3 COPD Recognition and Diagnosis: Approach to the Patient with Respiratory Symptoms

Key Points
1. Patients who present with respiratory symptoms such as cough, sputum production, wheezing, or breathlessness may have COPD, non-respiratory illnesses, or respiratory conditions other than COPD.
2. The initial evaluation of a patient who presents with respiratory symptoms includes a history, physical examination, spirometry testing, and a chest radiograph.
3. The diagnosis of COPD depends on the findings of appropriate symptoms in the right clinical context with airflow obstruction noted on spirometry testing.

3.1 Introduction

Patients who are seen in health care settings often present with respiratory symptoms including shortness of breath, cough, sputum production and chest discomfort or chest tightness. Although the focus of this primer is COPD, not every individual who has these respiratory symptoms and a history of smoking tobacco products has COPD. It is the task for the health care provider to be able to interview individuals who present with these symptoms and perform basic diagnostic tests to determine whether the cause for these symptoms is COPD or another respiratory or non-respiratory condition. This chapter will focus on the approach to a patient who presents with these respiratory symptoms. By obtaining the appropriate history and test results, the provider can determine the cause for the symptoms and, if it is COPD, initiate further management and treatment.

3.2 Patient Presenting with Respiratory Symptoms

An individual may present in a clinical setting with one of the following respiratory symptoms:
- Dyspnea or shortness of breath with activity or at rest
- Cough
- Sputum Production
- Chest Discomfort or Chest Tightness
- Wheezes or Rhonchi
These symptoms are not specific to COPD or even to other respiratory illnesses and can be seen in other conditions that will require further investigation. Table 3.1 includes other conditions or causes of these respiratory symptoms other than COPD.
3.2.1 Further Discussion of Dyspnea/Shortness of Breath

Of the respiratory symptoms that individuals with COPD may have, dyspnea or breathlessness is a very common presenting symptom. Fifty percent of patients seen in acute care clinical settings present with the symptom of dyspnea (Parshall, 2012). The various descriptors of dyspnea can include: shortness of breath, air hunger, labored breathing, can’t get a deep breath, chest tightness, or heavy breathing. The American Thoracic Society’s definition of dyspnea is as follows: **Dyspnea is a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity** (Parshall, 2012). Like other symptoms that an individual may experience (pain, hunger, thirst, etc.), dyspnea is actually comprised of two separate but interacting elements: sensation and perception.

1. **Sensation:** the neural activation resulting from stimulation of peripheral neural receptors that varies based on the load, intensity and duration of the stimulation. Also, there are differences among the responses of different peripheral neural receptors.
2. **Perception:** the reaction of the individual to the neural activation that includes processing of that neural information along with other input including psychological, cultural, and behavioral factors.

In other words, dyspnea, like pain, is comprised of sensory and affective components. The sensory elements are the peripheral neural receptors as shown in Table 3.2.

In normal physiological states (e.g., exercise) and in disease states, stimulation of these peripheral receptors results in neural activation that is transmitted from the thorax to the central nervous system through pathways such as the vagus nerve and spinal cord afferents.

The neural traffic is then received in nuclei in the pons of the brainstem such as the nucleus of the tractus solitarius and in the medulla oblongata. From these locations, there are neural connections to the cortical sensory centers where this neural input is processed in the cortex along with other input depending on behavioral and cultural influences with the resulting sensation being noted as dyspnea or breathlessness. The latter processing is the affective component of the sensation of dyspnea.

Although an individual with disease may note breathlessness as a symptom of hypoxemia and hypercarbia, the input from chemoreceptors is only one signal that can cause the sense of dyspnea. In other scenarios, it is the input from other peripheral receptors that is noted as shortness of breath. As a result, for those individuals who do not exhibit hypoxemia but still note dyspnea, addition of supplemental oxygen will not relieve their dyspnea unless there is some placebo effect that is part of the behavioral input for the perception of dyspnea.

Dyspnea can be scored by different scales noted in Table 3.3. Dyspnea can be an alarming and distressing symptom for many individuals; it is influenced by both the sensory input from peripheral neural receptors; and it can be the result of disease
states in the lungs (airways and interstitium), the respiratory muscles, the chest wall, or the central vasculature.

