Asthma

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Asthma

• The scope of the problem
• Asthma in children
• Common and uncommon symptoms
• Diagnosis

Break

• Treatment principles
• Interesting cases
Every Life Deserves World Class Care

Asthma: the scope of the problem
Asthma in children

What is Asthma?

- Chronic disease of the airways that may cause
  - Wheezing
  - Breathlessness
  - Chest tightness
  - Nighttime or early morning coughing

- Episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.
Asthma

- Loss of epithelium
- Thickening of basal membrane
- Submucosal edema
- Mucus plugging
- Smooth muscle hypertrophy

ASTHMA: Definition

• Asthma is a clinical syndrome characterized by
  – airway obstruction, which is partially or completely reversible either spontaneously or with treatment;
  – airway inflammation;
  – and airway hyperresponsiveness (AHR) to a variety of stimuli

• Whereas past definitions of asthma emphasized AHR and reversible obstruction, current and more accurate definitions of asthma focus on asthma as a primary inflammatory disease of the airways, with clinical manifestations
  – increased bronchial hyperreactivity
  – and airflow obstruction due to the inflammation.
Asthma: Etiology and Pathogenesis

- In the genetically susceptible host, allergens, respiratory infections, certain occupational and environmental exposures, and many unknown host or environmental stimuli can produce the full spectrum of asthma, with persistent airway inflammation, bronchial hyperreactivity, and subsequent airflow obstruction.

- Once the inflammation and bronchial hyperreactivity are present, asthma can be triggered by additional factors, including exercise; inhalation of cold, dry air; hyperventilation; cigarette smoke; physical or emotional stress; inhalation of irritants; and pharmacologic agents, such as methacholine and histamine.

- When a patient with asthma inhales an allergen to which he or she is sensitized, the antigen cross-links to specific IgE molecules attached to the surface of mast cells in the bronchial mucosa and submucosa.

- The mast cells degranulate rapidly (within 30 minutes), releasing multiple mediators including leukotrienes, histamine, prostaglandins, platelet activating factor, and other mediators.

- These mediators lead to smooth muscle contraction, vascular congestion, and leakage resulting in airflow obstruction. This is the early (acute) asthmatic response (EAR), which is an immediate hypersensitivity reaction that usually subsides in about 30 to 60 minutes.

- In approximately 50% of asthmatic patients, however, airflow obstruction recurs in 3 to 8 hours. This late asthmatic response (LAR) is usually more severe and lasts longer than the EAR. The LAR is characterized by increasing influx and activation of inflammatory cells such as mast cells, eosinophils, and lymphocytes.

What Can Trigger Asthma?

Not all factors affect all people. It’s important to identify what affects a particular individual’s asthma.

- Infections in the upper airways, such as colds
- Changes in weather and temperature
- Exercise
- Physical expressions of strong feelings (crying or laughing hard, yelling)

Allergens such as:
- Furred and feathered animals
- Dust mites
- Cockroaches
- Pollens from grass and trees
- Molds (indoors and outdoors)

Irritants such as:
- Environmental tobacco smoke
- Scented products
- Strong fumes or odors
- Outdoor air pollution

Source: NHLBI
Asthma Health Burden

- Asthma affects over 20 million individuals in the USA alone.
- Approximately 8.6 million children under the age of 18 have been diagnosed with asthma in their lifetimes.
- Asthmatic children have 1.7 times increased risk of learning disabilities compared with non-asthmatic children.
- 1.5 million emergency room visits.
- 5500 deaths each year, 500,000 hospitalizations.
- The annual healthcare cost of asthma is over $10 billion.

Asthma is a Major Health Problem in the U.S.

- 5 million school-aged children have asthma.
- Students miss almost 13 million school days each year due to asthma.
- Asthma is the 3rd-ranking cause of hospitalization among children under 15.

On average, 3 children in a classroom of 30 are likely to have asthma.4

**Child and Adult Asthma Prevalence, United States, 1980-2007**

- **Child**
- **Adult**

**Asthma Prevalence by Sex, United States, 1980-2007**

- **Female**
- **Male**

Source: National Health Interview Survey; CDC National Center for Health Statistics
Current Asthma Prevalence for Youth by Race/Ethnicity, Ages 5-17, 2005-2007

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Asthma Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic Black</td>
<td>10.1%</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>7.1%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14.2%</td>
</tr>
<tr>
<td>Asian</td>
<td>10.2%</td>
</tr>
<tr>
<td>American Indian / Alaska Native</td>
<td>10.1%</td>
</tr>
</tbody>
</table>

