Advances in Pediatric Asthma

Stacy L Bichl APN, CPNP, AE-C
Advocate Children’s Outpatient Pediatrics

Kim Watts, MD, MS
Advocate Children’s Pediatric Pulmonology
Objectives

- Describe the basic pathophysiology of asthma and diagnostic considerations when evaluating a child for asthma
- Restate the utility of the four components of asthma management as delineated in the NHLBI National Asthma Education and Prevention Program
- Explain the different purposes of rescue and controller asthma medications, their correct administration.
- Identify barriers to asthma control
- Describe health outcome disparities in children with asthma
The Burden of Pediatric Asthma
The Scope of Asthma

• Most common chronic disease of childhood
• Affects more than 7 million children in the United States
• Approximately 9% of all US children have asthma
  – This rate has increased more than 160% in children under 5 in the last 20 years
• The annual economic cost of asthma is $19.7 billion
  – Direct costs such as medications and indirect costs such as loss of productivity
• 13 million school days are missed each year
Healthcare Utilization

Figure 4. Asthma health care encounters per 100 persons with asthma: United States, 2001–2009

NOTE: Access data table for Figure 4 at: http://www.cdc.gov/nchs/data/databriefs/db94_tables.pdf#4.

SOURCES: CDC/NCHS, National Ambulatory Medical Care Survey, National Hospital Ambulatory Medical Care Survey, National Hospital Discharge Survey, and National Health Interview Survey.
Rising Prevalence of Asthma

- Increase in asthma prevalence from 1980 to 1996 is greater than 50%
- Estimated current asthma prevalence in general increased between 2001-2009
- Largest increase in patients younger than 18 years old
Why the increasing numbers?

• Improved hygiene
  – Less exposure to pathogens disrupting innate immunity

• Increased indoor air pollution
  – Caused by increase in energy efficient building

• Increased incidence of early onset viral infections

• Increase in host susceptibility
  – Small lungs due to prematurity or maternal smoking

• Increased recognition and awareness
Pathophysiology
Pathophysiology of Asthma... “in a nutshell”

Asthma is a complex, chronic disorder with three main components.

• **Bronchoconstriction**—bronchial smooth muscle contraction that quickly narrows the airways in response to exposure to a variety of stimuli, including allergens or irritants.

• **Airway hyper-responsiveness**—an exaggerated bronchoconstrictor response to stimuli. (allergens, pollutants, histamine, viruses, cold air)

• **Airway edema**—persistent airway inflammation which left untreated becomes progressive with airway edema, mucus hypersecretion and mucous plugs that create additional obstruction.
Asthma Pathophysiology Overview

Diagram showing the comparison between a normal airway and one during asthma symptoms:

- **A Normal Airway:**
  - Airways
  - Airway wall
  - Muscle

- **C During Asthma Symptoms:**
  - Narrowed airway (limited airflow)
  - Tightened muscles constrict airway
  - Inflamed/thickened airway wall
  - Mucus

- **Airway x-section:**
  - Muscle
  - Airway wall
  - Mucus

- **Thickened airway wall:**
  - Muscle
  - Mucus
Diagnosis
The diagnosis of asthma is a clinical diagnosis:

- **Classic symptoms**
  - Recurrent wheezing… not always presenting symptom.
  - Cough
  - Chest tightness
  - Dyspnea

- **Exacerbating factors**
  - Cough or wheezing more prominent with exercise
  - Viral infections
  - Inhaled allergens (pollen, dust, mold)
  - Irritants (tobacco smoke exposure, perfumes)
  - Stress, emotion (crying, laughing)
  - Symptoms worsen at night/towards early morning

- **Response to therapy**
  - Improves with asthma therapy.
Cough

- Most common cause of cough in children over 3 years
- Persistent in nature—lasting more than 3 weeks at a time
- Night time to early morning cough
- Cough to specific exposures, more prominent with activity
- The “Wet-dry” asthma cough
  - Can be dry and hacking—reflective of airway edema
  - Can be productive with clear to white sputum—reflective of cellular infiltration, (with eosinophils, neutrophil and increased airway secretions)

