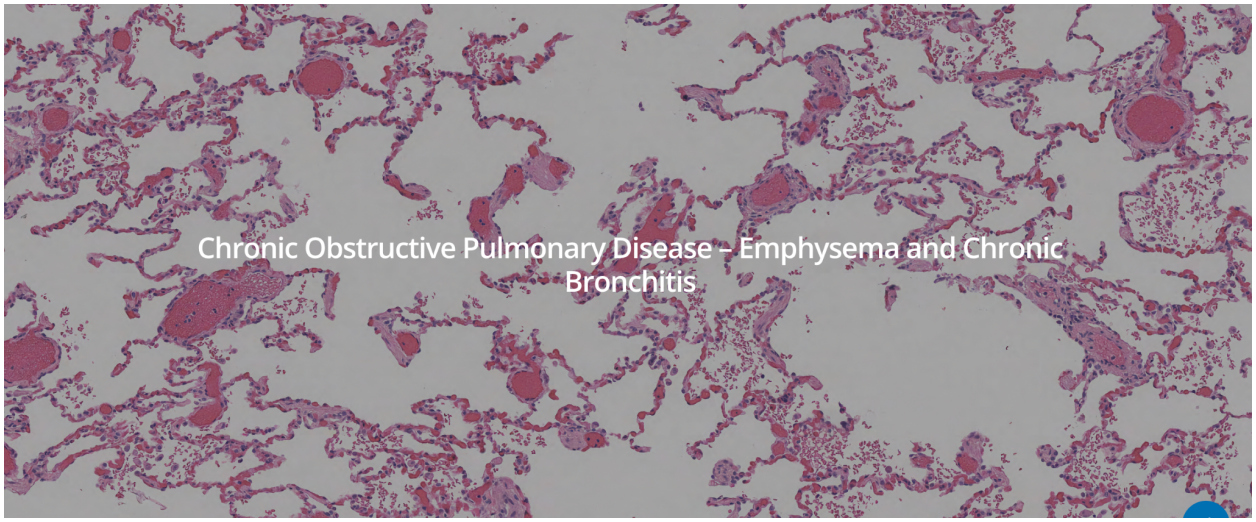

Chronic Obstructive Pulmonary Disease

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Background

Chronic obstructive airway disease (COPD) represents a spectrum of airway diseases including emphysema, chronic bronchitis, and asthma. It is characterized by airflow limitations. It is a top 10 cause of death in the United States.

This article includes findings associated primarily with emphysema and chronic bronchitis.

Quick Tips at Time of Autopsy

Clinical history

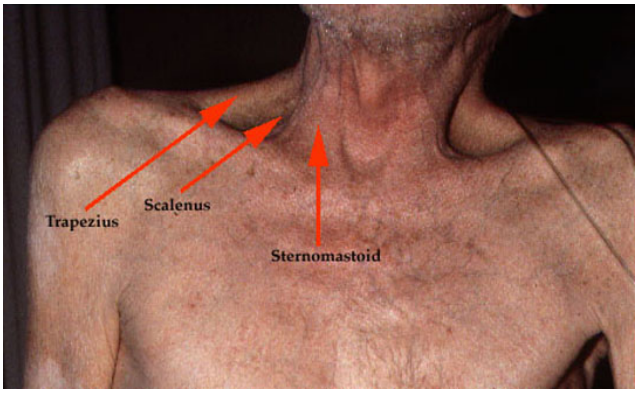
- Check the clinical history for the underlying cause:
    - Smoking is the most common cause, but other inhaled irritants (industrial particulates, agricultural dusts, biomass fuel) have also been implicated
    - Genetic alterations in alpha-1-antitrypsin are common in cases with an early onset and genetic testing results may be present in the health record. (The median age at presentation for alpha-1 antitrypsin deficiency is 46 years old)
- Not all patients will have an existing diagnosis of COPD, and it is a common new diagnosis at autopsy. (20% of pathologically proven cases show negative CT scans)

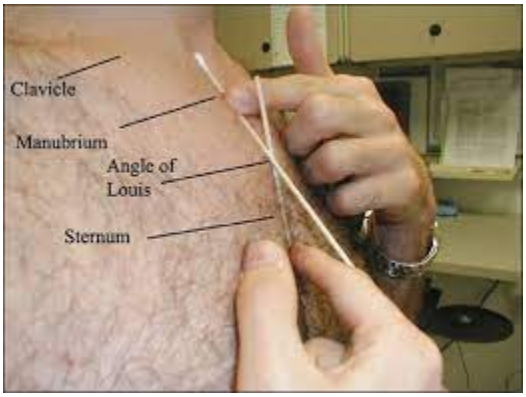
External examination

There are many external examination findings that can be associated with a diagnosis of COPD:

- “Pink puffer” - the classic physique in emphysema is a thin/emaciated patient with a large/barrel shaped chest due to air trapping (pulmonary hyperinflation). In contrast, those with chronic bronchitis are the “blue bloater” with excess weight gain

- The accessory muscles of respiration and the Angle of Louis can be prominent (see images below)





Images: (Top) increased accessory respiratory muscles and (Bottom) increased Angle of Louis. (Image Credit: (Top) Loyola University Medical Education Network and (Bottom) UC San Diego Practical Guide to Clinical Medicine)

- Cyanosis (but usually not clubbing)

- Edema in those with right heart failure

- Yellow discoloration of fingertips in active smokers
- Calluses on elbows, forearms, or thighs from tripod posture (leaning forward with elbows on thighs)

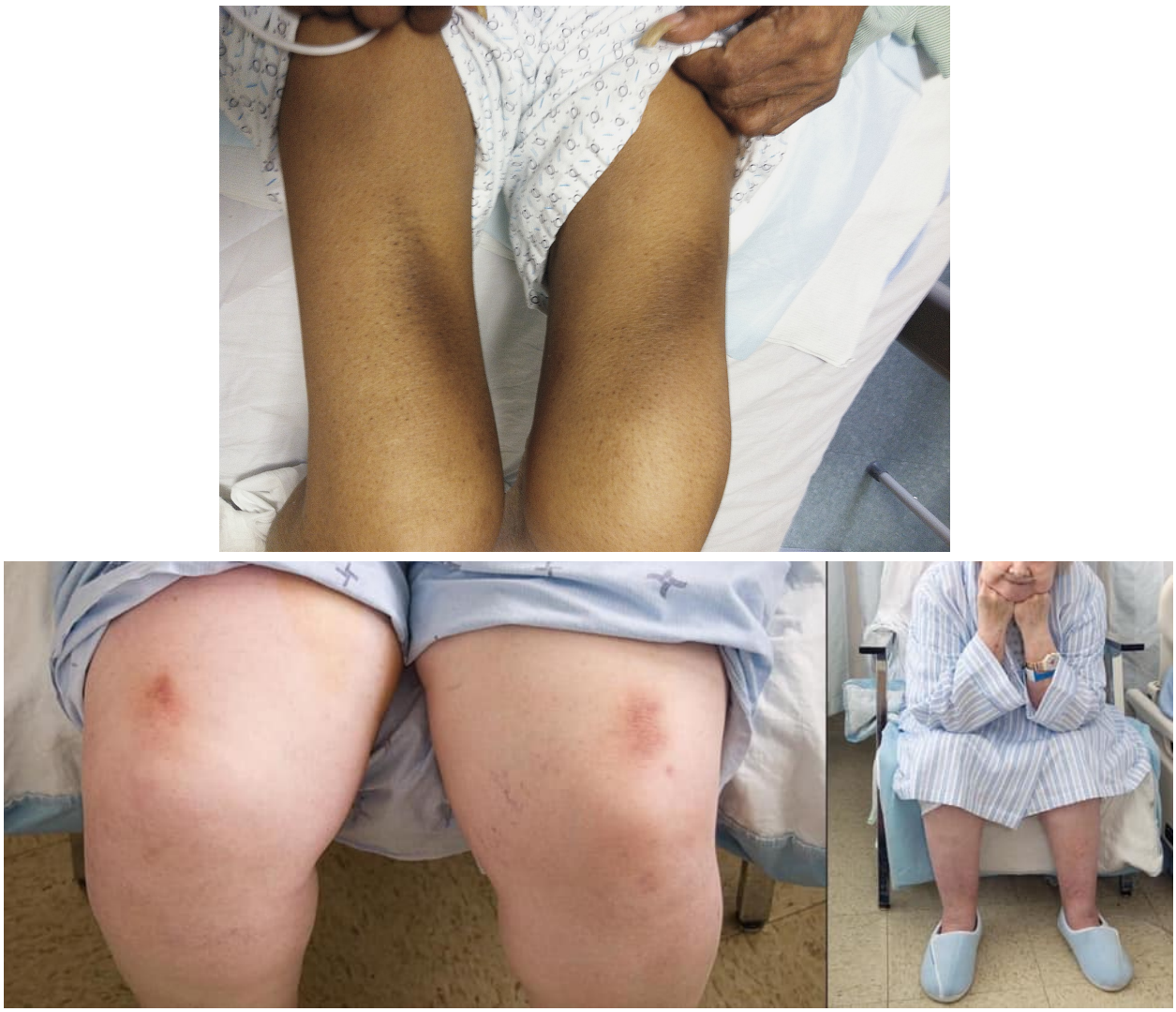


Image: Dahl's sign - calluses/hyperpigmentation from a tripod posture. (Image credits: (Above) Elliot Miller. Dahl's Sign, (Below) Gabriel Rebick 2008)

- Skin changes such as thinning and bruising from chronic steroids
- Alpha-1 antitrypsin deficiency is associated with dermatologic manifestations. The most common is necrotizing panniculitis, followed less commonly by systemic vasculitis, psoriasis, urticaria, and angioedema

Gross examination

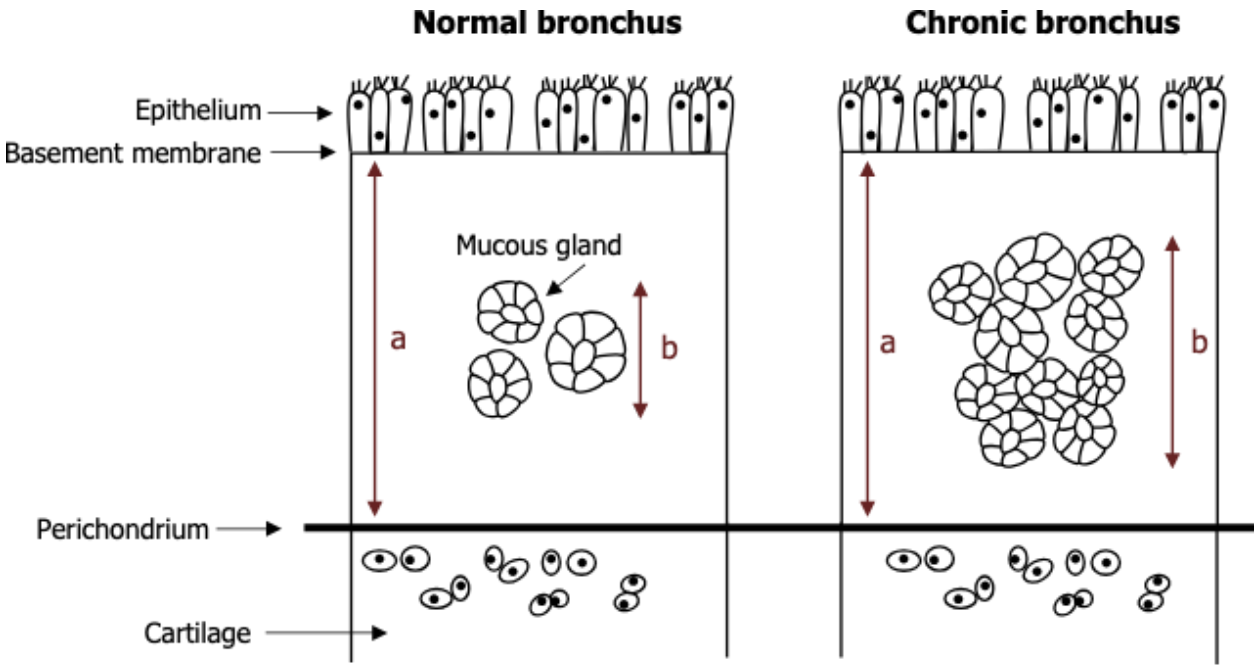
- Before opening: checking for a pneumothorax prior to opening the chest cavity can be useful in COPD cases as pneumothorax are common with COPD (esp. emphysema), can trigger exacerbations, and can be part of the cause of death. Checking for a pneumothorax at autopsy is a special dissection technique which is described here