Population Disparities in Asthma

- Current asthma prevalence is higher among
  - children than adults, boys than girls, women than men
- Asthma morbidity and mortality is higher among
  - African Americans than Caucasians

Asthma Mortality Rates by Sex, United States: 1979-2005

Asthma Mortality Rates by Race, United States: 1979-2005

Source: MMWR 2007;56(No. SS-8):1-54

ISAAC Phase Three

Wheeze in last 12 mths
13-14 yr age grp

Asthma prevalence increase in poor countries

Presented by Innes Asher, ERS Meeting Glasgow, September 2004
Special features of asthma in children

• More atopy: 60-70%
• Increased morbidity
• More episodic
• More difficult to define and diagnose
  – <5 yrs and 5-12 yrs
    – reactive airways vs asthma (young wheezers)
    – No standard PFTs
    – Co-morbid conditions (sinusitis, reflux)

Therapeutic approach in children

• Inhaled corticosteroids are the most effective therapy
  – Risk / benefit ratio
  – Growth velocity on ICS not different
• Same dose as adult
  – Deposition and absorption issues: 1/8th of dose ends up absorbed
• Intermittent inhaled steroids do not work
  – Make sure they are taken regularly
• Technique, technique, technique
• Involve child and parent in action plan
• Medications: what works is what they will take!!
  – ICS still first line
  – Steroid phobia: consider leukotriene antagonists
Common and uncommon asthma symptoms

• Common asthma symptoms:
  – Wheezing
  – Shortness of breath
  – Coughing, especially at night
  – Chest tightness, pain, or pressure

• Uncommon symptoms:
  – Chest Pain: need to r/o other etiologies
  – Dizziness: especially during exercise
  – Anxiety: Cause or effect?
Cough-Variant Asthma

- Coughing may be the sole complaint of patients with asthma.
- In such patients, the cough may be relieved by a bronchodilator or the avoidance of inhaled allergens.
- If bronchospasm is not present at the time of examination and spirometry is normal (which is often the case), the diagnosis can be confirmed by demonstrating reversible airway obstruction by a methacholine challenge test.

Exercise-Induced Asthma

- Common in asthmatics, especially after participation in outdoor activities in cold weather.
- The causes are not fully understood.
- Heat loss from the airways appears to be one of the causes.
- Diagnosis:
  - History
  - Spiro before and after exercise
  - Methacholine challenge
Occupational Asthma

• An estimated 2% to 5% of all asthma episodes may be caused by exposure to a specific sensitizing agent in the workplace.

• Occupational asthma is now the most common form of occupational lung disease in many industrialized countries.

• In an attempt to distinguish occupational from preexisting asthma, occupational asthma is defined as a disease characterized by a variable airflow limitation and/or AHR due to causes and conditions attributable to a particular working environment and not to stimuli encountered outside the workplace.

• Toluene diisocyanate is the most common cause of occupational asthma and is the best studied.

Nocturnal Asthma

• Nocturnal asthma is a characteristic problem in poorly controlled asthma and is reported by more than two thirds of suboptimally treated patients.

• It probably is due to the known physiologic decrease in the airway tone during sleep, which has been attributed to variation in catecholamine and cortisol secretion.

• Aspiration of gastric acid also may play a role in some patients with increased symptoms at night.

• ? Just poorly controlled asthma
Aspirin Sensitivity

• At least 5% of adults with asthma will experience severe and even fatal exacerbation of asthma after taking aspirin or other nonsteroidal antiinflammatory drugs (NSAIDs).

• Many of these patients have nasal polyps, although the relationship is not causal.

• The presumed mechanism is the inhibition of the cyclooxygenase pathway by aspirin and NSAIDs, with subsequent shunting of all arachidonic acid into the 5-lipoxygenase pathway, causing overproduction of bronchoconstrictor leukotrienes.

• Individuals with asthma should avoid these medications and instead use alternatives such as acetaminophen (e.g., Tylenol).

• Patients also should be informed that many over-the-counter medications contain aspirin and should be avoided as well.

Important Co-morbidities

• Gastroesophageal Reflux
  – The relationship between asthma and gastroesophageal reflux (GER) remains controversial
  – GER is nearly three times more prevalent in patients with asthma than it is in persons without asthma.
  – Presumably, acid reflux into the esophagus causes vagal stimulation, resulting in a reflex increase in bronchial tone in patients with asthma.

• Sinusitis
  – Acute and chronic sinusitis have been related to exacerbations and poor control of asthma by causing postnasal drip and interfering with nasal patency.
Asthma Mimetics: All that wheezes is not asthma!

