COPD: Pathophysiology and Management

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Objectives

After today, you will be able to:

• Identify patients at risk for COPD
• Utilize pulmonary function testing and clinical information to diagnose and stage COPD
• Understand mechanisms of dyspnea in COPD patients
• Utilize current guidelines to develop a COPD treatment plan
• Recognize the role for non-medical therapy in COPD including transplant
What is meant by “COPD?”

• Any smoking related respiratory disease?
• Emphysema?
• Chronic bronchitis?
• Emphysema + chronic bronchitis?
• Abnormality on spirometry?
• **Chronic**
  – slowly progressive, worsening over years to decades

• **Obstructive**
  – Spirometry with incompletely reversible airway obstruction (AKA airflow limitation).

• **Pulmonary Disease**
  – Involves pulmonary parenchyma and/or airways
COPD is common

• Over 5% of the adult US population
• Third leading cause of death in the US
  1. Heart disease 597,689
  2. Cancer 574,743
  3. COPD 138,080
  4. Stroke 129,476
• 12th leading cause of morbidity
• Economic impact of nearly $50,000,000,000/yr
Worldwide impact

- 4\textsuperscript{th} leading cause of death worldwide per WHO
  1. Ischemic heart disease
  2. Cerebrovascular disease
  3. Lower respiratory tract infections
  4. COPD
- Worldwide prevalence of GOLD 2 (moderate severity) or greater COPD in adults >40y = 9-10%  
  - 22% of men and 17% of women in Cape Town, South Africa
Development of COPD

Irritant activates Proteases

Protases

CD8 Cells
Macrophages
Neutrophils

Parenchymal Destruction
Airway Inflammation
Mucus Hypersecretion
WARNING
CIGARETTES CAUSE FATAL LUNG DISEASE

Irritant
Active smoking in adults and high school students

Nearly 1 in 5 people actively smoke.
Risk with smoking marijuana?

Symptoms

- Increase in chronic cough and sputum
- Increased risk of upper and lower respiratory tract infection*

Pulmonary function**

- No accelerated decline in FEV1, FVC
- Possible decrease in FEV1/FVC
- No change in diffusion capacity

*Particular concern for fungal infections

**Long-term effects may be underestimated

Tashkin DP. Ann Am Thorac Soc 103, 10:239
COPD and e-cig?
Smoking = only 29-39% of new cases worldwide

- Alpha-1 Antitrypsin (A1AT) deficiency
- Burned biomass
  - wood, animal dung, crop residue, coal
- Occupational exposures
- Childhood infections, tuberculosis
- Low birth weight
- Poor air quality
Alpha-1 Antitrypsin Deficiency

- Prevalence 1 : 1,000 - 1 : 5,000
- Require 2 copies of abnormal gene
- Classically causes basilar emphysema
- May be associated with liver disease
- Replacement therapy is available
- Screen all patients w/COPD
- Smoking cessation is most important goal
COPD in non-smokers

- Occupational exposures
  - Cadmium – electroplating, industrial paints, smelting, welding, battery production, plastics production,
  - Coal
  - Silica – mining, stonecutting, rock drilling, tunneling, abrasive blasting
COPD in non-smokers

• Occupational exposures
  – sulfur dioxide – burning of sulfur-containing compounds; exposure to bleaching agents, disinfectants, food additives, solvents; working in the mining industry, working near ore smelters, foundries, power plants
  – mineral dusts – mining
  – Vanadium – ceramics production and decoration, accelerator for drying paint, aniline black dye, textile coloring
Chronic Bronchitis

Emphysema

Persistent Airflow Obstruction

COPD

Asthma

Clinical spectrum


Chronic Bronchitis

Clinical diagnosis:
- Chronic productive cough for at least 3 months for 2 years
- Inflammation of airways.
- Bacterial colonization
Emphysema

Radiopathological dx
- Loss of alveoli and capillary surface area
- Loss of elastic recoil in the lung
Asthma

- Airway hyperreactivity
- Environmental triggers
Classic patient descriptions

Emphysema: “Pink Puffer”

Chronic bronchitis: “Blue Bloater”

Most COPD patients have features of both!
COPD symptoms

Dyspnea
Cough
Sputum production
Weight loss
Weight gain/edema
Poor functional capacity
COPD exam findings

- Underweight
- Thoracic hyperinflation
- Peripheral edema
- Cyanosis
- Accessory muscle use
- Poor air movement
- Wheezing
The COPD “comorbidome”
Chest x-ray
Flattened diaphragm and increased AP diameter → lung hyperinflation

Normal lateral CXR

Patient’s lateral CXR
COPD = obstruction on spirometry

**Normal**
- FEV1 > 80%
- FVC > 80%
- FEV1/FVC > 90%

**Obstruction**
- FEV1/FVC < LLN OR < 70%
- Long expiratory time

Flow (L/Sec)

Volume (L)
Airflow limitation:
• Increased smooth muscle tone
• Loss of elastic recoil, dynamic airway collapse
• Mucus burden
Severity based on FEV1

<table>
<thead>
<tr>
<th>GOLD Grade</th>
<th>FEV1 (% predicted)</th>
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<tbody>
<tr>
<td>I: mild</td>
<td>&gt;80</td>
</tr>
<tr>
<td>II: moderate</td>
<td>50 &lt; FEV1 &lt; 79</td>
</tr>
<tr>
<td>III: severe</td>
<td>30 &lt; FEV1 &lt; 49</td>
</tr>
<tr>
<td>IV: very severe</td>
<td>&lt;30 or &lt;50 with chronic respiratory failure</td>
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<tr>
<td>RISK</td>
<td>GOLD Classification</td>
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<td>------</td>
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<tr>
<td>C</td>
<td>High Risk, Less Symptoms</td>
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<tr>
<td>D</td>
<td>High Risk, More Symptoms</td>
</tr>
<tr>
<td>A</td>
<td>Low Risk, Less Symptoms</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk, More Symptoms</td>
</tr>
</tbody>
</table>

