Chronic Obstructive Pulmonary Disease (COPD)

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Objectives

- Describe current definition of chronic obstructive pulmonary disease as an inflammatory condition.
- List at least four risk factors developing COPD.
- Describe important clinical features of COPD. Be familiar with overlapping pathophysiologic and clinical characteristics of individuals with features of emphysema and chronic bronchitis.
Objectives – cont’d

- List key abnormalities of pulmonary function in COPD. Identify differences in flow-volume curve patterns in obstructive and restrictive respiratory disorders.
- Describe complications that affect quality of life and longevity in COPD.
- Discuss key therapeutic modalities in the management of COPD, including pulmonary rehabilitation.
A 65-yr-old man with an 60-pack-year history of smoking complains of shortness of breath on exertion of several months’ duration. On inspection, there is increased anteroposterior diameter of the chest, pursed lip breathing, and dyspnea during conversation. He is unable to complete more than 4 or 5 words at a time.
Physical examination

- Tachycardic
- Hyperresonant lungs with decreased breath sounds, no crepitations (rôles)
- No hepatomegaly or liver nodules on palpation

Which of the following is the most likely diagnosis?

A. Alpha-1-antitrypsin deficiency
B. Asthma
C. Bronchiectasis
D. Centriacinar emphysema
E. Chronic bronchitis
F. Panacinar emphysema
COPD -- definition

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

The chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person.

Older terms for COPD which are not used as often

Emphysema – A pathologic term that is often (but incorrectly) clinically used and describes only one of several structural abnormalities present in COPD.

Chronic bronchitis – Cough, sputum production for at least 3 mos in each of 2 consecutive years, but actually only seen in few patients; when mucus hypersecretion is more broadly applied, especially in older people exposed to environmental or occupational pollutants, the prevalence of chronic bronchitis is greater.

GOLD 2018
COPD – Some statistics

- About 15 million adults suffer from COPD in the U.S.
- Third leading cause of death in U.S.
- Women make up the majority, accounting for 52% (in 2011)
- Approx. 135,000 deaths in 2011
- Nearly 80% of COPD deaths are in non-Latino whites; Latinos exhibit the least number of deaths, approx. 3,700 (in 2011)

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6146a2.htm?s_cid=mm6146a2_w. Accessed April 7, 2016.
COPD – Risk factors

- Tobacco smoke (>20 pack-years)
- Passive smoking
- E-cigarettes alter host response in smokers
- Air pollution – harmful to people with heart and lung problems
- Hyperreactive airways (asthma → COPD)
- Ethnic, racial, socioeconomic factors
- Bacterial infections
Sources of air pollution

(a) Heating and cooking

(b) Biomass stacks for fuel

(c) Agricultural fires

(d) Moorburn
Indoor air pollution

A burning issue

Nearly 3 billion people burn wood, dung and other types of biomass in open stoves to cook their food and heat their homes. The World Health Organization has estimated the number of deaths caused by household air pollution (HAP) from burning biomass and coal.

Cause of death from household air pollution in 2012

- 6% Lung cancer
- 22% Chronic obstructive pulmonary disease
- 26% Ischemic heart disease
- 34% Stroke

Total deaths attributable to HAP in 2012, by region

- Africa: 581,300
- The Americas: 81,300
- Eastern Mediterranean: 200,800
- Europe: 117,200
- Southeast Asia: 1,691,600
- Western Pacific: 1,620,100

Number of deaths (millions)
OUTDOOR POLLUTION
Vicious Circle Hypothesis

Initiating factors
e.g. smoking, childhood respiratory disease

Impaired mucociliary clearance

Airway epithelial injury

Bacterial products

Bacterial colonization

Inflammatory response

Progression of COPD

Altered elastase - anti-elastase balance

Increased elastolytic activity

from Sethi Chest. 2000;117:286S-291S.
Scanning electron micrograph of normal ciliated columnar bronchial epithelium
Electron micrograph of bronchial epithelium injured by chronic smoking. Note missing and damaged columnar epithelial cells.
COPD – Genetic/Molecular Factors (examples)