Wheeze

- Polyphonic, musical, squeaky
- Generally expiratory but sometimes inspiratory

Advocate Children’s Hospital
Symptom Patterns

• Intermittent exacerbations but asymptomatic when well.
• Or chronic symptoms that worsen with exacerbations
• Morning “dipping”
  – Worsening of symptoms in the early morning corresponding to the physiologic dip in pulmonary function
• September epidemics
  – Viral infections, mycoplasma pneumoniae or Chlamydia pneumoniae infection
Diagnostic tools - Spirometry

- NAEPP recommends spirometry to be performed in patients older than 5 years:
  - $\text{FEV}_1 < 80\%$ predicted is abnormal
  - Reversibility (improvement in airflow of 12\%) after albuterol is abnormal.

- However, even in children with normal $\text{FEV}_1$, more subtle changes in the small airways ($\text{FEF}_{25-75}$) correlate with reversible airflow obstruction.

Even children with moderate asthma can have normal spirometry!
Spirometry loops
Diagnosis – Peak Flow

• More variable and effort dependent
• Wide variability in published predicted peak expiratory flow reference values
  – Can alter brand to brand
  – Predicted target changes quickly with linear growth
• Peak flows should not be used to diagnose asthma
• Limited usefulness in monitoring acute changes in those with known diagnosis.
Other Diagnostic Modalities

• Impulse Oscillometry
  – Passive cooperation
  – Evaluates resistance pre and post bronchodilator

• Bronchoprovocation Testing
  – Methylcholine, histamine, cold air, exercise
  – If patient fails empiric trial of asthma medications

• Chest x-ray
  – Hyperinflation, increased perihilar markings, non-specific signs of asthma
Risk Factors: The Asthma Predictive Index

- Risk factors in children <3 years that predict asthma symptoms at school age. The predictive index is positive when there is episodic wheezing during the preceding year AND
- One of 3 major criteria:
  - Physician diagnosed atopic dermatitis
  - Physician diagnosed parental asthma
  - Evidence of sensitization to aeroallergens
- OR 2 of the following minor criteria:
  - Peripheral blood eosinophilia ≥ 4%
  - Wheezing apart from colds
  - Evidence of sensitization to food allergens

More than 75% of children with a positive index had symptoms of asthma between 6 and 13 years of age.
Other risk factors?

• Parental History: Odds of a child with asthma
  – 25-30% greater with one asthmatic parent
  – About 50% greater with two asthmatic parents

• Obesity (as measured by BMI, higher fasting triglyceride levels, rate of acanthosis nigricans)

• Other Atopy… “the allergic triad”
  – Asthma
  – Atopic Dermatitis
  – Allergic Rhinitis

• Food Allergies (also a risk factor for intubation with exposure)

• Low fetal growth

• Recent/early Acetaminophen exposure
Other diagnostic considerations in infants

- Infection (post viral inflammation)
- Dysphagia with Aspiration
- GERD
- Sequelae of BPD
- Laryngotracheomalacia
- Interstitial Lung Disease
- Primary Ciliary Dyskinesia
- Cystic Fibrosis
- Congenital Heart Disease with L -> R shunt
- Immune Deficiency
- Vascular malformations/rings/slings
- Cystic Pulmonary Lesions (Congenital Lobar emphysema, CCAM)
- Tracheo-esophageal fistula
Other diagnostic considerations in children

- Allergic Rhinitis
- Chronic/acute sinusitis
- Foreign Body Aspiration
- Cystic Fibrosis
- Habit cough
- Vocal Cord Dysfunction
- Deconditioning +/- obesity
- Anemia
- GERD
Making a Diagnosis: Key Points

• Normal PFTs do not exclude a diagnosis of asthma

• The presence of wheezing is not a sure diagnostic sign nor does the absence of wheezing preclude a diagnosis of asthma.

