# Respiratory Disease: An Update for Radiologists

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## AN EDUCATIONAL UPDATE ON RESPIRATORY DISEASES

Many radiologists are working harder than ever before, and radiology is such a rapidly evolving field that many of its practitioners find it challenging just to keep up with developments in imaging, let alone other medical specialties. Yet the rest of medicine is evolving as well, and it is important that radiologists remain abreast of new developments in fields that are likely to impact their practice.

Because the single most commonly performed radiological study is the chest radiograph, and because respiratory signs and symptoms are among the most common reasons for patients to seek medical attention, new developments in pulmonary medicine are likely to be particularly relevant. This article provides a brief refresher on four of the most common and life-threatening pulmonary disorders that radiologists are likely to encounter on a regular basis: asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and acute respiratory distress syndrome (ARDS).

## ASTHMA

The word asthma comes from a Greek root meaning "panting." It is estimated that about 37 million Americans have been diagnosed with asthma at some point in their life, but only about 23 million currently carry the diagnosis. This amounts to a little over 7% of the US population. Perhaps in part because airways are smaller to begin with, asthma tends to be a more serious problem in younger populations, with a peak prevalence between the ages of 5 and 14 years. In patients younger than 18 years, asthma is more common in males, but in adulthood it is more common in females (1).

Asthma is a common reason patients seek medical attention, with approximately 14 million primary care visits and nearly 2 million emergency department visits each year (2). It is the most common reason children are admitted to the hospital from the emergency department. On the other hand, the mortality rate of asthma is relatively low, with fewer than 4000 deaths per year in the United States (3).

Asthma is an inflammatory disease that affects the larger, conducting airways to a greater extent than COPD, which predominates in smaller airways. It has a strong genetic component and tends to be associated with atopy, a predisposition to allergic rhinitis and eczema. Yet there is also an important environmental component, which may include exposure to a variety of allergens, as well as cold air and exercise.

The principal factors involved in the pathogenesis of asthma include bronchial smooth muscle hyperreactivity, inflammatory bronchial wall thickening, and increased mucus production. In the early phases of an attack, the release of histamine from mast cells and acetylcholine from parasympathetic neurons cause bronchoconstriction and mucus production, followed by leukotriene release from other inflammatory cells such as eosinophils and neutrophils. Long term, asthma can result in permanent airway narrowing (4).

One of the hallmarks of asthma is its intermittent nature, with patients often returning to normal function between attacks. Symptoms include dyspnea, chest tightness, coughing, and wheezing. Wheezing is usually most notable during expiration (5). Signs of a severe attack include dyspnea at rest, dyspnea that interferes with conversation, and a peak expiratory flow that is less than 40% predicted (6). Other predictors of a poor clinical course include a heart rate greater than 110 beats per minute and the presence of other serious medical conditions (7).

To make the formal diagnosis of asthma requires the exclusion of alternative diagnoses, a history of episodic airflow obstruction, and improvements in forced expiratory volume after the administration of a short-acting beta$_2$-agonist that exceed specified thresholds (6).

Most patients presenting with asthma have normal chest radiographs. However, common radiographic findings in asthma include hyperinflation, bronchial wall thickening (often referred to as peribronchial cuffing), and occasionally pulmonary edema. One of the most important reasons to obtain radiographs in suspected or confirmed asthma is to rule out mimics such as pneumothorax, pneumonia, and foreign-body aspiration, and to rule out complications, such as

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pneumomediastinum, pneumothorax, atelectasis, pneumonia, and mucoid impaction.

Computed tomography (CT) findings are generally nonspecific but may include bronchial wall thickening, expiratory air trapping, and attenuation of bronchial lumens. In some cases, CT can help diagnose important associated diseases, such as allergic bronchopulmonary aspergillosis.

## COPD

It is estimated that nearly 13 million Americans have been diagnosed with COPD, which represents the third most common cause of death in the United States, after heart disease and cancer. The disorder is more common in non-Hispanic whites, who account for about 80% of deaths. The diagnosis of COPD should be considered in any patient with chronic cough, dyspnea, and sputum production, and risk factors such as smoking or exposure to occupational hazards such as smoke or fine dust (8,9).

The diagnosis can be confirmed when the ratio of a patient's forced expiratory volume in 1 second over forced vital capacity ($FEV_1/FVC$) is less than 0.7 after the administration of bronchodilators. These criteria are a simplification of prior criteria, which were based on a lower limit of normal, rather than the strictly defined ratio of 0.7. These criteria were changed in 2010, and reaffirmed by the Global Initiative for Chronic Obstructive Lung Disease in 2015 (10,11). Because COPD includes both emphysema and chronic bronchitis, we will consider each of them in turn.