• Infants and children:
  – Congenital anomalies
  – Bronchopulmonary dysplasia
  – Bronchomalacia
  – Vascular rings
  – Cystic fibrosis
  – Foreign body aspiration

• Adults:
  – Chronic obstructive pulmonary disease (COPD)
  – Congestive heart failure (CHF)
  – Primary endobronchial tumors
  – Endobronchial metastasis (from colon, breast, melanoma, kidney, pancreas)

• Acute onset:
  – CHF (cardiac asthma)
  – Pneumonia
  – Pulmonary embolism
  – Anaphylaxis
  – Aspiration syndromes
  – Foreign body aspiration

• Insidious onset:
  – CHF
  – Bronchogenic carcinoma
  – Tracheal tumor
  – Endobronchial metastasis

• Intermittent:
  – CHF
  – Aspiration syndromes
  – COPD
  – Carcinoid syndrome
  – Vocal cord dysfunction
Diagnosis of asthma

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Asthma diagnosis

Symptoms

Airflow obstruction

Bronchial hyperresponsiveness

Airway inflammation

H&P

PEFR

Spirometry

Challenge
Asthma is a clinical diagnosis

To establish a diagnosis of asthma the clinician should determine that:
✓ Episodic symptoms of airflow obstruction or airway hyperresponsiveness are present.
✓ Airflow obstruction is at least partially reversible.
✓ Alternative diagnoses are excluded.

Recommended methods to establish the diagnosis are:
- Detailed medical history.
- Physical exam focusing on the upper respiratory tract, chest, and skin.
- Spirometry to demonstrate obstruction and assess reversibility
- Methacholine challenge
- Additional studies to exclude alternate diagnoses.

Diagnosis of Asthma: symptoms

➢ Wheezing – high-pitched whistling sounds when breathing out.
➢ History of (any):
  — Cough, worse particularly at night
  — Recurrent wheeze
  — Recurrent difficulty in breathing
  — Recurrent chest tightness
➢ Symptoms occur or worsen in the presence of known triggers.
➢ Symptoms occur or worsen at night awakening patient.
Asthma Severity

Once diagnosis is established:
- Identify precipitating factors (triggers).
- Identify comorbidities that aggravate asthma
- Assess patient’s knowledge & skills for self-management.
- Classify severity using impairment & risk domains.

Pulmonary function testing (spirometry) to assess severity.

Diagnosing Asthma: Medical History

- Symptoms
  - Coughing, Wheezing, Shortness of breath, Chest tightness

- Symptom Patterns
  - Troublesome cough, particularly at night
  - Awakened by coughing
  - Colds that last more than 10 days
  - Relief when medication is used

- Triggers
  - Coughing or wheezing after physical activity
  - Breathing problems during particular seasons
  - Coughing, wheezing, or chest tightness after allergen exposure

- Severity
- Family History
Diagnosing Asthma: physical examination

- Wheezing sounds during normal breathing
- Hyperexpansion of the chest
- Increased nasal secretions or nasal polyps
- Atopic dermatitis, eczema, or other allergic skin conditions

Diagnosing Asthma: testing

- Peak flow
- Spirometry
- Methacholine challenge
- Therapeutic trial
- Exhaled nitric oxide (FENO)
Diagnosing Asthma: Peak Flow Chart

People with moderate or severe asthma should take readings:
- Every morning
- Every evening
- After an exacerbation

Diagnosing asthma: spirometry

Reduced FEV1/FVC ratio = obstruction
Reduced FEV1
Normal FVC = pure obstruction
Significant Bronchodilator response
Reversible airway obstruction: asthma
Diagnosing asthma: exhaled nitric oxide

- Loss of epithelium
- Thickening of basal membrane
- Submucosal edema
- Mucus plugging
- Smooth muscle hypertrophy

ASTHMA

- Airflow obstruction
- Bronchial hyperresponsiveness
- Airway inflammation

H&P, PEFR, Spirometry, Challenge
### eNO Levels in Lung Disease: NO Levels in the Lower Airway


### FE$_{NO}$ and Sputum Eosinophils (%)


$r = 0.48$

$p = 0.003$
Dose-Response Relationship and Reproducibility of the Fall in Exhaled Nitric Oxide After Inhaled Steroids in Asthma


Diagnosing Asthma: Comparisons between Exhaled Nitric Oxide Measurements and Conventional Tests


<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>2 wk</th>
<th>Initial</th>
<th>2 wk</th>
<th>Visit 3</th>
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<tbody>
<tr>
<td>Clinical asthma assessment</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FE$_{NO}$ measurement</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Skin allergy test</td>
<td>X</td>
<td></td>
<td></td>
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<td>Spirometry</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Bronchodilator reversibility</td>
<td>X</td>
<td></td>
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<tr>
<td>Hypertonic saline challenge</td>
<td>X</td>
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<td>Sputum induction</td>
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<td>Peak flow measurements</td>
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<td>Trial of oral prednisone</td>
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<td>X</td>
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</tbody>
</table>
Diagnosing Asthma: Comparisons between Exhaled Nitric Oxide Measurements and Conventional Tests


(A) expiratory flow variation (solid) and peak expiratory flow steroid response (dotted).

