“Fighting for Air,"
The Mechanism of Shortness of Breath
In Emphysema

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COPD = Chronic Bronchitis and Emphysema

Multiple efforts are being put in place to help raise the awareness of COPD

Joint Commission

Development of COPD Certification Program

- Collaboration with American Lung Association
- Task force utilized GOLD and ATS/ERS guidelines as resources and created draft addendum
- Preliminary requirements for public comment April, 2007
- Public comments and pilot site visits considered by Task Force
- Product launch September, 2007
COPD: Guideline Definitions

**GOLD** – “…preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.”

**ATS/ERS** – “…preventable and treatable disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, primarily caused by cigarette smoking. Although COPD affects the lungs, it also produces significant systemic consequences.”

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Agenda

- COPD: A Major Public Health Burden
- Understanding the Clinical Course of COPD
- Simplifying the Diagnosis of COPD
- Managing and Treating COPD
Tobacco Use Contributes to Preventable Causes of Death

- 18% of total deaths and 37.5% of preventable causes of death in the United States are tobacco-related

- According to the US Department of Health and Human Services, 1/3 of all tobacco users in this country will die prematurely from tobacco-related diseases, shortening their own life span by an average of 13.2 years in men and 14.5 years in women

Preventable Causes of Death in the United States in 2000

- Tobacco Use (435,000)
- Illicit Use of Drugs (17,000)
- Motor Vehicles (43,000)
- Sexual Behavior (20,000)
- Firearms (29,000)
- Toxic Agents (55,000)
- Microbial Agents (55,000)
- Alcohol (85,000)
- Diet/Activity (400,000)

U.S. Mortality From Smoking-Related Disease

Smoking-Related Disease Mortality*

- Neoplasms 40%
- Ischemic Heart Disease 22%
- Respiratory Disease 25%
- Cerebrovascular Disease 4%
- Other Cardiovascular Disease 8%
- Other <1%

* Percentage of deaths attributable to specific smoking-related diseases, 1997 – 2001 based on estimates using smoking-attributable fraction and relative risk estimations

- More than 399,000 US deaths annually are attributable to cigarette smoking
- Every eight seconds, someone dies from tobacco use

Society’s Problem

- The deaths
  - Smoking kills more people than alcohol, AIDS, car accidents, illegal drugs, murders, and suicides combined
    - People who die each year from their own cigarette smoking: 400,000
    - People who die each year from others smoking: 38,000 to 67,500

- The dollars
  - Health care costs: $75.5 billion
    - $1677 per smoker per year
  - Productivity costs: $92 billion
    - $2044 per smoker per year

National Cancer Institute. Monograph 10: Health Effects of Exposure to Environmental Tobacco Smoke. NIH.
Smoking Is Not Just a Personal Matter

- Secondhand smoke increases health risks for family members
  - lung cancer and heart disease in spouses
  - smoking by children of tobacco users
  - low birth weight, sudden infant death syndrome, asthma, middle ear disease, respiratory infections in children of smokers

- 38,000 annual deaths are attributed to secondhand smoke

Economic Costs of Smoking

- Direct medical expenditures attributed to smoking:
  - $75 billion per year
  - 14% of all Medicaid expenditures are related to smoking
- Lost productivity:
  - $92 billion per year

Health Benefits of Stopping Smoking

Time After Stopping

20 minutes
BP, HR, and peripheral circulation improve

24 hours
CO levels drop

48 hours
Nicotine eliminated; taste and smell improved

2-12 wk
Lung function improves up to 30%

3-9 mo
Shortness of breath and coughing decrease

15 years
Risk of MI and stroke fall to the same level as a nonsmoker

10 years
Risk of lung cancer reduced by 50%

1 year
Risk of MI reduced by 50%

COPD is a Common Chronic Disease

- **COPD**: 12.6 million
- **Diabetes**: 15.1 million
- **Asthma**: 14.4 million
- **Heart Disease**: 24.7 million
- **HTN**: 47.5 million
- **Obesity**: 49.5 million

HTN = Hypertension

Some Facts

- In the US
  - 12 million diagnosed with COPD
  - 12 million with signs/symptoms undiagnosed
- Death rate among women doubled last 20 years
- Costs
  - 14.7 billion direct
  - 15.7 billion indirect
- Rising prevalence and mortality especially in women and African Americans
- Fourth leading cause of death in the US and estimated to climb to third by 2020
Percent Change in Age-Adjusted Death Rates in the U.S., 1965-1998

Coronary Heart Disease: -59%
Stroke: -64%
Other CVD: -35%
COPD: +163%
All Other Causes: -7%

CVD=Cardiovascular disease.
Source: NHLBI/NIH/DHH
COPD: 5th Leading Cause of Death Worldwide

- Ischemic Heart Disease: 7,208,000
- Cerebrovascular Disease: 5,509,000
- Lower Respiratory Tract Infection: 3,884,000
- HIV/AIDS: 2,777,000
- COPD: 2,748,000
- Perinatal Conditions: 2,462,000
- Diarrheal Disease: 1,798,000
- Tuberculosis: 1,566,000
- Trachea/Bronchus/Lung Cancer: 1,243,000
- Road Traffic Accidents: 1,192,000

