COPD Pathology with 3D Interactive
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COPD: Change in Definition

• COPD used to include 5 disease processes
  1 Chronic Bronchitis
  2 Emphysema
  3 Asthma
  4 Bronchiectasis
  5 Cystic fibrosis & fibrosis from Tb

• Differential diagnosis separates 3 to 5

COPD: Definitions of 21st Century

• Preventable and treatable
• Airflow limitation that is not fully reversible
• Progressive disease
• Abnormal inflammatory response of the lungs
• Subsets of patients

COPD Includes Chronic Bronchitis

• Productive cough for 3 months in 2 consecutive years with intermittent wheezing and variable degrees of recurring dyspnea on exertion
• Inflammation of cells that line the bronchus resulting in excess sputum
• Mucous glands enlarge and bronchial walls thicken, resulting in a deformed and narrow airway lumen
COPD Includes Emphysema

- Abnormal permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis.
- Destruction occurs in the alveoli and the orderly appearance of the acinus is disturbed.
- Normal elasticity is lost, air becomes trapped in over-inflated lungs.

COPD: Airway Effects

Pathology, Pathogenesis, & Pathophysiology

- Pathology
  - Characteristics and effects of COPD
- Pathogenesis
  - Origin and cause of COPD
- Pathophysiology
  - Biologic and physical manifestations of COPD
    - Processes within the body that result in signs and symptoms
**COPD: Anatomy Review**

Divisions of lower respiratory tract

1. **Trachea** – cartilage; conducting airway
2. **Mainstem bronchi** – β2 smooth muscle; conducting airway
3. **Secondary bronchi** – β2 smooth muscle; conducting airway
4. **Tertiary bronchi** – β2 smooth muscle; conducting airway
5. **Bronchioles** – β2 smooth muscle; conducting airway
6. **Terminal bronchioles** – β2 smooth muscle; conducting airway
7. **Respiratory bronchioles** – gas exchange starts here
8. **Alveoli** – gas exchange; septa are alveolar walls

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**COPD: Pathology**

COPD Compromises Four Compartments of the Lung

1. **Central airways** – cartilaginous >2mm diameter
   - Bronchial glands hypertrophy – increased sputum production
   - Airway epithelium metaplasia changes – loss of cilia and ciliary dysfunction, increased smooth muscle and connective tissue
   - Inflammatory cells predominate – lymphocytes (CD8+), neutrophils, and macrophages

2. **Peripheral airways** – non-cartilaginous <2mm diameter
   - Bronchiolitis present in early stages of COPD
   - Increased number of goblet cells and epithelial metaplasia
   - Inflammatory cells predominate – lymphocytes (CD8+), neutrophils, and macrophages
   - Advanced disease reveals fibrosis and more collagen in walls

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**Inflammatory Cells Involved in COPD**

- Neutrophil elastase
- Cathepsins
- MMPs

### Alveolar wall destruction
- Emphysema

- Mucus hypersecretion

### Fibrosis
- Obstructive bronchiolitis

- Source: Peter J. Barnes, MD
COPD: Pathology

COPD Compromises Four Compartments of the Lung

1. Lung parenchyma – respiratory bronchioles, alveoli, and capillaries
   - Emphysema – enlargement of air spaces distal to terminal bronchioles, Two types
     1. Centrolobular – dilation and destruction of respiratory bronchioles
     2. Panlobular – destruction of entire acinus, Alpha1-antitrypsin
   - Loss of alveolar attachments – airway collapse
   - Inflammation similar to previous
   - Development of bullae

2. Pulmonary vasculature
   - Begins early in disease
   - Vessel wall thickening and endothelial dysfunction
   - Increased vascular smooth muscle tone
   - Infiltration of vessel wall with CD8+ and T lymphocytes
   - Advanced stages – develop collagen deposition and capillary bed destruction leading to pulmonary hypertension and cor-pulmonale

Source: Peter J. Barnes, MD
Not everyone that smokes gets **COPD**
COPD: Pathogenesis

- Tobacco smoking is the main risk factor for COPD
- Some smokers display an exaggerated protected inflammatory response, which causes tissue destruction, impairs defense and repair mechanisms, thus leading to characteristics of COPD

COPD: Pathogenesis

Three processes important to Pathogenesis

1. Inflammation cascade
   - Differs from bronchial asthma cascade
2. Proteinase and antiprotease imbalance
   - Released by inflammatory cells
3. Oxidative Stress
   - Oxidizing biological molecules leads to cell dysfunction and/or death

Inflammation in Asthma & COPD

COPD
- Macrophages
- PMNs
- CD8 T cells
- proteases
- LTB4
- IL-8, TNF-α

Asthma
- Eosinophils
- Mast cells
- CD4 T cells
- mediators
- LTD4
- IL-4, IL-5, IL-13

Source: Peter J. Barnes, MD
Pathogenic mechanisms produce pathological changes, giving rise to four physiological abnormalities in COPD

1. Mucous hypersecretion and ciliary dysfunction
   - First physiologic abnormality developed in COPD
   - Enlarged mucous glands and epithelial cell metaplasia