(B) FEV₁% predicted (solid), FEV₁/FVC ratio (dotted), and FEV₁ steroid response (dashed).

(C) FENO₅₀ (solid) and sputum eosinophils (dotted).

The NEW ENGLAND JOURNAL of MEDICINE

Use of Exhaled Nitric Oxide Measurements to Guide Treatment in Chronic Asthma

Andrew D. Smith, M.B., Ch.B., Jan O. Cowan, Karen P. Brassett, G. Peter Herbison, M.Sc., and D. Robin Taylor, M.D.

Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city adolescents and young adults: a randomised controlled trial

Esterling | Saffier | Hamer | Mitre | Coker | Peter | Groom | George | T'Connors, Wayne | Magan, Moir Katten

The Lancet; Sep 20-Sep 26, 2008

Cleveland Clinic
**Potential Uses of FENO in Asthma**

- Diagnosis
- Monitoring
- Titration of medications
- Evaluate adherence

**Gartner Hype Cycle**

- Peak of Inflated Expectations
- Plateau of Productivity
- Slope of Enlightenment
- Trough of Disillusionment
- Technology Trigger

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**American Thoracic Society Documents Review**

**American Thoracic Society Documents: version 8**

Guidelines for the Interpretation of Exhaled Nitric Oxide Levels (FENO) for Clinical Application

Raad A. Dweik (Chair) (1, 2), Peter B. Boggis (3), Serpil C. Erzurum (1, 2), Charles G. Irvin (4), Margaret W. Leigh (5), Jon O. Lundberg (6), Anna-Carin Olin (7), Alan L. Flummer (8), D. Robin Taylor (9)


**Revised: Fall 2009,...., Fall 2010**

**To be presented to the Board of Directors: Spring 2011**
Clinically Useful FENO cut-points

A. Diagnosis

<table>
<thead>
<tr>
<th>Symptoms present during past 2-4 weeks</th>
<th>FENO &lt;25 ppb</th>
<th>FENO 25-50 ppb</th>
<th>FENO &gt;50 ppb</th>
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</thead>
<tbody>
<tr>
<td>- eosinophilic airway inflammation unlikely</td>
<td>- Consider alternative diagnosis</td>
<td>- Interpret with caution</td>
<td>- Consider clinical context - Monitor change in FENO over time - Consider variables like anxiety and smoking</td>
</tr>
<tr>
<td>- unlikely to benefit from ICS</td>
<td></td>
<td></td>
<td>- eosinophilic airway inflammation present - Likely to benefit from ICS</td>
</tr>
</tbody>
</table>

B. Monitoring (in patients diagnosed with asthma)

<table>
<thead>
<tr>
<th>Symptoms present</th>
<th>FENO &lt;25 ppb</th>
<th>FENO 25-50 ppb</th>
<th>FENO &gt;50 ppb</th>
</tr>
</thead>
<tbody>
<tr>
<td>- consider alternative diagnosis</td>
<td>- Persistent allergen exposure</td>
<td>- Persistent allergen exposure - Poor compliance - Inadequate ICS dose - Steroid resistance</td>
<td></td>
</tr>
<tr>
<td>- unlikely to benefit from increase in ICS</td>
<td>- Poor compliance - Inadequate ICS dose - Steroid resistance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symptoms absent</th>
<th>FENO &lt;25 ppb</th>
<th>FENO 25-50 ppb</th>
<th>FENO &gt;50 ppb</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Adequate ICS dose - Good compliance - Consider ICS taper</td>
<td>- Adequate ICS dosing - Good compliance - Monitor change in FENO</td>
<td>- ICS withdrawal or dose reduction may result in relapse - Poor compliance or inhaler technique</td>
<td></td>
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</tbody>
</table>
Asthma: Key take home points

• Asthma is a huge medical burden in adults and children:
  – In the US
  – Globally
  – Among different racial and ethnic groups

• 2 components of asthma:
  – **Inflammation**
  – Airway reactivity / bronchospasm

• Diagnosis of asthma:
  – Clinical Diagnosis
  – no one specific test: PEFR, Spirometry, BD response, Methacholine challenge, FENO
Keep it Simple…

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Every life deserves world class care.