A. Alpha 1 – antitrypsin (anti-protease) deficiency

- The only definitely proven genetic abnormality leading to COPD.
- Associated with lower lobe and panlobular emphysema.
- Over 95% of persons with A₁AT deficiency are homozygous for the Z allele, i.e., PiZZ, but it is rare.
- Those with heterozygous deficiency (Pi MZ) may also become affected with increased airway hyperreactivity, but not all necessarily progress to COPD.
EXOGENOUS PROTEASES (INFECTIONS):
CENTRILOBULAR EMPHYSEMA -

ENDOGENOUS PROTEASES
(LEUKOCYTE SEQUESTRATION, MACROPHAGES):
PANACINAR EMPHYSEMA
Panlobular emphysema caused by alpha-1 antitrypsin deficiency:

Note large bulla in RLL. The lower lobes are involved initially because they receive more blood flow, with high concentrations of proteases delivered to these areas.

Patients homozygous to this gene (PiZZ) develop accelerated tissue destruction and succumb to the disease at a younger age.
B. Genome studies have identified genetic links with specific clinical phenotypes of COPD: emphysema, chronic bronchitis (both with and without acute exacerbations), and asthma-COPD overlap syndrome (ACOS).
History

- Smoking at least one pack of cigarettes daily for 20 years.
- Cough with mucoid to mucopurulent sputum.
- Dyspnea (breathlessness)—first with exertion then progressively at rest.
- Increased frequency of respiratory illnesses, i.e., chest colds, upper respiratory infections, “flu” episodes.
- May experience wheezing.
- Late symptoms and signs are: hypoxemia, heart failure, weight loss, poor appetite, early satiety, secondary erythrocytosis (in chronic bronchitis)
Dyspnea -- Factors

- Dyspnea (breathlessness) – first with exertion, ultimately at rest. Exercise intolerance is due to many contributing factors:
  
a. Ventilatory limitation – hyperinflation, dead-space ventilation, impaired gas exchange, deconditioning, peripheral muscle dysfunction.
  
b. Gas exchange limitations – Hypoxemia, hypercarbia increase ventilatory demands → lactic acid production from fatiguing respiratory muscles.
Dyspnea – Factors (cont’d)

c. Cardiac dysfunction – right ventricular hypertrophy → cor pulmonale → left ventricular dysfunction.

d. Skeletal muscle dysfunction – due to deconditioning, oxidative stress, systemic inflammation, hypoxemia, chronic steroid use, weight loss.

e. Respiratory muscle dysfunction – from chronic overload and hyperinflation.
COPD is a systemic disease!
Emphysema:
- Thin
- Weight loss
- Using accessory neck muscles
- Barrel chest
- Tense abdominal muscles (to try to push the air out)
- Very dyspneic
- ABGs surprisingly preserved until advanced phase in emphysema
- “Pink puffer”
Hyperinflation in obstructive disorders

Excessive air trapped in the lungs, such as occurs during an acute exacerbation of asthma or chronic obstructive pulmonary disease (COPD).

When chest is percussed, it sounds like a hollow drum (hyperresonant) – one can even feel the vibrations coming through the chest wall.

Figure courtesy of Dr. Keens
Normal CXR

CXR of severe COPD – note low, flat diaphragms, paucity of lung markings, long, narrow heart
Lateral upright view of chest in severe COPD:

- Large retrosternal air space
- Flat, low-set diaphragms – all consistent with hyperinflated lungs, increased FRC, RV and TLC (see lung volumes, below).
Domed diaphragm with area of apposition
Bronchitic:

- Ruddy complexion – may be related to secondary erythrocytosis
- May be fatigued, but not dyspneic
- ABGs show hypoxemia and hypercarbia
- Cor pulmonale due to hypoxemia-induced pulmonary hypertension
- “Blue bloater”
Arterial Blood Gases

- Hypoxemia - clinically significant when PaO$_2$ falls below 55 mm Hg because of the risk for developing cor pulmonale

- Hypercapnia – later in the disease when FEV$_1$ falls below 1.0 L.