As dyspnea is often distressing and anxiety-provoking and can lead to overall limitation in activities, the use of anxiolytics for patients with COPD is often a useful adjunctive therapy. Respiratory depression is a potential complication of the medications used to relieve anxiety (such as benzodiazepines).

For patients with COPD, the greater the impairment as determined by clinical scores such as the BODE Index (BMI, airflow obstruction, dyspnea and exercise capac-

<table>
<thead>
<tr>
<th>Table 3.2: Sensory: Pulmonary Afferent Neural Receptors and other Afferent Neural Input</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Airway Irritant Receptors</strong></td>
</tr>
<tr>
<td><strong>Within Lung Parenchyma/Interstitial</strong></td>
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<tr>
<td>Slowly Adapting Stretch Receptors</td>
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<td>Rapidly Adapting Stretch Receptors</td>
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<tr>
<td>C-Fibers (bronchial and pulmonary)</td>
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<tr>
<td><strong>Respiratory Muscles/Chest Wall</strong></td>
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<tr>
<td>Muscle spindles</td>
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<td>Golgi tendon organs</td>
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<tr>
<td><strong>Carotid Bodies, aortic bodies, central medullary chemoreceptors</strong></td>
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<td><strong>Vascular receptors</strong></td>
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<td>Right Atrial and Left Atrial mechanoreceptors</td>
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<td>Pulmonary Artery baroreceptors</td>
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<tr>
<td>Right Ventricular strain receptors</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Table 3.3: Scales for scoring Dyspnea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scales for Scoring Dyspnea</strong></td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
</tr>
<tr>
<td>Borg Score: 6 to 20</td>
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<tr>
<td>Visual Analog Scale (VAS): 100 mm</td>
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<tr>
<td>Oxygen Cost Diagram (OCD): 13 activities with increasing oxygen requirements</td>
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ity index), the increased use of more extreme affective descriptors such as frightening and awful for the symptom of dyspnea (Williams, 2010).

### 3.3 Initial Screening Evaluation for a Patient Presenting with Respiratory Symptoms including Dyspnea

The presence of a respiratory symptom such as dyspnea does not necessarily indicate the disease process is in the lungs but could be in the heart, the circulation, the respiratory muscles or the chest wall. When a patient presents with respiratory symptoms such as dyspnea, the approach to determining the cause for these symptoms is described in Figure 3.1.

**Figure 3.1: Approach to the Evaluation of an Individual who Presents with Respiratory Symptoms**

This figure presents a basic algorithm for the evaluation of an individual who presents with respiratory symptoms such as shortness of breath, cough, wheezing, and/or phlegm production. Once non-respiratory causes are excluded, a respiratory evaluation including history, physical examination, imaging studies, and physiologic testing is initiated. Based upon spirometry, the respiratory physiology can be classified as normal, restrictive, or obstructive. (Recognition of a mixed restrictive and obstructive pattern requires additional lung function testing as discussed in Chapter 4, Pulmonary Function Testing.)
3.3.1 Exclude Causes of Symptoms other than Lung Disease

Based upon the initial presentation, relevant medical history and initial evaluation, it may be determined that the cause for the symptoms of dyspnea, chest discomfort, etc. is due to disease processes such as cardiac disease (see Table 3.1). For example, if the cause for these symptoms is cardiac, then the following would be useful: medical history especially relating to cardiac disease, diagnostic testing including electrocardiogram, echocardiogram, and stress testing. Once non-respiratory diseases are excluded or are not considered to be the prime reason for the current symptoms, then evaluation of respiratory causes can be initiated.

3.3.2 Respiratory Causes for Symptoms

The respiratory causes for symptoms of dyspnea, cough, sputum production, and chest tightness or discomfort can be divided into primarily airways diseases (such as COPD, asthma, bronchiectasis) or interstitial/parenchymal diseases (interstitial lung disease, pneumoconiosis, alveolar filling disease). Other possible respiratory diseases such as pulmonary vascular disease, pleural disease, or neuromuscular disease involving the respiratory muscles may also be considered.

3.3.2.1 Initial Evaluation of Respiratory Processes

The first steps for the evaluation of possible respiratory disease include history, physical examination, spirometry testing and chest radiograph.

- **History**: Detailed respiratory, environmental and occupational history will need to be performed, including all personal habits such as smoking.

- **Physical Examination**: focusing on the respiratory system for signs of respiratory insufficiency including use of accessory muscles, chest wall abnormalities, and auscultation for adventitial sounds.

