Asthma

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Objectives

- Identify barriers to effective control of asthma symptoms
- Perform an initial assessment of asthma severity and identify appropriate medication options
- Integrate the Asthma Control Test (ACT) Score as a tool to monitor asthma control in the office setting
- Counsel patients on medication use and administration techniques to improve adherence

What is Asthma?

- Chronic inflammatory disorder of the airways
  - Cells: mast cells, eosinophils, T lymphocytes
  - Chemical mediators: histamine, leukotrienes, platelet-activating factor, bradykinin
  - Chemotactic factors: cytokines, eotaxin
  - Eventual remodeling of airways

- Airway hyperresponsiveness
  - Acute inflammation
  - Smooth muscle constriction with airflow limitation (at least partially reversible)
Atopy: complex interaction between multiple genes and environmental factors, leading to IgE mediated response to allergens
- Link to chromosome 5 and 11
- If one parent with atopy, risk for child 25%
- If both parents, risk is 50-75%
- Atopy is present in 40% of children
- Manifested as asthma, allergic rhinitis, atopic dermatitis (eczema), allergic conjunctivitis, urticaria, food and drug allergies
Asthma Pathophysiology

- Smooth muscle dysfunction
- Airway inflammation
- Airway remodeling


Bronchoconstriction

Before

10 Minutes After Allergen Challenge

Asthma Pathophysiology

- Asthma is a common disease with significant morbidity, mortality and cost: 15-20% of children
- Suspect asthma in any child with recurrent wheezing
- Differential of cough and wheezing in infant/child
  - C - Cystic Fibrosis
  - R - Respiratory tract infections
  - A - Aspiration (foreign body, TEF, GERD)
  - D - Dyskinetic cilia
  - L - Lung and airway malformations (vascular rings, tracheal stenosis, laryngotracheomalacia, laryngeal webs, BPD, tumor)
  - E - Edema (congestive heart failure due to congenital heart dz)
Differential of Asthma in Adults

- COPD
- Congestive heart failure
- Pulmonary embolism
- Mechanical obstruction (tumor)
- Pulmonary infiltrate with eosinophilia
- Cough secondary to drugs (ACE inhibitors)
- Vocal Cord Dysfunction

Asthma Triggers

- Exercise
- Viral infections
- Smoke (tobacco, wood)
- Pollen
- Changes in weather
- Cold air
- Animals with fur or feathers
- Acid reflux
- Airborne chemicals or dusts (pollution, perfumes)
- Molds
- House-dust mites
- Cockroach allergens
- Strong emotional expression

What are the Therapeutic Targets?

Smooth muscle dysfunction
- Bronchoconstriction
- Bronchial hyperreactivity
- Hyperplasia/hypertrophy
- Inflammatory mediator release

Airway inflammation
- Inflammatory cell infiltration/activation
- Mucosal edema
- Cellular proliferation
- Epithelial damage
- Basement membrane thickening

Symptoms/Exacerbations

### Short Acting Products

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Dosing</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol</td>
<td>Pro-Air HFA®</td>
<td>Metered dose aerosol</td>
<td>β2-agonist</td>
</tr>
<tr>
<td></td>
<td>Proventil HFA®</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ventolin HFA®</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td>Maxair Autohaler®</td>
<td>Inhalation solution</td>
<td>β2-agonist</td>
</tr>
<tr>
<td>Levalbuterol</td>
<td>Xopenex®</td>
<td>Breath-actuated Metered dose inhaler</td>
<td>β2-agonist</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>Atrovent HFA®</td>
<td>Inhalation solution</td>
<td>Anticholinergic</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>Combinent®</td>
<td>Metered dose inhaler</td>
<td>Anticholinergic and β2-agonist</td>
</tr>
</tbody>
</table>

### Meter Dose Inhalers

- Breath actuated MDIs
  - May be useful for elderly and others unable to coordinate propellant actuation and inhalation
- Dry Powder Inhalers (DPI)
  - Rapid, 1-2 sec, deep inhalation
  - Most children cannot generate sufficient inspiratory flow to activate inhaler
  - Dose is lost if patient exhales through device
- β-agonists, ICS, anticholinergics

### Delivery Devices: Inhalers (cont)
**Breath Actuated and Dry Powder Inhalers**

- Spacer or Valved Holding Chamber (VHC)
  - Actuate only once into spacer/VHC per inhalation
  - Slow, 3-5 sec, deep inhalation, followed by 10 sec breathhold
  - Improves lung delivery of medication, decreases oropharyngeal deposition (thus decrease risk of thrush from steroids)
  - Use anti-static VHCs or rinse plastic non-anti-static VHCs with dilute household detergents
  - Can be bulky