### Emphysema

Nearly 5 million Americans have been diagnosed with emphysema, which is strongly correlated with age. Historically, the prevalence was higher in men, but recently women have surpassed men (8). The disease results from an imbalance of inflammatory and anti-inflammatory forces that eventually leads to tissue destruction. Cigarette smoke and other irritants increase oxidative stress, leading to chemotaxis of inflammatory cells and the release of inflammatory mediators and proteases.

Conditions associated with diminished antioxidant or antiprotease activity, such as alpha-1-antitrypsin deficiency, are associated with increased risk. In all types, this imbalance between inflammatory and anti-inflammatory activity results in the destruction of alveolar, interstitial, and vascular tissue, meaning that there is less tissue to tether the airways open, and the airways collapse more readily. The end result is hyperexpanded lungs (the term emphysema derives from the Greek for "puff up") that lack the ability to increase air movement during periods of exercise and therefore cannot exchange gases as effectively as disease free lungs (10).

There are four principal types of emphysema, each of which results in a characteristic pattern of tissue destruction and hyperinflation that can be detected on chest CT. These are categorized with respect to their pattern of acinar involvement. Acinus comes from the Latin for "berry" and refers to a raspberry-like cluster of alveoli in which the respiratory bronchioles terminate.

Centriacinar, the type most commonly seen in cigarette smokers, results in tissue destruction at the center of the acinus, near the end of the respiratory bronchiole. Panacinar, the variant most often seen with alpha-1-antitrypsin deficiency, results in enlargement of airspaces throughout the acinus. Terminal acinar emphysema results in the destruction of tissue around the periphery of the acinus, and is often responsible for the spontaneous pneumothoraces that result from ruptured bullae. Finally, the irregular variant demonstrates an inconsistent pattern of tissue destruction that is likely to be accompanied by scarring (4).

Patients with emphysema are sometimes described as "pink puffers." The destruction of airspaces and vasculature is generally balanced, meaning that there is relatively little mismatch of ventilation and perfusion and therefore no cyanosis, at least at rest. Patients often expire against pursed lips, as a means of increasing end-expiratory pressure and keeping the airways open (4). The definitive diagnosis is pathological, but most patients exhibit a combination of dyspnea, cough, wheezing, and a barrel chest (12).

Plain radiographic findings include large, lucent lungs with flattened hemidiaphragms and increased retrosternal clear space. However, such changes may be subtle or even absent, and the principal role of plain radiography is to exclude mimics and treatable causes of exacerbations, such as infection, bronchiectasis, and cancer. Treatment consists of smoking cessation, oxygen supplementation, and symptomatic therapy such as bronchodilators. In patients with severe bullous disease, lung reduction therapy may be helpful.

### Chronic Bronchitis

Chronic bronchitis afflicts approximately 10 million Americans, and is nearly two times as common in women as in men (8). It, too, is caused by inflammation, but in this case inflammatory mediators lead to proliferation of glandular tissue, hypersecretion of mucus, and fibrosis of smaller airways. These changes in turn increase resistance to airflow in the airways in inverse proportion of the fourth power of the reduction of airway radius, meaning that a reduction of airway diameter by a factor of one-half increases resistance 16 times.

This reduction in air movement means that affected areas of the lung remain perfused but are no longer well aerated, resulting in a ventilation-perfusion mismatch and cyanosis. Cigarette smoke exacerbates these problems, in part by undermining the efficiency of the mucociliary apparatus that normally clears particulate matter and mucus from the airways (4,10). Patients present with dyspnea, productive cough, and frequent respiratory infections.

Clinically, the diagnosis of chronic bronchitis is made when the patient experiences regular mucus production for 3 or more months of the year for at least two consecutive years (10). Because of cyanosis, patients are sometimes referred to as "blue bloaters," as opposed to emphysema's "pink puffers." The

radiographic findings of chronic bronchitis are nonspecific, but may include increased bronchovascular markings, cardiomegaly, and enlargement of the pulmonary vessels, particularly in patients who have developed pulmonary hypertension and cor pulmonale.

On CT, enlargement of the pulmonary vessels is often accompanied by thickening of the bronchial walls, which can progress to scarring. As with emphysema, the principal reason for chest radiography in chronic bronchitis is not to make the diagnosis but to assess for complications, such as pneumonia. In both disorders, chest CT is likely to play an increasing role to assess for the development of another sequela of long-term cigarette smoking, lung cancer.

