Bronchial Asthma
Sections

• Epidemiology
• Pathophysiology
• Diagnosis
• Medications
• Approach to Management
• Treatment Steps
• Special Situations
• Acute Asthma
What is Asthma.....Definition (GINA)

– A **chronic inflammatory disorder** of the airways in which many cells and cellular elements play a role.

– The chronic inflammation is associated with **airway hyper-responsiveness** that leads to **recurrent episodes of wheezing, breathlessness, chest tightness** and coughing particularly at night or early morning.

– These episodes are usually associated with widespread, but **variable airflow obstruction** within the lung that is **often reversible** either spontaneously or with treatment.
Asthma classification

• Child-onset asthma (extrinsic asthma)
  – Associated with atopy
  – **IgE** directed against common **environmental antigens** (house-dust mites, animal proteins, fungi
  – **Viral wheezing** Infants/children, allergy/allergy history associated with **continuing asthma** through childhood
• **Adult-onset asthma**
  
  – Many situations
  
  – Allergens important
  
  – Non-IgE asthma have nasal polyps, sinusitis, aspirin sensitivity or NSAID sensitivity
  
  – Idiosyncratic asthma less understood
• Adult-onset asthma
  – Occupational exposure
    • animal products, biological enzymes, plastic resin, wood dusts, metal
    • removal from workplace may improve symptoms although symptoms persist in some
Prevalence

• Most common chronic disease currently affecting appx. 300 million people worldwide.
• 10-12% of adults
• 15% of children
• Most have periodic wheezing attacks separated by symptom-free period.
• attacks can last minutes to days, and can become dangerous if the airflow becomes severely restricted.
PRECIPITATING OR AGGRAVATING FACTORS

- viral respiratory infections
- exercise
- endocrine factors
- drugs: aspirin beta blockers
- exposure to irritants and occupational chemicals
- weather changes: cold air
- allergens
- environmental changes
- food additives: sulfites
- emotional expression: anger, laughing
Epidemiology

- Age – any (peak age 3 yrs)
- Current asthma prevalence is higher among
  - children than adults
  - boys than girls (2:1)
  - women than men
- Children grow out of their asthma
- Asthma morbidity and mortality is higher among
  - African Americans than Caucasians

Source: MMWR 2007; 56(No. SS - 8): 1-54
Risk Factors for Developing Asthma: Genetic Characteristics

Atopy

- Major risk factor
- The body’s predisposition to develop an antibody (IgE) in response to exposure to environmental allergens
- Can be measured in the blood
- Includes allergic rhinitis, asthma, hay fever, and eczema
Causes/ Risk factors

- **Endogenous Factors**
  - Genetic predisposition
  - Atopy
  - Airway hyperresponsiveness
  - Gender
  - Early viral infection

- **ENVIRONMENTAL RISK FACTORS**
  - Perinatal Factors
  - Indoor and Outdoor Allergens
  - Smoking and Environmental Tobacco Smoke
  - Other Pollutants
  - Respiratory Illnesses
Triggers

- Allergens
- URI
- Exercise and hyperventilation
- Cold air
- Sulphur dioxide and irritant gases
- Drugs (β-blocker, aspirin)
- Stress
- Irritants (household sprays, paintfumes)
Pathology of Asthma

Inflammation

Airway Hyper-responsiveness

Airway Obstruction

Symptoms of Asthma
Mechanisms: Asthma Inflammation

Allergens
Sensitizers
Viruses
Air pollutants?

INFLAMMATION 'Chronic eosinophilic bronchitis

AIRWAY HYPERRESPONSIVENESS

SYMPTOMS
Cough  Wheeze
Chest  Dyspnea tightness

TRIGGERS
Allergens
Exercise
Cold air
SO₂
Particulates

Source: Peter J. Barnes, MD
Asthma Inflammation: Cells and Mediators

- Allergen
- Macrophage/Dendritic cell
- Mast cell
- Th2 cell
- Neutrophil
- Eosinophil

- Mucus plug
- Mucus hypersecretion
- Hyperplasia
- Vasodilatation
- New vessels (angiogenesis)
- Plasma leak
- Edema
- Nerve activation
- Epithelial shedding

- Airway smooth muscle
- Hypertrophy/hyperplasia
- Subepithelial fibrosis
- Sensory nerve activation
- Cholinergic reflex
- Bronchoconstriction

