## **COPD: Differential Diagnosis**

## **Educational Objectives**

At the end of this presentation, the learner should be able to ...

- Describe constellation of symptoms and evaluation leading to consideration of chronic obstructive pulmonary disease (COPD) as diagnosis.
- Delineate modifiable and non-modifiable risk factors for chronic obstructive pulmonary disease.
- Understand diagnostic criteria for COPD.
- Describe other diseases that need to be considered in the workup of a patient with dyspnea, chronic cough, and sputum production.

## Differential Diagnosis

- Evaluation
- Risk Factors
- Diagnostic Criteria
- Other Conditions to Consider

Assessment of symptoms

- Severity of breathlessness, cough, sputum production, wheezing, chest tightness, weight loss or anorexia
- Change in alertness or mental status, fatigue, confusion, anxiety, dizziness, pallor or cyanosis
- COPD should be considered in any patient with a chronic cough, dyspnea or sputum production

Assessment of symptoms

- Severity of breathlessness, cough, sputum production, wheezing, chest tightness, weight loss or anorexia
- Change in alertness or mental status, fatigue, confusion, anxiety, dizziness, pallor or cyanosis
- COPD should be considered in any patient with a chronic cough, dyspnea or sputum production

### **Medical History**

- Allergies
- Sinus problems
- Other respiratory disease
- Risk factors
- Exposures (occupational and environmental)
- Family history
- Co-morbidities that may affect activity
- Medications
- Prior hospitalizations or evaluation to date

- Vital Signs
  - Respiratory rate, pattern, effort
  - Pulse oximetry
- Extremities
  - Inspection for cyanosis
- Chest
  - Inspection to assess AP diameter (barrel chest)
  - Palpation and percussion of chest
- Lungs
  - Auscultation for wheezing, crackles, and/or decreased breath sounds

Stephens, 2008

### Question

The differential diagnosis of COPD should be considered in patients who present with which of the following symptoms?

- A. Chronic cough
- B. Any sputum production
- C. Dyspnea
- D. Increased sputum production
- E. All of the above

## **Differential Diagnoses**

### Pulmonary

- Asthma
- Bronchogenic carcinoma
- Bronchiectasis
- Tuberculosis
- Cystic fibrosis
- Interstitial lung disease
- Bronchiolitis obliterans
- Alpha-1 antitrypsin deficiency
- Pleural effusion
- Pulmonary edema
- Recurrent aspiration
- Tracheobronchomalacia
- Recurrent pulmonary emboli
- Foreign body

### Non-pulmonary

- Congestive Heart Failure
- Hyperventilation syndrome/panic attacks
- Vocal cord dysfunction
- Obstructive sleep apnea undiagnosed
- Aspergillosis
- Chronic Fatigue Syndrome



### Question

Which of the following is the most appropriate to use to confirm the diagnosis of COPD?

- A. Chest X-ray
- B. Arterial blood gas
- C. Spirometry
- D. High resolution CT scan of chest
- E. Clinical examination

Studies that may help in diagnosis:

- Chest X-ray (SOR: C)
- Spirometry (SOR: C)
- Arterial blood gas (SOR: C)
- Alpha-1 antitrypsin levels (SOR: C)
- High resolution CAT scan of chest (SOR: C)

SOR: Strength of Recommendation

Stephens, 2008

Spirometry

- Gold standard for diagnosis
- Standard to establish severity and stage
- Perform both pre- and post-bronchodilator
  - Irreversible airflow limitation is the hallmark of COPD

- Smoking
  - Major risk factor (duh!)
  - Risk increases with number of pack years smoked
  - Secondhand smoke in large amounts presents risk
- Environmental pollution
  - Smog and exhaust from vehicles
  - Smoke from burning wood or other biomass fuels
  - Particulates in occupational dust

### **Occupational Irritants**

**Occupation** Irritant Agricultural worker Coal miner Concrete worker **Construction worker** Dust Gold miner Silica Hard rock miner Rubber worker

Endotoxin Coal dust Mineral dust Dust Silica Mineral dust Industrial chemicals

Nonmodifiable Risk Factors

- Gender (Risk about equal in men and women)
  - Attributed to smoking habits of both genders
- Age
  - Develops slowly
  - Most people  $\geq$  40 years old when symptoms start
- Alpha-1 antitrypsin deficiency
  - Mostly Northern European heritage
  - Rare cause (2% of COPD population)

Additional risk factors

- Severe lung infections as a child
- Previous tuberculosis
- Gastroesophageal reflux disease
  - Possible cause as recurrent irritant
  - May worsen COPD
- Lower socioeconomic status

Global Initiative for Chronic Obstructive Lung Disease (GOLD) Criteria

- Program to provide guidelines for management of COPD; started 1998; international effort.
- Consider COPD in any patient with following:
  - Dyspnea
  - Chronic cough or sputum production and/or
  - Exposure to risk factors

GOLD Criteria (continued)