- The chest cavity: hyperinflation can enlarge the lungs and obscure the heart when viewing the chest cavity
- Lung/airway gross examination:
    - The bronchi/large airways in chronic bronchitis patients may show boggy mucosa with excessive mucinous secretions and prominent mucosal pits overlying the orifices of bronchial mucous glands
    - The lung parenchyma in emphysematous patients will show variably sized cystic air spaces
    - Evidence of smoking may include increased anthracotic pigment deposition in lung parenchyma and mediastinal nodes
    - **Sections: routine lung sections should include apical and basal lung parenchyma, as well as bronchial wall and associated vasculature**
- Heart gross examination: the heart may show changes associated with cor pulmonale (such as right ventricular hypertrophy).
    - Right heart failure will in turn demonstrate findings of hepatosplenomegaly, nutmeg liver/centrilobular congestion, and/or ascites.
    - Findings of pulmonary hypertension (from right heart failure) include yellow atherosclerotic plagued in large pulmonary arteries
- Gross exam findings in genetic cases of COPD (alpha-1-antitrypsin)
    - Liver disease is common in cases of alpha-1 antitrypsin deficiency, which should be worked up based on routine liver section(s) at autopsy. Since liver disease can include hepatocellular carcinoma, close inspection for an undiagnosed malignancy is also warranted
    - Vascular pathology is also increased in AAT including abdominal and intracranial aneurysms, arterial fibromuscular dysplasia, and venous thromboembolism (VTE)