Source: Peter J. Barnes, MD
Asthma Inflammation: Cells and Mediators

**Inflammatory cells**
- Mast cells
- Eosinophils
- Th2 cells
- Basophils
- Neutrophils
- Platelets
- **Structural cells**
  - Epithelial cells
  - Sm muscle cells
  - Endothelial cells
  - Fibroblast
  - Nerves

**Mediators**
- Histamine
- Leukotrienes
- Prostanoids
- PAF
- Kinins
- Adenosine
- Endothelins
- Nitric oxide
- Cytokines
- Chemokines
- Growth factors

**Effects**
- Bronchospasm
- Plasma exudation
- Mucus secretion
- AHR
- Structural changes

Source: Peter J. Barnes, MD
Pathophysiology


Copyright © The McGraw-Hill Companies, Inc. All rights reserved.
Pathophysiology of asthma

APC = Antigen presenting cell
ILs = Interleukins
TH2 = T-lymphocyte Helper cell 2
Inflammation ➔ Remodeling

- Inflammation
- Airway Hypersecretion
- Subepithelial fibrosis
- Angiogenesis
Antigen
    ↓
    IgE
    ↓
Mast cell
    ↓
Proinflammatory
    Cytokines, IL-4
    ↓
T cell
    ↓
    IL-4
    ↓
B cell
    ↓
Macrophages
    ↓
    Proinflammatory
    Cytokines
Histamines
    Leukotrienes
    ↓
Chemoattractants
    LTB-4
Bronchospasm
    ↓
Tryptase
    ↓
Neutrophils
    Activated
    ↓
    Cytokines
    ↓
Eosinophil
    ↓
    Inflammation
    ↓
    Acute
    Subacute
    Chronic
Anatomy of an Asthma Attack

- Inspired air
- Expired air
- Primary bronchi
- Larynx (voice box)
- Trachea (windpipe)
- Right lung
- Left lung
- Bronchial tube
- Bronchus
- Bronchioles
- Alveoli (air pockets)
- Smooth muscle
- Blood vessels
- Lumen
- Mucous lining

Normal airway:
- Uninflamed
- Normal diameter
- No excess mucus

Obstructed airway:
- Inflamed
- Decreased diameter
- Excess mucus

Blood vessels infiltrated by immune cells:
- Inflammation and swelling

© 2001 Encyclopædia Britannica, Inc.
Asthma: Pathological changes

- Normal Airway:
  - Mucus
  - Submucosa
  - Airway
  - Mucosa
  - Muscle
  - Production of mucus

- Airway during an Asthma Attack:
  - Swollen submucosa
  - Airway narrows
  - Excess mucus
  - Secretion of mucus from gland increases
Pathology and consequences

- Smooth muscle mass increase
  - Severe bronchospasm during exacerbation

- Mucous glands increase
  - Important mucous secretion during exacerbation

- Inflammatory cells persistence
  - Ongoing inflammation

- Fibrogenic growth factor release
  - Collagen deposition on RBM and ECM

- Elastolysis
  - Reduced elasticity of airway wall
Asthma - Pathophysiology

- Genetic predisposition
- Intrinsic vulnerability
- Atopy/allergy

Inflammation underlies disease processes
Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time
COPD
- Neutrophils
- No airway hyperresponsiveness
- Less bronchodilator response
- Limited steroid response

Asthma
- Eosinophils
- Airway hyperresponsiveness
- Bronchodilator response
- Steroid response