Symptoms:
- mMRC 0-1
- CAT <10
- mMRC ≥2
- CAT ≥10

Source: US Pharm © 2013 Jobson Publishing
Causes of Dyspnea

- Resting and exertional (dynamic) hyperinflation
- Increased demand for ventilation
- Muscle weakness (limb and respiratory)
Try breathing at higher lung volume

1) Breathe in to full vital capacity
2) Exhale half way
3) Take 5 more breaths starting at this new starting point
Acute COPD Exacerbations

- Increase cough frequency
- Increase in sputum volume
- Change in sputum appearance
- May have
  - Increased work of breathing,
  - Wheezing or poor air movement
  - Hypercapnia, hypoxemia
AE-COPD triggers

**Infectious (60–80% of all exacerbations)**
- Frequent (70–85% of all infectious exacerbations)
  - *Haemophilus influenzae*
  - *Streptococcus pneumoniae*
  - *Moraxella catarrhalis*
  - Viruses (influenza and parainfluenza viruses, rhinoviruses, coronaviruses)
- Infrequent (15–30% of all infectious exacerbations)
  - *Pseudomonas aeruginosa*
  - Opportunistic gram-negative species
  - *Staphylococcus aureus*
  - *Chlamydophila pneumoniae*
  - *Mycoplasma pneumoniae*

**Non-infectious (20–40% of all exacerbations)**
- Heart failure
- Pulmonary embolism
- Non-pulmonary infections
- Pneumothorax
- Pneumonia

**Precipitating and environmental factors**
- Cold air
- Air pollution
- Allergens
- Tobacco smoking
- Non-adherence to respiratory medication
Making a treatment plan

Factors to consider

- Symptom severity
- Airflow impairment
- Exacerbation frequency
- Financial limitations
- Barriers to compliance
**Goals of therapy**

1. **Stop the progression**
   - Smoking cessation!

2. **Reduce hypoxemia**
   - Oxygen if hypoxemic (<88%)

3. **Improve airflow and reduce hyperinflation**
   - Bronchodilators: LABA, LAMA, SABA, SAMA
   - Lung volume reduction (LVR)

4. **Reduce exacerbations**
   - Inhaled corticosteroids
   - Daily macrolide, roflumilast

5. **Improve endurance/muscle strength**
   - Pulmonary rehabilitation
Oxygen Therapy

Striking *mortality benefit*, proportional to length of time spent on oxygen

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**Mortality in men**

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**Mortality in women**

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Lancet 1981:681

Ann Intern Med 1980; 93:391
Bronchodilators: symptom control

**Short acting agents**

**Short-acting β-agonist (SABA)**
- Albuterol
- Levalbuterol

**Short-acting anticholinergic (SAMA)**
- ipratropium

**Long acting agents**

**Long-acting β-agonist (LABA)**
- Formoterol
- Salmeterol
- Indacaterol
- Indacaterol
- Vilanterol

**Long-acting anticholinergic (LAMA)**
- Tiotropium
- Aclidinium
- Umeclidinium
- Glycopyrronium
Inhaled corticosteroids (ICS): reduce exacerbations

- Fluticasone
- Mometasone
- Beclamethasone
- Budesonide
- Ciclesonide
GOLD recommendations for initial therapy

**Group A**
Short-acting bronchodilator

**Group B**
Long-acting bronchodilator

**Group C**
ICS + LABA
OR
LAMA

**Group D**
ICS + LABA
AND/OR
LAMA

Increasing disease severity
2nd line agents

• Roflumilast
  – PDE4 inhibitor
  – Reduced exacerbations

• Theophylline
  – Nonspecific PDE inhibitor
  – Possibly reduced exacerbations

• Daily macrolide antibiotic therapy
  – Azithromycin, clarithromycin
  – Reduced frequency of exacerbations, improve QoL
Other Treatments

Vaccinations:

• Influenza Vaccination
• Pneumovax

Pulmonary rehabilitation
Pulmonary Rehabilitation

- Improved QoL
- Improved functional capacity
- Improved exercise capacity
- Reduced hospital admissions

Cochrane Database of Systematic Reviews. 2015, CD003793
Surgical therapy

LVRS
• Removal of apical portions of lungs in patients with apical predominant emphysema
• Goal to reduce hyperinflation

Lung transplant
• May be candidates for single or double lung transplant
• Listing generally when BODE >7, FEV1 <20%, DLCO <20%
• 80% 1-year survival, 60% 3 year survival, 50% 5 year survival
COPD Exacerbations

• **Corticosteroids**
  – 5 days of prednisone 40mg/day adequate for most exacerbations
  – Hospitalized patients often receive IV methylprednisolone

• **Antibiotics**
  – Azithromycin, doxycycline, TMP-SMX, amoxicillin-clavulanate → cover most common infections
  – Levofloxacin, ciprofloxacin → cover Pseudomonas if at risk

• Frequent bronchodilator administration
• Respiratory support if needed
Summary

• COPD is a common, preventable pulmonary disease that causes significant morbidity
• COPD is chronic airflow obstruction in the setting of emphysema and/or chronic bronchitis
• Smoking is the most important risk factor for smoking but numerous other predisposing factors exist
• Dyspnea is common and is due to multiple factors
• Treatment should involve an assessment of the patient’s disease severity, symptoms, and ability to manage medical treatments