**Delivery Devices: Spacers and Chambers**

- Comfort seal mask or mouthpiece
- Anti-static polymer chamber

**Spacers and Valved Holding Chambers**
Nebulizers

Inhaled Corticosteroids (ICS): The Most Effective Long-Term Controller Medications for Asthma

The daily use of ICS results in the following:
- Asthma symptoms will diminish and improvement continues gradually
- Occurrence of severe exacerbations is greatly reduced
- Use of quick-relief medication decreases
- Lung function improves significantly, as measured by PEF, FEV₁, and airway hyperresponsiveness
- Problems due to asthma may return if patients stop taking ICS
- Must rinse mouth after use to decrease risk oral thrush


Effects of Inhaled Corticosteroids on Inflammation

Types of Inhaled Corticosteroids

- Fluticasone (Flovent) HFA/DPI alone or with Salmeterol (Advair)
  - 1 puff BID – dose depends on severity
- Budesonide (Pulmicort) DPI alone or with Formoterol (Symbicort)
  - 2 puffs BID – dose depends on severity
- Beclomethasone (Beclovent, QVAR) HFA
- Flunisolide HFA
- Mometasone DPI

Leukotrienes as Mediators of Asthma

- In vitro and in vivo evidence supports the role of leukotrienes as important mediators of asthma by:
  - The ability to contract the human airway in vitro and in vivo
  - The ability to recruit eosinophils into the airway
  - The recovery of LTs from the airways of asthmatics
  - The ability to improve clinical asthma by blocking CysLT₁ receptors

Leukotriene Modifiers

- Montelukast (Singulair)
  - 4 mg 1-4 yrs, 5 mg 5-11 yrs, 10 mg > 12 yrs
  - chewable tabs 4, 5 mg; tabs 10 mg
- Zafirlukast (Accolate)
  - 10 mg BID for 7-11 yrs;
  - 40 mg qd or 20 mg BID for > 12 yrs
  - tabs 10, 20 mg
- Zileuton (Zyflo)
  - 600 mg QID for > 12 yrs only (with meals and bedtime)
  - elevation of liver enzymes reported
  - tabs 600 mg
Available LABA-Containing Products

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Formulation</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmeterol</td>
<td>Serevent®</td>
<td>DPI</td>
<td>1 inh BID</td>
</tr>
<tr>
<td>Formoterol</td>
<td>Foradil®</td>
<td>DPI</td>
<td>1 inh BID</td>
</tr>
<tr>
<td>Formoterol +</td>
<td>Symbicort®</td>
<td>MDI</td>
<td>2 inh BID</td>
</tr>
<tr>
<td>Salmeterol +</td>
<td>Advair®</td>
<td>DPI (Diskus)</td>
<td>1 inh BID</td>
</tr>
<tr>
<td>Fluticasone</td>
<td></td>
<td>MDI</td>
<td>2 inh BID</td>
</tr>
</tbody>
</table>

DPI = dry powder inhaler. Advair and Serevent are registered trademarks of GlaxoSmithKline. FORADIL is a registered trademark of Schering-Plough.

Management of Acute Mild Exacerbation

**Mild:** dyspnea only with activity; PEF ≥ 70% pred or best
- If known asthmatic, usually cared for at home
- If first time wheezing, check CXR
- Short-acting inhaled ß₂-agonists via spacer, valved holding chamber (VHC) or nebulizer (with prompt relief)
  - Albuterol (Ventolin, ProAir®): via inhaler: 1-2 puffs; via nebulizer: 0.63 – 2.5 mg in 3 cc saline
  - Levalbuterol (Xopenex): inhaler: 1-2 puffs; via nebulizer: 0.31-1.25 mg in 3 cc saline
  - Possible short course of oral systemic steroids

Use of Peak Flow Meter

Portable, handheld monitor for peak expiratory flow
- Forced exhalation after full inhalation while standing
- Record 3 readings
- Compare to predicted value or personal best reading
- Repeat after treatment to assess response
- Also used for chronic monitoring
Comparison Normal CXR (left) to Asthma (right)

Note Air trapping with hyperinflation and flattened diaphragms

Management of Acute Moderate Exacerbation

- **Moderate**: dyspnea interferes with normal activity; FEV1 or PEF 40 - 69% pred/personal best
- Usually requires office or ED visit
- Oxygen if needed to achieve SaO2 ≥ 90%
- Short-acting inhaled β2-agonists via spacer, valved holding chamber (VHC) or nebulizer up to 3 doses in 1st hr
  - Albuterol (Ventolin, ProAir): via inhaler: 1-2 puffs; via nebulizer: 0.63 – 2.5 mg in 3cc saline
  - Levalbuterol (Xopenex): inhaler: 1-2 puffs; via nebulizer: 0.31-1.25 mg in 3 cc saline
- Continue SABA q 60 min for 1-3 hrs; then decide to admit
- Oral systemic steroids, followed by inhaled steroids