• “Reactive airways” is a symptom, not a diagnosis…and is given the same ICD-9 code as asthma.

• There are identifiable risk factors that should raise suspicion for a diagnosis of asthma

• Transient intermittent wheezing should be treated as asthma unless another underlying cause is identified.

• Take a step outside the asthma box- consider the age appropriate differential list.
Components of asthma management

NAEPP 2007 GUIDELINES

1. Assessment
   • Initially = severity
   • Ongoing = control

2. Treatment (medication)
   • Initiate treatment based on severity
   • Adjust treatment based on control

3. Education

4. Reduction of environmental and co-morbid influences
Assessment:
Assessment: Dual domains to consider

• **Impairment** = impact on functioning:
  • Daily symptoms
  • Exercise intolerance
  • Poor sleep quality
  • Missed school/work
  • Rescue medication use

• **Risk** = likelihood of the following:
  • asthma exacerbation
  • loss of lung function
  • Impaired lung growth
  • Risk for adverse medication effects
Classifying Asthma Severity and Initiating Treatment in Youths ≥ 12 Years of Age and Adults

Assessing severity and initiating treatment for patients who are not currently taking long-term control medications.

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity ≥ 12 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
</tr>
<tr>
<td>Impairment</td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>≤2 x/month</td>
</tr>
<tr>
<td>Short-acting beta agonist use for symptom control (not prevention of EIB)</td>
<td>&lt;2 days/week</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
</tr>
<tr>
<td>Lung function</td>
<td>● Normal FEV₁ between exacerbations</td>
</tr>
<tr>
<td></td>
<td>● FEV₁/FVC normal</td>
</tr>
<tr>
<td>Risk</td>
<td>Exacerbations requiring oral systemic corticosteroids</td>
</tr>
</tbody>
</table>

Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV₁.

Recommended Step for Initiating Treatment

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4 or 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>and consider short course of oral systemic corticosteroids</td>
</tr>
</tbody>
</table>

In 2-6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.

FEV₁ - forced expiratory volume in one second; FVC - forced vital capacity.
Assessment: Who should get controller therapy?

- 0 to 4 years old
  - Greater than 4 episodes of wheezing
  - Parental history of asthma
  - Patient with atopic dermatitis or allergies
  - Food allergies with eosinophilia or wheezing without colds
  - Require albuterol more than two days per week
  - Experiences severe illness < 6 weeks apart
  - 2 rounds of steroids in 6 months
  - Intermittent disease with severe exacerbation
Assessment: Who should get controller therapy?

- 5 Years and older:
  - For any persistent asthma
  - Any symptoms > 2 days a week
  - Night time symptoms greater than 2 times a month
  - Albuterol more than 2 days a week
  - Any interference with normal activity
  - Requires oral steroids more than once a year
  - Severity and interval of exacerbations
Treatment: Maintenance Therapy
Choosing controller therapy?

Intermittent - - > Step 1
Mild - - > Step 2
Moderate - - > Step 3
Severe - - > Step 3 or 4
Inhaled Corticosteroids

• Inhibiting steps in the inflammatory cascade
• Associated with reduction in
  – Symptoms
  – Irreversible decline in lung function
  – Asthma exacerbations
  – Functional limitations
  – Side effects from other medications
• Reduction in parameters better than with leukotriene antagonist
• First line control therapy for persistent asthma
Key points in the inhaled steroid debate

• New literature in adults suggest possibility of ICS use episodically with symptoms for **mild** persistent asthma or titrated low dose ICS during time of symptoms in mild-moderate asthma
  – these recommendations remain outside the NHLBI guidelines for children.

• Research showed initial slowing in height velocity in prepubertal children using ICS for > 2 years persisted as a reduction in adult height, although the average decrease was 1.2 cm and neither progressive or cumulative.

The usual dose of an oral steroid burst is 40mg for 5 days
=200mg or 200,000ug
...almost all of which is bioavailable.

