COPD

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“You’ve come a long way, baby.”

Wayne McLaren…Former Marlboro Man

Age 30…a robust young man
Age 51…riding into the sunset

% Change in Age Adjusted Death Rate
US 1965-1998…gotta die of something

Other Sad Facts

- Direct Cost 2002- 18 Billion; Indirect Costs- 14 Billion
- WHO: 1 billion smokers worldwide…to increase to 1.6 billion 2025. Increasing in lower income areas
- It is expected to be the third leading cause of death by 2020

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Disease Trajectory of a Patients with COPD

New Definition
• Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease state characterised 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.

Risk Factors
• Smoke from home cooking and heating fuel
• Occupational dust and chemicals
• Gender: More common in men. M:F ratio is 5.2:2.7% (in India)
• Increasing age
• Others: Infection, nutrition and deficiency of α1 antitrypsin

Pathophysiology of COPD
• Increased mucus production and reduced mucociliary clearance - cough and sputum production
• Loss of elastic recoil - airway collapse
• Increase smooth muscle tone
• Pulmonary hyperinflation
• Gas exchange abnormalities - hypoxemia and/or hypercapnia

The Real Story
• Noxious particles and gases
  - Host factors
  - Anti-oxidants
  - Anti-proteinases
• Lung inflammation
• Oxidative stress
• Proteinases
• SUPH vasodilators
• COPD pathology
INFLAMMATION

Small airway disease
Airway Inflammation
Airway remodeling

Parenchymal destruction
Loss of alveolar attachments
Decrease of elastic recoil

AIRFLOW LIMITATION

COPD Patients

Stereotypical pictures of COPD patients

Blue Bloater
Pink Puffer

Physical signs

• Large barrel shaped chest (hyperinflation)
• Prominent accessory respiratory muscles in neck and use of accessory muscle in respiration
• Low, flat diaphragm
• Diminished breath sound

THE Guideline

• Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung and Blood Institute (NHLBI)

COPD classification based on spirometry

GOLD 2003

<table>
<thead>
<tr>
<th>Severity</th>
<th>Postbronchodilator FEV1/FVC</th>
<th>Postbronchodilator FEV1% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>At risk</td>
<td>&gt;0.7</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Mild COPD</td>
<td>&lt;0.7</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Moderate COPD</td>
<td>&lt;0.7</td>
<td>50-80</td>
</tr>
<tr>
<td>Severe COPD</td>
<td>≤0.7</td>
<td>30-50</td>
</tr>
<tr>
<td>Very severe COPD</td>
<td>≤0.7</td>
<td>&lt;30</td>
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</table>

SPIROMETRY is not to substitute for clinical judgment in the evaluation of the severity of disease in individual patients.

Stage 0 At Risk

• Normal spirometry
• +/- Chronic symptoms (cough, sputum, production)
Stage I  Mild COPD

- FEV1/FVC <70%
- FEV1 >80% predicted
- With or without chronic symptoms (cough, sputum production)

Stage II  Moderate COPD

- FEV1/FVC <70%
- 50% <FEV1 <80% predicted
- With or without chronic symptoms (cough, sputum production)

Stage III  Severe COPD

- FEV1/FVC <70%
- 30% <FEV1 <50% predicted
- With or without chronic symptoms (cough, sputum production)

Stage IV  Very Severe COPD

- FEV1/FVC <70%
- FEV1 <30% predicted or FEV1 <50% predicted plus chronic respiratory failure

Key Indicators for COPD Diagnosis

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic cough</td>
<td>Present intermittently or every day; often present throughout the day, seldom only nocturnal</td>
</tr>
<tr>
<td>Chronic sputum production</td>
<td>Present for many years, worst in winters. Initially mucoid – becomes purulent with exacerbation</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Progressive, Persistent (present every day)</td>
</tr>
<tr>
<td>History of exposure to risk factors</td>
<td>Tobacco smoke (including beedi), occupational dusts and chemicals, smoke from home cooking and heating fuel</td>
</tr>
</tbody>
</table>

Assess: Who Has Early Stages And Who Do You Test?