Ancillary testing

- If tested, pre-mortem or ante-mortem blood samples may show polycythemia, increased hemoglobin, and increased hematocrit in chronically hypoxic patients

Quick Tips at Time of Histology Evaluation

- Bronchial sections in chronic bronchitis
    - Early changes include hypertrophy of submucosal glands in the tracheobronchial tree while later changes include increased goblet cells in small airways
    - The Reid Index (see illustration below) can be used to measure the percentage of bronchial wall occupied by submucosal mucous glands. This directly correlates with sputum production, variable dysplasia, squamous metaplasia, and bronchiolitis obliterans. (Of note, the Reid Index is useful in emphysema, chronic bronchitis, and asthma). <0.4 is a normal Reid Index
    - Chronic inflammatory infiltrates are variable
    - Peri-bronchial vessels can be enlarged



Reid index = b/a = thickness of mucous gland layer/thickness of wall between epithelium and cartilage

Image: How to calculate the Reid Index in bronchial histology. Image Credit: Andrew Binks, COPD in Pulmonary Pathophysiology, available online at LibreTexts Medicine)

- Lung parenchyma sections in emphysema
    - Sections demonstrate enlarged airspaces, irregular acini, and thin septae with nodular “club-like” tips

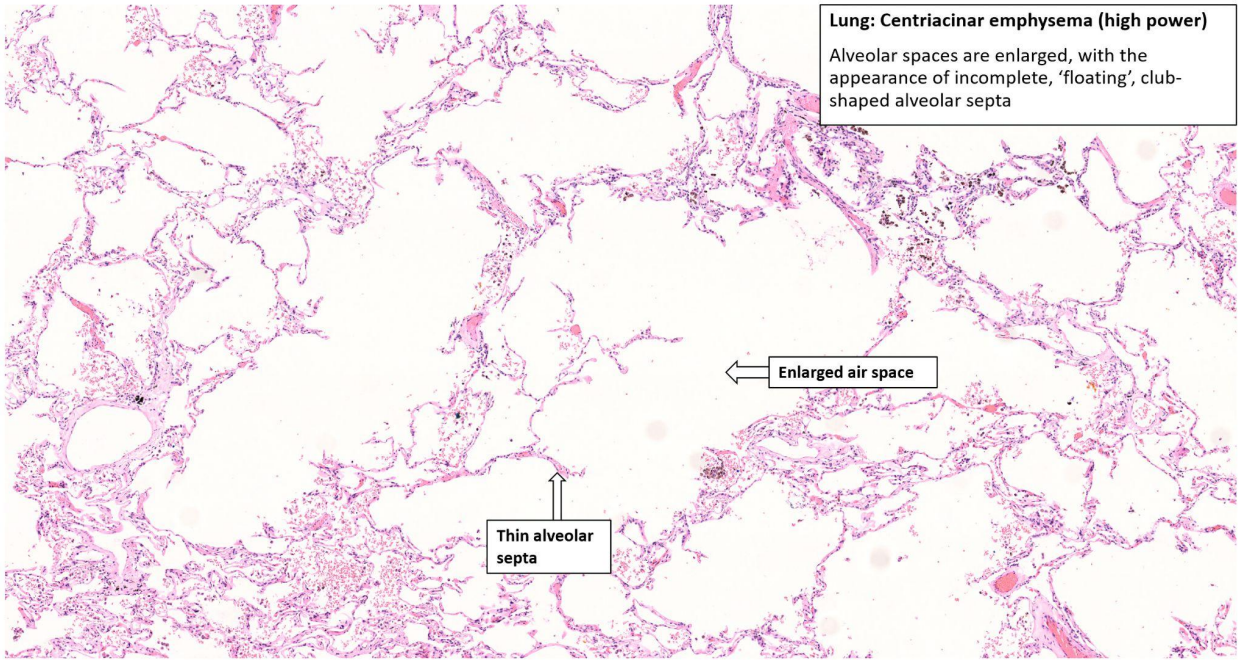
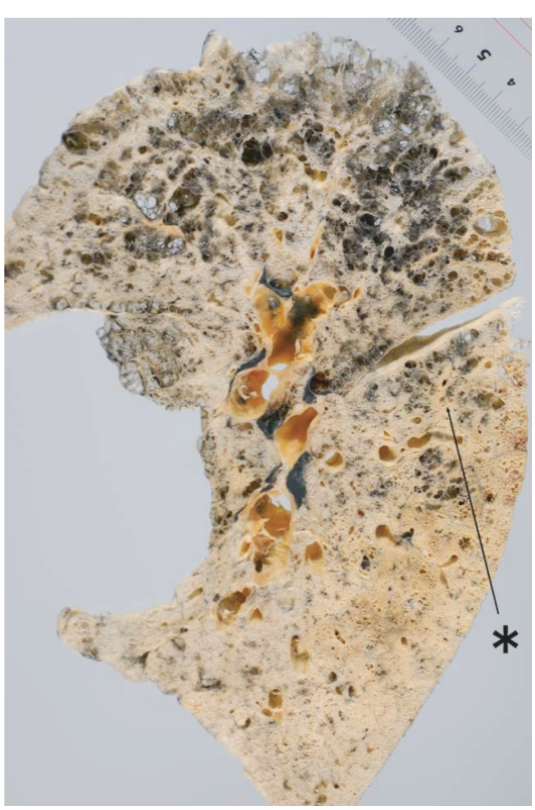


Image: Histology of emphysema with enlarged airspaces, thin alveolar septa, and club-shaped alveolar septa. (Image credit: University of Singapore)

- There are three patterns of emphysema

Pattern	Location	Histology	Etiology
Centriacinar	lung apex	terminal bronchiole disease with sparing of peripheral respiratory lobule	smoking
Panacinar	lung base	the entire respiratory lobule is involved	alpha-1 antitrypsin