Wheezy bronchitis 10%
**Asthma**
Sensitizing agent

Asthmatic airway inflammation
CD4+ T-lymphocytes
Eosinophils

**COPD**
Noxious agent

COPD airway inflammation
CD8+ T-lymphocytes
Macrophages
Neutrophils

**Airflow limitation**
Completely reversible

Completely irreversible
Physiologic Differences

**Asthma**
- Normal DLCO
- Normal lung volume
- Normal elastic recoil
- Flow dominant BD response

**COPD**
- Abnormal DLCO
- Hyperinflation
- Decreased elastic recoil
- Volume dominant BD response

Sciurba FC, CHEST 2004;117S-124S
<table>
<thead>
<tr>
<th>Disease Pathology</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversible airflow obstruction</td>
<td>+ ++</td>
<td>+</td>
</tr>
<tr>
<td>Airway inflammation</td>
<td>+ +++</td>
<td>+ +</td>
</tr>
<tr>
<td>Mucus hypersecretion</td>
<td>+</td>
<td>+ + +</td>
</tr>
<tr>
<td>Goblet cell metaplasia</td>
<td>+</td>
<td>+ +</td>
</tr>
<tr>
<td>Impaired mucus clearance</td>
<td>+ ++</td>
<td>+ +</td>
</tr>
<tr>
<td>Epithelial damage</td>
<td>++</td>
<td>—</td>
</tr>
<tr>
<td>Alveolar destruction</td>
<td>—</td>
<td>++</td>
</tr>
<tr>
<td>Smooth muscle hypertrophy</td>
<td>+ +</td>
<td>—</td>
</tr>
<tr>
<td>Basement membrane thickening</td>
<td>+++</td>
<td>—</td>
</tr>
</tbody>
</table>
Asthma-Classic presentation

- Episodic wheeze, dyspnea, chest tightness, or cough often triggered by allergens or sinusitis/rhinitis.
- Physical examination: wheezing, prolonged end-expiration, and decreased air movement. However, the examination can be normal.
- Uncontrolled symptoms in spite of aggressive therapy warrant evaluation to rule out other etiologies of the patient's symptoms and assess whether there are any triggers that can be controlled
Is it Asthma?

- Recurrent episodes of wheezing
- Troublesome cough at night
- Cough or wheeze after exercise
- Cough, wheeze or chest tightness after exposure to airborne allergens or pollutants
- Colds “go to the chest” or take more than 10 days to clear
How Does Asthma present ??

Clinical Presentations

- Episodic Attack
- Status Asthmatics
- Chronic Asthma

Always Describe diseases in following manner:

- Patient Symptoms
- Clinical features
- Inspection
- Palpation/percussion
- Auscultation
# Extrinsic vs intrinsic asthma

<table>
<thead>
<tr>
<th>Points</th>
<th>Early Onset</th>
<th>Late Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Early</td>
<td>Late</td>
</tr>
<tr>
<td>Atopy</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Allergen involvement</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Family history</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>IgE in Serum</td>
<td>Increased levels</td>
<td>Normal levels</td>
</tr>
<tr>
<td>Skin Hypersensitivity test</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Provocation test result</td>
<td>Positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>
## Differential diagnosis

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases causing recurrent episodic dyspnea</td>
<td>Chronic obstructive pulmonary disease, coronary artery disease, congestive heart failure, pulmonary emboli, recurrent gastroesophageal reflux with aspiration, recurrent anaphylaxis, systemic mastocytosis, carcinoid syndrome</td>
</tr>
<tr>
<td>Common diseases causing cough</td>
<td>Rhinitis, sinusitis, otitis, bronchitis (chronic or postviral), bronchiectasis, cystic fibrosis, pneumonia, diffuse pulmonary fibrosis</td>
</tr>
<tr>
<td>Common diseases causing airflow obstruction</td>
<td>Chronic obstructive bronchitis and emphysema, bronchiolitis obliterans, cystic fibrosis, organic or functional laryngeal narrowing, extrinsic or intrinsic narrowing of trachea or major bronchus.</td>
</tr>
</tbody>
</table>
DIAGNOSIS
Cough, wheezing and Breathlessness

- Minimal or no expectoration
  - Associated chest tightness
- Symptoms variable, Intermittent, recurrent, seasonal, worse at night and provoked by triggers
- History of atopy in self or atopy/eczema in family
- Breath Sound intensity normal
  - Prominent rhonchi – bilateral, diffuse, polyphonic, expiratory

**MANAGE AS ASTHMA**

- Expectoration mucoid or mucopurulent
- Symptoms chronic/progressive/persistent
- History of smoking (active or ETS exposure)

**Hyperinflation, pursed lip breathing, diminished intensity of breath sounds**

**Sputum for AFB (x3)**

- Positive
  - **TUBERCULOSIS** (Refer to RNTCP)
- Negative
  - **MANAGE AS COPD**