- Contribute to pulmonary hypertension and cor pulmonale.
Typical spirometric curves: Normal, obstructed and restrictive patterns

A. NORMAL
FEV = 4.0
FVC = 5.0
% = 80

B. OBSTRUCTIVE
FEV = 1.3
FVC = 3.1
% = 42

C. RESTRICTIVE
FEV = 2.8
FVC = 3.1
% = 90

From J. West – Respiratory Physiology: The Essentials
Spirometry - The Sixth Vital Sign

<table>
<thead>
<tr>
<th></th>
<th>FEV₁</th>
<th>FVC</th>
<th>FEV₁/FVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>4.15</td>
<td>5.20</td>
<td>80 %</td>
</tr>
<tr>
<td>COPD</td>
<td>2.35</td>
<td>3.90</td>
<td>60 %</td>
</tr>
</tbody>
</table>

FEV₁ (Forced Expiratory Volume in 1 second) and FVC (Forced Vital Capacity) are compared in healthy individuals (Normal) and in individuals with Chronic Obstructive Pulmonary Disease (COPD).
Flow-volume curves:

Compare normal curve (the larger one) against the curve in a COPD patient.

Note the downward convexity ("scooping") of the obstructed curve.
Flow-volume curve from patient with severe COPD:

Note the immediate decrease in flow during expiration (portion above zero flow line) -----------------

This is seen with dynamic airway collapse due to loss of lung elastic recoil. The airways have lost their normal tethering support due to tissue destruction.

The small curve in the middle is the tidal breathing curve.
Flow-volume curves

Dashed F-V curves represent normal pattern
Lung Volumes: In obstructive airway disease, volumes are increased; in restrictive conditions, volumes are reduced.
DIFFUSION CAPACITY:

Cut section of lung to show why diffusion capacity ($D_L CO$) is reduced in emphysema.

The extensive tissue destruction reduces surface area available for gas exchange, an important factor in the determination of $D_L CO$. In asthma, $D_L CO$ is normal or slightly increased.
This cut section also explains why:

• Lung compliance is increased in emphysema due to reduced lung elastic recoil

• Producing ventilation/perfusion mismatching...

• And gas exchange abnormalities (increase in AaDO$_2$)
Lung compliance in emphysema is increased
Clinical-Physiologic-Pathologic correlations:

**Acute exacerbations of COPD**

- Defined as sudden worsening in airway function and respiratory symptoms in patients with COPD.
- Associated with airway inflammation and physiologic deterioration.
- Bacteria, viruses, and changes in air quality (including smoking) interact to produce increased inflammation.
- Cause morbidity, hospital admissions, mortality, and adversely affect quality of life.
### Table 2.5. Modified MRC dyspnea scale

**PLEASE TICK IN THE BOX THAT APPLIES TO YOU**  
**(ONE BOX ONLY) (Grades 0-4)**

<table>
<thead>
<tr>
<th>mMRC Grade</th>
<th>Description</th>
<th>Ticked</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on the level or walking up a slight hill.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 meters or after a few minutes on the level.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing or undressing.</td>
<td></td>
</tr>
</tbody>
</table>

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a Fletcher CM. BMJ 1960; 2: 1662.
The COPD assessment test

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy  0 1 2 3 4 5  I am very sad

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I never cough</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>I cough all the time</td>
<td></td>
</tr>
<tr>
<td>I have no phlegm (mucus) in my chest at all</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>My chest is completely full of phlegm (mucus)</td>
<td></td>
</tr>
<tr>
<td>My chest does not feel tight at all</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>My chest feels very tight</td>
<td></td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am not breathless</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>When I walk up a hill or one flight of stairs I am very breathless</td>
<td></td>
</tr>
<tr>
<td>I am not limited doing any activities at home</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>I am very limited doing activities at home</td>
<td></td>
</tr>
<tr>
<td>I am confident leaving my home despite my lung condition</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>I am not at all confident leaving my home because of my lung condition</td>
<td></td>
</tr>
<tr>
<td>I sleep soundly</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>I don't sleep soundly because of my lung condition</td>
<td></td>
</tr>
<tr>
<td>I have lots of energy</td>
<td>0 1 2 3 4 5</td>
</tr>
<tr>
<td>I have no energy at all</td>
<td></td>
</tr>
</tbody>
</table>

Reference: Jones et al. ERU 2009; 34 (3); 648-54.
In the refined assessment scheme, patients should undergo spirometry to determine the severity of airflow limitation (i.e., spirometric grade). They should then undergo assessment of either dyspnea, using the mMRC, or symptoms using the CATTM. Finally, their history of exacerbations (including prior hospitalizations) should be recorded (GOLD 2017).
Figure 7. Therapy at Each Stage of COPD

Postbronchodilator FEV₁ is recommended for the diagnosis and assessment of severity of COPD.