Risk Factors for COPD

Cigarette smoke
Occupational dust and chemicals
Environmental tobacco smoke (ETS)
Indoor and outdoor air pollution

Nutrition
Infections
Socio-economic status
Aging Populations
Epidemiology

- 80-90% cases related to smoking
- A smoker is 10 times more likely to die of COPD
  - No markers to predict who will develop
  - All smokers are candidates for cessation
- Irreversible decline in lung function with smoking
- More women than men die from COPD annually
- Mortality rate in men stable
- Mortality rate in women and African Americans steadily rising
- 15-20% of population over age 50 have COPD

Source: US Centers for Disease Control and Prevention, 2002
COPD in Women Is on the Rise

**Perception**

- In 2004, women accounted for approximately 63% of all self-reported cases of COPD
- From 1980 to 2000, COPD mortality rates for women nearly tripled
- In 2000, COPD hospitalizations for women outnumbered those for men
- Increased morbidity and mortality in women likely reflects increased smoking by women

**Reality**


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COPD in Younger Patients Is on the Rise

Perception

Reality

- COPD afflicts the working age population\textsuperscript{1,2}
- \textasciitilde 70\% of COPD patients are younger than age 65\textsuperscript{3}
- Patients < 65 accounted for 67\% of COPD office visits and 43\% of hospitalizations\textsuperscript{1}
- COPD is as common as asthma and diabetes in population aged 45-64\textsuperscript{3}

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Pathophysiology of COPD

**INFLAMMATION**

- Airway resistance – cm H2O/L/sec
- Compliance - L/cm H2O

**Small airway disease**
- Airway inflammation
- Airway remodelling

**Parenchymal destruction**
- Loss of alveolar attachments
- Decrease of elastic recoil

**AIRFLOW LIMITATION**

Overview of COPD Pathophysiology

- Cigarette Smoke
- Susceptibility Genes
- Gender
- Proteinases/Cell Mediators
- Oxidative Stress
- Environmental Irritants
- Respiratory Infections

Lung Inflammation, Hyperinflation, Airway Obstruction, Elastic Recoil Loss

Exacerbations
- Chronic Bronchitis
- Emphysema
- Systemic/Extrapulmonary Effects
- Mucociliary Dysfunction
- Structural Changes

COPD is a Disease Characterized by Inflammation

- Cigarette Smoke
- Epithelial Cells
- Macrophage/Dendritic Cell
- Neutrophil
- Monocyte
- Fibroblast
- CD8+ Tc Cell
- Proteases
- Fibrosis
- Obstructive Bronchiolitis
- Emphysema
- Mucus Hypersecretion

Pathology: Airflow Limitation

- Irreversible
  - Airway fibrosis
  - Loss of elastic recoil
  - Destruction of “tethering” alveolar tissue
- Reversible
  - Inflammatory component
  - Smooth muscle contraction
  - Dynamic hyperinflation
Inflammation Destruction of Alveolar Architecture

Normal

COPD

COPD: A Long-Term Progressive Disease

COPD

- Expiratory flow limitation
- Air trapping
- Hyperinflation
- Dyspnea

Deconditioning

Activity Limitation

Decrease in quality of life

Exacerbations

Reduced Exercise Endurance

Characteristics of Air Trapping and Hyperinflation

- Low, Flattened Diaphragm
- Increased A-P Diameter
- Air Trapping
Co-Morbidities of COPD

- Weight loss with decreased fat-free mass
- Increased cardiovascular mortality
- Muscle wasting and weakness
- Other systemic effects:
  - osteoporosis
  - anemia
  - depression

Related to Systemic Inflammation?
Diagnosis of COPD

SYMPTOMS
- cough
- sputum
- shortness of breath

EXPOSURE TO RISK FACTORS
- tobacco
- occupation
- indoor/outdoor pollution

SPIROMETRY
Why is the Burden of COPD Increasing?

- Poor recognition by patient
  - Do not present early for diagnosis
  - Under-rate symptoms
- Difficulty in diagnosis
  - Diagnosis of exclusion
  - Diagnosis is complicated by discrepancy between symptoms and the degree of airway obstruction
  - Inadequate utilization of lung function tests

Under-diagnosed
Why is the Burden of COPD Increasing?