- Associated fever, chest pain, constitutional symptoms

**SUSPECT OTHER DIAGNOSES OR COMPLICATIONS**

**Referral**
Key indicators for considering a diagnosis of asthma

- Typical history
- Intermittent symptoms (reversible)
- Association of symptoms to weather changes, dust, smoke, exercise, viral infection, animals with fur or feathers, house-dust mites, mold, pollen, strong emotional expression (laughing or crying hard), airborne chemicals or dust
- Diurnal variation
- Family history
- Presence of atopy, allergic rhinitis, skin allergies
Routine Investigations

• Hemogram including eosinophil count
• Blood gas analysis
• X-ray chest
• ECG
• Serum electrolytes (Mg, Na, K)
• spirometry
Spirometry

- Spirometry measurements (FEV₁, FVC, FEV₁/FVC) before and after bronchodilator helps determine whether there is airflow obstruction and whether it is reversible over the short term.

- (12% in increase in FEV₁ and absolute increase in 200ml after 200ug of salbutamol inhalation)
Spirometry

• Spirometry should be done
  – at the time of initial assessment
  – after treatment is initiated and symptoms and peak expiratory flow (PEF) have been stabilized
  – at least every 1 to 2 years to assess the maintenance of airway function
# Classification of Severity

<table>
<thead>
<tr>
<th>STEP 4</th>
<th>Severe Persistent</th>
<th>Symptoms</th>
<th>Nocturnal Symptoms</th>
<th>FEV₁ or PEF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Continuous</td>
<td>Frequent</td>
<td>≤ 60% predicted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limited physical activity</td>
<td></td>
<td>Variability &gt; 30%</td>
</tr>
<tr>
<td>STEP 3</td>
<td>Moderate Persistent</td>
<td>Daily</td>
<td>&gt; 1 time week</td>
<td>60 - 80% predicted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Attacks affect activity</td>
<td></td>
<td>Variability &gt; 30%</td>
</tr>
<tr>
<td>STEP 2</td>
<td>Mild Persistent</td>
<td>&gt; 1 time a week but &lt; 1 time a day</td>
<td>&gt; 2 times a month</td>
<td>≥ 80% predicted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Variability 20 - 30%</td>
</tr>
<tr>
<td>STEP 1</td>
<td>Intermittent</td>
<td>&lt; 1 time a week</td>
<td>≤ 2 times a month</td>
<td>≥ 80% predicted</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asymptomatic and normal PEF between attacks</td>
<td></td>
<td>Variability &lt; 20%</td>
</tr>
</tbody>
</table>

The presence of one feature of severity is sufficient to place the patient in that category.
TREATMENT
Goals of Asthma Therapy

- Prevent recurrent exacerbations and minimize the need for emergency department visits or hospitalizations
- Maintain (near-) “normal” pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Provide optimal pharmacotherapy with minimal or no adverse effects
- Prevent asthma mortality
Asthma Management and Prevention
Five Components

1. Develop Patient/Doctor Partnership
2. Identify and Reduce Exposure to Risk Factors
3. Assess, Treat and Monitor Asthma
4. Manage Asthma Exacerbations
5. Special Considerations
Asthma Management and Prevention Program

- Asthma can be effectively controlled in most patients by intervening to suppress and reverse inflammation as well as treating bronchoconstriction and related symptoms

- Early intervention to stop exposure to the risk factors that sensitized the airway may help improve the control of asthma and reduce medication needs.
Asthma Management and Prevention Program

- Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control
Component 1: Develop Patient/Doctor Partnership

- Educate continually
- Include the family
- Provide information about asthma
- Provide training on self-management skills
- Emphasize a partnership among health care providers, the patient, and the patient’s family
Component 1: Develop Patient/Doctor Partnership

Key factors to facilitate communication:

✓ Friendly demeanor
✓ Interactive dialogue
✓ Encouragement and praise
✓ Provide appropriate information
✓ Feedback and review
Factors Involved in Non-Adherence

Medication Usage
- Difficulties associated with inhalers
- Complicated regimens
- Fears about, or actual side effects
- Cost
- Distance to pharmacies

Non-Medication Factors
- Misunderstanding/lack of information
- Fears about side-effects
- Inappropriate expectations
- Underestimation of severity
- Attitudes toward ill health
- Cultural factors
- Poor communication
Component 2: Identify and Reduce Exposure to Risk Factors

- Measures to prevent the development of asthma, and asthma exacerbations by avoiding or reducing exposure to risk factors should be implemented wherever possible.

- Asthma exacerbations may be caused by a variety of risk factors – allergens, viral infections, pollutants and drugs.

