

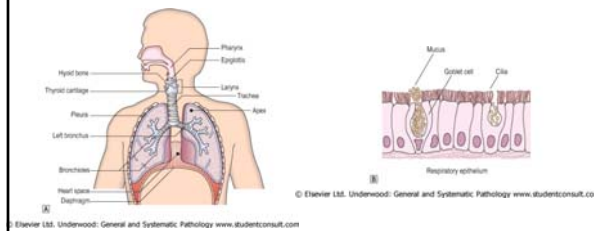
Pulmonary Pathology

Obstructive Airways Disease

Respiratory disease

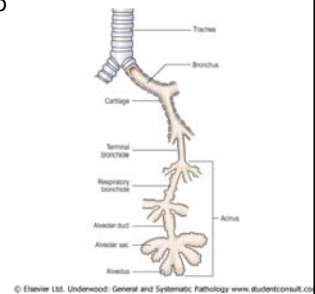
- Pulmonary diseases (especially infective) together with gastrointestinal infection are the commonest cause of death in the developing world
- Pulmonary disease is almost entirely *environmental* rather than *genetic*

Basic anatomy!



The respiratory acinus

- Cartilage is present to level of proximal bronchioles
- Beyond terminal bronchiole gas exchange occurs
- The distal airspaces are kept open by elastic tension in alveolar walls



Function of lungs....

- Gas exchange (O₂, CO₂)
 - Depends on compliance (stretchability) of lungs
 - Can only occur in alveoli that are *both* ventilated and perfused

Ventilation-perfusion defects

- Alveoli that are ventilated but not perfused is ventilatory “dead space”
- Alveoli that are perfused but not ventilated leads to “shunting” of non-oxygenated blood from pulmonary to systemic circulation (a mechanism of cyanosis)

Spirometry (pulmonary physiology)

- FEV1: volume of air blown out forcibly in 1 second. A function of large airways. Dependent on body size.
- Vital capacity (VC): total volume of expired air. Ratio FEV1/VC compensates for body size
- T_{CO} (transfer factor): absorption of carbon monoxide in 1 breath (gas exchange)

Functional Classification of Lung Disease

Distinctive clinical and physiological features define:

- Obstructive lung disease: decreased FEV1 and FEV1/VC
- Restrictive lung disease: decreased FEV1. Normal FEV1/VC. Decreased T_{CO} .

Respiratory failure (causes)

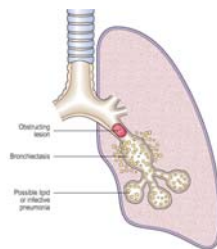
- Ventilation defects (CNS, neuromuscular defects, drugs)
- Perfusion defects (cardiac failure, pulmonary emboli)
- Gas exchange defects (fibrosis, consolidation, emphysema)
 Lead to hypoxia and hypercapnia
 Often more than factor one will operate

Airway Narrowing/Obstruction

- Muscle spasm
- Mucosal oedema (inflammatory or otherwise)
- Airway collapse due to loss of support
- (Localised obstruction due to tumour or foreign body)

Localised obstruction

- Collapse
- Lipid pneumonia
- Infection
- Bronchiectasis (if longstanding)



Main Categories of (diffuse) Obstructive Disease

- Asthma
- Chronic obstructive pulmonary disease (COPD/COAD/COLD)

Chronic Obstructive Disease

- Chronic bronchitis
- Emphysema

Symptomatic patients often have both

Bronchial Asthma

A chronic *inflammatory* disorder characterised by hyperreactive airways leading to *episodic reversible bronchoconstriction*

Asthma

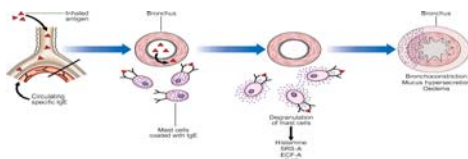
- Extrinsic - response to inhaled antigen
- Intrinsic - non-immune mechanisms (cold, exercise, aspirin)

Immunological Mechanisms

Type I hypersensitivity - allergen binds to IgE on surface of mast cells

- Degranulation (histamine)
 - muscle spasm
 - inflammatory cell influx (eosinophils)
 - mucosal inflammation/oedema
- Inflammatory infiltrate tends to chronicity

