Outline COPD

• Pathophysiology
• Etiology
• Signs & symptoms
• Diagnostic testing & data interpretation
• Respiratory therapeutic interventions
100% COPD patients

90% Chronic Bronchitis
5% Emphysema

5% Chronic Bronchitis

5% Emphysema
COPD Pathophysiology

“Blue Bloater”

“Pink Puffer”

COPD phenotypes
COPD Pathophysiology

**Chronic Bronchitis**
- Inflammation & swelling of airways
- Excessive production of mucus
- Partial & total mucous plugging
- Bronchial smooth muscle contraction
- Hyperinflation

**Emphysema**
- Destruction & enlargement of peripheral airways
- Destruction of pulmonary capillaries
- Loss of elastic recoil
- Less surface area for gas exchange
- Hyperinflation
COPD Pathophysiology

Emphysema

- Compressed duct
- Collapsed alveolar sac

Normal lungs

- Bronchiole
- Alveolar duct
- Alveolar sac
- Alveolar pore
- Capillary network
Pathogenesis of emphysema

TOBACCO

Nicotine

Reactive oxygen species ("free radicals")

Inactivation of antiproteases ("functional" $\alpha_1$-AT deficiency)

Neutrophil elastase

Congenital $\alpha_1$-AT deficiency

Tissue damage

Capillary

IL-8

LTB$_4$

TNF

Neutrophil

Alveolar macrophage

Macrophage elastase and metalloproteinases

EMPHYSEMA
COPD Pathophysiology

COPD patients have:

- Increased $R_{aw}$
- Increased $C_L$
- Expiratory airflow obstruction
- Lengthened ventilation time constant
- Air trapping (auto-PEEP)
COPD Pathophysiology

- **Causes of cor pulmonale:**
  - Chronic hypoxemia
  - Chronic hypercapnia
  - Chronic acidemia
  - Polycythemia

  - Increase RV workload
  - Cause RV hypertrophy
  - Increases blood viscosity

Lead to RV failure:
- Peripheral edema
- Hepatosplenomegaly
- Jugular venous distention
- Ascites
COPD Pathophysiology

• COPD is characterized also by chronic inflammation of:
  – conducting airways
  – lung parenchyma
  – pulmonary vasculature
Signs & Symptoms

• Chronic cough
  – Intermittent or non-productive
• Mucus production
  – Persistent sputum production suggests COPD
• Dyspnea on exertion (later progressing to dyspnea at rest)
  – Worsens with exercise and becomes persistent
Diagnostic Testing & Data Interpretation

- Spirometry
- Arterial blood gas analysis
- Chest radiography
- Electrocardiography
Diagnostic Testing & Data Interpretation

Spirometry

- Mild COPD (Stage I):
  - FEV₁% < 70%
  - FEV₁ ≥ 80%
- Moderate COPD (Stage II):
  - FEV₁% < 70%
  - FEV₁ < 80% to > 50%
- Severe COPD (Stage III):
  - FEV₁% < 70%
  - FEV₁ < 50% to > 30%
- Very Severe COPD (Stage IV):
  - FEV₁% < 70%
  - FEV₁ < 30%

FVC generally > SVC
Lung Volumes & Capacities

4 lung volumes:
- RV
- $V_T$
- ERV
- IRV

4 lung capacities:
- TLC
- VC
- IC
- FRC

Restrictive Disease

Obstructive Disease

Normal
Diagnostic Testing & Data Interpretation

DlCO

- Chronic bronchitis: usually normal
- Emphysema: decreased
Diagnostic Testing & Data Interpretation

Arterial Blood Gas Analysis

- ABG values change over time as COPD progresses.
- Early stages, ABGs may show mild hypoxemia and normal PaCO$_2$ caused by ventilation-perfusion mismatch.
- As COPD progresses, low PaO$_2$ stimulates peripheral chemoreceptors, causing slight respiratory alkalosis.
- As airflow obstruction and alveolar hypoventilation become severe, hypoxemia worsens, chronic CO$_2$ retention and respiratory acidosis occur.
- In stable COPD, renal compensation provides a metabolic alkalosis to “normalize” arterial pH.
- Exacerbations worsen acidemia despite chronically elevated bicarbonate levels.
Diagnostic Testing & Data Interpretation

Arterial Blood Gas Analysis

• Example, stable COPD:
  pH 7.36; PaCO₂ 79 mm Hg; HCO₃⁻ 43 mEq/L; PaO₂ 61 mm Hg

• Example, impending respiratory failure:
  pH 7.52; PaCO₂ 52 mm Hg; HCO₃⁻ 40 mEq/L; PaO₂ 46 mm Hg