- Reducing exposure to some categories of risk factors improves the control of asthma and reduces medications needs.
Component 2: Identify and Reduce Exposure to Risk Factors

- Reduce exposure to indoor allergens
- Avoid tobacco smoke
- Avoid vehicle emission
- Identify irritants in the workplace
- Explore role of infections on asthma development, especially in children and young infants
Influenza Vaccination

- Influenza vaccination should be provided to patients with asthma when vaccination of the general population is advised.
Component 3: Assess, Treat and Monitor Asthma

• The goal of asthma treatment, to achieve and maintain clinical control
• can be achieved in a majority of patients with a pharmacologic intervention strategy.
## GINA Levels of Asthma Control

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled</th>
<th>Partly controlled (Any present in any week)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td>3 or more features of partly controlled asthma present in any week</td>
</tr>
<tr>
<td>Limitations of activities</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Nocturnal symptoms / awakening</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Need for rescue / “reliever” treatment</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>Lung function (PEF or FEV&lt;sub&gt;1&lt;/sub&gt;)</td>
<td>Normal</td>
<td>&lt; 80% predicted or personal best (if known) on any day</td>
<td></td>
</tr>
<tr>
<td>Exacerbation</td>
<td>None</td>
<td>One or more / year</td>
<td>1 in any week</td>
</tr>
</tbody>
</table>
# Asthma drug classification

## CONTROLLERS

<table>
<thead>
<tr>
<th>Inhaled corticosteroids</th>
<th>Leukotriene modifiers</th>
<th>Oral corticosteroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Fluticasone</td>
<td></td>
<td>3. Methylprednisone</td>
</tr>
</tbody>
</table>

**Anti-inflammatory action to prevent asthma attacks**

**Sustained bronchodilator action but weak or unproven anti-inflammatory effect**

## RELIEVERS

<table>
<thead>
<tr>
<th>Long-acting beta-agonists</th>
<th>Short-acting beta-agonists</th>
<th>Anti-cholinergenics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Salmeterol</td>
<td>1. Salbutamol</td>
<td>Ipratropium bromide</td>
</tr>
<tr>
<td>2. Formoterol</td>
<td>2. Fenoterol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Terbutaline</td>
<td></td>
</tr>
</tbody>
</table>

**For quick relief of symptoms and use in acute attacks as PRN dosage only**
Methods of Medication Delivery

- Metered-dose inhaler (MDI)
  - Spacer/holding chamber/face mask
- Dry-powder inhaler (DPI)
- Nebulizer
- Oral Medication
  - Tablets, Liquids
- Intravenous Medication
  - IV Corticosteroids, IV Aminophylline
What are Controllers?

- Prevent future attacks
- Long term control of asthma
- Prevent airway remodeling
What Are Relievers?

- Rescue medications
- Quick relief of symptoms
- Used during acute attacks
- Action lasts 4-6 hrs
CONTROLLERS

Inhaled Corticosteroids

- **Treatment of choice for** long-term control of persistent asthma
- **Benefits**
  - Reduced airway inflammation through topical activity
  - decreases airway hyper-responsiveness.
  - Improve lung function and quality of life
  - Reduce the frequency of exacerbations
  - Reduced use of quick-relief medicine

**NEVER FOR RESCUE PURPOSES**
CONTROLLERS
Corticosteroids

• Inhaled
  ▪ Bectolmethasone
  ▪ Fluticasone
  ▪ Triamcinolone
  ▪ Budesonide
  ▪ Flunisolide
Anti-inflammatory Effect of Glucocorticoid

**inflammatory cells**

- Eosinophil: \( \downarrow \) Numbers (apoptosis) → T-lymphocyte
- \( \downarrow \) Cytokines → Mast cell
- \( \downarrow \) Numbers → Macrophage
- \( \downarrow \) Cytokines → Dendritic cell

**Structural cells**

- Epithelial cell: \( \downarrow \) Cytokines Mediators
- Endothelial cell: \( \downarrow \) Leak
- Airway smooth muscle: \( \uparrow \) \( \beta_2 \)-Rece
- Mucus gland: \( \downarrow \) Mucus secretion