Management of Acute Severe Exacerbation

- **Severe**: dyspnea at rest, interferes with conversation; FEV1 or PEF < 40% pred/personal best
- Usually requires ED visit and likely hospitalization
- Oxygen to achieve SaO2 ≥ 90%
- High dose inhaled short acting β2-agonist plus ipatropium (Atrovent) via nebulizer or MDI with valved holding chamber every 20 minutes or continuously up to one hour
- Continue inhaled SABA (albuterol or levalbuterol) and ipatropium (Atrovent) q 60 min or continuously for 1-3 hrs
- Systemic steroids – po or IV
- If incomplete response, admit to hospital
 Subset of Severe: Life-Threatening

- Life threatening: too dyspneic to speak, perspiring; PEF < 25% pred/personal best
- Requires ED/hospitalization, possibly ICU
- Oxygen to achieve SaO2 ≥ 90%
- Treatment as above; may need hourly or continuous SABA
- IV systemic steroids
- Possible intubation and mechanical ventilation

 Steroid Dosing in Acute Asthma

- Systemic corticosteroids
  - Prednisone (Deltasone, Liquid Pred)
  - Prednisolone (Orapred, Prelone, Pediapred)
  - Methylprednisolone (Medrol)
  - Dosing: 1-2 mg/kg with max 40-60 mg/day single or divided dosing bid x 3-10 days

2007 Guidelines: Long Term Goals of Therapy

- Reduce Impairment
  - Prevent chronic symptoms
  - Require infrequent use of short-acting beta2-agonist (SABA)
  - Maintain (near) normal lung function
  - Maintain normal activity levels
- Reduce Risk
  - Prevent exacerbations
  - Minimize need for ER care or hospitalization
  - Prevent loss of lung function /reduced lung growth
  - Minimize adverse effects of therapy

Four Components of Care

1. Assessment and monitoring
   - Assess asthma severity to initiate therapy
   - Assess asthma control to adjust therapy
   - Schedule follow up care

2. Education
   - Provide self management education
   - Develop written action plan
   - Integrate education into all points of care (medical providers, nurses, pharmacists, RTs, asthma educators in clinic, ER, hospital, school, home)

3. Control Environmental Factors and Comorbid Conditions
   - Measures to control exposures to allergens and pollutants or irritants (including smoke); consider immunotherapy
   - Treat comorbid conditions (GERD, obesity, obstructive sleep apnea, rhinitis and sinusitis, stress, depression, aspergillosis)
   - Influenza vaccine

4. Medications
   - http://www.nhlbi.nih.gov/guidelines/asthma
   - Use stepwise approach to determine options to meet patient’s needs and circumstances
   - Inhaled corticosteroids (ICS) are the most effective long term control
   - Consider domain of relevance, patient’s history of response to the medication, and patient’s willingness and ability to use the medication

Four Components of Care (cont)
2007 Guidelines: Asthma Severity vs. Control

- **Severity**
  - The intrinsic intensity of the disease process
  - Assess asthma severity to initiate therapy

- **Control**
  - The degree to which asthma symptoms are minimized by therapy
  - Assess and monitor control to adjust therapy
  - See attached Asthma Control Test

Classification of Asthma Severity

- **Severe Persistent**
  - Step 3
  - Throughout the day
  - > 1x/wk

- **Moderate Persistent**
  - Step 2
  - Daily
  - 3-4 x/month

- **Mild Persistent**
  - Step 1
  - Daily
  - Not daily and not > 1 x/day

- **Mild Intermittent**
  - Step 1
  - NA
  - NA

Severity Classification for Adults and Children < 5 yrs

<table>
<thead>
<tr>
<th>Severity Class</th>
<th>PEF or PEFR</th>
<th>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC</th>
<th>Inhaled Medication Use</th>
<th>Maintenance with Control Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Persistent</td>
<td>NA</td>
<td>NA</td>
<td>Daily</td>
<td>None</td>
</tr>
<tr>
<td>Moderate Persistent</td>
<td>NA</td>
<td>NA</td>
<td>Daily</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Mild Persistent</td>
<td>NA</td>
<td>NA</td>
<td>Daily</td>
<td>Minor limitation</td>
</tr>
<tr>
<td>Mild Intermittent</td>
<td>NA</td>
<td>NA</td>
<td>Daily</td>
<td>None</td>
</tr>
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</table>

