Asthma Outline

- Pathophysiology
- Etiology
- Signs & symptoms
- Diagnostic testing & data interpretation
- Respiratory therapeutic interventions
Asthma: Pathophysiology

- Bronchial smooth muscle constriction (spontaneously or therapeutically reversible)
- Increased airway responsiveness (hypersensitivity) to certain stimuli
- Increased bronchopulmonary secretions
- Airway wall edema (inflammation)
Asthma: Pathophysiology

- Airway inflammation
- Increased airway responsiveness (hypersensitivity) to certain stimuli

Clinical expression of a reversible lower airway obstruction
Asthma: Pathophysiology

A. Normal Airway
- Airways
- Airway wall
- Muscle

B. Normal Airway (limited air flow)
- Tightened muscles
- Constricted airway

C. During Asthma Symptoms
- Inflamed/thickened airway wall
- Mucus

Muscle
Airway wall
Airway x-section
Thickened airway wall
Muscle
Mucus
Asthma: Pathophysiology

- Airway remodeling is associated with chronic asthma, but the cause of remodeling remains unclear whether it results from:
  - (1) airway inflammation in response to allergens, or
  - (2) immune-mediated events such as viral infections.
Asthma: Pathophysiology

Definition of Airway Remodeling

Persistent changes in airway structure including:

- Subepithelial fibrosis (thickening of airway walls)
- Increased smooth muscle mass
- Mucous gland & goblet cell hyperplasia
- Increased bronchial wall vascularity
- Inflammatory cellular infiltrates
Asthma: Pathophysiology

- The physiological consequences of airway remodeling:
  - not reversed by asthma therapy
  - determinant of airway hyperresponsiveness
  - accelerated loss of lung function over time
- Changes documented *post mortem*
Timeline to Airway Remodeling

**Acute phase**
- Allergen
- Mast cell
- Leukotrienes
- Histamine
- IgE
- IL-4
- IL-5

**Chronic phase**
- TNF-α
- Macrophage
- Goblet cell
- Epithelial cell
- Mucus
- Airway damage/inflammation
- Degranulation
- Eosinophil
- IL-4
- IL-5
- IL-13
- T_H2

**Remodelling**
- Smooth muscle hyperplasia and hypertrophy
- Mucus gland hyperplasia
- Mucus
- Chronic inflammation
- Airway remodelling
- Collagen deposition
- Fibroblast activation
- Neutrophil
- Cytokines
- Chemokines
- Prostanoids
Acute Inflammation

Chronic Inflammation

Airway Remodeling

Time

Symptoms (Bronchoconstriction)

Exacerbations (Nonspecific Hyperreactivity)

Persistent Airflow Obstruction
ASM = airway smooth muscle; ECM = extracellular matrix
Airway Remodeling

Transformation toward the asthmatic airway: Exposure of normal airway to insults:

- allergens,
- microbes,
- viruses, or
- environmental factors
  - pollutants,
  - tobacco smoke, or
  - nanoparticles

Causing changes throughout:
- epithelium
- airway smooth muscle (ASM)
- extracellular matrix (ECM)

Remodeled asthmatic airway involves:

- infiltration of various immune cells,
- thickened epithelium with goblet cell hyperplasia,
- increased mucus,
- thickened, more fibrotic ASM layer with increased cell size (hypertrophy) and numbers (hyperplasia),
- altered ECM composition
Airway Remodeling in Asthma over Time

- Smooth muscle mass increase
- Mucous glands increase
- Inflammatory cells persistence
- Fibrogenic growth factor release

- Severe bronchospasm during exacerbation
- Ongoing inflammation

- Important mucous secretion during exacerbation
- Collagen deposition on RBM and ECM

- Elastolysis
  - Reduced elasticity of airway wall
Regardless of the triggers of asthma, repeated cycles of inflammation in the lungs with injury to the pulmonary tissues followed by repair may produce long-term structural changes, i.e., "remodeling" of the airways.
Etiology

The development of asthma appears to involve an interplay between:

- host factors (genetics) and
- environmental exposures occurring at crucial times during the development of the immune system.