**GLUCOCORTICOIDs**
## Estimated Comparative Daily Dosages for Adults of Inhaled Corticosteroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low Dose</th>
<th>Medium Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Step 2</td>
<td>Step 3</td>
<td>Step 4</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>1-3 puffs</td>
<td>3-6 puffs</td>
<td>&gt;6 puffs</td>
</tr>
<tr>
<td></td>
<td>80 - 240 mcg</td>
<td>240 - 480 mcg</td>
<td>&gt; 480 mcg</td>
</tr>
<tr>
<td>Budesonide DPI</td>
<td>1-3 puffs</td>
<td>3-6 puffs</td>
<td>&gt; 6 puffs</td>
</tr>
<tr>
<td></td>
<td>200 – 600 mcg</td>
<td>600 – 1,200 mcg</td>
<td>&gt; 600 mcg</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>2-4 puffs</td>
<td>4-8 puffs</td>
<td>&gt; 8 puffs</td>
</tr>
<tr>
<td></td>
<td>500–1,000 mcg</td>
<td>1,000–2,000 mcg</td>
<td>&gt; 2,000 mcg</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>2-6 puffs (44)</td>
<td>2-6 puffs (110)</td>
<td>&gt; 6 puffs (110)</td>
</tr>
<tr>
<td></td>
<td>88-264 mcg</td>
<td>264-660 mcg</td>
<td>&gt; 660 mcg</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>4-10 puffs</td>
<td>10-20 puffs</td>
<td>&gt; 20 puff</td>
</tr>
<tr>
<td></td>
<td>400-1,000 mcg</td>
<td>1,000–2,000 mcg</td>
<td>&gt; 2,000 mcg</td>
</tr>
</tbody>
</table>
## Corticosteroid Side Effects

<table>
<thead>
<tr>
<th>Inhaled Local</th>
<th>Systemic (oral, IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dysphonia</td>
<td>• Fluid retention</td>
</tr>
<tr>
<td>• Cough/throat irritation</td>
<td>• Muscle weakness</td>
</tr>
<tr>
<td>• Thrush</td>
<td>• Ulcers</td>
</tr>
<tr>
<td>• Impaired growth (high dose)?</td>
<td>• Malaise</td>
</tr>
<tr>
<td></td>
<td>• Impaired wound healing</td>
</tr>
<tr>
<td></td>
<td>• Nausea/Vomiting, HA</td>
</tr>
<tr>
<td></td>
<td>• Osteoporosis (adults)</td>
</tr>
<tr>
<td></td>
<td>• Cataracts (adults)</td>
</tr>
<tr>
<td></td>
<td>• Glaucoma (adults)</td>
</tr>
</tbody>
</table>
The Fate of Inhaled Steroids

Mouth and Pharynx

Swallowd fraction ~ 80-90%

GI tract

Absorption from the gut

Liver

Active drug from the gut

Inactivation in the liver “first pass”

Lung deposit ~ 10-20%

Absorption from the lung (A)

Systemic Concentration = A+B

Systemic Circulation
CONTROLLERS

Long-acting Beta$_2$-agonists

- Salmeterol, Formoterol
  - Indication: Daily long-term control

  *Bronchodilate by long-term stimulation of beta$_2$ receptors*

- Advantages
  - Blunt exercise induced symptoms for longer time
  - Decrease nocturnal symptoms
  - Improve quality of life

- Combination therapy beneficial when added to inhaled corticosteroids

  Decrease the need to increase inhaled corticosteroid dose by dose
CONTROLLERS
Long-acting Beta$_2$-agonists

- **NOT** for acute symptoms or exacerbations
  - Onset of effect $\rightarrow$ 30 minutes
  - Peak effect $\rightarrow$ 1-2 hours
  - Duration of effect $\rightarrow$ up to 12 hours
- **NOT** a substitute for anti-inflammatory therapy
- **NOT** appropriate for monotherapy
Useful Beta Adrenergic Effects

- Relax bronchial smooth muscle
- Inhibit mediator release from mast cells, eosinophils, macrophages
- Decrease mucous secretion (submucosal gl)
- Increase mucociliary transport
- Inhibit bronchial oedema
- Inhibit cholinergic transmission
- Decrease airway hyperresponsiveness
CONTROLLERS
Leukotriene Modifiers

- Cysteinyl Leukotriene Receptor Antagonists
  - **Montelukast** – Once a day in PM – indicated at age 1
  - **Zafirlukast** – Twice daily – Empty Stomach
    - Many drug interactions