• Example, severe COPD exacerbation:
  pH 7.28; PaCO₂ 99 mm Hg; HCO₃⁻ 45 mEq/L; PaO₂ 34 mm Hg
Time and Progression of Disease

Point at which $\text{PaO}_2$ declines enough to stimulate peripheral chemoreceptors 

60 mm Hg

Point at which COPD worsens causing chronic $\text{CO}_2$ retention
Diagnostic Testing & Data Interpretation

Chest Radiography

• Chronic Bronchitis:
  – Increased bronchovascular markings
  – Cardiomegaly (cor pulmonale)

• Emphysema
  – Hyperinflation
  – Flattened diaphragms
  – Widened costophrenic angles
  – Horizontal ribs

Seldom diagnostic, but useful for excluding alternative diagnoses and comorbidities.
Diagnostic Testing & Data Interpretation

**Electrocardiography**

- EKG rarely specific in COPD
- Often done to evaluate elderly patients comorbidities to exclude other disease processes
- EKG may diagnose significant dysthymia, STEMI, or show acute ischemic changes suggestive of acute coronary syndrome
- Right axis deviation
Pharmacological Considerations

β-2 Agonists: Short-Acting and Long-Acting

• SABAs (4-6 hours)
  – albuterol (Ventolin, ProAir)
  – levalbuterol (Xopenex)

• LABAs (12 hours)
  – salmeterol (Serevent)
  – formoterol (Foradil)
  – aformoterol (Brovona)
Pharmacological Considerations

Muscarinic Antagonists: Short-Acting and Long-Acting

• SAMAs (4 hours)
  – ipratropium bromide (Atrovent)

• LAMAs (24 hours)
  – tiotropium bromide (Spiriva) blocks Ach release from M1 & M3 receptors
  – aclidinium (Tudorza)
  – umeclidinium (Incruse)

SAMAs & LAMAs are:
• anticholinergic bronchodilators
• parasympatholytics
Pharmacological Considerations

LABA and ICS: Long-Acting

• salmeterol and fluticasone (Advair)
• formoterol and budesonide (Symbicort)
• vilanterol and fluticasone (Breo Ellipta)

Systemic Corticosteroids

• methyprednisolone (Medrol, Solu-Medrol)
• hydrocortisone (Solu-Sortef)

Phosphodiesterase-4 Inhibitor

• roflumilast (Daliresp)

**NOTE:** Emphasis of these drugs is to reduce airway, parenchymal, and pulmonary vascular inflammation in COPD.
Pharmacological Considerations

LABAs and LAMAs

• vilanterol and umeclidinium (Anoro Ellipta)
• olodaterol and tiotropium bromide (Stiolto Respimat)

What’s next? The “Triple Crown,” i.e., LABA + LAMA + ICS?
In drug pipeline: formoterol (LABA)
glycopyrronium (LAMA)
budesonide (ICS)
Inhaled irritants or endogenous inflammatory mediators activate sensory nerve fibers which send signals to the central nervous system and trigger reflex firing of parasympathetic nerves in the airway. Parasympathetic, post-ganglionic cholinergic (releasing acetylcholine - ACh) neurons are located within the airway wall and send fibers to airway smooth muscle and glands causing contraction and secretion respectively. Both of these actions occur when the released acetylcholine binds to muscarinic receptors on target cells. Anti-muscarinic drugs block these receptors, preventing acetylcholine from binding. NOTE: Preganglionic nerves, carried to the airways in branches of the vagus nerve, synapse with post-ganglionic parasympathetic nerves and are themselves cholinergic (as are all preganglionic neurons). The released acetylcholine in this case binds to nicotinic receptors which have a different pharmacological profile and are not affected by anti-muscarinic drugs.
Anticholinergic bronchodilators (parasympatholytics or muscarinic antagonists): block Ach release at M1 & M3 receptors.
NOTE: Flu and pneumonia vaccinations are highly recommended for COPD patients in all stages.
Surgical Interventions

• Lung Volume Reduction Surgery (LVRS)
  – severe emphysema patients
  – remove up to 30 percent of each lung
  – beneficial for patients with predominant upper lobe disease and low exercise capacity

• Lung Transplant
  – Relatively common among COPD patients (SLT/BLT)
Non-Surgical Interventions

- Bronchoscopic Lung Volume Reduction (BLVR)
  - Bronchoscopy: patient assessment
  - Pulmonary rehabilitation program: conditioning, etc.
  - 2nd bronchoscopy: one-way valves (3 average) placed in airways of the pre-determined lung lobe, designed to promote atelectasis by blocking inspiratory flow
  - If successful, significant improvement in function and quality of life is potentially achievable
COPD Exacerbation

