Special Considerations in Children

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- Asthma burden
- Case study
- Changes in lung function with age
- Impact of therapy
Asthma Burden for Children

- 6.8 million children currently have asthma
  - 22.9 million Americans currently have asthma
  - almost 1.2 million under age 5
  - 50-80% are diagnosed before their 5th birthday

- Highest lifetime prevalence 10% for ages 5-17 yrs
  - lifetime prevalence for all ages 7.7%
  - second highest in those >age 65 years

Asthma Burden

- 12.8 million school days
  - 54% of children missed school or daycare in the past year as a result of their asthma
  - average of nearly four days missed/year

- 10.1 million lost work days
  - $5 billion in lost productivity
Asthma Burden in Children

- 34% with asthma are awakened at night with asthma symptoms
- 49% experienced asthma symptoms during play, exercise, or exertion in the last month
- 62% report limited activity
- 54% experienced a sudden, severe asthma attack in the last year

http://www.asthmainamerica.com/

Asthma Burden for Children

- Ambulatory care visits: Almost 2% (4 million)
- ED visits: 2.3% (593,000)
- Hospitalizations: 5.6% (155,000)
- Mortality: 138 deaths per year
  - 3,563 deaths in all age groups
## Current Asthma Prevalence

received the diagnosis of asthma and still have the disease

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adults</th>
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</thead>
<tbody>
<tr>
<td>Female</td>
<td>8.5</td>
<td>9.0</td>
</tr>
<tr>
<td>Male</td>
<td>9.7</td>
<td>5.4</td>
</tr>
</tbody>
</table>

- Pattern reverses between children and adults

[www.lungusa.org](http://www.lungusa.org)

## Race Specific Asthma Prevalence

<table>
<thead>
<tr>
<th></th>
<th>Hispanic</th>
<th>Non-Hispanic White</th>
<th>Non-Hispanic Black*</th>
<th>Non-Hispanic Other</th>
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</thead>
<tbody>
<tr>
<td>Lifetime prevalence</td>
<td>10.2</td>
<td>11.5</td>
<td>13.3</td>
<td>10.5</td>
</tr>
<tr>
<td>Current prevalence</td>
<td>6.8</td>
<td>7.6</td>
<td>10.2</td>
<td>5.4</td>
</tr>
<tr>
<td>Attack prevalence</td>
<td>4.9</td>
<td>4.1</td>
<td>5.2</td>
<td>3.2</td>
</tr>
</tbody>
</table>

*Mortality also highest among children in this group

Trends in Asthma Morbidity and Mortality, American Lung Association, January 2009
### State Specific Asthma Prevalence

<table>
<thead>
<tr>
<th>State</th>
<th>Lifetime prevalence</th>
<th>Current prevalence</th>
<th>Asthma attack</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>12.4</td>
<td>8.8</td>
<td>5.7</td>
</tr>
<tr>
<td>Delaware</td>
<td>15.3</td>
<td>11.9</td>
<td>6.5</td>
</tr>
<tr>
<td>Maine</td>
<td>14.6</td>
<td>10.6</td>
<td>7.1</td>
</tr>
<tr>
<td>Hawaii</td>
<td>17.1</td>
<td>11.8</td>
<td>6.0</td>
</tr>
<tr>
<td>Wyoming</td>
<td>8.1</td>
<td>6.4</td>
<td>4.2</td>
</tr>
</tbody>
</table>

*Asthma attack rate in Indiana also 7.1

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### Current asthma prevalence among children 0 to 17 years of age in the United States in 2003

Which is the worst place to live in the United States if you suffer from asthma and allergies?

- Philadelphia, Pennsylvania
- Cleveland, Ohio
- St. Louis, Missouri
- Detroit, Michigan
- Boston, Massachusetts

http://www.AsthmaCapitals.com
Factors include asthma rates, pollution, allergens, smoking, medications, number of specialists
Case Study: 18 month old referred for evaluation of cough

- Cough began 2 weeks ago following a cold
- Sibling had a runny nose and fever but was fine after 2 days
- Full term baby with uneventful perinatal course
- Attends day care 5 days per week

Medical and Family History

- Eczema noted at age four months
- Wheezing noted at age 6 months during a sick visit to your office
- Mother has a history of allergic rhinitis and had asthma when she was a child
- 4 year old brother gets “bronchitis” every winter
- His father coughs but only when he exercises too much.
- At home there is an “outdoor” cat
Physical Exam