### Stepwise Approach for Adults and Children (>12 years)

<table>
<thead>
<tr>
<th>Severity Class</th>
<th>Symptoms/Day</th>
<th>Symptoms/Night</th>
<th>Rescue Medication Use</th>
<th>Daily Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Persistent</td>
<td>Daily</td>
<td>&gt;60%</td>
<td>Reduced 3%</td>
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</tr>
<tr>
<td>Step 2</td>
<td>2x/week, but not daily</td>
<td>&gt;2 x/week, but not daily</td>
<td>Minor limitation</td>
<td></td>
</tr>
<tr>
<td>Mild Persistent</td>
<td>Daily</td>
<td>&gt;80%</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td>2 days/week</td>
<td>≥80%</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Mild Intermittent</td>
<td>Daily</td>
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### Control Classification for Adults and Children ≥ 12 yrs

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<th>Daily Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not well controlled</td>
<td>&gt;2 x/week or multiple times</td>
<td>&gt;2 nights/week, but not nightly</td>
<td>&gt;2 days/week</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Step up 1 step after 2 weeks; consider short course oral steroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extremely limited</td>
<td>&gt;2 x/week or multiple times</td>
<td>&gt;2 nights/week, but not nightly</td>
<td>&gt;2 days/week</td>
<td>Some limitation</td>
</tr>
<tr>
<td>Step 1</td>
<td>2 days/week</td>
<td>≥80%</td>
<td>&gt;80%</td>
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</tr>
<tr>
<td>Well controlled</td>
<td>Daily</td>
<td>&gt;75%</td>
<td>&gt;80%</td>
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<tr>
<td>Maintenance step: 1-2 x/week, moderate limitation, daily rescue until 33 days</td>
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<td>Minor limitation</td>
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</tr>
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<td>Daily</td>
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Patient Perceptions of Asthma Control

- Lack of adherence to clinical practice guidelines
- <50% employ environmental control measures
- 55% still have nicotine exposure
- Controller medications are underused
- Adherence estimated at 30-70%
- Controller therapy is not consistently provided following an acute exacerbation requiring urgent care
- Clinicians, patients and caregivers overestimate the degree of asthma control
- Asthma management may not be sufficiently personalized, especially in difficult-to-treat patients


Barriers to Effective Control of Asthma

- http://www.asthma.com/resources/asthma-control-test.html
- Designed to become a vital sign at every visit
- Support staff can read questions to patient
- Parent can administer at home
- Simple 5-question quiz
- Reflects multidimensional nature of asthma control
- Aligns with NIH goals of asthma therapy
- Encourages patient/provider communication
- Score of ≤ 19 suggests asthma may not be controlled adequately
Control Medications used in Asthma

- Inhaled corticosteroids once or twice a day
- Cromolyn sodium (Intal), Nedocromil (Tilade) QID
- Long-acting inhaled β₂-agonists
  - Salmeterol (Serevent) twice a day
  - Formoterol (Foradil) twice a day
- Leukotriene Receptor Antagonists (LTRA)
  - Montelukast (Singular) once a day
  - Zafirlukast (Accolate) once a day
- Methylxanthines
  - Theophylline, Aminophylline QID

http://www.asthma.com/resources/asthma-control-test.html
Long Term Control - Environmental
- Limit exposure to viral infections (daycare with fewer children); Influenza vaccine
- Limit exposure to smoke
  - No smoking allowed in house
  - Aid in smoking cessation
- Eliminate use of wood stoves and fireplaces
- Dust mite control
  - Encase pillow, mattress, box springs
  - Wash bedding weekly
- Mold/mildew control
  - Fix leaky pipes, clean bathtub/shower area

Long Term Control – Environment (cont)
- Avoid sleeping on upholstered furniture
- Minimize number of stuffed animals
- Reduce indoor humidity to < 50% (no vaporizers)
- Remove carpets or vacuum frequently
- Avoid overhead fans
- Pets – remove or keep out of bedroom
- Use filter on air ducts in bedroom
- Control cockroaches – don’t leave food or garbage exposed; use boric acid traps

Cough – Variant Asthma
- Consider in patient with chronic cough – cough is triggered by allergens, but airways don’t narrow as much, therefore peak flow may not be abnormal
- Symptom diary; provocation test
- Treatment same
Persistent asthma requires daily long-term controller medication, specifically anti-inflammatory therapy.

- Stepwise approach to pharmacologic therapy to first gain and then maintain control.
- Regular follow-up visits imperative.
- Patient education reinforces recommendations.
- Avoiding or controlling asthma triggers essential.
- Consider referral to specialist for difficult-to-control patients.

Summary: Managing Asthma Long Term

Website Resources

National Asthma Education And Prevention Program (NAEPP) Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma
  * www.nhlbi.nih.gov/guidelines/asthma/asths

- Asthma Control Tests for children and adults:
  * www.asthmacontrol.com

- Asthma Action Plan
  * http://www.dcasthma.org/dc_revised_asthma_action_plan_an_english.pdf