I: Mild
- FEV₁/FVC < 0.70
- FEV₁ ≥ 80% predicted

II: Moderate
- FEV₁/FVC < 0.70
- 50% ≤ FEV₁ < 80% predicted

III: Severe
- FEV₁/FVC < 0.70
- 30% ≤ FEV₁ < 50% predicted

IV: Very Severe
- FEV₁/FVC < 0.70
- FEV₁ < 30% predicted or FEV₁ < 50% predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

Add regular treatment with one or more long-acting bronchodilators (when needed); Add rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure

Consider surgical treatments
Complications of COPD

- Hypoxic pulmonary hypertension
- Right heart failure (cor pulmonale)
- Frequent respiratory infections (>2/yr)
- Weight loss, loss of appetite
- Respiratory failure with hypoxemia, hypercapnia and respiratory acidosis
COPD and cor pulmonale:

- Cyanotic lips and nailbeds (indicates $\text{PO}_2 < 45 \text{ mmHg breathing room air}$)
- Jugular venous distention
- Hepatomegaly
- If legs were seen this picture, one would note dependent edema
COPD -- Management

- Smoking cessation
- Oxygen therapy
- Bronchodilators – mainly inhaled
  - Beta-agonists (albuterol, salmeterol)
  - Anticholinergics (anti-muscarinic agents: ipratropium, tiotropium, glycopyridium)
- Steroids – for acute exacerbations; ICSs for maintenance, but they are being replaced by LAMAs
- Phosphodiesterase inhibitors (roflumilast, theophylline)
- Antibiotics (increased sputum, cough, dyspnea)
- Mechanical ventilation
- Surgery – lung volume reduction; transplantation
- Pulmonary rehabilitation
Proper Position of Head and Inhaler During Inhaler Use
Spacers to be used with MDIs
Spacers -- usefulness

Improve aerosol delivery in patients not able to coordinate the meter dose inhaler.
Long-term oxygen trial study: Demonstrates survival benefit for 24 hr continuous use of supplemental oxygen in patients with COPD (circles: continuous oxygen; squares: intermittent oxygen).
Pulmonary rehabilitation: Key concept

Pulmonary rehabilitation attempts to return the patient to the highest possible functioning level allowed by the pulmonary disability and overall life situation.
Remember, COPD is a systemic condition!
A 65-yr-old man with an 80-pack-year history of smoking complains of shortness of breath on exertion of several months’ duration. On inspection, there is increased anteroposterior diameter of the chest, pursed lips, and dyspnea during conversation. He is unable to complete more than 4 or 5 words at a time.
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- Tachycardic
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Practice question 1

Which of the following sequences concerning average lung volumes and capacities of a healthy person at rest is in the correct order of descending magnitude? (Note: TLC = total lung capacity; VC = vital capacity; FRC = functional residual capacity; TV = tidal volume)

A. TLC>VC>TV>FRC
B. TLC>FRC>VC>TV
C. TLC>VC>FRC>TV
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A. TLC>VC>TV>FRC
B. TLC>FRC>VC>TV
C. TLC>VC>FRC>TV *******
D. TLC>FRC>TV>VC
Practice question 2

For a patient being evaluated for chronic dyspnea the results of pulmonary function tests were as follows:

**Spirometry:**
- Forced vital capacity: 2.43 L (81% predicted)
- FEV$_1$: 0.42 L (18%; no reversal)
- FEV$_1$/FVC: 17%

**Lung volumes by body plethysmography:**
- Total lung capacity: 7.47 L (155%)
- Residual volume: 5.05 L (269%)
- Diffusion capacity for carbon monoxide: 4.7 mL/min/mmHg (26%)

These results are most consistent with:
A. Chronic bronchitis
B. Idiopathic pulmonary fibrosis
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E. Asbestosis
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OVERALL KEY POINTS

- COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator
- \( \text{FEV}_1/\text{FVC} < 0.70 \) confirms the presence of persistent airflow limitation.
- The goals of COPD assessment are to determine the severity of the disease, including the severity of airflow limitation, the impact of disease on the patient’s health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

GOLD 2017
Concomitant chronic diseases occur frequently in COPD patients, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety, and lung cancer.

These comorbidities should be actively sought and treated appropriately when present as they can influence mortality and hospitalizations independently.
No more butts!
THANK YOU --
QUESTIONS ?
COMMENTS?