- Symptoms and risk factors are not diagnostic in themselves but should prompt spirometry in patients >40 yrs of age
- Diagnosis should be confirmed by pre- and postbronchodilator spirometry

### **Key Indicators**

- Dyspnea
  - Progressive, usually worse with exercise, persistent, described as increased effort to breathe
- Chronic cough
  - May be intermittent, may be nonproductive
- Chronic sputum production
  - Any pattern
- History of exposure to risk factors
  - Tobacco smoke, occupational dust, chemicals, fumes or smoke from cooking or heating fuels

### Spirometry Classification for COPD

Stage	FEV1:FVC	FEV1
1: Mild	<0.70	≥80% of predicted value
2: Moderate		50% to 79% of predicted value
3: Severe		30% to 49% of predicted value
4: Very severe		<30% of predicted value OR <50% of predicted value with chronic respiratory failure

Adapted from GOLD, 2009

## **Differential Diagnoses**

#### Pulmonary

- Asthma
- Bronchogenic carcinoma
- Bronchiectasis
- Tuberculosis
- Cystic fibrosis
- Interstitial lung disease
- Bronchiolitis obliterans
- Alpha-1 antitrypsin deficiency
- Pleural effusion
- Pulmonary edema
- Recurrent aspiration
- Tracheobronchomalacia
- Recurrent pulmonary emboli
- Foreign body

#### Non-pulmonary

- Congestive heart failure
- Hyperventilation syndrome/panic attacks
- Vocal cord dysfunction
- Obstructive sleep apnea (undiagnosed)
- Aspergillosis
- Chronic fatigue syndrome

Stephens, 2008

### Asthma

- Episodic symptoms of airflow obstruction or airway hyper-responsiveness
- Airflow obstruction partially reversible by spirometry
- Characterized by reversibility and variability in symptoms and airflow
- Alternative diagnosis excluded by history and exam

Global Initiative for Asthma (GINA) Report, 2009

Asthma – Key indicators

- Cough, worse particularly at night
- Recurrent wheezing, chest tightness or difficulty breathing
- Wheezing on physical examination
- Symptoms that occur or worsen in presence of known triggers
- Symptoms that occur/worsen at night

Asthma – Spirometry

- Establishes diagnosis of asthma
- Perform when key indicators present
- Demonstrates obstruction and assesses for reversibility
  - Reversibility defined as >12% increase in FEV1 from baseline

NHLBI/NIH NAEP Guidelines, 2007

### Asthma – Similarities with COPD

- Major epidemiologic causes of chronic obstructive airway disease
- Involve underlying airway inflammation
- Can cause similar chronic respiratory symptoms and fixed airflow limitation
- Can co-exist with the other making diagnosis more difficult

Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2009 Global Initiative for Asthma (GINA) Report, 2009

Asthma – Differences from COPD

- Underlying immune mechanism of chronic inflammation different
- Age of onset
  - Earlier in life with asthma
  - Usually > age 40 in COPD
- Symptoms in asthma vary; COPD slowly progressive
- Smoking associated with COPD
- Asthma with reversible airflow limitation; irreversible airflow limitation in COPD

Asthma –

Using spirometry to differentiate from COPD

- Post-bronchodilator FEV1 <80% predicted together with FEV1/FVC <0.70 confirms airflow limitation that is not fully reversible
- Asthma may show similar changes in chronic and more severe cases; PFT's may be needed to distinguish it from COPD

NHLBI/NIH Asthma Guidelines , 2007

# Clinical Features in Differentiating COPD from Asthma

<b>Clinical Feature</b>	COPD	Asthma
Age	Older than 35 years	Any age
Cough	Persistent, productive	Intermittent, usually nonproductive
Smoking	Typical	Variable
Dyspnea	Progressive, persistent	Variable
Nocturnal symptoms	Breathlessness, late in disease	Coughing, wheezing
	Adapted with pe	ermission from Stephens, 2008

# Clinical Features in Differentiating COPD from Asthma (continued)

<b>Clinical Feature</b>	COPD	Asthma
Family history	Less common	More common
Atopy	Less common	More common
Diurnal symptoms	Less common	More common
Spirometry	Irreversible airway limitation	Reversible airway limitation

Adapted with permission from Stephens, 2008

### **Heart Failure (HF)**

Characteristics	Midlife to late-life onset; associated with risk factors such as hypertension and coronary artery disease
Clinical presentation	Fatigue, exertional and paroxysmal nocturnal dyspnea, and peripheral edema, crackles on auscultation
Pulmonary function test	Decreased DLCO, predominantly used to exclude other diagnoses

### Heart Failure (HF, continued)

Chest radiography	Increased heart size, pulmonary vascular congestion, pleural effusions
Other recommended testing	Echocardiography, BNP measurement, electrocardiography; cardiac catheterization in selected patients

### **Bronchiectasis**

Characteristics	Usually midlife onset; progressive with exacerbations
Clinical presentation	Productive cough with large volumes of thick, purulent sputum; dypsnea; and wheezing associated with bacterial infections, crackles, and clubbing on exam
Pulmonary function test	Obstructive airflow limitation, both fixed and reversible

### **Bronchiectasis (continued)**

Chest radiography	Focal pneumonia, atelectasis; dilated bronchial tree, thickened airways (ring shadow)
Other recommended testing	Bacterial, microbacterial, and fungal sputum culture, chest CT.