- **Spirometry Testing**: The technical details for the performance of spirometry testing will be discussed in greater detail in Chapter 4 of this primer. The interpretation of spirometry test results to help identify the type of respiratory condition will be discussed in greater detail in Chapter 4.

- **Chest Radiograph**: A standard PA and lateral chest radiograph can be performed as part of the initial evaluation for any individual who presents with respiratory symptoms. It may not show any specific findings (not sensitive for some airways diseases or mild involvement with interstitial lung disease (ILD) or pulmonary vascular disease). However, there may be findings that will help identify certain patterns of disease presentations such as emphysematous changes in patients with COPD or interstitial markings in patients with ILD. Further description of the radiographic images for patients with COPD can be found in Chapter 5 of this COPD Primer.
3.3.2.2 Further evaluation of Causes of Respiratory Symptoms after Spirometry Test Results

If the initial evaluation suggests that the patient’s respiratory symptoms are most likely due to a respiratory condition/disease, then the initial spirometry test results can provide information as to the type of impairment and in turn the type of disease that is being considered. Figure 3.2 is an algorithmic approach based on the results of the spirometry testing.

After excluding non-pulmonary causes of the symptoms and performing the initial screening tests including spirometry, the interpretation of spirometry can reveal normal results, airflow obstruction, or possible restriction (as mentioned, further explanation for the performance and interpretation of spirometry testing will be discussed in Chapter 4).

If airflow obstruction is found on the screening spirometry, possible conditions include COPD or asthma; other airways diseases could also present with airflow obstruction and asthma may present with a normal spirometry.
3.4 COPD

As the algorithm indicates, if the spirometry test results show airflow obstruction and the most likely disorder is COPD, then other clinical information and further diagnostic test results can help establish that COPD is present. Recent research indicates that COPD is not a single disease with a common pathogenesis but a syndrome composed of symptoms and findings in the presence of known risk factors.

3.4.1 Definition of COPD

As stated in the Key Points at the beginning of this chapter, the diagnosis of COPD depends on the findings of appropriate symptoms in the right clinical context with airflow obstruction noted on spirometry testing.

The following factors are considered when determining whether a patient has COPD:

- COPD is a syndrome related to the appropriate history, clinical signs and symptoms, physiologic and radiographic findings including the presence of airflow obstruction by spirometry (ATS, 2004).
- The airflow obstruction does not normalize or is not fully reversible.
- Various organizations define airflow obstruction differently. The American Thoracic Society-European Respiratory Society (ATS/ERS) definition uses the lower limit of normal (LLN) for the ratio of FEV₁/FVC based on reference equations, primarily NHANES III reference equations for spirometry (Hankinson, 1999) whereas the Global initiative for chronic Obstructive Lung Disease (GOLD, 2013) criterion uses a fixed cutoff of 70% for the ratio of FEV₁/FVC. In either case, airflow obstruction is considered to be a reduced FEV₁/FVC ratio (either below LLN or 70%). However, just like the syndrome of COPD is a continuum from no disease to severe disease, the presence of airflow obstruction itself can be a continuum from no airflow obstruction to very severe airflow obstruction. There are instances with borderline airflow obstruction with values of FEV₁/FVC above the threshold value (whether it is the LLN or 70%) that still may have some likelihood of abnormality of airways disease that would be consistent with a clinical diagnosis of COPD. For these borderline cases, the use of reduced mid-expiratory flow values would be helpful to identify instances where there would be intermediate probability or likelihood of airflow obstruction that would be consistent with COPD. The mid-expiratory flow ratio (MEFR) can be useful in these circumstances. When this ratio (actual FEF₂₅-₇₅%/actual FVC)/(predicted FEF₂₅-₇₅%/predicted FVC) is < 0.70, at a time when the FEV₁/FVC ratio is above the lower cutoff for airflow obstruction, there is an intermediate probability that there is airflow obstruction that would be consistent with COPD.
- Clinical manifestations of COPD and asthma can overlap.
Historically, COPD was considered to be composed of two disorders: chronic bronchitis and emphysema. More recent information suggest that as a syndrome, COPD is a heterogeneous disorder that is actually composed of several phenotypes. (See further discussion of COPD phenotypes in Chapter 5 on Radiology).