- Test patients with:
  - chronic cough and sputum
  - exposure to risk factors
  - even if no dyspnea
- Early Stage:
  - airflow limitation that is not fully reversible
  - with or without the presence of symptoms
**Spirometry**
- Diagnosis
- Assessing severity
- Assessing prognosis
- Monitoring progression

**Assess: Additional Investigations > Stage II: Moderate COPD**
- Bronchodilator reversibility testing
  - rule out asthma
  - establish best attainable lung function
  - gauge a patient’s prognosis
  - guide treatment decisions
- Chest x-ray
  - seldom diagnostic unless obvious bullous disease
  - valuable in excluding alternative diagnoses
  - CT not routinely recommended

**Multiple Factors Lead to Hyperinflation and Air Trapping**
- Low, Flattened Diaphragm
- Increased A-P Diameter

**Assess: Additional Investigations > Stage II: Moderate COPD**
- Arterial blood gas measurement
  - In advanced COPD: FEV1 <40% predicted or signs suggestive of respiratory failure or right heart failure
  - central cyanosis, ankle swelling, JVD
  - Respiratory failure
    - PaO2 < 60 mm Hg +/- PaCO2 >50 mm Hg
  - Alpha-1 antitrypsin deficiency screening
    - COPD at a young age
    - strong family history of the disease

**Differential Diagnosis**
- A major differential diagnosis is asthma
- In some patients with chronic asthma, a clear distinction from COPD is not possible
- In these cases, current management is similar to that of asthma
- Other potential diagnoses are usually easier to distinguish from COPD

**COPD**
- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history
- Dyspnea during exercise
- Largely *irreversible* airflow limitation
Asthma

- Onset early in life (often childhood)
- Symptoms vary from day to day
- Symptoms at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma
- Largely reversible airflow limitation

Congestive Heart Failure

- Fine basilar crackles on auscultation
- Chest x-ray shows dilated heart, pulmonary edema
- PFTs indicate restriction- not obstruction
- BNP can help

Other Diff Dx to Consider

- Bronchiectasis
  - Large volumes of purulent sputum
  - Bacterial infection
  - CXR/CT shows bronchial dilation, bronchial wall thickening
- TB
  - History with the usual suspects

Monitoring: This is a progressive disease

- Lung function worsens over time- even with best care
- Monitor symptoms and objective measures of airflow limitation to determine when to adjust therapy
- Spirometry should be performed if there is a substantial increase in symptoms or a complication
- ABG should be considered in all patients with an FEV1 <40% predicted or clinical signs of respiratory failure or right heart failure (JVD/edema)

Reduce Risk Factors

- Reducing exposure to tobacco smoke, occupational dusts, and chemicals, and indoor and outdoor air pollutants
- Smoking cessation is the single most effective -- and cost-effective -- intervention to reduce the risk of developing COPD and stop its progression (Evidence A)
Smoking Cessation
Physician Interventions

- Ask about tobacco use at every visit
- Advise all smokers to quit
- Assess smokers readiness to quit
- Assist the patient in quitting
- Arrange follow up visit

Manage Stable COPD
Key Points 1

- Stepwise increase in treatment based on disease severity
- Health education can play a role in improving skills, ability to cope with illness, and health status. It is effective in accomplishing certain goals, including smoking cessation (Evidence A).
- None of the existing medications for COPD affects long-term decline in lung function that is the hallmark of this disease (Evidence A).
- Pharmacotherapy for COPD is used to decrease symptoms and/or complications

Manage COPD Key Points

- Add inhaled steroids to bronchodilators for symptomatic COPD patients with an FEV1 <50% predicted (Stage III: Severe COPD and Stage IV Very Severe COPD) and repeated exacerbations (Evidence A)
- Avoid chronic treatment with systemic steroids - unfavorable benefit-to-risk ratio (Evidence A)

Manage COPD Key Points 2

- The long-term O2 with chronic respiratory failure increases survival (Evidence A)
- Improves exercise tolerance
- If hypercapnic titrate SpO2 to 88-90%
- Walk your clinic patients if RA SpO2 OK
**Manage COPD Key Points 3**

- All COPD patients benefit from exercise training program
- Improves both exercise tolerance and symptoms of dyspnea and fatigue (Evidence A)

**Management of COPD**

- Smoking cessation
- Pulmonary rehabilitation
- Pharmacologic
- Supplemental oxygen
- Non-invasive ventilation
- Surgical remedies

**Medications**

**Pharmacotherapy for Stable COPD**

**Bronchodilators**

- Short-acting $\beta_2$-agonist – Salbutamol
- Long-acting $\beta_2$-agonist – Salmeterol and Formoterol
- Anticholinergics – Ipratropium, Tiotropium
- Methylxanthines – Theophylline

**Steroids**

- Oral – Prednisolone
- Inhaled – Fluticasone, Budesonide

**How Do Bronchodilators Work?**

- Reverse the increased bronchomotor tone
- Relax the smooth muscle
- Reduce the hyperinflation
- Improve breathlessness

“Bronchodilator medications are central to the symptomatic management of COPD”

**GOLD Report 2003**
Bronchodilators
Beta2-agonists

- Short-acting
  - Fenoterol
  - Salbutamol (albuterol)
  - Terbutaline
- Long-acting
  - Formoterol
  - Salmeterol

