GOAL: Describe the basic morphologic and pathophysiologic changes in various conditions of the respiratory system. Define (describe) and correlate the symptoms and signs of a disease with the structural changes of diseased organs.

OBJECTIVES:
1. Review the normal gross and histologic anatomy of the lung.
2. Describe the morphologic characteristics of common pulmonary disorders.

CLINICAL CASES:

Case 1
Normal lung review

Case 2
A 37-year-old woman develops dyspnea and pleuritic chest pain 1 day post-partum. She has a 20 pack-year history of smoking, which she gave up at the beginning of her pregnancy. On physical exam she has a fever of 38°C and a pulse of 102. Her lungs sound clear to auscultation. Her heart exam is normal, aside from tachycardia. Her left calf is swollen and tender. On chest x-ray a peripheral opacity is seen in the right lower lobe

a. Identify organ: Lung

b. Describe the characteristic pathologic changes in the histologic and gross specimen.
   Gross: Wedge-shaped, hemorrhagic (red-blue) area. Near the apex of the wedge an occluded vessel may be identified.
   Histologic: Ischemic/hemorrhagic necrosis of the lung. “Ghost-like” remnants of alveolar walls, bronchioles, and vessels. Red blood cells may fill the alveoli.

c. Diagnosis: Pulmonary Infarct

d. What are risk factors for the development of this condition?
   Congestive heart failure
   Cancer
   Immobilization for a long period
   Hypercoagulable states – primary or secondary
   Obesity
Recent surgery
Oral contraceptives
Pregnancy

>95% of all pulmonary emboli arise from thrombi within the large deep veins of the lower legs.

d. What underlying genetic disorders may pre-dispose this individual to this problem?

Inherited hypercoagulable states such as Factor V Leiden, Prothrombin II gene mutation, and Protein C, Protein S and Antithrombin III deficiencies.

e. How often do pulmonary emboli actually cause pulmonary infarction?

Only ~10%
Why? Infarcts are generally associated with concomitant abnormality of bronchial circulation, as in patients with heart disease. Thus, pulmonary infarcts tend to be uncommon in the young.

Case 3

A 63-year-old man presents with dyspnea. He also complains of cough, which is worse in the mornings, off and on for several years. There is no history of fever or purulent sputum or cyanosis. He smokes two packs of cigarettes/day for the last 50 years. On exam there is hyper-resonance of the chest by percussion and prolonged expiratory phase on auscultation.

a. Identify organ: **Lung**

b. Describe the characteristic pathologic changes in the specimen.

-Destruction of septal walls of alveoli.
-Fusion of adjacent alveoli producing large abnormal airspaces (blebs or bullae).

c. Correlate the clinical findings with the pathology.

Prolonged expiration and purse-lip breathing – attempt to “squeeze” air out of lungs
Cough – associated bronchitis
Hyperresonance – increased lung volumes/hyperexpansion

d. Diagnosis: **Emphysema**

e. What is the most common etiology of this disorder?
Tobacco/cigarette smoking

f. What underlying genetic disorder(s) can contribute to this disorder?
   Homozygous alpha₁ antitrypsin deficiency, PiZZ phenotype (autosomal recessive)

Case 4

A newborn develops respiratory insufficiency. He was born at 25 weeks gestation and weighed 500 gm at birth. The mother had fever for 3 days before delivery and the amniotic fluid was purulent. Surfactant and antibiotics were administered. The baby’s condition deteriorated rapidly and he died 8 hours later.

a. Identify organ: Lung

b. Describe the characteristic pathologic changes in the tissue.
   Some alveoli are atelectatic and collapsed.
   Necrotic cellular debris is present within bronchioles and alveolar ducts
   Eosinophilic hyaline membranes, composed of fibrin admixed with cellular debris, line alveoli

c. Diagnosis: Hyaline Membrane Disease

Case 5

A 44-year-old female undergoing chemotherapy for metastatic ovarian cancer is admitted to the hospital with a severe infection and sepsis. Over the next 2 days she develops progressive dyspnea. She becomes hypoxic and cyanotic and requires increasing oxygen concentration.

Chest X-ray shows diffuse bilateral infiltrates.

a. Identify organ: Lung

b. Describe the characteristic pathologic changes in the tissue.
   Congestion; interstitial and alveolar edema; collapsed alveoli; alveoli contain proteinaceous debris, desquamated cells, hyaline membranes

c. Diagnosis: Adult Respiratory Distress Syndrome (Diffuse alveolar damage)
Case 6

A 56 year-old man develops progressive dyspnea over 6-8 months. He denies fever, chest pain or hemoptysis. He has never smoked cigarettes. On physical exam he is hypoxemic. On chest auscultation there are fine bibasilar inspiratory crackles (sound like Velcro)

Chest X-ray shows bilateral interstitial infiltrates with a peripheral distribution.

a. Identify the organ: **Lung**

b. Describe the characteristic pathologic changes in this specimen.

   - Thickening and fibrosis of the interstitial septum
   - Focal chronic inflammation of the septum
   - Dilated airspaces separated by fibrous tissue
   - “Honeycomb lung”

c. Diagnosis. **Diffuse Interstitial Fibrosis**

   The diseases that cause diffuse interstitial fibrosis are heterogeneous.
   - Idiopathic pulmonary fibrosis
   - Nonspecific interstitial pneumonia
   - Cryptogenic organizing pneumonia
   - Collagen vascular disease
   - Pneumoconioses
   - Drug and therapy related (ie bleomycin, radiation)

The unifying pathogenetic factor is injury to the alveoli with activation of macrophages and the release of fibrogenic cytokines, such as TFG-beta.

d. What pattern would be seen on this patient’s pulmonary function test?

   **Restrictive pattern** – reduced total lung capacity