Paraseptal	subpleural, esp. fissures		

    - Fibrosis and inflammation are usually minimal but can be seen focally. (Of note, chronic inflammation in the lungs can be underlying cause of emphysematous changes)
    - In smokers, intraalveolar pigmented macrophages (“smoker’s macrophages”) and increased anthracotic pigment deposition can be seen
- Genetic cases
    - Accumulation of altered alpha-1 antitrypsin in hepatocytes will stain with PAS
    - Liver disease can also include chronic hepatitis, cholestasis, cholangitis, cirrhosis, and/or hepatocellular carcinoma



Images: (Left) Distribution of centriacinar emphysema. Photograph of an inflated and fixed lung showing emphysematous foci with anthracosis mainly distributed in the upper lobe and superior segment of the lower lobe (*). (Right) Panacinar emphysema. An inflated-fixed lung does not demonstrate obvious anthracosis. Enlargements of airspaces are diffusely observed and in some areas the disease is bordered by the interlobular septum (arrow). (Bottom) Distal acinar emphysema. Photograph of an inflated and fixed lung specimen showing subpleural airspaces with smooth wall structures. (Image credits: Akira Yoshikawa et. al., Obstructive pulmonary disease: Emphysema on PathOutlines)

Quick Tips for Autopsy Report

- The sub-classification of emphysema can be challenging with multiple recognized subtypes including combined pulmonary fibrosis and emphysema, interstitial emphysema, bullous emphysema, senile emphysema, irregular emphysema, and congenital lobar emphysema. Atypical presentations or unusual histologic findings may be the key to exploring one of these less common/incidental manifestations of emphysema

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