- Host factors (genetics): intrinsic asthma
- Environmental factors: extrinsic asthma
Signs & Symptoms

- Wheezing (All that wheezes is **NOT** asthma.)
- Coughing (not always productive)
- Shortness of breath
- Tightness of chest (chest pain)
- Agitation
- Increased respiratory rate
- Tachycardia
- Accessory muscle use
- $O_2$ desaturation
Signs & Symptoms

- **Wheezing:**
  - Mildest form: end-expiratory only
  - Increasing severity: wheezing lasts throughout expiration
  - More severe episode: present during inspiration & expiration
  - Most severe episode: may be absent because of severe limitation of airflow (decreased air velocity) associated with airway narrowing and respiratory muscle fatigue
Signs & Symptoms

Cough:

- May be only symptom of asthma, especially in cases of exercise-induced or nocturnal asthma
- Usually nonproductive and non-paroxysmal
Factors causing symptoms to occur or worsen:

- Exercise
- Viral infection (rhinovirus, RSV)
- Inhalation of allergens (animal dander, pollen, etc.)
- Inhalation of irritants (smoke, chemicals, etc.)
- Weather (seasonal) changes
Signs & Symptoms

Factors causing symptoms to occur or worsen:
- Stress
- Strong emotional expressions (laughing, crying)
- Intensifying during sleep
- Awakening person from sleep
Diagnostic Testing & Data Interpretation

- **PFTs**
  - **Spirometry:** FVC, FEV<sub>1</sub>, FEV<sub>1</sub>%
    - **Obstructive pattern:**
      - FEV<sub>1</sub> < 70% predicted
      - FEV<sub>1</sub>% < 75%
    - **Post-bronchchodilator data:**
      - FEV<sub>1</sub> ≥ 12% predicted
      - FEV<sub>1</sub> ≥ 200 ml
      - PEF > 60 L/min (or > 20% of pre-bronchodilator)

 reversable expiratory air-flow limitation consistent with asthma
Diagnostic Testing & Data Interpretation

- PFTs
  - Bronchoprovocation testing ($\text{FEV}_1 \geq 80\%$)
    - Overcomes difficulty diagnosing asthma despite normal PFTs and persistent asthma-like symptoms (e.g., cough, SOB, etc.)
      - Methacholine ($\text{FEV}_1$ decreases $> 20\%$ with 8 mg/ml dose or less)
      - Histamine and mannitol (other provocative agents used)
      - Cold air
      - Exercise
Diagnostic Testing & Data Interpretation

- **Radioallergosorbent test (RAST)**
  - Skin testing
  - Allergy blood testing (serum IgE)

- **FENO (exhaled NO and inflammation)**
  - Normal: adults < 25 ppb; children < 20 ppb
  - FENO increases with airway inflammation

- **Chest radiography**
  - Stable asthma: normal
  - Asthma exacerbation: hyperinflation depending on severity
Diagnostic Testing & Data Interpretation

- **ABGs**
  - Stable asthma: normal
  - Asthma exacerbation:
    - Early episode: uncompensated respiratory alkalosis with mild hypoxemia
    - Late episode: uncompensated respiratory acidosis with moderate to severe hypoxemia (respiratory failure, a.k.a. status asthmaticus)
Respiratory Therapeutic Interventions

- **Classifications of asthma:**
  - Intermittent
  - Mild persistent
  - Moderate persistent
  - Severe persistent
## Classification of Asthma ≥ 12 Years

