Asthma and Chronic Obstructive Pulmonary Disease (COPD)
Diagnostic and management fundamentals
Preston Seaberg, M.D.
Learning Objectives

• Contrast pathophysiology of asthma and COPD
• Recite diagnostic criteria for asthma and COPD
• Create a management plan for a patient with asthma, COPD or asthma-COPD overlap syndrome
• Identify the interventions associated with improved or worsened mortality in those with asthma or COPD
Overall, Things are Better Today than in the Past

• Preventable deaths decreasing!
• Extreme poverty decreasing!
  • More manufacturing, roads, cars
• But with these, more pollution
COPD: It’s Even Worse than I Thought

- Year 2000, COPD 4th leading cause of death
- Year 2016: COPD 3rd leading cause of death
  - > 3 million COPD deaths globally
- In all but low-income countries, now a leading cause of death

Source: WHO
Pathophysiology of Asthma

- Bronchial inflammation
  - Generally, the cells involved in allergic response

- Bronchial hyper-responsiveness
  - Inhaled stimuli and cell-based mediators (e.g., histamine)
  - Dust, fumes, allergens, exercise, extreme temperatures, respiratory infections

- Result: airflow limitation, most pronounced in expiration, generally with high degree of reversibility with bronchodilators
  - Plus, 12-fold risk of developing COPD

Source: GINA, GOLD
Pathophysiology of COPD

- Repetitive or chronic insults
  - Inhalational exposure (e.g. cigarette smoke)
  - Chronic inflammation
  - Protease activity (e.g. alpha 1-antitrypsin deficiency)

- Causing some mixture of
  - Airway fibrosis and narrowing
  - Alveolar wall destruction
  - Goblet cell hyperplasia
  - Ciliary impairment

- Resulting in airflow limitation poorly responsive to bronchodilators
  - +/- hypoxia, hypercapnia, or increased pulmonary vascular resistance

Source: GOLD
Clinical Presentation of Asthma or COPD

• Chronic cough
• Wheeze
• Dyspnea, especially on exertion
• Recurrent lower respiratory tract infections (COPD > asthma)
• Increased perceived severity of respiratory tract infections
• Variability in symptom severity (asthma >> COPD)
Diagnosis of Asthma and COPD

Spirometric diagnosis with symptoms

There is no substitute

...but let us try to find one!
Can Airflow Limitation be Diagnosed Without Spirometry? (1/2)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Likelihood of Airflow Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well 54-year-old US man with wheezing</td>
<td>21%</td>
</tr>
<tr>
<td>Well 54-year-old US man with 19 pack-years of cigarette smoking</td>
<td>6%</td>
</tr>
<tr>
<td>Well 54-year-old US man, 41 pack-years of cigarette smoking, in the US</td>
<td>60%</td>
</tr>
<tr>
<td>As above, but in Southeast Asia*</td>
<td>55%</td>
</tr>
<tr>
<td>As above, but in Africa*</td>
<td>68%</td>
</tr>
<tr>
<td>70-year-old wheezing man with 55 years of cigarette smoking and maximum laryngeal height of 3.8 cm</td>
<td>99%</td>
</tr>
</tbody>
</table>

Note: establishing presence of airflow limitation is only the first step. Plus, even among heavy smokers, < 50% will develop COPD.
Can Airflow Limitation be Diagnosed Without Spirometry? (2/2)

<table>
<thead>
<tr>
<th>Single Best Findings That Are the Easiest to Measure</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status, &gt; 40 pack-years</td>
<td>12</td>
</tr>
<tr>
<td>Auscultated wheezing or laryngeal height ≤ 4 cm</td>
<td>×4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>To “Rule In” Obstructive Disease, Must Use a Multivariate Model</th>
<th>Posterior Odds of Disease, Probability (%)</th>
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<tbody>
<tr>
<td>Smoking &gt; 55 y and wheezing symptoms and auscultated wheezing</td>
<td>156 (99)</td>
</tr>
<tr>
<td>History of OAD and smoking &gt; 40 pack-years and age ≥ 45 y and laryngeal height ≤ 4 cm</td>
<td>220 (99)</td>
</tr>
</tbody>
</table>

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<th>To “Rule Out” Obstructive Disease, Must Use a Multivariate Model</th>
<th>Posterior Odds of Disease, Probability (%)</th>
</tr>
</thead>
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<tr>
<td>Smoking &lt; 30 y and no wheezing symptoms and no auscultated wheezing</td>
<td>0.02 (1.5)</td>
</tr>
<tr>
<td>No history of OAD and smoking &lt; 40 pack-years and age &lt; 45 y and laryngeal height &gt; 4 cm</td>
<td>0.03 (3)</td>
</tr>
</tbody>
</table>