- More air trapping
- Hypoventilation
- Muscle fatigue
- Increased WOB
COPD Exacerbation

- Increased Exp. Raw
- Increased RR
- Intrinsic PEEP
- Alveolar hypoventilation
- Respiratory muscle work
- Increased O$_2$ consumption
Acute-on-Chronic Respiratory Failure

Uncompensated respiratory acidosis superimposed on compensated respiratory acidosis
Respiratory failure No intervention

DEATH
O₂ Therapy

Bronchodilators

Conventional Therapy

Anti-inflammatory agents

NPPV

ANTIBIOTICS??
Antibiotics are given when:

1) Increased dyspnea
2) Increased sputum volume
3) Increased sputum purulence

1) Severe exacerbation
2) Mechanical ventilation (invasive or noninvasive)
Common bacteria recovered from lower airways during COPD exacerbation:

- Hemophilus influenzae
- Streptococcus pneumoniae
- Moraxella catarrhalis
Current Standard of Care

• Conventional Therapy:
  – $O_2$ therapy
  – bronchodilators
  – anti-inflammatory agents
  – NPPV
  – ABX?
Current Standard of Care

- NPPV:
  - Reduces WOB
  - Reduces inspiratory muscle activity
  - Reduces RR
  - Increases VT
  - Improves minute ventilation
  - Enables better gas exchange
  - Rests respiratory muscles
Current Standard of Care

**NPPV Selection Criteria**

- **Determine need for ventilatory assistance**
  - Dyspnea (moderate to severe respiratory distress)
  - Excessive accessory muscle use/paradoxical breathing
  - $\text{pH} < 7.35$ and/or $\text{PaCO}_2 > 45 \text{ mm Hg}$
  - $\text{PaO}_2/\text{FiO}_2 < 200$
  - RR $> 25$ breaths/minute
  - Potential reversibility of the disease process

- **Exclusion criteria**
NPPV Exclusion Criteria

- Respiratory arrest
- Need for immediate ET intubation
- Hemodynamic instability
- Inability to protect airway (impaired cough)
- Excessive secretions
- Agitated & confused
- Uncooperative or unmotivated
- Facial deformities
- Brain injury/unstable respiratory drive
Inactivity

Muscle wasting

Increased shortness of breath

Poor O₂ Utilization

Pulmonary Rehabilitation Breaks this Vicious Cycle
Pulmonary Rehabilitation

• Assessment of efficacy:
  – fewer exacerbations per year
  – less severe exacerbations
  – reduced LOS when hospitalized
  – fewer MD office visits per year
  – improved ADL and QOL
Pathophysiology of COPD

**Normal**
- Alpha-1 antitrypsin coats lungs, protecting them from neutrophil elastase.
- Alpha-1 antitrypsin Protects lungs from neutrophil elastase.
- Neutrophil elastase Produced by white blood cells to break down harmful bacteria. Potentially damaging to lungs.

**Alpha-1 Antitrypsin Deficiency**
- Lungs lack alpha-1 antitrypsin coating, leaving them open to damage by neutrophil elastase
- Alpha-1 antitrypsin Trapped in liver, causing liver damage
- Neutrophil elastase Uninhibited, causing lung damage.
Each parent has 2 versions of α-1 AT genes. "M" is most common, and produces normal levels of α-1 AT. Most people have 2 copies of "M" genes (MM) in each cell. "Z" gene produces less α-1 AT. Persons with 2 copies of "Z" in each cell are likely to have α-1 AT deficiency. Figure shows possible outcomes for children of 2 parents with "MZ" genes, with children getting one gene from each parent. One child in 4 children of such parents will have α-1 AT deficiency, and 3 in 4 will have at least one "Z" gene.
<table>
<thead>
<tr>
<th>Stage I Mild</th>
<th>Stage II Moderate</th>
<th>Stage III Severe</th>
<th>Stage IV Very Severe</th>
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<tbody>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; % &lt; 70% FEV&lt;sub&gt;1&lt;/sub&gt; ≥ 80%</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; % &lt; 70% FEV&lt;sub&gt;1&lt;/sub&gt; 50% - 79%</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; % &lt; 70% FEV&lt;sub&gt;1&lt;/sub&gt; 30% - 49%</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; % &lt; 70% FEV&lt;sub&gt;1&lt;/sub&gt; ≤ 30%</td>
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**Active reduction of risk factors: influenza vaccination**  
**Add: SABA when indicated**

**Add: regular RX with one or more LABAs**  
**Add: pulmonary rehabilitation**

**Add: ICS if repeated exacerbations occur**

**Add: LTOT when chronic respiratory failure present**  
**Consider: lung volume reduction surgery**
Cigarette Smoking Facts