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Intermittent</th>
<th>Mild Persistent</th>
<th>Moderate Persistent</th>
<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤ 2 days/wk</td>
<td>&gt; 2 days/wk</td>
<td>daily</td>
<td>throughout day</td>
</tr>
<tr>
<td><strong>Nighttime Awakenings</strong></td>
<td>≤ 2 X/mon</td>
<td>3 – 4 X/mon</td>
<td>1 X/month; not weekly</td>
<td>7 X/week</td>
</tr>
<tr>
<td><strong>SABA Use for Control</strong></td>
<td>≤ 2 days/wk</td>
<td>&gt; 2 days/wk; no more than 1X/day</td>
<td>daily</td>
<td>several times/day</td>
</tr>
<tr>
<td><strong>Interference with Activity</strong></td>
<td>none</td>
<td>minor</td>
<td>some</td>
<td>extreme</td>
</tr>
<tr>
<td><strong>Lung Function</strong></td>
<td>FEV$_1$ &gt; 80%; FEV$_1$% normal</td>
<td>FEV$_1$ &gt; 80%; FEV$_1$% normal</td>
<td>FEV$_1$ 60%-80%; FEV$_1$% reduced 5%</td>
<td>FEV$_1$ &lt; 60%; FEV$_1$% reduced &gt;5%</td>
</tr>
</tbody>
</table>
### Classification of Asthma ≥ 12 Years

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<tr>
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<th>Severe Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk (Exacerbations Requiring OCS)</td>
<td>0 to 1/yr</td>
<td>≥ 2/year</td>
<td>≥ 2/year</td>
<td>≥ 2/year</td>
</tr>
<tr>
<td>Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommended STEP for Initiating Treatment</td>
<td>STEP 1</td>
<td>STEP 2</td>
<td>STEP 3</td>
<td>STEP 4 or 5</td>
</tr>
</tbody>
</table>
## Classification of Asthma ≥ 12 Years

### Intermittent Asthma

Consult with asthma specialist if Step 4 care or higher is required. Consider consultation at Step 3.

<table>
<thead>
<tr>
<th>Persistent Asthma: Daily Medication</th>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
<th>STEP 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA PRN</td>
<td>Lose dose ICS</td>
<td>Low dose ICS + LABA</td>
<td>Medium dose ICS + LABA</td>
<td>High dose ICS + LABA and consider omalizumab for patients who have allergies.</td>
<td>High dose ICS + LABA + OCS and consider omalizumab for patients who have allergies.</td>
</tr>
</tbody>
</table>

### Quick Relief for All Patients:

- SABA PRN for symptoms. Intensity of treatment depends on severity of symptoms up to 3 treatments at 20-minute intervals as needed. Short course OCS may be needed.
- SABA use ≥ 3 days/week for symptom relief generally indicates inadequate control & the need to step up treatment.
Classification of the Severity of Asthma Exacerbations

- Mild
- Moderate
- Severe
- Very Severe (Life Threatening)
Asthma Exacerbation

- Treatment settings for asthma exacerbation:
  - Home
  - MD office or urgent care
  - Emergency room
<table>
<thead>
<tr>
<th>Classification of Severity</th>
<th>Signs &amp; Symptoms</th>
<th>Initial PEF Predicted or Personal Best</th>
<th>Clinical Course</th>
</tr>
</thead>
</table>
| Mild                       | Dyspnea on exertion | PEF $\geq 70\%$                   | • Home treatment  
• Prompt relief SABA  
• OCS |
| Moderate                   | Dyspnea limiting activity | PEF 40% to 69% | • Office or ED visit  
• Frequent SABA needed  
• OCS  
• Symptoms last 1-2 days after treatment begun |
<table>
<thead>
<tr>
<th>Classification of Severity</th>
<th>Signs &amp; Symptoms</th>
<th>Initial PEF Predicted or Personal Best</th>
<th>Clinical Course</th>
</tr>
</thead>
</table>
| Severe                      | Dyspnea at rest interfering with speaking | PEF 25% to 39% | • Usually requires ED; hospitalization likely  
                          |                  |                        | • Partial relief from SABA  
                          |                  |                        | • OCS  
                          |                  |                        | • Symptoms lasting 1-3 days after treatment  
                          |                  |                        | • Adjunctive therapies |
| Life Threatening           | Too dyspneic to speak; diaphoresis       | PEF < 25% | • Requires ED & hospitalization  
                          |                  |                        | • No relief from frequent SABA  
                          |                  |                        | • IV corticosteroids  
                          |                  |                        | • Adjunctive therapies |
Asthma Exacerbation: Home