The history that is usually associated with the development of COPD is related to tobacco smoking with or without environmental or occupational risk factors. There may also be genetic predisposition or susceptibility for the development of COPD combined with exposure to personal or environmental/occupational risk factors.

The deficiency of the enzyme α-1 antitrypsin is seen in about 1% of patients with COPD.

When COPD is considered a syndrome, there may be a different approach to establish the presence or diagnosis of COPD. As with other clinical conditions or disorders (e.g., pulmonary embolus, obstructive sleep apnea), there may be a degree of certainty or likelihood for the establishment of the diagnosis that in turn is dependent on physiological, historical, and clinical factors. Stated differently, we use Bayes Theorem for the determination of the likelihood for the presence of a disorder that is dependent upon the context or the pre-test probability of the disorder or condition.

The factors used for the diagnosis of COPD are:

1. Physiological:
   - Presence of airflow obstruction defined primarily by a reduced FEV₁/FVC but may include other spirometric parameters as well (e.g., reduced mid-expiratory flow rates).
   - Other physiological factors as described below that may be confirmatory for the presence of COPD (e.g., air-trapping, hyperinflation, increased airways resistance, reduced diffusing capacity).

2. Historical:
   - Smoking history that is considered substantive (e.g., greater than 20–40 pk-ysrs).
   - Previous clinical diagnosis of COPD by a health care provider.
   - Other environmental or occupational exposures that are associated with the development of airways diseases.

3. Clinical:
   - Appropriate respiratory symptoms: dyspnea, cough, sputum production, chest tightness, wheezing.
   - Other clinical diagnostic testing: CT scans or chest radiographs showing emphysematous changes.
   - Use of medications for airways diseases including inhaled bronchodilators, inhaled and/or oral corticosteroids.
The weighting of these factors for the determination of the likelihood of COPD is not entirely clear but some of these factors are probably more significant than others (airflow obstruction, smoking history, previous diagnosis of COPD, presence of respiratory symptoms). See Figure 3.3 for illustration of this approach to the diagnosis of COPD.

3.4.2 Other Diagnostic Tests to Help Confirm the Presence of COPD

As mentioned above, there are other physiological test results that support the diagnosis of COPD. These confirmatory diagnostic tests include more complete pulmonary function testing such as measurement of lung volumes by body plethysmography or nitrogen washout testing. In some patients with COPD, the lung volume measurements show hyperinflation (a total lung capacity that is greater than the upper limits of normal for that parameter) or air-trapping (a residual volume values that is greater than the upper limits of normal for that parameter).
Diffusing capacity measurement could also be performed. Diffusing capacity values give an indication of the lungs ability to take up oxygen (using carbon monoxide as the surrogate gas for oxygen). Patients with COPD who have emphysematous changes may have a reduced diffusing capacity since there is a loss of pulmonary capillary surface area.

As will be discussed in Chapter 5, radiographic imaging beyond chest radiographs can be useful for patients with COPD. A CT scan of the chest is a more sensitive approach to identify the presence of emphysematous changes as well as any interstitial changes that may be present that are not obvious by a standard chest radiograph.

Cardiopulmonary exercise testing may also be useful for the determination of exercise performance for these patients and, if there is limitation to exercise performance, whether the cause of the limitation is due to COPD (Eschenbacher, 1990).

If the confirmatory tests indicate that the disease process is COPD, then the severity of the disease and recommendations for management can be found in other chapters in this COPD Primer (e.g. Chapter 14).

### 3.5 Asthma

If airflow obstruction is interpreted from the screening spirometry and the disease is thought to be asthma instead of COPD, then confirmatory testing can also be done. Although there may be clinical overlap between these two obstructive airways diseases, there can be differences that help distinguish one condition from the other as shown in Table 3.4.