- General: alert and playful
- Respiratory rate 24, oxygen saturation 98%
- Temperature 98.4 °F
- Height & weight both 40th percentile
- HEENT: moderate nasal congestion
- Chest: no retractions, clear breath sounds
- Skin: mild eczema

Does he have asthma?
Asthma Predictive Index (API)

✓ Wheezing during the first 3 years of life
PLUS

1 Major Criterion  OR  2 Minor Criteria
✓ Physician-diagnosed parental history of asthma
✓ Physician-diagnosed atopic dermatitis

• Physician-diagnosed allergic rhinitis
✓ Wheezing unrelated to colds
• Eosinophilia (≥4%)

Children with atopic dermatitis and a parental or sibling history of atopic dermatitis, allergic rhinitis or asthma have a 50-80% increased risk of developing asthma


What is the probability that he will have another exacerbation?
The “September Epidemic” of asthma: Emergency Department Visits


Monthly Admissions for Wheezing

Heymann et al JACI 2004
What causes worsening of asthma?

Etiology of Asthma Exacerbations

- Compared with asthmatic controls, children with asthma who presented to the ED were
  - More likely to have any viral infection
    (62% vs. 41%; \(P=.011\))

Children Hospitalized for Wheezing

**Children < Age 3 Years**

- Adenovirus
- Parainfluenza 1,2,3
- RSV
- Metapneumovirus
- Influenza A,B
- Rhinovirus
- Enterovirus
- Coronavirus

**Percent of Patients Who Tested Positive for Each Virus**

- Wheeze
- Control

- p<0.001
- p<0.04
- p=0.01

**Children Hospitalized for Wheezing**

**Children ≥ Age 3 Years**

- Adenovirus
- Parainfluenza 1,2,3
- RSV
- Metapneumovirus
- Influenza A,B
- Rhinovirus
- Enterovirus
- Coronavirus

**Percent of Patients Who Tested Positive for Each Virus**

- Wheeze
- Control

- p<0.001

Heymann et al JACI 2004
Etiology of Asthma Exacerbations

- Compared with asthmatic controls, children with asthma who presented to the ED in September were
  - More likely to have any viral infection (62% vs 41%; $P = .011$)
  - Less likely to have $\beta_2$-adrenergic agonist prescription (75.4% vs 94.3%; $P < .001$)
  - Less likely to have an ICS prescription (84.7% vs 49.1%; $P < .001$)

Johnston and Sears. *Am J Respir Crit Care Med*. 2001;163:A359

Will he wheeze in the future?
Tucson Children’s Respiratory Study

- Birth cohort study began in 1980 and continues today (n=1246)
- In the first 6 years, 49% reported symptoms of wheezing

Asthma and Wheezing in the First 6 Years

**Transient wheezing**
- Smaller airway caliber
- No bronchial hyperresponsiveness
- Wheezing resolved by age 6

**Persistent wheezing**
- Atopy
- Bronchial hyperresponsiveness
- Significant deterioration in lung function by age 6

Asthma and Wheezing in the First Six Years of Life

What happens over time?
The Melbourne Asthma Study

- Community-based longitudinal study of subjects with a history of wheezing in childhood
- Subjects from a 1957 birth cohort were prospectively followed at age 7, 10, 14, 21, 28, 35, and 42
- 87% of survivors from the original cohort participated in the 1999 review


The Melbourne Asthma Study: Initial Patient Groups

- Control group (n=105)
- Mild wheezy bronchitis group (n=74)
  - No episodes of wheezing
  - <5 episodes of wheezing associated with bronchitis or respiratory tract infection
- Wheezy bronchitis group (n=104)
  - ≥5 episodes of wheezing associated with bronchitis or respiratory tract infection
- Asthma group (n=113)
  - Wheezing unassociated with respiratory tract infection
- Severe asthma group (n=83)
  - Onset of symptoms before age 3, persistent symptoms at age 10, FEV₁/FVC ≤50%, and/or barrel chest deformity

Melbourne Asthma Study: FEV$_1$ from 7 to 42 Years

![Graph showing FEV$_1$ % Predicted over age at review (years) for different categories: Controls, Mild wheezy bronchitis, Wheezy bronchitis, Asthma, Severe asthma.]