Two Approaches

- Increase dose & frequency of usual reliever
- Add OCS (prednisone) and contact physician
**Asthma Exacerbation: Home**

**SABA:**
- Repeated dosing
- Temporary relief until cause of worsening passes
- Repeated doses for more than 1-2 days; need for review of controlling regimen

**Dosing of albuterol:**
2.5 to 5.0 mg per 20 minutes for three treatments. If no improvement, then:
2.5 to 10.0 mg every 1 to 4 hours as needed, or 10 to 15 mg/hour continuously.
Asthma Exacerbation: Home

OCS:

- Prednisone 40-60 mg/day in single or 2 divided doses for 5-10 days.
- No need to taper OCS dose if course of treatment is less than 1 week.
Asthma Exacerbation: MD Office/Urgent Care

- O₂ therapy
- Repetitive/continuous SABA
  - 2.5 to 10.0 mg every 1-4 hours as needed, or
  - 10 to 15 mg/hour continuously.
- OCS
  - prednisone 40-60 mg single dose
Asthma Exacerbation: ER

- O₂ therapy
- Repetitive/continuous SABA
- OCS

Adjunctive therapies considered

- IV Magnesium sulfate (MgSO₄)
  - Inhibit smooth muscle contraction
  - Decrease histamine release
  - Inhibit acetylcholine release (Acetylcholine causes smooth muscle contraction.)
- Heliox (80-20 or 70-30)
Primary Care Management

SABA

Systemic corticosteroids

Controller medications

Thank You!
Obstructive Sleep Apnea
OSA Outline

- Pathophysiology
- Etiology
- Signs & symptoms
- Diagnostic testing & data interpretation
- Respiratory therapeutic interventions
Upper airway anatomy

- Composed of numerous muscles & soft tissue
- Lack rigid bony support
- Collapsible portion extends from hard palate to larynx
- Ability to change shape and momentarily close is essential for speech and swallowing during wakefulness
OSA: Pathophysiology

- Upper airway anatomy
  - Suppleness provides for collapse at inopportune times such as during sleep
  - OSA caused by soft tissue collapse in pharynx during sleep
  - Transmural pressure across pharyngeal wall decreases
  - X-sectional area of pharynx decreases
  - Pharynx collapses and obstruction occurs
OSA: Pathophysiology

- Causes of occlusion of pharynx:
  - Micrognathia (small lower jaw/chin)
  - Retrognathia (recessed lower jaw/chin)
  - Macroglossia (large tongue)
  - Large tonsils
  - Deviated nasal septum
Retrognathia

Before corrective surgery

After corrective surgery

Micrognathia

Macroglossia

Enlarged tongue
OSA: Pathophysiology

- Upper airway relaxes during sleep
- Upper airway becomes occluded
- Increased upper airway R
- Inspiratory muscles contract forcefully
  - - 70 to – 80 cm H\textsubscript{2}O
- Pharyngeal airway collapses
  - Decreased transmural pressure
OSA: Pathophysiology

- Apnea: cessation of airflow through the nose and mouth for at least 10 seconds.
- Hypopnea: slow, shallow breathing
  - reduction in ventilation of at least 50%, resulting in a decreased $\text{SaO}_2$ of $\geq 4\%$ due to partial airway obstruction
Characteristics of OSA during sleep include:

- hypoxemia
- hypercapnia
- large intrathoracic pressure swings to -120 cm H$_2$O
- surges of systemic BP to 250/150 mm Hg associated with sleep arousals
- sleep fragmentation up to 100 times/hour
### OSA Signs & Symptoms

#### Nighttime
- Snoring
- Choking
- Gasping
- Restless sleep
- Sweating
- Sleep fragmentation
- Enuresis
- Frequent urination

#### Daytime
- Morning headaches
- Sleepiness
- Fatigue
- Personality changes
- Memory loss
- Impotence
- Poor job performance
- Concentration loss
OSA Medical Consequences