## PNEUMONIA

Pneumonia is generally divided into two categories: community-acquired pneumonia (CAP) and healthcare-associated pneumonia (HCAP). CAP applies when the pneumonia was acquired in the outpatient setting or within 48 hours of hospitalization (13), whereas HCAP occurs after 48 hours of admission, or in a patient who has recently been in the hospital, who resides in a long-term care facility, or visits a hospital or hemodialysis clinic regularly (14).

Each year, nearly 6 million cases of pneumonia are diagnosed in the United States, and it represents the number two cause of hospitalization. More than 1 million patients are hospitalized annually for CAP, which results in about 50,000 deaths (13). Although HCAP is less common, its incidence is much higher in ventilated patients, and its mortality is also considerably higher. Overall, pneumonia is the eighth leading cause of death in the United States, although it ranks higher in small children (sixth) and those whose age is more than 65 years (seventh) (13,15).

The clinical and radiologic manifestations of pneumonia represent the interaction of microorganisms invading the lung and the host immune response. A common route of infection is microaspiration during sleep, due to altered consciousness, or impaired swallowing and gag reflexes. Microorganisms can also be inhaled or the lung can be seeded hematogenously.

Host defenses include the hairs and turbinates and the mucus lining the tracheobronchial tree. The cilia lining the respiratory epithelium help to propel trapped microorganisms and other particles out of the respiratory passages and into the pharynx, where they can be swallowed or expectorated. Organisms that do make it into the smaller airways are engulfed by macrophages, which are also cleared by the mucociliary elevator. If a sufficient number of microorganisms manage to evade these defenses, pneumonia can result. Inflammation ensues, which may result in the accumulation of pus in the airspaces. The fever associated with pneumonia is often secondary to the release of tumor necrosis factors and interleukins (5).

The clinical presentation of pneumonia is variable. Classically, CAPs present with the abrupt onset of high fever and productive cough. Patients may also complain of pleuritic chest pain. A variety of systemic symptoms including fatigue, nausea, vomiting, diarrhea, headaches, myalgias and arthralgias, and confusion may also manifest. Physical examination findings include tachypnea, use of accessory muscles of respiration, crackles, bronchial breath sounds, dullness to percussion, and tactile fremitus (5). The diagnosis is made by a combination of lower respiratory signs and symptoms and a chest radiographic abnormality (14,16).

As its name implies, lobar pneumonia, most often due to *Streptococcus pneumoniae*, usually demonstrates radiographic findings including lobar airspace opacification, often accompanied by pleural effusion and atelectasis due to small-airway obstruction. Atypical pneumonias, most often due to *Mycoplasma*, *Chlamydia*, *Legionella*, and viral pathogens, more often present with an interstitial pattern of opacities, often in a perihilar distribution.

## ARDS

It is estimated that there are nearly 200,000 cases of ARDS per year in the United States. The incidence increases as patients age, becoming highest in the elderly. In-hospital mortality is relatively high, with a mortality rate of approximately 40%, resulting in approximately 75,000 deaths per year (17). The pathogenesis of the disorder begins with injury to the alveolar walls.

A number of different insults may be responsible, including sepsis, aspiration, pneumonia, trauma, transfusions, toxic inhalation, and near-drowning. As capillary endothelial cells and type 1 pneumocytes die, they release cytokines such as tumor necrosis factors, which increase capillary permeability, resulting in the leakage of proteins and migration of inflammatory cells into the alveoli. Surfactant is displaced and degraded and the distance across which diffusion of gases must take place increases. After the exudative phase, a proliferative phase ensues, during which type 2 pneumocytes begin rebuilding alveolar architecture (5).

ARDS typically presents 12–36 hours after an insult such as the development of sepsis or pneumonia (5,18). It begins with increasing dyspnea and tachypnea, which may be followed by tachycardia and respiratory failure. Many patients require increasing concentrations of inspired oxygen leading to intubation (5).

To make the diagnosis of ARDS, onset must be within a week of a known insult, chest imaging must show bilateral opacities consistent with airspace pulmonary edema, and arterial oxygen levels must be significantly below those of inspired oxygen levels. The greater this gap, the more severe the ARDS (19). The chest radiograph resembles airspace pulmonary edema or hemorrhage, usually manifesting as diffuse, bilateral, and confluent airspace opacities. In contrast to cardiogenic edema, ARDS is not accompanied by cardiomegaly, and the pulmonary opacities do not clear in response to diuretics. The process usually evolves over days to weeks. Many survivors develop chronic lung disease.

## CONCLUSION

Radiologists interpreting chest imaging studies are not merely detecting findings and generating differential diagnoses based on what they see. What they see and say depends to a great degree on what they understand. As biomedical science's understanding of respiratory diseases progresses, the knowledge base of radiologists needs to advance apace, so that radiologic interpretations can remain as accurate, relevant, and useful as possible.

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