Anticholinergics

- Mode of Action
  - Cholinergic tone is only reversible component of COPD
  - Normal airway have small degree of vagal cholinergic tone

- Short-acting
  - Ipratropium bromide
  - Oxitropium bromide

- Long-acting
  - Tiotropium

Mode of Action

- Airways are narrowed in COPD therefore vagal cholinergic tone has greater effect on airway resistance ($\text{Resistance} \propto 1/\text{radius}^4$)
- Therefore, the need for anticholinergic drugs that will act as muscarinic receptor antagonist and block the acetylcholine induced bronchoconstriction

Bronchodilators-Methylxanthines

- Methylxanthines
  - Aminophylline (slow release preparations)
  - Theophylline (slow release preparations)
  - RARELY OF SIGNIFICANT BENEFIT
  - LEVEL 8-12 mcg/ml

"All guidelines recommend inhaled bronchodilator as first line therapy. The ATS suggest initial therapy with an anticholinergic drug if regular therapy is needed”


Drugs of Today 2002; 38(9): 585-600
LA Bronchodilators in COPD

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Lung function</th>
<th>Symptoms</th>
<th>Exercise tolerance</th>
<th>Decrease exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmeterol</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Formoterol</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>+++</td>
<td>++</td>
<td>?</td>
<td>++</td>
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Other Med Adjuncts?

- Influenza vaccines significantly reduce serious illness and death (Evidence A)
- Pneumococcal vaccine – OK to use but data lacking (Evidence B)
- **Antibiotics**: other than treating infectious exacerbations not recommended (Evidence A)
- **Mucolytic Agents**: a few patients with viscous sputum may benefit but widespread use cannot be recommended (Evidence D)
- **Antitussives**: Cough, a troublesome symptom in COPD, has a protective role. Regular use of antitussives contraindicated (Evidence D)
- **Narcotics**: The use of PO and IV opioids effective for dyspnea in advanced disease

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Therapy by Stage- Pretty Simple

- “Make everything as simple as possible, but not one bit simpler”
  Einstein

Manage Exacerbations

- Do you admit? You and your patient decide… little guidance in the literature

Manage Exacerbations 1

- Infection of tracheobronchial tree and air pollution are most common causes
- Cause of about 1/3 of severe exacerbations cannot be identified
Manage Exacerbations 2

- (Evidence A) treatment
  - Inhaled bronchodilators (beta2-agonists and/or anticholinergics)
  - Systemic, preferably oral, glucocorticosteroids
- (Evidence B) Antibiotic treatment if signs of airway infection
  - increased volume/change of color of sputum
  - fever
- O2 of course but caution with retainers
- Little evidence for Methylnxanthines

Manage Exacerbations 3

- Noninvasive intermittent positive pressure ventilation (NIPPV) improves blood gases and pH, reduces in-hospital mortality, decreases the need for invasive mechanical ventilation and intubation, and decreases the length of hospital stay (Evidence A)
- BIPAP is Best!
  - Set FiO2, inspiratory (IPAP) and expiratory (EPAP)
  - Difference between IPAP and EPAP augments tidal volume and improves minute ventilation
  - CO2 gets blown off

Noninvasive Ventilation

Stable outpatient management
Acute exacerbation treated in hospital
increases pH
reduces PaCO2
reduces breathlessness first 4 hours of Rx
reduces length of hospital stay
reduces intubation rate

Indications for O2 Therapy

- PaO2 55 mmHg or less
- PaO2 56 – 59 mmHg with complication, such as erythrocytosis or cor pulmonale
- SaO2 88% or less

Volume Reduction Surgery

A procedure in which 20-30% of the most diseased portions of the lung are removed
- Reduces lung hyperinflation
- Dilates bronchi by increased traction forces
- Places diaphragm at better mechanical advantage

Volume Reduction Surgery Outcomes

- Improved dyspnea index scores
- Improved elastic recoil of the lung
- Decreased residual volume and FRC
- Decreased PaCO2
- Improved FEV1
- Improved 6-minute walk distance
Lung Transplantation

Over 1500 lung transplants/year in the United States
4000 candidates awaiting transplant in the US late 2003
Provides significant improvement in both health-related and overall quality of life

Lung transplantation

Inclusion Criteria
- Life expectancy less than 3 years
- Failure of medical therapy
- Age less than 60 years
- No extrapulmonary organ failures

Lung Transplantation Exclusion Criteria
- Coronary artery disease
- Continuing substance abuse
- Inadequate psychosocial support
- Extreme cachexia or obesity
- Recent malignancy (<5 years)
- Long term, high dose corticosteroid use