Pediatric Asthma Updates

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International
Disclosures

- I have none relevant to this presentation
Pediatric Asthma Updates

- Asthma epidemiology in children
- Different ways to determine asthma severity
- Inner city asthma
- Effect of inhaled steroids on growth
Asthma: Definition and Symptoms

- The diagnosis of asthma in children is clinical. It is based on recognising a characteristic pattern of episodic symptoms in the absence of an alternative explanation.

- Symptoms are caused by inflammation causing narrowing of small airways and may include:
  - wheezing
  - cough
  - difficulty breathing
  - chest tightness
Pediatric Asthma is the Most Common Chronic Respiratory Disease in the Developed World

- The highest prevalence found in the US, the UK and Australia

  - The increasing prevalence previously reported appears to have plateaued or even declined

2. O'Byrne PM, et al. Severe exacerbations and decline in lung function in asthma. Am J Respir Crit Care Med. 2009;179:19-24
Asthma Prevalence Among Children

- Prevalence remains high
- No impact on exacerbations
7 million (10 %) currently have asthma
- more common in children than adults (7.3 %)
10 million children (14 %) diagnosed with asthma during their lifetimes

CDC National Center for Health Statistics, National Health Interview, Survey (NHIS)
National Surveillance of Asthma: United States, 2001-2010
Asthma in Children in the U.S. is Not Well Controlled

- 6.7 million office visits
- Nearly 4 million exacerbations
- 640,000 Emergency Department visits
- 157,000 hospitalizations
  - 3rd most common cause for hospitalization
- 185 deaths

Persistent asthma prevalence ranged from 45.0% in Oregon to 74.4% in Mississippi.
Pediatric Asthma is the Most Common Chronic Respiratory Disease in the Developed World

- The highest prevalence found in the US, the UK and Australia
  1. The increasing prevalence previously reported appears to have plateaued or even declined

- In resource poor countries, asthma prevalence is generally increasing

2. O'Byrne PM, et al. Severe exacerbations and decline in lung function in asthma. Am J Respir Crit Care Med. 2009;179:19-24
Why does asthma prevalence vary?

- Geography
- Genetics
- Allergens
- Pollution
- Poverty
- Variability in making the diagnosis
Easy Breathing Survey

- Questionnaire designed to assist primary care providers in diagnosing asthma in children

- Four questions on the survey were shown to be sensitive and specific for asthma
Easy Breathing Survey

1. Has your child had wheezing or whistling in the chest at any time in the last 12 months?

2. Has your child awakened at night because of coughing in the last 12 months?

3. Has your child had coughing, wheezing or shortness of breath with exercise or activity and had to stop because of these symptoms at any time in the last 12 months?

4. When your child has a cold, does the cough usually last more than 10 days?
Easy Breathing Survey

- A positive response to any 1 of the 4 questions was over **94% sensitive** for asthma
  - sensitivity was greater for persistent asthma than for intermittent asthma.

- A negative response to all 4 questions was **55% specific** for ruling out asthma.

J Pediatr 2001;139:267-72
Stepwise Approach for Managing Asthma

- 10 year old boy with asthma coughs three days per week. He usually uses albuterol 3-4 times per week. His mother does not hear him cough at night or when he is playing. He has missed two days of school because of asthma.

- How severe is his asthma?
- What would you recommend for therapy?
## Easy Breathing Survey: Symptom Evaluation

<table>
<thead>
<tr>
<th>Severity*</th>
<th>Intermittent</th>
<th>Mild persistent</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of episodes of cough, wheeze, shortness of breath</td>
<td>&lt;2x/wk</td>
<td>&gt;2x/wk &lt;qd</td>
<td>daily</td>
<td>continuously</td>
</tr>
<tr>
<td>Frequency of nocturnal symptoms</td>
<td>&lt;3x/mo</td>
<td>&gt;2x/mo</td>
<td>&gt;1x/wk</td>
<td>&gt;4x/wk</td>
</tr>
<tr>
<td>Exercise impairment even with pretreatment with beta-agonist</td>
<td>none</td>
<td>occasionally</td>
<td>some</td>
<td>always</td>
</tr>
<tr>
<td>Use of beta-agonist (for symptoms not related to exercise)</td>
<td>0–&lt;2x/wk</td>
<td>&gt;2x/wk &lt;qd</td>
<td>qd</td>
<td>&gt;qd</td>
</tr>
<tr>
<td>Use of prednisone therapy in past year</td>
<td>0–2</td>
<td>&gt;2</td>
<td>&gt;3</td>
<td>&gt;4</td>
</tr>
<tr>
<td>School absenteeism for asthma past year (days/month)</td>
<td>none</td>
<td>3–5</td>
<td>6–8</td>
<td>&gt;8</td>
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</table>