- Pulmonary hypertension
  - Nocturnal hypoxemia
  - Nocturnal hypercapnia
- Cor pulmonale
- Systemic hypertension
- Congestive heart failure
- Cardiac dysrhythmias
- Stroke
OSA Risk Factors

- Excessive body weight
- Neck circumference
  - Short, thick neck
  - Males > 17 inches; females > 16 inches
- Having a narrowed airway
- Sinus issues with constant nasal congestion
- Males twice as prone than females
- Blacks under 35 years old
OSA

Normal airway during sleep  Obstructed airway during sleep
Mallampati Score

- Mallampati I
- Mallampati II
- Mallampati III
- Mallampati IV

Class 1
Class 2
Class 3
Class 4
Normal Anatomy
Open airways allow air to flow easily.

Common Causes of Sleep Apnea
Large tonsils and adenoids make airflow more difficult.
Palatine tonsils

- Pair of soft tissue masses
- Rear of throat in pharynx
- Tissue similar to lymph nodes
- Part of lymphatic system
- Removal does not seem to increase susceptibility to infection
- Vary in size and swell in response to infection
Hypertrophic Tongue
Size may obstruct airway:
• vascular malformations
• muscle hypertrophy
• amyloidosis (amyloids accumulating in a tissue or organ; certain proteins become insoluble in water enlarging tissue)

Nasal Fossae
Obstruction may be caused by:
• nasal polyps
• deviated septum
• tumor growth

Soft Palate
Obstruction may be caused by:
• soft palate too long
• soft palate too thick

Hypertrophic Tonsils
• seen frequently in children
• surgical removal alleviates problem

Fatty Tissue
• adipose tissue deposited in pharyngeal walls
Recurrent Obstructive Apneas and Hypopneas

Physiological Alterations
- Chronic
- Intermittent
- Hypoxia
- Increased
- Sympathetic
- Nervous
- System Activity
- Intrathoracic
- Pressure
- Swings
- Hypercapnia
- Increased
- Arousals/Sleep
- Fragmentation

Intermediate Mechanisms
- Increased
- Inflammation
- Increased
- Oxidative
- Stress
- Metabolic
- Dysfunction/
- Insulin
- Resistance/
- Glucose
- Dysregulation
- Weight Gain
- Hyper-
- coaguability
- Endothelial
- Dysfunction

Clinical Outcomes
- Systemic hypertension
- Atherosclerosis
- Pulmonary hypertension
- Diastolic dysfunction
- Congestive heart failure
- Stroke
- Cardiac dysrhythmias
- Diabetes mellitus
- Increased mortality and sudden death
Cardiovascular Responses to Normal Sleep

- ↓ Sympathetic activity
- ↓ Heart rate
- ↓ Arrhythmogenicity
- ↑ Parasympathetic activity
- ↑ Cardiac refractory periods

Sleep Apnea

Physiological Effects
- Hypoxemia
- Increased sympathetic Activity
- Intrathoracic pressure changes
- Cortical arousal

Biological Effects
- Inflammation
- Oxidative stress
- Endothelial dysfunction
- Adipokines

Cardiovascular Disease
- Systemic hypertension
- Congestive heart failure
- Pulmonary hypertension
- Cor pulmonale
- Cardiac ischemia
- Cardiac dysrhythmias
- Cerebrovascular disease
Diagnostic Testing & Data Interpretation

- **Apnea-Hypopnea Index (AHI)**
  - Normal: $\text{AHI} < 5$ per hour
  - Mild: $\text{AHI} \geq 5$, but $< 15$ per hour
  - Moderate: $\text{AHI} \geq 15$, but $< 30$ per hour
  - Severe: $\text{AHI} \geq 30$ per hour
Diagnostic Testing & Data Interpretation

- Polysomnography
  - Electroencephalogram (EEG)
  - Electro-oculogram (EOG)
  - Electrocardiogram (ECG)
  - Electromyogram (EMG)
  - Nasal/oral thermistor (airflow)
  - Chest and abdominal excursions
  - Pulse oximeter (SpO₂)
CPAP Therapy

A potential life saving and changing option for the treatment of sleep apnea.
**Before**
Appearance of throat prior to UPPP surgery. Note the anatomy which is common to sleep apnea patients to include the large tonsils, long uvula and narrow arch behind the tonsils.