Note: establishing presence of airflow limitation is only the first step

Simel DL and Keitz S (2009)
Diagnosis of Asthma and COPD

- Consider other causes of similar symptoms
  - Lung cancer
  - Chronic infections (e.g. tuberculosis)
  - Congestive heart failure
  - Interstitial lung disease
  - For cough, upper airway cough syndrome, gastroesophageal reflux disease or medications

- Spirometry for chronic, bothersome symptoms
  - No role for spirometry if no symptoms!
Diagnosing Asthma or COPD

- FEV1/FVC ratio < 70% of predicted = airflow obstruction
  - Forced expiratory volume over 1 second (FEV₁)
  - Forced vital capacity (FVC)
  - Reference values by age, height, sex, race
  - Persistent limitation after bronchodilator: COPD
- FEV₁ improves ≥12% and ≥ 200 mL after bronchodilator: asthma
Pitfalls

- Restrictive disease
- Poor quality study
- Intermittent obstruction

Source: MKSAP 18
Notes on Airway Obstruction

Flow-volume loops in upper airway obstruction

(A) Normal flow-volume loop: the expiratory portion of the flow-volume curve is characterized by a rapid rise to the peak flow rate, followed by a nearly linear fall in flow. The inspiratory curve is a relatively symmetrical, saddle-shaped curve.

(B) Fixed upper airway obstruction (can be intrathoracic or extrathoracic): flow limitation and flattening are noted in both the inspiratory and expiratory limbs of the flow-volume loop.

(C) Dynamic (or variable, nonfixed) extrathoracic obstruction: with flow limitation and flattening are noted on the inspiratory limb of the loop.

(D) Dynamic (or variable, nonfixed) intrathoracic obstruction: flow limitation and flattening are noted on the expiratory limb of the loop.

Aboussouan LS and Stoller JK. “Flow-volume loops.” In: UpToDate, Barnes PJ and Wood RA (Eds), UpToDate, Waltham, MA, 2019.
Special Asthma Variants

- Allergic variant: high sputum eosinophils, high exhaled nitric oxide
  - If refractory, anti-IgE, anti-IL4 or anti-IL5 treatment may be considered

- Cough variant asthma

- Exercise-induced asthma
  - Give $\beta_2$-agonists prior to exercise

- Occupational asthma

- Aspirin-exacerbated respiratory disease

- Reactive airways dysfunction syndrome
  - New, persistent (3 months or longer) asthma symptoms after intense inhalational exposure

- Allergic bronchopulmonary aspergillosis
  - High IgE, Aspergillus hypersensitivity, imaging findings
  - Treat with steroids ± antifungals
Chronic Cough with Normal Spirometry

- Spirometry after “provoking” with exercise, cold air, or methacholine (known as “bronchoprovocation”)
- Chest radiograph, especially if at risk for lung cancer or indolent infection (e.g. TB)
- Exclude medication side effect (e.g. ACE inhibitors)
- Consider empiric, stepwise treatment
  - Upper airway cough syndrome: nasal corticosteroid
  - Gastroesophageal reflux disease: PPI or H₂ blocker
  - If no bronchoprovocation, could trial asthma treatment
Asthma/COPD Pharmacotherapy

Acronyms

- SABA = short-acting β₂-agonist (e.g. albuterol)
- SAMA = short-acting muscarinic antagonist (e.g. ipratropium)
- LABA = long-acting β₂-agonist (e.g. salmeterol)
- LAMA = long-acting muscarinic antagonist (e.g. tiotropium)
- LTRA = leukotriene receptor antagonist (e.g. montelukast)
- ICS = inhaled corticosteroid (e.g. beclomethasone)
- OCS = oral corticosteroid (e.g. prednisone)
Asthma Treatment

Most adults and adolescents start at step 2

Reference: GINA
Special Note

• Don’t use LABA without concomitant ICS
  • Associated with higher risk of asthma-related death
GINA Questionnaire to Assess Asthma Control

• In the past 4 weeks, as the patient had:
  • Daytime symptoms more than 2x/week?
  • Any night waking due to asthma?
  • SABA reliever needed more than 2x/wk?
  • Any activity limitation due to asthma?