• 16 million Americans live with a smoking related disease

• For every person who dies from smoking, at least 30 people live with serious smoking-related illness

• Smoking causes cancer, heart disease, stroke, lung diseases, diabetes, and COPD

• Smoking increases risk for TB, eye diseases, and immune system problems, including rheumatoid arthritis
Cigarette Smoking Facts

• On average, smokers die 10 years earlier than nonsmokers
• Cigarette smoking about 480,000 deaths per year in the US, including nearly 42,000 deaths resulting from secondhand smoke
• Total economic cost of smoking > $300 billion a year, including
  – nearly $170 billion in direct medical care for adults
  – more than $156 billion in lost productivity due to premature death and exposure to secondhand smoke
COPD Resources

Outline Bronchiectasis

• Pathophysiology
• Etiology
• Signs & symptoms
• Diagnostic testing & data interpretation
• Respiratory therapeutic interventions
Bronchiectasis Pathophysiology

Three pathophysiological forms of bronchiectasis

- Saccular
- Varicose
- Cylindrical
Bronchiectasis Pathophysiology

- Chronic (permanent) dilatation & distortion of conducting airways
- Airways inflamed
- Bronchial wall, blood vessels, cilia, smooth muscles, destroyed & airway walls weakened
- Mucociliary clearance compromised
- One or both lungs
- Generally limited to a lobe (lower) or segment
Bronchiectasis Pathophysiology

- Mucociliary impairment:
  - copious, viscous secretions
  - foul-smelling (fetid) mucus
  - anaerobes cause foul smell
  - insensitive cough mechanism in affected airways
  - Cough initiated when mucus “spills” into normal airways
3 distinct layers emerge after mucus settles (24 hours):
- top foamy (supernatant layer)
- clear middle liquid
- bottom purulent

Streaks of blood may be present, as a result of erosion of airway walls and blood vessels.
Bronchiectasis Etiology

- cystic fibrosis
- primary pulmonary dyskinesia (immotile cilia)
- frequent (chronic) lung infections (recurring pneumonia)
- tuberculosis
- GERD
- aspiration (prolonged) of foreign objects
Bronchiectasis Etiology

• Kartagener syndrome (genetic disorder)
  – situs inversus
  – chronic sinusitis
  – bronchiectasis
    • no curative treatment
    • management aimed at infection and symptom control
    • prophylactic antibiotics (i.e., azithromycin), mucolytics, bronchodilators, inhaled corticosteroids, and pulmonary hygiene
    • lung transplantation may be an option
Kartagener Syndrome

- Dextrocardia
- Right sided aorta
- Dextrocardia with cardiomegaly
- Right sided gastric bubble
- Bronchiectasis
- Left sided liver
- Chronic scar tissue

Frontal CXR

Axial CT w/ Contrast
Abnormal airway widening and dilatation caused by frequent airway inflammation and respiratory infections.
Parts of some airways become widened.

Extra mucus collects in the widened airway. This is prone to infection.
Bronchiectasis: Signs & Symptoms

- Daily occurring over months or years
- Daily production of large amounts of sputum
  - may contain mucus, trapped particles, and pus
- Shortness of breath and wheezing
- Pleuritic chest pain
- Clubbing of digits
- Weakness & weight loss
Bronchiectasis: Lab Findings

**Spirometry, Lung Volumes, & Capacities**

- **Obstructive bronchiectasis**
  - Decreased expiratory flows
  - Increased lung volumes & capacities

- **Restrictive bronchiectasis (fibrotic changes)**
  - Expiratory flows mixed (N, increased, decreased)
  - Decreased lung volumes & capacities
Bronchiectasis: Lab Findings

Arterial Blood Gas Data

• Acute alveolar hyperventilation with hypoxemia (uncompensated respiratory alkalosis)
  mild to moderate disease
  – pH↑; PaCO₂↓; PaO₂↓; SaO₂↓; bicarb →

• Chronic respiratory failure with hypoxemia (compensated respiratory acidosis)
  severe disease
  – pH↓; PaCO₂↑; PaO₂↓; SaO₂↓; bicarb ↑
Bronchiectasis: Respiratory Therapeutic Interventions

- Oxygen therapy protocol
  - Hypoxemia often caused by capillary shunting
- Bronchopulmonary hygiene therapy protocol
  - PEP, HFCWO, CPT, suctioning, directed cough, etc.
- Lung expansion therapy protocol
- Aerosolized medication therapy protocol
  - β-2 agonists, anticholinergics
- Mechanical ventilation protocol