Pathology of asthma



- Airway inflammation with mucosal oedema
- Mucus plugging



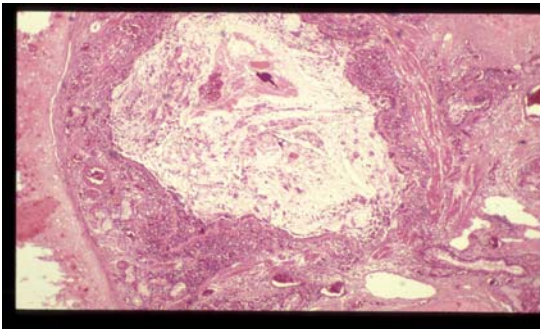
Mucosal oedema



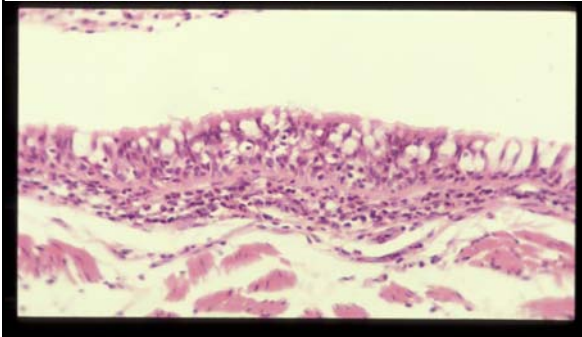
Mucus plugs



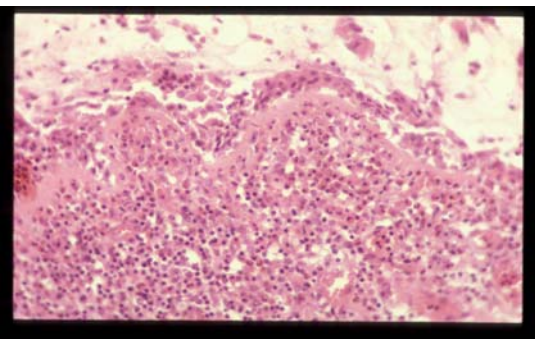
Mucus plug/inflammation



Inflammation



Inflammation/epithelial damage



Chronic Obstructive Pulmonary Disease

- Chronic bronchitis
- Emphysema

A smokers disease
Symptomatic patients usually have both

COPD

- In top 5 causes of death in Europe/N. America
- Clinical course characterised by infective exacerbations (*Haemophilus influenzae*, *Streptococcus pneumoniae*)
- Death by respiratory failure or heart failure ("cor pulmonale")

Chronic Bronchitis

Cough productive of sputum on most days for 3 months of at least 2 successive years

- An epidemiological definition
- Does not imply airway inflammation

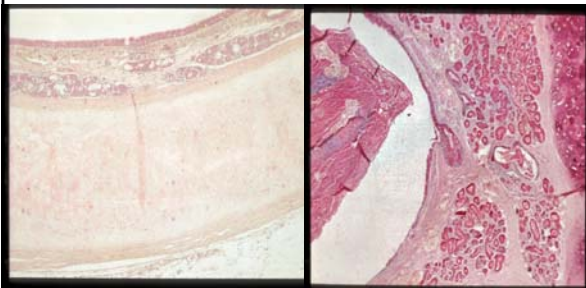
Chronic Bronchitis

- Chronic irritation \Rightarrow defensive increase in mucus production with increase in numbers of epithelial cells (esp goblet cells)
- Poor relation to functional obstruction
- Role in sputum production and increased tendency to infection

Chronic Bronchitis

- Non-reversible obstruction
- In some patients there may be a reversible ("asthmatic") component

Normal vs. Chronic Bronchitis



Small airways in Chronic Bronchitis

- More important than traditionally realised
- Goblet cell metaplasia, macrophage accumulation and fibrosis around bronchioles may generate functional obstruction

Emphysema

- Increase beyond the normal in the size of the airspaces distal to the terminal bronchiole
- Without fibrosis

The gas-exchanging compartment of the lung

Emphysema (types)

- Centriacinar (centrilobular)
- Panacinar
- Others (e.g. localised around scars in the lung)

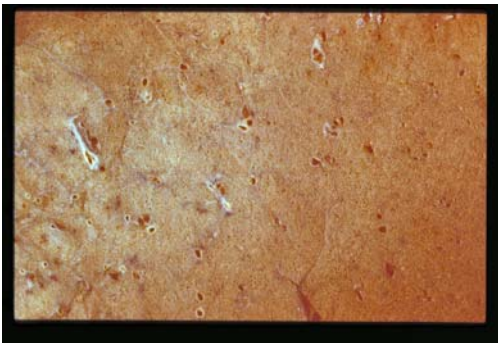
Emphysema

- Difficult to diagnose in life (apart from late disease – enlarged “barrel chest”)
- Radiology (CT) can show changes in lung density
- Correlation with function known from autopsy studies

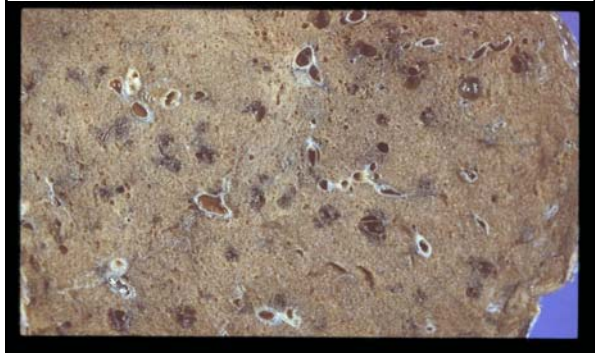
Emphysema

- “Dilatation” is due to loss of alveolar walls (tissue destruction)
- Appears as “holes” in the lung tissue