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**Table 3.4: Distinguishing Asthma and COPD**

<table>
<thead>
<tr>
<th>Distinguishing Asthma and COPD</th>
<th>Asthma</th>
<th>COPD</th>
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<tbody>
<tr>
<td>Predominant Inflammatory Cells</td>
<td>Eosinophils</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>Cytokines</td>
<td>Th2: IL-4,5,9,13</td>
<td>Th1: IFN-γ</td>
</tr>
<tr>
<td>Air Flow Limitation</td>
<td>Can normalize</td>
<td>Does not normalize</td>
</tr>
<tr>
<td>Age of onset</td>
<td>Younger</td>
<td>Older</td>
</tr>
<tr>
<td>Atopy/allergies</td>
<td>More likely</td>
<td>Less likely</td>
</tr>
<tr>
<td>Variability</td>
<td>Varies day-to-day</td>
<td>Less likely to vary</td>
</tr>
<tr>
<td>Medication</td>
<td>Inhaled corticosteroid initially</td>
<td>Inhaled corticosteroid after bronchodilators are used</td>
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</table>
For asthma, the inflammatory component found in the airways can be eosinophilic or neutrophilic but for COPD, it is usually neutrophilic. Other aspects of the inflammation found in asthma include t-helper type-2 lymphocytes with mediators that can include IL-4, 5, 9 and 13. For COPD, the inflammation may be more of t-helper type-1 lymphocytes with Interferon-γ (IFN-γ). The airflow obstruction with asthma can return to within normal limits at baseline or as a result of medication but this normalization usually does not occur with COPD. Asthma is clinically seen as developing in younger individuals who have an allergic component to their disease. There is usually more day-to-day variability in asthma as a result of exposure to different triggering agents such as environmental antigens. Finally, the management of these two airways diseases differs: inhaled corticosteroids are used as the primary controller medication for asthma and bronchodilators such as long-acting anticholinergic agents are more useful in COPD.

Confirmatory tests to identify asthma include standard lung function tests such as lung volume measurements and diffusing capacity and bronchoprovocation challenge test such as methacholine testing. The usefulness of such a bronchoprovocation challenge test for asthma was described in the NHLBI Guidelines for the Diagnosis and Management of Asthma EPR-3:

“The bronchoprovocation with methacholine, histamine, cold air or exercise challenge may be useful when asthma is suspected and spirometry is normal or near normal. A positive test is diagnostic for the presence of airway hyperresponsiveness, a feature of asthma but can be present in other conditions. A positive test is consistent with asthma; a negative test may be more helpful to rule out asthma” (NHLBI, 2007).

In patients with asthma, lung volume measurements may reveal hyperinflation and air-trapping but may also be within normal limits. For diffusing capacity measurements in asthma, the values can be normal or even elevated as compared to many patients with COPD where the diffusing capacity measurement is reduced (especially if emphysema is present).

### 3.6 Interstitial Lung Disease

If the screening spirometry for individuals who present with respiratory symptoms (including dyspnea and cough) reveals a possible restrictive impairment pattern instead of airflow obstruction and the chest radiograph shows interstitial markings, then the disease process could be an interstitial lung disease. Confirmatory testing to help establish the diagnosis of an interstitial lung disease includes further lung function testing with lung volume measurement and diffusing capacity. Lung volume values would be expected to confirm the presence of a restrictive lung defect that had been suggested by spirometry. Both total lung capacity and residual volume results might be below their respective lower limits of normal (LLN). Diffusing capacity measurement may also be reduced as the interstitial disease process has reduced
the pulmonary capillary surface area and reduced the ability of the lungs to take up oxygen.

CT scans of the chest, especially high-resolution CT scans, are useful in the diagnosis of interstitial lung diseases by showing specific patterns that may be associated with certain ILD classifications (Webb, 2009).

Cardiopulmonary exercise testing may reveal pulmonary or ventilatory limitation as well as possible pulmonary vascular limitation. The latter may be seen if there is associated pulmonary hypertension as a result of reduced pulmonary vascular compliance due to the interstitial disease process involving the pulmonary vasculature.

Finally, in some instances, a lung biopsy may be needed. This histopathologic diagnosis would not only help establish the specific type of ILD but may also be useful for prognosis and for disease management.

3.7 Summary Points

1. Patients who present with respiratory symptoms require a standardized approach to determine the cause for their symptoms.
2. Not all patients who experience respiratory symptoms and have a significant smoking history have COPD.
3. Other conditions that could explain the presence of symptoms of dyspnea, cough, and chest discomfort include other respiratory diseases (airways diseases such as asthma and bronchiectasis; or restrictive lung diseases including interstitial lung diseases) and non-pulmonary processes such as heart failure.
4. History, physical examination, chest radiograph and spirometry are part of the initial screening evaluation needed to help determine the type of disease process but more advanced testing may be needed subsequently.

References