*Severity based on the highest severity category in which any clinical symptom occurs.
Stepwise Approach for Managing Asthma in 5 to 11 Year Old Children

**Intermittent**

**Step 1**

*Preferred:*
SABA prn

**Alternative:***
Low-Dose ICS (A)

Cromolyn (B),
Nedocromil (B),
or Theophylline (B)

**Step 2**

*Preferred:*
Medium-Dose ICS (B)

or

Low-Dose ICS and either
LABA (B),
LTRA (B),
or Theophylline (B)

**Step 3**

*Preferred:*
Medium-Dose ICS + LABA (B)

or

Medium-Dose ICS and either
LTRA (B),
or Theophylline (B)

**Step 4**

*Preferred:*
High-Dose ICS + LABA (B)

*Alternative:*
High-Dose ICS and either
LTRA (B),
or Theophylline (B)

or

Theophylline (B)

and

Omalizumab May Be Considered for Patients Who Have Allergies

**Step 5**

*Preferred:*
High-Dose ICS + LABA + Oral Corticosteroid (D)

*Alternative:*
High-Dose ICS and either
LTRA or Theophylline and Oral Corticosteroid (D)

and

Omalizumab May Be Considered for Patients Who Have Allergies

**Step 6**

*Preferred:*
High-Dose ICS + LABA + Oral Corticosteroid (D)

Theophylline (B)

and

Omalizumab May Be Considered for Patients Who Have Allergies

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SABA=short acting beta-agonist

LABA= long acting beta-agonist

LTRA = leukotriene receptor antagonist.

ICS= inhaled corticosteroid

http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf
Severity Mismatch between Asthma Symptoms and Spirometry

- 894 children (ages 5-19 years)
  - 62% Medicaid insured
  - 88% ethnic or racial minority group

- Asthma Severity was determined by both
  1. Easy Breathing Survey symptom evaluation
  2. Spirometry

### Asthma Severity based on symptoms

*Severity be based on the highest severity category in which any clinical symptom occurs

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*Severity be based on the highest severity category in which any clinical symptom occurs

+based on National Asthma Education and Prevention Program
The two methods for determining asthma severity (survey vs. spirometry) were compared.

<table>
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<th>FEV&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent/mild persistent</td>
<td>( \geq 80% )</td>
</tr>
<tr>
<td>Moderate</td>
<td>60%-80%</td>
</tr>
<tr>
<td>Severe</td>
<td>( \leq 60% )</td>
</tr>
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Asthma Symptoms Underestimate Asthma Severity

- The concordance between clinical and spirometry determined asthma severity was poor.
- Spirometry severity was higher in 36% of these children.
Spirometry

- Without spirometry, providers often overestimate the degree of asthma control \(^1,^2\)

- Underestimating asthma severity results in
  - Suboptimal treatment
  - Increased morbidity
  - Increased cost
  - Decreased quality of life

Spirometry

- Recommended by the Expert Panel Report
  - Continues to be underused

- Abnormal spirometry associated with increased risk of an asthma attack in the subsequent year

- Asthma symptoms underestimate asthma severity

Persistent asthma prevalence ranged from 45.0% in Oregon to 74.4% in Mississippi

Behavioral Risk Factors Surveillance System (BRFSS)—Adult Asthma Call-back survey Data, 2006-2010
Asthma Disparities Among U.S. Children

- 7 million (10%) currently have asthma

- The burden of asthma falls disproportionately on non-Hispanic black, American Indian/Alaskan Native and some Hispanic (i.e., Puerto Rican) populations. ²,³

Current Asthma Prevalence for children varies by Race/Ethnicity

- Puerto Ricans report 20.3% current prevalence
- Mexicans report 8.7% current prevalence

Asthma Disparities Among U.S. Children

- Low-income populations, minorities, and children living in inner cities experience more ED visits, more hospitalizations, more deaths due to asthma than the general population.


Are Inner Cities the Problem?

- Low-income populations, minorities, and children living in inner cities experience:
  - more ED visits
  - more hospitalizations
  - more deaths due to asthma than the general population.


Urban Asthma

- Urban areas have been shown to have a high burden of asthma

- The causes for this increased burden are not known
Inner City Asthma

- 23,065 children living in 5,853 census tracts were studied

- Tracts included inner-city and non-inner-city areas
Inner City Asthma

- The prevalence of current asthma was 12.9% in inner-city vs. 10.6% in non-inner-city areas.

- The difference was **not significant** after adjusting for race/ethnicity, region, age, and sex.