• None of these: well controlled
• 1-2 of these: partly controlled
• 3-4 of these: uncontrolled
Evaluation of Uncontrolled Asthma

• First, verify inhaler technique
• Next, evaluate for triggers – “AIR-SMOG”
  • Allergens
  • Irritants/infection
  • Rhinitis/sinusitis
  • Smoking/sleep apnea/stress
  • Medications (β-blockers, NSAIDs)
  • Occupational exposure
  • Gastroesophageal reflux disease
Step Up Asthma Treatment if Truly Uncontrolled

• First, verify inhaler technique and adherence
• Next, control triggers
• Next, step up therapy
  • If symptoms are severe, step up therapy while addressing the other components
Asthma Action Plan for Exacerbations

• Early and mild:
  • Increase use of reliever (e.g. albuterol)
  • Increase controller (quadruple dose)
  • Review response
Asthma Action Plan for Exacerbations

• Late or moderate
  • Peak expiratory flow or FEV1 < 60% of patient’s best
  • No improvement after 48 hours
  • Steps:
    • Continue reliever
    • Continue controller
    • Add prednisone or prednisolone 40-50 mg daily (adults; weight-based in children)
    • Evaluation by clinician
Treating Asthma Exacerbations in Clinic

• No tachypnea, hypoxia, increased work of breathing
  • Administer 4-10 puffs of short-acting $\beta_2$-agonist by metered dose inhaler+spacer, or nebulizer
  • If improving, can return home with close follow-up
  • If not improving, transfer to acute care facility
Treating Severe Asthma Exacerbations

• Tachypnea, hypoxia, increased work of breathing or decreased level of consciousness
  • Transfer to acute care facility
  • Nebulized bronchodilators, systemic corticosteroid, possibly IV magnesium sulfate, intensive care interventions if indicated
Asthma Treatments in Pregnancy

- Oral and inhaled corticosteroids
- Short- and long-acting $\beta_2$-agonists
- Leukotriene receptor antagonist antagonists

- No evidence of fetal harm for any of above
Principles of COPD Management

• **Smoking cessation**

• **Minimization of particulate exposure**
  - Indoor open fires, poorly functioning stove
  - Occupational dusts or fumes

• **Protect from infections**
  - Influenza virus, pneumococcus (PPSV-23 ± PCV-13)

• **Treatment intensity depends on symptoms, risk of exacerbations**

• **Pulmonary rehabilitation, if available**

• **Supplemental oxygen, if candidate**
Address Smoking at Each Visit

• One study in Nigeria
  • 70% of patients with COPD were smoking
  • 32% were counseled on smoking cessation

Desalu et al (2013)

• Counseling improves quit rates

• Use nicotine replacement therapy, pharmacotherapy or a combination
  • Varenicline, bupropion are main medications
## GOLD Grading: Spirometry

<table>
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<tr>
<th>Condition</th>
<th>Severity</th>
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</thead>
<tbody>
<tr>
<td>FEV1 ≥ 80%</td>
<td>Mild</td>
</tr>
<tr>
<td>FEV1 &lt;80% and ≥ 50%</td>
<td>Moderate</td>
</tr>
<tr>
<td>FEV1 &lt;50% and ≥ 30%</td>
<td>Severe</td>
</tr>
<tr>
<td>FEV1 &lt;30%</td>
<td>Very Severe</td>
</tr>
</tbody>
</table>

A single FEV1 has low predictive value for exacerbations. A decreasing FEV1 has more predictive value.
GOLD Staging: Symptoms and Exacerbations

- mMRC 0: breathless with strenuous exercise only
- mMRC 1: breathless when hurrying on level ground, or when walking up slight incline
- mMRC 2: must walk more slowly than peers, or breathless walking at own pace
- mMRC 3: breathless walking 100 m
- mMRC 4: breathless dressing

- Low risk: 0-1 exacerbation in one year
- High risk: 2+ exacerbations in one year
Pharmacotherapy for Stable COPD

LABA-ICS or LABA-LAMA + pulm rehab

≥2 exacerbations*

LABA-LAMA + ICS + pulm rehab + macrolide? + roflumilast?

Pharmacological treatment

Bronchodilator(s) ± anti-inflammatory

Bronchodilator(s) only

LABA and/or LAMA and pulmonary rehabilitation

ICS risky if frequent infections or history of mycobacterial infection

Reference: GOLD
COPD Medications that Reduce Mortality?