- 5-Lipoxygenase inhibitors
  - **Zileuton** – Four times daily
    - Many drug interactions
Add-on Controllers
Leukotriene Modifiers

- **Montelukast**
  - Improves lung function and asthma control
  - May protect against exercise induced bronchoconstriction
  - Improves lung function when added to inhaled corticosteroids
  - Not as effective as inhaled corticosteroids
- 4 mg, 5 mg chewable and 10 mg tablet
  - Once daily dosing (evening)
- Pediatric indication > 1 year
- No food restrictions
RELIEVERS

Short-Acting Beta$_2$-agonist

- Salbutamol
- Pirbuterol
- Terbutaline
- Levosalbutamol
RELIEVERS
Short-Acting Beta$_2$-Agonists

- Most effective medication for relief of acute bronchospasm
- Preferably use inhaled rather than oral preparations
- Increased need for these medications indicates uncontrolled asthma (and inflammation)
- Regularly scheduled use not generally recommended – use “as needed”
  - May lower effectiveness
  - May increase airway hyperresponsiveness
SHORT-ACTING BETA$_2$-AGONISTS

- Side Effects:
  - Increased Heart Rate
  - Palpitations
  - Nervousness
  - Sleeplessness
  - Headache
  - Tremor
Unwanted Beta Adrenergic Effects

- Hypokalemia (K shift into muscle tissue)
- Hyperglycemia (glycogenolysis)
- Hypoxia (pulmonary vasodilation causing increased ventilation/perfusion mismatch)
Oral Steroid Short Course

- Prednisone 30-40mg x 10-14 days for acute exacerbation of Asthma
- no weaning of dose unless long term use
Step 1 Treatment for Adults and Children > 5: Mild Intermittent

**Controller – Daily**
- Not needed

**Reliever – Quick Relief**
- Short-acting inhaled
  beta$_2$-agonist
- Increasing use, or use more than 2x/week, may indicate need for long-term-control therapy
- Intensity of treatment depends on severity of exacerbation
Step 2 Treatment for Adults and Children > 5: Mild Persistent

**Controller – Preferred Daily**
- Low dose inhaled corticosteroid

**Alternatives (alphabetically)**
- Cromolyn, leukotriene modifier,
  nedocromil

OR
- Sustained-release theophylline to serum concentration of 5-15mcg/ml
Step 3 Treatment for Adults and Children > 5: Moderate Persistent

**Controller – Preferred Daily**
- Low to medium dose inhaled corticosteroid (medium dose) and long-acting beta$_2$-agonist

**Alternatives (alphabetically)**
- Increase inhaled corticosteroids to medium-dose range
  OR
- Low to medium dose inhaled corticosteroid (medium dose) and either leukotriene modifier or theophylline
Step 3 Treatment for Adults and Children > 5: Moderate Persistent

(patients with recurring severe exacerbations)

**Controller – Preferred Daily**
- Medium dose inhaled corticosteroid
  (medium dose) and long-acting beta_2_-agonist

**Alternatives (alphabetically)**
- Medium dose inhaled corticosteroid
  (medium dose) and either leukotriene modifier or theophylline

- Consider referral to a specialist
Step 4 Treatment for Adults and Children > 5: Severe Persistent

**Controller - Daily**
- High-dose inhaled corticosteroid AND
- Long-acting inhaled beta₂-agonist AND, if needed,
- Corticosteroid tablets or syrup long term (2 mg/kg/day, generally ≤ 60 mg/day). (Make repeat attempts to reduce dose and maintain control with high-dose inhaled corticosteroid).

- Recommend referral to a specialist
Persistent asthma: Daily medication
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.