**After**
Appearance after UPPP surgery. The tissue in the front part of the throat is trimmed and the uvula is folded and sutured.
The Waking Dead: Dangers of Sleep Deprivation

More than 70 million Americans suffer from one or more of the 85 sleep disorders recognized by the American Sleep Disorders Association. What is the cost of our restless nights?

Late Night Aftermath

Sleep deprivation plays a major role in a variety of conditions and illnesses.

- Decreased alertness
- Cognitive impairment
- Increased stress
- Increased appetite

Reducing sleep by 90 minutes for just one night can reduce daytime alertness by up to 32%.

Untreated sleep disorders can have long-term effects.

- High blood pressure
- Heart failure
- Stroke
- Obesity
DROWSY DRIVING

The National Highway Traffic Safety Administration (NHTSA) estimates that, each year, drowsy driving is responsible for at least:

- 100,000 automobile crashes
- 71,000 injuries
- 1,550 fatalities

COGNITIVE IMPAIRMENT

<table>
<thead>
<tr>
<th>Awake for 18 hours</th>
<th>Awake for 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>similar to blood alcohol content of</td>
</tr>
<tr>
<td></td>
<td>0.05%</td>
</tr>
<tr>
<td></td>
<td>0.10%*</td>
</tr>
</tbody>
</table>

*higher than the legal limit in all states

2009-2010 study of 150,000 adults:

4.2% said they’d fallen asleep while driving at least once in the last 30 days.

SLEEP RECOMMENDATIONS

By age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Hours/Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns</td>
<td>16-18</td>
</tr>
<tr>
<td>Pre-schoolers</td>
<td>11-12</td>
</tr>
<tr>
<td>School-aged children</td>
<td>At least 10</td>
</tr>
<tr>
<td>Teens</td>
<td>9-10</td>
</tr>
<tr>
<td>Adults/Elderly</td>
<td>7-8</td>
</tr>
</tbody>
</table>

Mortality risk is increased for people getting less than six or seven hours of sleep per night. Severe insomnia triples the mortality risk in elderly men.
31% of high school students get an average of 8 hours or less of sleep each night.

29% of adults get an average of 6 hours or less of sleep each night.

$18 BILLION Est. cost to U.S. employers in lost productivity caused by sleep loss.

PEOPLE WITH INSOMNIA ARE...
10 times as likely to develop depression
17 times as likely to have significant anxiety

SLEEP RECOVERY

Sometimes sleep disorders can be corrected by lifestyle changes such as:

- Getting more exercise
- Reducing stress
- Cutting back on alcohol, nicotine and caffeine
- Hanging medications that are causing sleeplessness

Other sleep disorders require testing and diagnosis through a sleep study.

Natural treatments for sleep include:

- Chamomile tea
- Melatonin
- Valerian
- Kava

More serious sleep disorders like sleep apnea, narcolepsy and restless leg syndrome are treatable but require a physician’s care, medication and sometimes a CPAP (continuous positive airway pressure) device to keep the airways open during sleep.

SLEEP EXPERTS RECOMMEND “GOOD SLEEP HYGIENE” ON A CONSISTENT BASIS TO MAXIMIZE YOUR RESTFULNESS

- Sticking to a regular sleep schedule
- Avoiding naps
- Avoiding stressful activities and strenuous exercise at least two hours before bed
- Practicing relaxation techniques such as yoga, meditation and deep breathing before bedtime
- Creating a restful environment that is dark, comfortable and quiet

Sources:
- [WebMD: Sleep Disorder Features: Important Sleep Habits](http://www.webmd.com/sleep-disorders/features/important-sleep-habits)