- Black race, Puerto Rican ethnicity, and lower household income were independent risk factors for current asthma.
Inner City Asthma

- Prevalence of asthma is high in some inner-city areas

- This is largely explained by demographic factors

- Living in an urban neighborhood is not an independent risk factor for asthma
Inner City Asthma: Other Factors?

- Exposure to violence has been associated with:
  - more symptom days
  - higher hospitalization rates

- **Boston, Mass**
  - 10% < 6 years had witnessed a knifing or a shooting
  - 47% had heard gunshots

- **Chicago, Ill**
  - 42% between 7 and 13 years had witnessed a shooting


Concerns About Safety

- Close windows
  - potentially increasing exposure to indoor triggers
- Restrict children’s outdoor activity
  - sedentary lifestyle
  - linked to obesity
  - isolation and depression
- Increased stress
  - may potentiate asthma-inducing effects of other environmental pollutants (e.g. air pollution)

Stress: Biologic Manifestations

- 39 children with asthma and 38 healthy children
  - Recruited from the Vancouver, BC
- UCLA Life Stress Interview (Child Version)
  - Covers acute and chronic forms of stress over the past 6 months
- Measured beta receptor and glucocorticoid receptor mRNA from blood

PNAS April 4, 2006 vol. 103 no. 14 5496-5501
Children with asthma who experienced stress compared to those with asthma but no stress

- 9.5-fold reduction in $\beta_2$ adrenergic receptor mRNA
- 5.5-fold reduction in glucocorticoid receptor mRNA

Fewer receptors may diminish sensitivity to $\beta_2$-agonist and glucocorticoid medications
What is the effect of inhaled steroids on growth?

- Effective, well tolerated and safe at the recommended dosages
  - The potential but small risk of adverse events is well balanced by their efficacy
  - Concerns about growth persist

Cochrane Reviews: Inhaled corticosteroids in children with persistent asthma

- Six different steroids given at low or medium daily doses
- Growth velocity
  - 14 trials with 5717 participants
- Change from baseline in height
  - 15 trials with 3275 participants

How much was height reduced for children with asthma treated with inhaled steroids?

A. none
B. ¼ inch
C. ½ inch
D. 1 inch
E. 2 inches
Effect of Inhaled Steroids on Growth

- Height-change from baseline - 0.61 cm/y (0.24 in)

- Growth velocity - 0.48 cm/y (0.19 in)
## Effect of Inhaled Steroids on Growth

<table>
<thead>
<tr>
<th>Inhaled Steroid</th>
<th>Velocity (cm/y)</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone CFC 400 µg/day</td>
<td>-0.91 (0.36 inches)</td>
<td>-0.95 (0.37 inches)</td>
</tr>
<tr>
<td>Budesonide 400 µg/day</td>
<td>-0.59</td>
<td></td>
</tr>
<tr>
<td>Ciclesonide 200 µg/day</td>
<td>-0.08</td>
<td>-0.15</td>
</tr>
<tr>
<td>Flunisolide 400 µg/day</td>
<td>-0.22</td>
<td></td>
</tr>
<tr>
<td>Fluticasone 100-200 µg/day</td>
<td>-0.39</td>
<td>-0.46</td>
</tr>
<tr>
<td>Mometasone 200 µg/day</td>
<td>-0.47</td>
<td></td>
</tr>
</tbody>
</table>

- Growth velocity and height were reduced for all inhaled steroids.
- No impact:
  - daily dose (low vs. medium)
  - inhalation device
  - age

Effect of Budesonide on Adult Height

311 children followed for 13 years

- Initial rapid decline
- Nadir after 2-3 years of use
- Then stable with no further decline
- 1.2 cm (lower with higher dose)

![Graph showing height difference, Budesonide vs. Placebo](image)

<table>
<thead>
<tr>
<th>Mean Age (yr)</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Budesonide</td>
<td>9</td>
<td>11</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td>296</td>
<td>281</td>
<td>396</td>
<td>383</td>
<td>281</td>
<td>377</td>
</tr>
</tbody>
</table>

Effect of Inhaled Steroids on Growth

- Seen with all inhaled steroids
  - Further reduced with increased dose

- Growth suppression seemed to be maximal during the first few years of therapy and

- The decrease was neither progressive nor cumulative

Conclusions

- **Epidemiology**
  - Prevalence seems to have plateaued in US
  - Asthma severity based on symptoms and spirometry
    - Higher severity with spirometry than symptoms
  - Inner city asthma
    - Living in an urban neighborhood is not an independent risk factor for asthma
- **What is the effect of inhaled steroids on growth?**
  - The all modestly reduce velocity and growth