Melbourne Asthma Study: Key Findings

- 70% continued to have asthma symptoms
  - 90% of those with severe asthma
  - 24% of those who only wheezed with colds
- Differences in FEV$_1$ were seen before age 10 years
- The early loss of lung function did not appear to progress at a rate greater than controls

Natural History of Asthma

- Studies from around the world* report that many children with asthma experience remissions or improvement in early adulthood
- Loss of lung function happens early in childhood
- Severe asthma persists with age

*Aberdeen, Tasmania, Boston, national British study, Danish cohort, Isle of Wight, etc.

Therapy for Persistent Asthma

Potters Asthma Cure (circa 1927): —”pour powder to form a cone, light, inhale deeply”

Beck, H. History of Asthma Incidents, Treatments and Outcomes. Beck6mw.freeserve.co.uk
Stepwise Approach for Managing Asthma in Children Aged 5 to 11 Years: NAEPP Guidelines

**Step 1**
Preferred: SABA prn

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

**Step 3**
Preferred: Medium-Dose ICS (B) or Low-Dose ICS and either LABA (B), LTRA (B), or Theophylline (B)

**Step 4**
Preferred: Medium-Dose ICS + LABA (B)
Alternative: High-Dose ICS and either LABA (B), LTRA (B), or Theophylline (B)

**Step 5**
Preferred: High-Dose ICS + LABA (B)
Alternative: High-Dose ICS and either LTRA or Theophylline and Oral Corticosteroid (D)

**Step 6**
Preferred: High-Dose ICS + LABA + Oral Corticosteroid (D)
Alternative: High-Dose ICS and either LTRA or Theophylline and Oral Corticosteroid (D)
May Be Considered for Patients Who Have Allergies

ICS= inhaled corticosteroid; LTRA = leukotriene receptor antagonist.

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**Does treatment improve FEV₁?**
Childhood Asthma Management Program (CAMP) Study

Design: Multicenter, randomized, double-blind 4 year study of 1041 children aged 5 to 13 years with mild to moderate asthma

Treatments: Budesonide, Nedocromil, placebo

Primary endpoint: FEV₁ as an indicator of lung growth

Camp Study:
Lung Function as Measured by FEV₁

CAMP Study: Bronchial Hyperresponsiveness

![Graph showing PC_{20} (mg/mL) over time for Budesonide, Nedocromil, and Placebo.]

- Higher doses of methacholine were needed to induce bronchoconstriction.
- The benefits from inhaled steroids were only seen while they were being used.


Long-Term Inhaled Corticosteroids in Preschool Children at High Risk for Asthma

- 285 two or three year old children with a positive asthma predictive index

- Fluticasone vs. placebo for two years, followed by a one-year period without study medication.

- The primary outcome was the proportion of episode-free days during the observation year.

Guilbert, et al., *NEJM* 2006;354:1985-97
Long-Term Inhaled Corticosteroids in Preschool Children at High Risk for Asthma:

- **Results:** No significant differences were seen between the two groups proportion of episode-free days, the number of exacerbations, or lung function

- **Conclusions:** In children at high risk for asthma, two years of inhaled-corticosteroid therapy did not change the development of asthma symptoms or lung function during a third, treatment-free year.
What about leukotriene receptor antagonists?

**CLIC Study**

- Children 6-18 years of age with mild to moderate persistent asthma
  - FEV1 ≥ 70%
  - Bronchodilator response ≥12%
- Treatment with fluticasone or montelukast in a two-sequence crossover study
CLIC study

- Large proportion had similar response to both fluticasone and montelukast
- Some patients responded to one drug but not the other (fluticasone 23%, montelukast 5%)
- Unable to identify who was likely to respond to one therapy over another

Special Considerations in Children

- Asthma is common problem
- Heterogeneous in presentation, response to therapy and progression
- Early changes can be long-lasting
- Inhaled steroids to not appear to modify subsequent disease after the treatment is discontinued
The Growing Understanding of Asthma

1970s–1980s
Bronchoconstriction
Symptoms
Relieve symptoms
Prevent symptoms
Prevent exacerbations
Prevent early changes

1980s–1990s
Inflammation
Bronchial Hyperreactivity
Prevent symptoms
Prevent exacerbations
Prevent remodeling

1990s–
Bronchoconstriction
Remodeling
Fixed Obstruction
Prevent symptoms
Prevent exacerbations
Reduce side effects
Prevent early changes

2000s–
Bronchoconstriction
Inflammation
Early airway Obstruction
Environment
Infection
Allergy
Genetics

Symptoms
Prevent symptoms
Prevent exacerbations
Prevent remodeling