2. Airflow limitation and hyperinflation
   - Expiratory (largely irreversible) airflow limitation
     - Physiologic hallmark of COPD
   - Major site is smaller conducting airways <2mm
   - Loss of elastic recoil due to alveolar wall destruction
   - Destruction of alveolar attachments
   - Accumulation of inflammatory cells, mucous and plasma exudate in the bronchi
   - Smooth muscle contraction (tense vagal tone) and dynamic hyperinflation during exercise
     - Major factor affecting exercise limitation in patients

3. Gas exchange abnormalities
   - Occurs in advanced COPD characterized by hypoxemia with or without hypercapnia
   - Abnormal gas exchange as a result of anatomical alterations as described previously

4. Pulmonary hypertension
   - Occurs after severe gas exchange abnormalities
   - Results from hypoxic vasoconstriction, endothelial dysfunction, remodeling of pulmonary arteries and destruction of capillary bed
   - Leads to right sided heart failure – cor pulmonale
Pulmonary Hypertension in COPD

- Chronic hypoxia
- Pulmonary vasoconstriction
- Muscularization
- Intimal hyperplasia
- Fibrosis
- Obliteration
- Pulmonary hypertension
- Cor pulmonale
- Edema
- Death

Source: Peter J. Barnes, MD

Only Two Things Clinically Proven to Prolong Life for COPD Patients

1. Quitting Tobacco
2. LTOT only for those who qualify

Pro-Active vs. Passive Referral

- Fax Referral System
- 50% enrollment rate
- 35-45% abstinence at 6mos
- 25-35% abstinence at 1 year

- Leaving it up to the individual to call when ready
- According to research conducted at San Diego State University only 3% of clients receiving literature containing quit line information made a call to the quit line

- Results = 20 @ 6mos / 15@yr
- Results = 1.2 @ 6mos / 1@yr
QuitFax Referral Form – Quick and Easy!

ASHLine 1-800-55-66-222
www.ashline.org
National Quit Line
1-800-Quit Now

COPD: Treatment & Management

Four Components of Care
1. Assess and monitor disease
   • Spirometry is the tool
2. Reduce risk factors
3. Manage stable COPD
   • Pharmacologic and non-pharmacologic
4. Manage acute exacerbations
   • Steroids, antibiotics, ventilation support

GOLD Standards COPD Pharmacotherapy

Manage Exacerbations: Introduction

- An exacerbation of COPD is an event in the natural course of the disease characterized by a sudden change in the patient's baseline symptoms: dyspnea, cough, and/or sputum that is beyond normal day-to-day variations
- May warrant a change in regular medication usage

<table>
<thead>
<tr>
<th>Component</th>
<th>FEV₁/FVC &lt; 70%</th>
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<tbody>
<tr>
<td>I: Mild</td>
<td>FEV₁ &gt;60% pred</td>
</tr>
<tr>
<td>II: Moderate</td>
<td>FEV₁ 50-60% pred</td>
</tr>
<tr>
<td>III: Severe</td>
<td>FEV₁ 30-50% pred</td>
</tr>
<tr>
<td>IV: Very Severe</td>
<td>FEV₁ &lt; 30% pred</td>
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</tbody>
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Avoidance of risk factor(s); influenza vaccination
Add short-acting bronchodilator when needed: β₂ agonists
Add regular treatment with one or more long-acting bronchodilators: β₂ agonists and anticholinergics
Add rehabilitation
Add ICS for repeated exacerbations
Add LTOT
Surgical interventions
COPD Exacerbations: Epidemiology

- Exacerbations play a role in decline of FEV\textsubscript{1}
  - Decline in FEV\textsubscript{1} of 46.1 ml/yr with frequent (>1.5) exacerbations per year
  - Decline in FEV\textsubscript{1} of 25.3 ml/yr with infrequent (<1.5) exacerbations per year
  - Greater lung function decline value observed in COPD exacerbations amongst current smokers

Donaldson et al, Thorax 2002;57;847-52

COPD Exacerbations: Epidemiology

- Seasonality
  - 50% more likely in the winter

- Recurrent Exacerbations
  - 30% of those hospitalized have another exacerbation within 8 weeks

COPD Exacerbations: Epidemiology

- The most common causes are:
  - Infection of the tracheobronchial tree
  - Air pollution

- Cause of 1/3 of severe exacerbations unknown

- Conditions that mimic exacerbations: pneumonia, CHF, PE, pneumothorax, pleural effusions, arrhythmia
  - Important to Differential Diagnosis

WORLD COPD DAY

November 16, 2011

Raising COPD Awareness Worldwide
Interactive COPD Education System

This interactive module is provided by Syandus, Inc.

Click to Launch the COPD Active Learning Module

References


14. American Lung Association of Minnesota, COPD Educator Course, 2006. Cheryl Sasse; Jeff Rubens, MD; Kathy Schultz, RRT; Charles McArthur, RRT, RPFT; Janet Maliekiewicz, RN, PHN; Lynn Sieben, RRT; Dick Sternholz LS; Bob McNall, RRT, MAARC; Charlene McVeay, MD


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