This is equal to:

- 400 days of Pulmicort 0.25 mg BID
- 625 days of QVAR 160ug BID
- 1,136 days of Flovent 88ug BID

... of which only 1-6% is bioavailable.
Leukotriene Receptor Agonists

- Cysteinyl leukotrienes found in BAL in asthmatic patients
- Inhibit production at various points in the cascade
- Adjuvant therapy to ICS in patients > 1 year old
- No evidence to support use as first line controller agent or as intermittent therapy
- Can be used to step down therapy from ICS or in mild patient who cannot tolerate ICS
Montelukast

**VS. Placebo**
- 2-5 years olds
- Intermittent asthma associated with viral symptoms
- Better than placebo with a reduced rate of exacerbations and decreased use of ICS

**Vs. ICS**
- Meta-analysis in mild to moderate persistent asthma children ICS had better pulmonary function and better asthma control
- ICS more cost effective
Long Acting Beta Agonists

• Used as an adjuvant to ICS
• Should not be used for acute exacerbations
• Once control is obtained, effort should be made to go to a single agent ICS
• Reserved for patients who “fail” medium dose ICS
• Black box warning
  – May increase the chance of severe asthma episodes and asthma related deaths
Chronic Oral Steroids

• Severe persistent asthma
• Long term effects
  – Adrenal suppression
  – Weight gain
  – Diabetes
  – Hypertension
  – Cataracts
  – Delayed growth
  – Immune suppression
  – Osteoporosis
  – Behavioral effects
• Lowest possible dose, every other day administration, trying all other modalities is preferable
Anti IgE (Omalizumab)

- Monoclonal anti IgE
- Moderate to severe asthma
- Not controlled on ICS
- Elevated IgE levels
- Approved if > 12 year old in US
- IgE levels 30 - 700
- Positive allergy testing
Other Therapies

• Cromolyn
  – Systemic review found no clear therapeutic effect vs. placebo
  – No evidence to support the concurrent use of cromolyn with ICS

• Theophylline
  – Use limited secondary to potentially serious short term side effects (arrhythmia, seizures and death)
  – Needs frequent serum monitoring as well as monitoring with drug interactions
Treatment: Exacerbation Management
Asthma Exacerbations:

• **Who is the child at risk for death?**
  - Previous severe exacerbations (intubation, ICU admit)
  - > 2 hospitalizations or > 3 ED visits in the last year
  - Use of > 2 canisters of rescue meds per month
  - Dysfunctional family units, low SES, inner city residence
  - Poor perception of airway obstruction
  - Concurrent food allergies
  - Illicit drug use
  - Co-morbidities- GERD, OSA, sinusitis, chronic rhinitis, obesity, ABPA, Stress/anxiety/Depression

• **Always respect a child’s complaint of breathing difficulty**

• **Even a child with mild asthma can have a fatal exacerbation**
Short Acting Beta Agonists

- Act to relax smooth muscles around the airways
- Overuse or regular use is associated with poor control
- Theoretical concern regarding down regulation of beta receptors with chronic use
  - Can impact medication needed for urgent care
Short acting medications

• Albuterol
  – MDI with spacer or nebulizer
  – No role for oral albuterol given side effects

• Levalbuterol
  – R- enantiomer – active isomer only
  – Approved MDI > 4 years old and nebulizer > 6 years old
  – Comparable, no evidence for superiority
Ipratropium Bromide

- Anti-cholinergic
- Bronchodilator through smooth muscle relaxation
- Adjuvant for albuterol in emergency settings
  - Reduce hospital admissions
  - Improve lung function in severe asthma
- Also can use as an alternative agent to albuterol
  - Tracheomalacia
- MDI not administered to soy or peanut allergy patients as it contains soy lecithin
Steroids

• **INHALED STEROIDS**
  
  • 2007 NAEPP expert panel does NOT recommend increasing dosing of inhaled steroids for treatment of acute exacerbations
  
  • Not found effective in reducing severity or progression of exacerbation
  
  • Higher dose (> 2 times the normal dose) may be an alternative to oral steroids in mild exacerbations if patient does not tolerate oral steroids - limited data.

