2019 Lancet: 885 New Zealanders, mild asthma
  – 30% fewer severe exacerbations, 50% less steroid
• SiT limitations:
  - Off label, not FDA approved
  - Only ages 12+ studied
  - Only budesonide/formoterol Turbohaler studied (not in US)

LTRA as Adjunct

• 2011 pragmatic trial (N=352 adults and children)
  - LTRA equivalent at 2 months to ICS+LABA
  - Non-equivalent at 2 years
• 2010 trial (N=182 children) compared adjuncts:
  - Increased ICS dose
  - Added LABA
  - Added LTRA
  - Overall best response on ACT with added LABA
Tiotropium for Asthma

• 2012 industry funded RCT (N=900)
  - All with asthma not controlled on LABA or ICS
  - DOE improvements of pulmonary function
  - 1 less exacerbation after 8 yrs of treatment!
• Multiple Cochrane Reviews in 2015/2014
  - LAMA add on therapy improves lung function
  - Reduces exacerbations compared to ICS alone
  - No difference in exacerbations vs ICS/LABA
• FDA approved ages 6+

Biologics: “The Mab’s”

• Omalizumab, benralizumab, mepolizumab, dupilumab
• Anti-IgE, anti-IL 5, anti-IL 4/13
• “Mab’s”:
  - Reduce asthma exacerbations
  - Reduce hospitalizations
  - Generally well-tolerated
  - Reduce/withdraw steroids
• Step 5 medications, rx with pulmonary/allergy consultation
• Expensive! One vial omalizumab: $826! dupilumab: $3K/month!
• Risks: anaphylaxis (esp omalizumab), shingles (mepolizumab)
Acute Asthma Management

Poll Question 5

In a 6-y.o. presenting with an asthma exacerbation, which of the following is the best initial action?

A. Administer albuterol via MDI
B. Start albuterol nebulizer
C. Administer IV albuterol
D. Administer ICS
Albuterol

• 2009 Cochrane review:
  - MDIs as effective as nebulizers
  - MDIs may reduce hospital length of stay compared to nebulizers

• 2003 RCT (N=168) children 2-24 months:
  - Less admissions with MDI vs. nebulizer

Albuterol/Ipratropium

• 2016 Systematic review (N=2497):
  In children under 3 years with an exacerbation
  - 44% reduction in admissions with MDI vs. neb (NNT=10)
  - Ipratropium did not appear to help (but evidence is poor)

  In children 3-18 years, and adults
  - No likely difference between MDI and nebulizer
  - Ipratropium reduced hospitalizations vs SABA alone
  - Most guidelines rec combo; stop once stable/admitted
**Steroids in Exacerbations**

- **ICS = NO! ORAL = YES!**
- **ICS** in the ER for acute exacerbations
  - 2016 Cochrane: no decrease in admissions
- **Choice of oral steroid?**
  - Prednisone vs. dexamethasone
  - 2 days of dex as good as 5 days of prednisone
  - Single dose of dex as good as 3 days of prednisone

**Novel ICS Use**

- **Quadruple-dose ICS for worsening symptoms**
  - Two 2018 RCT’s tested this hypothesis
  - Completely ineffective in children; minimal benefit in adults
  - Use oral/IM steroids for exacerbations
- **As-needed ICS without daily maintenance therapy**
  - Two 2018 studies with 8000 patients with mild persistent asthma
  - Compared daily ICS to as need budesonide/formoterol inhaler
  - No difference in exacerbations, less ICS exposure, more symptoms
- **Single maintenance and reliever therapy (“SMART”)**
  - Budesonide/formoterol for BOTH maintenance and rescue therapy
  - No albuterol inhaler
  - 2018 meta-analysis: SMART decreased exacerbations, not symptoms
**Exercise-Induced Bronchoconstriction**

- Formal postexercise spirometry for diagnosis
- SABA 15 min prior to exercise
- Alternatn: mast cell stabilizer, anticholinergic
- NO LABA’s!
- If use SABA daily: ICS or LRA
- Nondrug: warm up first, use mask or scarf

**Influenza Vaccine**

- 2013 Cochrane Review of 18 trials
  - No reduction in influenza-related exacerbations
  - No apparent risk from inactivated vaccine
  - No risk from live intranasal influenza vaccination
  - Vaccines do not worsen asthma
- 2017 meta-analysis of 35 studies (142K)
  - Pooled efficacy of 81%
  - Reduced febrile illness by 72%
  - Reduced exacerbations by 59-78%
Asthma and Supplements

• Vitamin D MAY prevent exacerbations
  - 2018 RCT (N=250): vitamin D vs placebo; no difference in time to 1st exacerbation
  - 2016 Cochrane: 9 trials, 435 children, 658 adults showed reduction in exacerbations (0.44 to 0.28 per person-year), ER visits, and hospitalizations (6% to 3% per year)

• Caffeine improves airways function for up to four hours
  - 7 studies of 75 patients
  - Improved FEV1 by 12-18%
  - May need to avoid caffeine for at least four hours prior to spirometry

• Probiotics during pregnancy or early infancy do not prevent asthma
  - Meta-analysis of 20 RCTs included 4866 children
  - Various combinations/doses of probiotics
  - Followed children from 2 to 6 years after birth
  - No evidence of benefit
  - 2017 RCT (N=184 infants) found no reduction at 5 years

• Vitamin C not beneficial in asthma
  - 9 studies, 330 participants
  - One study with drop in FEV1 post-exercise
Asthma and Pregnancy

• Asthma may improve, worsen or stay the same
  - Mild: 12.6% exacerbation/2.3% hospitalization
  - Moderate: 25.7%/6.8%
  - Severe: 51.9%/26.9%

• 15-20% increased risk of complications
  - Mortality, pre-e, preterm delivery, low birth weight

• Monitor peak flows bid +/- spirometry

Asthma and Pregnancy

• Medication safety
  - Albuterol (C), ICS (B/C), LABA (C), LRA (B), Ipratrop (B)
  - Carboprost (avoid!)

• “Best” data: albuterol, budesonide, salmeterol

• Less data: formoterol, LRA’s

• No diff in malformations b/t ICS vs. LABA/ICS

• AEA in pregnancy tx’ed the same!!

Smoking cessation!
Nuts and Pregnancy

- Avoiding nuts during pregnancy controversial
- Danish Birth Cohort of 101,045 pregnancies
- Self-report data from validated questionnaire
- Nut intake inversely associated with asthma
- Consumption may decrease risk of allergies
- Nut consumption not harmful

Fish Oil in Pregnancy

- 2016 RCT in Danish women (N = 695): LCPUFA during pregnancy to reduce wheezing disorders in children
- Compared 1g of fish oil to identical olive oil
- Supplementation 22-26 weeks gestation until 1 week after; children followed at least 5 years
- Wheezing disorders lower in fish oil group
  (16.9% vs 23.7%; HR 0.69; 95% CI 0.49 - 0.97, NNT 15)
- Women with lowest baseline LCPUFA levels benefited most
  (17.5% vs 34.1%; HR 0.46; 0.25 - 0.83, NNT 5.6)
- No reduction in exacerbations, allergic sensitization, or eczema
Practice Recommendations

• ICS are best first line maintenance therapy
• LABAS are safe and can be used second line
• Consider novel treatments: SMART, tiotropium
• MDIs are as effective as nebulizers
• Consider 2 days of dexamethasone for AEA

Questions