### **Tuberculosis**

Characteristics	Onset at any age; associated with history of exposure, local prevalence may suggest diagnosis
Clinical presentation	Productive cough, hemoptysis, fever, and weight loss
Pulmonary function test	Not used for diagnosis

### **Tuberculosis (continued)**

Chest radiography	Infiltrate, nodular lesions, hilar adenopathy, cavitary lesions or granulomas
Other recommended testing	Sputum AFB culture, PPD, sputum cultures confirm diagnosis

### **Bronchiolitis obliterans**

Characteristics	Onset at any age but often younger; may be associated with history of flu-like illness, collagen vascular disease, or toxic fume exposure, non-smokers
Clinical presentation	Often subacute presentation with dyspnea, cough, and fever
Pulmonary function test	Decreased vital capacity, decreased DLCO, usually no obstructive component

### **Bronchiolitis obliterans (continued)**

Chest radiography	Multifocal, bilateral alveolar infiltrates
Other recommended testing	ESR, high-resolution CT shows hypodense areas, lung biopsy

### Tracheobronchomalacia

Characteristics	Onset usually more middle age; idiopathic or acquired during the course of other illnesses
Clinical presentation	Cough, difficulty in clearing secretions, wheezing, recurrent bronchitis, pneumonia
Pulmonary function test	Obstructive ventilatory impairment not responsive to conventional treatment with bronchodilators or inhaled corticosteroids
	Adapted with permission from DeWar, 2006

Continued on next slide

### Tracheobronchomalacia, (continued)

Chest radiography (dynamic CT)	Allows volumetric acquisition of data both at end-inspiration and during dynamic expiration; reduction in airway caliber of 50% or more between inspiration and expiration may help in diagnosis
Other recommended testing	Flexible bronchoscopy; endobronchial ultrasonography

### **Cystic fibrosis**

Characteristics	Usually early-life onset; progressive with exacerbations; associated with pancreatic disease, failure to thrive, intestinal obstruction, cirrhosis, and steatorrhea.
Clinical presentation	Predictive cough with purulent sputum, dyspnea, and wheezing
Pulmonary function test	Predominantly fixed airflow obstruction

### **Cystic fibrosis (continued)**

Chest radiography	Bronchiectasis frequent in upper lobes
Other recommended testing	Sweat chloride test (diagnostic), bacterial sputum culture

### Key Points

- COPD is associated with several chronic respiratory symptoms that suggests its diagnosis
- Symptoms overlap with other conditions -- asthma in particular
- History, risk factors and progression of disease assist with diagnosis
- Spirometry, with and without bronchodilator, usually necessary to make diagnosis

## References

- American Thoracic Society/European Respiratory Society Statement: Standards for the Diagnosis and Management of Individuals with Alpha-1 Antitrypsin Deficiency. Am J Respir Crit Care Med 2003;168;818–900.
- Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J 2004;23:932.
- Cosio MG, Saetta M, Agust A. Immunologic Aspects of Chronic Obstructive Pulmonary Disease. N Engl J Med 2009;360:2445-54.
- Dewar M, Curry RW. Chronic Obstructive Pulmonary Disease: Diagnostic Considerations. Am Fam Physician 2006;73(4):669-676.
- Global Initiative for Asthma (GINA) Report, 2009: Diagnosis and Classification, pg 16-24.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Report, 2009. http://www.goldcopd.org.
- Muller NL, Coxson H. Chronic obstructive pulmonary disease. 4: imaging the lungs in patients with chronic obstructive pulmonary disease. Thorax. 2002;57:982–5.

## References (continued)

- Murgu, SD and Colt, HG. Symptoms often mimic those of asthma and COPD -- Recognizing tracheobronchomalacia.(chronic obstructive pulmonary disease); J Respir Dis. 2006;27(8):327-335
- Niewoehner DE. Outpatient Management of Severe COPD. N Engl J Med 2010;362:1407-16
- NHLBI/NIH National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, 2007.
- Qaseem A, Snow V, Shekelle P, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2007;147:633-8.
- Price DB, et al. Symptom-based questionnaire for identifying COPD in smokers. Respiration 2006; 73(3):285-95.
- Stephens MB, Yew KS. Diagnosis of Chronic Obstructive Pulmonary Disease. Am Fam Physician 2008;78(1):87-92.
- Sutherland ER, Cherniack, RM. Management of Chronic Obstructive Pulmonary Disease. N Engl J Med 2004;350:2689-97.
- Tinkelman DG, et al. Symptom-based questionnaire for differentiating COPD and asthma. Respiration 2006; 73(3):296-305.

## THANK YOU

Capaid Phaima



Shalima