• Poor knowledge of disease
  – Patient and Health professionals
  – Poor understanding of pathophysiology and pharmacotherapy
• Nihilistic attitudes towards COPD
  – Myth that the condition is untreatable
COPD: Patient Misperceptions

• Patients may misunderstand or minimize symptoms such as fatigue, dyspnea, cough. They may neglect to mention these symptoms to the physician

• Misperception and denial are significant barriers to diagnosis and management

• Symptoms may be misattributed to “asthma” or “getting older”

  ✓ “I’ve been coughing when I wake up each morning, **but it’s just smoker’s cough. This is normal and not harmful to my health.**”

  ✓ “Carrying these groceries is harder than it used to be. **I must be old and out of shape.**”

  ✓ “**I don’t need meds for my breathing because it’s not a serious problem.**”

COPD Diagnosis Is Confirmed by Spirometry

- Spirometry is the standard for measurement of airflow limitation\(^1\)
- Common spirometry measurements include FEV\(_1\) and FVC\(^1,2\)
- FEV\(_1\)/FVC is used to diagnose COPD\(^1-3\)
- FEV\(_1\) is used to classify severity\(^1\)

FEV\(_1\)= Forced expiratory volume in one second.
FVC=Forced vital capacity.

Portable Office Spirometer
Flow-Volume Loops

Representative, prebronchodilator flow-volume loop from a patient with COPD compared with a representative normal loop.

- Peak expiratory flow rate
- FEV₁ (notch added by auto timer)
- Forced exhalation
- Maximal inhalation
Spirometry measures maximal volume of air forcibly exhaled from the point of maximal inhalation and the volume of air exhaled during the first second.

Smoking Cessation: The Single Most Important Way to Prevent COPD Onset and Progression

If exposure to noxious agents stops, disease progression slows

*Average and range of FEV₁ decline.

Why is Nicotine Addictive?

- Nicotine releases “gratification” producing chemicals in the brain.
- Long term use of nicotine produces changes in brain function and structure.
- Addictive properties are related to the rate of delivery to the brain.
Pharmacologic Aids for Smoking Cessation

- 35% of smokers attempt to quit each year
- Nicotine Replacement Therapy
- Bupropion: inhibits reuptake of dopamine and norepinephrine
- Varenicline: partial agonist-antagonist for nicotine receptor
- Vaccine: antigen-antibody complex
Spirometry Is a Useful Tool to Assess COPD Severity and Progression\textsuperscript{1,2}

<table>
<thead>
<tr>
<th>Stage</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity</td>
<td>$\text{FEV}_1/FVC &lt; 0.70$</td>
<td>$\text{FEV}_1/FVC &lt; 0.70$</td>
<td>$\text{FEV}_1/FVC &lt; 0.70$</td>
<td>$\text{FEV}_1/FVC &lt; 0.70$</td>
</tr>
<tr>
<td>Chronic cough and sputum production</td>
<td>$\text{FEV}_1 \geq 80%$ predicted</td>
<td>$50% \leq \text{FEV}_1 &lt; 80%$ predicted</td>
<td>$30% \leq \text{FEV}_1 &lt; 50%$ predicted</td>
<td>$\text{FEV}_1 &lt; 30%$ predicted or $\text{FEV}_1 &lt; 50%$ predicted plus chronic respiratory failure</td>
</tr>
<tr>
<td>Typical symptoms</td>
<td>Stage I symptoms + dyspnea</td>
<td>Progressive dyspnea</td>
<td>Stage III symptoms + respiratory failure, right heart failure, weight loss, arterial hypoxemia</td>
<td></td>
</tr>
</tbody>
</table>


Pharmacologic Therapy to Manage COPD

Bronchodilators Used in COPD

- Beta 2 Agonists (short acting)
  - Albuterol
  - Levalbuterol
  - Pirbuterol
- Anticholinergic (short acting)
  - Ipratropium bromide
- Fixed Combinations (short acting)
  - Albuterol/ipratropium bromide
## Bronchodilators Used in COPD

- **Beta 2 Agonists (long acting)**
  - Salmeterol (Serevent)
  - Formoterol (Foradil)
  - Arformoterol (Brovana)
  - Formoterol fumarate (Perforomist)
- **Anticholinergic (long acting)**
  - Tiotropium (Spiriva)
- **Fixed Combinations (long acting)**
  - Fluticasone/salmeterol (Advair)
  - Formoterol/budesonide (Symbicort)
- **Methylxanthines (Theophyllines)**
Inhaled Corticosteroids Used in COPD

- Fluticasone/Salmeterol (Advair 250/50)
- Budesonide/Formoterol (Symbicort 160/4.5)
### Comprehensive Treatment Approach to COPD

#### Treatment Goals
- Relieve symptoms
- Prevent disease progression
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality

#### Management Approach
- Smoking cessation
- Pharmacotherapy
- Nonpharmacologic interventions

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Nonpharmacologic Therapy to Manage COPD

- Smoking Cessation
- Patient Education
- Vaccination
- Pulmonary Rehabilitation
- Oxygen Therapy
- Surgical and Non-surgical Alternatives

Conclusions

• COPD is a leading cause of death in the U.S. and is on the rise

• COPD is a long-term, progressive disease

• Hyperinflation is an underlying physiological mechanism of activity-related breathlessness and subsequent activity limitation

• COPD can be identified early in its course, by assessing smoking history, age, and symptoms

• A comprehensive treatment approach to COPD management includes smoking cessation, pharmacotherapy, and nonpharmacological interventions
Questions?
And
Thank You!

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