Step 1
Preferred: Low-dose ICS
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

Step 2
Preferred: Low-dose ICS + LABA
Alternative: Low-dose ICS + either LTRA, Theophylline, or Zileuton

Step 3
Preferred: Medium-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton

Step 4
Preferred:
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies

Step 5
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Step up if needed
(first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible
(and asthma is well controlled at least 3 months)

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-relief medication for all patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
Monitor Asthma Control

**PARTLY CONTROLLED**
- Daytime symptoms > twice/week
- Any limitation of activity
- Any nocturnal symptoms/awakening
- Need for reliever medication > twice/week
- Lung function <80% predicted or personal best
- <1 exacerbation per year

Check adherence and inhaler technique
Step up treatment

**CONTROLLED**
- < 2 daytime symptoms per week
- No limitation of activity
- No nocturnal symptoms/awakening
- Reliever medication - twice/week
- Normal lung function
- No exacerbations

Consider step down if controlled for 3 or more months

**UNCONTROLLED**
- Three or more features of partly controlled asthma in any week.
- An exacerbation in any week

Check adherence and inhaler technique
Step up treatment

**Assess control**
- Daytime symptoms
- Limitation of activities
- Nocturnal symptoms/awakening
- Need for reliever medication
- Lung function (PEF or FEV1)
- Exacerbations
Treating to Maintain Asthma Control

Stepping down treatment when asthma is controlled

- When controlled on medium- to high-dose inhaled glucocorticosteroids: 50% dose reduction at 3 month intervals (Evidence B)
- When controlled on low-dose inhaled glucocorticosteroids: switch to once-daily dosing (Evidence A)
Treating to Maintain Asthma Control

Stepping up treatment in response to loss of control

- Rapid-onset, short-acting or long-acting inhaled β2-agonist bronchodilators provide temporary relief
- Need for repeated dosing over more than one/two days signals need for possible increase in controller therapy
Managing the well controlled patient

As soon as good control:

- Reduce oral steroids first, then stop
- Reduce relievers before controllers

When good control for 3+ months:

- Reduce inhaled steroids
Therapy to avoid!

- Sedatives & hypnotics
- Cough syrups
- Anti-histamines
- Immunosuppressive drugs
- Immunotherapy
- Maintenance oral prednisone >10mg/day
Managing partly/uncontrolled asthma

• Check the inhaler technique
• Check adherence and understanding of medication
• Consider aggravation by:
  – Exposure to triggers/allergens at home or work
  – Co-morbid conditions: GI reflux, rhinitis/sinusitis, cardiac problem
  – Medications: Beta-blockers, NSAIDs, Aspirin
The Asthma Action Plan

- Helps patients/caregivers manage asthma
  - Uses Peak Flows
  - Spells out medication instructions

- Green Zone 80-100% Peak Flow
- Yellow Zone 50-80% Peak Flow
- Red Zone Below 50% Peak Flow
Medication Delivery Demonstrations

- Breath Actuated Inhalers
- Metered Dose Inhalers with Spacer/Holding Chamber
- Dry Powder Inhalers
- Nebulizers
## pMDIs

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small and portable</td>
<td>difficult to learn technique</td>
</tr>
<tr>
<td></td>
<td>Unsuitable for children $&lt; 5-6$</td>
</tr>
<tr>
<td>Quick to use</td>
<td>Unsuitable for the elderly, Cold jet may irritate throat</td>
</tr>
<tr>
<td></td>
<td>Limited amount of drug delivered per puff</td>
</tr>
</tbody>
</table>
Spacers and Holding Chambers

A spacer device enhances delivery by decreasing the velocity of the particles and reducing the number of large particles, allowing smaller particles of drug to be inhaled.

- A spacer device with a one-way valve, i.e., holding chamber, eliminates the need for the patient to coordinate actuation with inhalation and optimizes drug delivery.

- A simple spacer device without a valve requires coordination between inhalation and actuation.
DPIs

• Generally easier to use
• A minimal inspiratory flow rate is necessary to inhale from a DPI; difficult for some pts to use during an exacerbation
• More ecological than MDIs
• Storage may be difficult in humid climates
Nebulizer

Advantages

No Coordination required
Can be used for all ages
Effective in severe asthma

Disadvantages

Cumbersome
Expensive
Noisy
Treatment takes time
Which inhalation device for which patient?

- Infants and children up 5 y/o: pMDI+spacer, nebulizer
- Children 5-9 y/o: pMDI+spacer, nebulizer, DPI
- Competent older children and adults: pMDI, DPI
- Incompetent older children/adults: pMDI+spacer, nebulizer
Key Messages

• Asthma is common—can happen to anybody
• Asthma can be effectively controlled, although it cannot be cured.
• Effective asthma management programs include education, objective measures of lung function, environmental control, and pharmacologic therapy.
• A stepwise approach to pharmacologic therapy is recommended.
• The aim is to accomplish the goals of therapy with the least possible medication.