• Just one, but only for some

• Supplemental oxygen indications:
  • Resting SpO2 < 90% with right heart failure or erythrocytosis, or
  • Resting SpO2 < 89% without right heart failure
    • Mortality benefit really for those with resting SpO2 < 81%
Treatment of COPD Exacerbation

• Nonsevere: bothersome symptoms without decompensation
  • Alert
  • Minimal if any tachypnea
  • Minimal change in SpO2 from baseline
  • Any one of these:
    • Increased dyspnea
    • Increased sputum volume
    • Increased sputum production

• Treat nonsevere exacerbations at home (or possibly hospital)
  • SABA ± SAMA every 4-6 hours and as needed
  • Steroids: 5 days of prednisone 40 mg daily
  • Antibiotics: only if evidence of pneumonia
Treatment of COPD Exacerbation

• Severe: respiratory failure, or any two of
  • Increased dyspnea
  • Increased volume of sputum
  • Increased purulence of sputum

• Treat severe exacerbations in hospital:
  • SABA ± SAMA every 4-6 hours and as needed
  • Steroids: 5 days of prednisone 40 mg daily
    • Occasionally (but not often) longer and more
  • Antibiotics: ceftriaxone or levofloxacin
    • Cefepime or piperacillin-tazobactam if risk of drug-resistant organisms
  • Respiratory failure
    • CPAP or BiPAP if awake
    • Intubation and mechanical ventilation if obtunded
  • Nonresolving: consider pulmonary embolism
Asthma-COPD Overlap Syndrome (ACOS)

- **Major Criteria (need 2)**
  - Positive bronchodilator response (FEV1 ≥15% and ≥400 ml)
  - Sputum eosinophilia
  - Personal history of asthma

- **Minor Criteria (need 2)**
  - High total IgE
  - Personal history of atopy
  - Positive bronchodilator (FEV1 ≥12% and ≥200 ml)

- **Reach for ICS earlier here than for those with COPD alone**
  
  Soler-Cataluna et al. Archivos de Bronconeumologia 2012; 48(9).
Advanced COPD

- Severe symptoms despite optimal medications
- Numerous exacerbations despite optimal medications
- Consider procedural treatments, if available
- Consider specialty palliative care ± hospice, if available
  - Opioids may be used for dyspnea
Procedural Treatment Options for Severe Disease

- Bronchial thermoplasty for severe, refractory asthma
  - Radiofrequency ablation of airway smooth muscle
  - Only if FEV$_1$ > 60%
  - Recommended in context of clinical trial
  - Quality of life purposes

- Lung volume reduction surgery for some with severe, refractory COPD
  - Only for very carefully selected patients
  - Quality of life purposes

- Lung transplantation
  - Only for very carefully selected patients
  - Potential to improve quality and length of life
Summary
Diagnosing Asthma or COPD

- FEV1/FVC ratio < 70% of predicted = airflow obstruction
  - Forced expiratory volume over 1 second (FEV₁)
  - Forced vital capacity (FVC)
  - Reference values by age, height, sex, race
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Pharmacotherapy for Stable COPD

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≥2 exacerbations*  
0 or 1 exacerbation

SABA and/or SAMA

LABA and/or LAMA and pulmonary rehabilitation

ABC assessment

LABA-LAMA + ICS + pulm rehab + macrolide? + roflumilast?

Pharmacological treatment

Bronchodilator(s) ± anti-inflammatory

Bronchodilator(s) only

ICS risky if frequent infections or history of mycobacterial infection

Reference: GOLD
Asthma Action Plan for Exacerbations

• Increase use of reliever (e.g. albuterol)
• Quadruple dose of controller
• Add oral corticosteroids if no improvement, or if severe
  • Prednisone 40 mg daily reasonable to start
  • Duration less clear than in COPD, and based on symptoms
    • 5-14 days, typically
Treatment of COPD Exacerbation

- Nonsevere: bothersome symptoms without decompensation
- Severe: two cardinal manifestations or clinical decompensation
- Treat nonsevere exacerbations at home (or possibly hospital)
- SABA ± SAMA every 4-6 hours and as needed
- Steroids: 5 days of prednisone 40 mg daily
- Antibiotics:
  - Nonsevere exacerbation: only if evidence of pneumonia
  - Any severe exacerbation
- CPAP or BiPAP if awake with respiratory failure
- Intubation with mechanical ventilation if respiratory failure and obtunded
References (1/2)


- Inhaled corticosteroid doses for NICE’s asthma guideline. https://www.nice.org.uk/guidance/ng80/resources/inhaled-corticosteroid-doses-pdf-4731528781


References (2/2)