• Short course of oral steroids in addition to short acting beta agonists should be mainstay of treatment for acute exacerbations
Delivery Considerations for Inhaled Medications

- Inhaled medications have equal delivery and efficacy when given properly by nebulizer or MDI/spacer/mask techniques.
- “Blow-by” nebulized therapies are ineffective!!
- Dry powder inhalers require a higher inspiratory flow rate for appropriate deposition (generally for children > 5 yrs)
- Appropriate spacer device should ALWAYS be used for MDI delivery. (combination with a correctly facemask in young children)
Medication administration: MDI with spacers

Every MDI needs a spacer... No matter the age/medication!
Medication administration: Diskus
Medication administration: Nebulizers
Medication administration: Turbohalers/Twisthalers

Budesonide = Controller
(Pirbuterol) = Rescue med
Key points in medication management

• Have clear agreed upon goals of therapy
• Always consider risk of taking medication vs not taking medication.
• Know your medications…
  – ICS dose response curve is relatively flat.
  – Leukotriene inhibitors can also treat Allergic rhinitis and EIA
  – LABA should be reserved for difficult to treat situations and risks should be discussed before prescribing.
• Consider seasonal treatment for those with asthma symptoms only in relation to certain times of year
Maintaining Asthma Control

- Patient follow up at 1-6 month intervals
- Reassess Impairment and Risk at all visits
- Incorporate self-assessment (Asthma Control test)
- Monitor height at every visit
- **Consider stepping up** if exacerbation requires oral steroids/ED
- **Consider stepping down** therapy when asthma has been well controlled for at least 6 months:
  - Make sure the changes are made gradually. This is necessary to identify minimum therapy associated with good control
  - Closely monitor after changing any therapy to assure sustained control of asthma
Education & Environmental Prevention Strategies:
Asthma Education

• Basic facts of asthma
  – Normal airways vs. asthma airways
  – What happens to airways in exacerbations

• Medications
  – Long acting “controller meds”
  – Short- acting “rescue meds”

• Patient skills
  – Medication administration techniques reviewed at every visit.
  – Knowing triggers/ reducing environmental factors
  – Self monitoring- recognizing exacerbations
  – Accessing medical care appropriately

• Understanding of an asthma action plan
  – Reviewed and provided in writing
Management Components:
The asthma action plan

<table>
<thead>
<tr>
<th>1. GREEN GO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing is good</td>
</tr>
<tr>
<td>No coughing or wheezing</td>
</tr>
<tr>
<td>Can work, play &amp; sleep</td>
</tr>
</tbody>
</table>

Medicine | How much? | When? |
|----------|-----------|-------|

10-20 minutes before sports or other strenuous activity, use this medicine.

<table>
<thead>
<tr>
<th>2. YELLOW CAUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>Wheezing</td>
</tr>
<tr>
<td>Tight chest</td>
</tr>
<tr>
<td>Wakes up at night</td>
</tr>
</tbody>
</table>

Medicine | How much? | When? |
|----------|-----------|-------|

Continue this plan until your child is well and without symptoms for three full days. Then return to green zone plan.

<table>
<thead>
<tr>
<th>3. RED STOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reliever medicine isn't working</td>
</tr>
<tr>
<td>Breathing is hard</td>
</tr>
<tr>
<td>Nose opens wide</td>
</tr>
<tr>
<td>Can't speak well</td>
</tr>
<tr>
<td>Can't walk</td>
</tr>
<tr>
<td>Ribs show</td>
</tr>
</tbody>
</table>

DANGER - CALL 911
Get help from a doctor now!

Medicine | How much? | When? |
|----------|-----------|-------|

Take these medicines until you talk with the doctor.