Normal lung



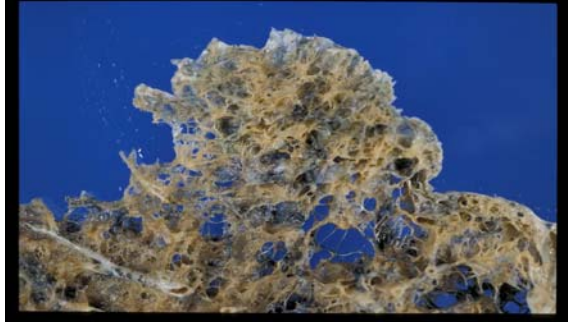
Centriacinar emphysema



Panacinar emphysema 1



Panacinar emphysema 2

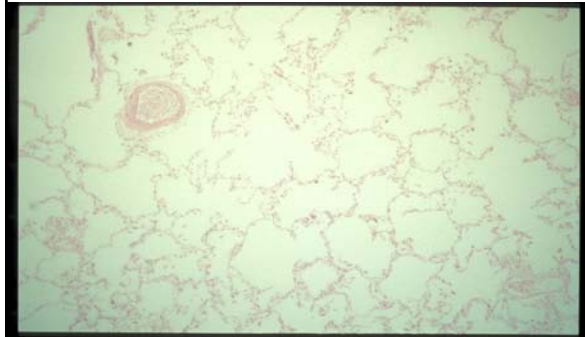


Emphysema

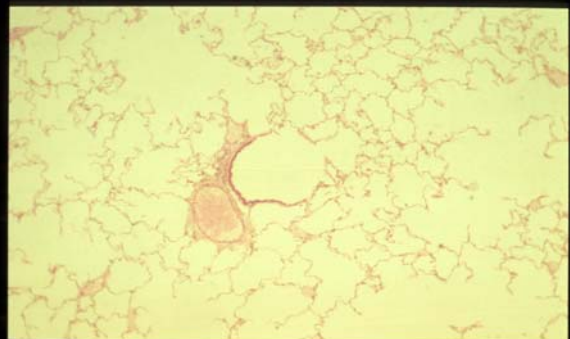
How do these changes relate to functional deficit?

- Poorly at macroscopic level
- Better with microscopic measurement

Normal



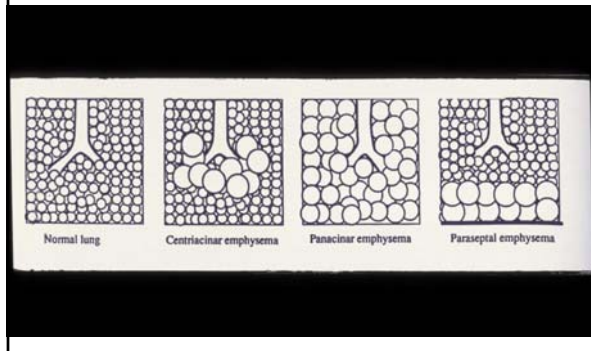
Early emphysema



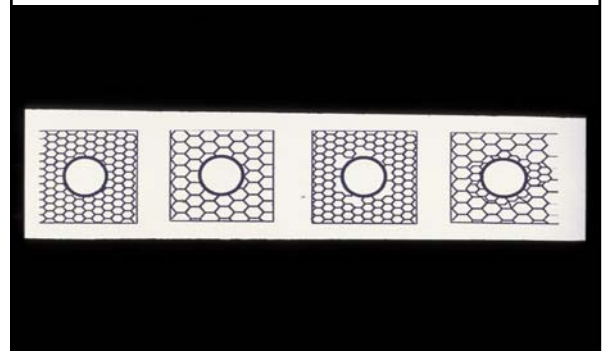
Emphysema Impairs Respiratory Function

- Diminished alveolar surface area for gas exchange (decreased T_{CO})
- Loss of elastic recoil and support of small airways leading to tendency to collapse with obstruction

Loss of surface area (emphysema)



Loss of support on bronchiolar walls



As disease advances....

↓ Pa O₂ leads to:

- Dyspnoea and increased respiratory rate
- Pulmonary vasoconstriction (and pulmonary hypertension)



Epidemiology of COPD

- Smoking
- Atmospheric pollution
- Genetic factors

Pathophysiology of Emphysema

High rate of emphysema in the rare genetic condition of α 1 antitrypsin deficiency

- THE PROTEASE/ANTIPROTEASE HYPOTHESIS

Elastic Tissue

- Sensitive to damage by *elastases* (enzymes produced by neutrophils and macrophages)
- $\alpha 1$ antitrypsin acts as an anti-elastase

Imbalance in either arm of this system predisposes to destruction of elastic alveolar walls (emphysema)

Tobacco smoke.....

- Increases nos. of neutrophils and macrophages in lung
- Slows transit of these cells
- Promotes neutrophil degranulation
- Inhibits $\alpha 1$ antitrypsin