- **Red Alert**
  - Abuterol 0.5cc + 2 cc saline by nebulizer
  - Abuterol 2 puffs

- **Yellow Alert**
  - Abuterol 2 puffs

- **Green Alert**
  - pediatric dummy

In the right language
Check literacy
Reviewed at each visit
One for each household
One for school
Accessible in the EMR
Convenient for clinicians
Environmental/ Prevention Strategies

• Animal dander
• Pollen, outdoor molds, grasses
• Tobacco smoke
• Dust mites
• Live plants, christmas trees
• Cockroaches
• Smoke, strong odors, cleaning sprays
• Bedroom environment
  • Limit stuffed animals
  • Allergy covers on pillows
  • NO pets in bed/bedroom
Barriers to Care
Unequal burden of asthma

- About 1 in 6 or (17%) of non-Hispanic black children had asthma in 2009
- In 2001-2009 the greatest rise in asthma rates was among black children with an almost 50% increase
- About 40% of uninsured people with asthma reported not being able to afford their medications
- About 11% of insured people can not afford their asthma medications
Affects of Poverty and Race on Pediatric Asthma Prevalence

• Definitions of poor, near poor and non-poor are based on federal poverty levels that take into account annual/monthly income and family size.

• Prevalence data 2006-2008

MMRW, Jan. 14, 2011
Differences in Prevalence

- African American = 12.7 %
- Puerto Ricans = 25.7 %
- Mexican Americans = 6.6%
- Whites = 8.8%
- Higher among children
  - Living below the poverty threshold
  - Living in an urban setting
  - Northeastern portion of the US
Signals of Poor Asthma Control

• Utilization of ER
• Frequency of hospitalizations
• Repeated use of oral glucocorticoids
• School absenteeism
• Inability to participate in physical activity
Co-morbidities affecting Asthma control

- Gastroesophageal reflux (GERD)
- Obesity
- Obstructive Sleep Apnea
- Seasonal or Allergic Rhinitis
- Sinusitis
- Allergic bronchopulmonary Aspergillosis (ABPA)
- Vitamin D Deficiency
- Stress
- Depression
Considerations for Poor Asthma Control

- Environmental Exposures
  - ETS, mice, cockroaches
- Inadequate inhaler technique, broken or missing equipment
- Ineffective drug dose or dosing interval
- Other complicating medical problems
- Substitution of inappropriate treatment
- Response variability to certain medications
- Non-adherence
Factors affecting adherence

- Family disagreement about diagnosis
- Peer rejection
- Concern about adverse side effects of controllers
- Financial consequences
- Disruption of family routines
- Fear of inability to obtain health insurance with a pre-existing condition
- Limitations of social interactions because of triggers
If you never ask the question, you will never know the answer.
Goals of asthma therapy

• **Reduce Current Impairment**
  – Prevent symptoms
  – Infrequent need (<2 days a week) for relief medications (not including prevention of exercise-induced bronchospasm)
  – Maintain normal, or near normal pulmonary function.
  – Maintain normal activity levels (including exercise and other physical activity and attendance at school).
  – Meet patients’ and families’ expectations of and satisfaction with asthma care.
Goals of asthma therapy

• **Reduce Risk**
  • Prevent recurrent exacerbations of asthma
  • Minimize the need for ED visits or hospitalizations.
  • Prevent loss of lung function; for children, prevent reduced lung growth.
  • Provide optimal pharmacotherapy with minimal or no adverse effects of therapy…
    “lowest effective dose”.

[Image] Advocate Children’s Hospital
When is a Referral to an Asthma Specialist Needed?

- Difficulty achieving or maintaining asthma control
- Patient requires > 2 bursts of systemic steroids in 1 year
- Exacerbation that requires hospitalization
- Step 4 or higher care is required (Step 3 or higher for children 0-4 years of age)
- Immunotherapy or Monoclonal therapy is considered
- When additional testing is indicated
- When parent or provider is concerned with symptoms, response to treatment or long term prognosis
Thank you

Stacy Bichl, APN CPNP

Stacy.Bichl@advocatehealth.com