Chronic obstructive pulmonary disease

COPD

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COPD

FEV1 ↓

Chronic bronchitis

inflammatory thickening of the wall and intermittent luminal plugging

or

chronic obstructive bronchiolitis

inflammatory thickening of the wall and peribronchiolar fibrosis

Emphysema

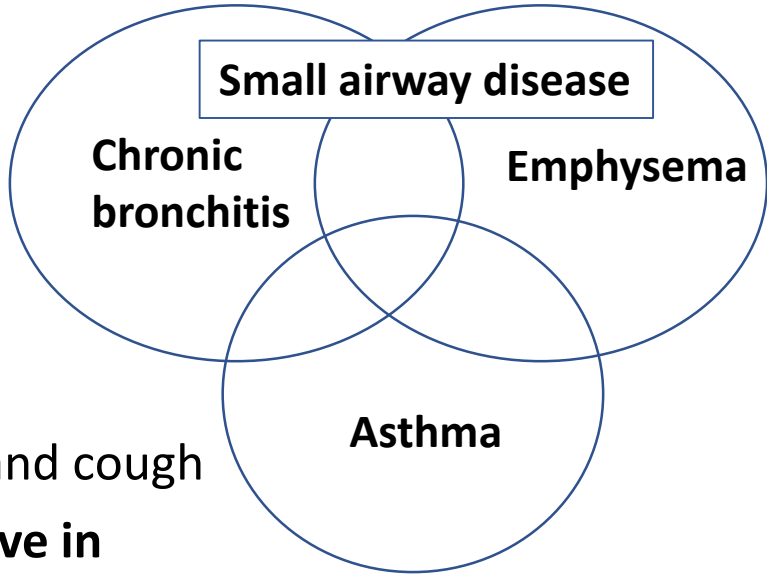
premature closure of basically normal airways because of diminished pulmonary elastic recoil

Asthma

airway narrowing is caused by increased amounts of mucus, inflammatory oedema and muscular hypertrophy

airflow limitation

Clinical presentations of COPD



- Breathlessness, impaired exercise tolerance and cough
- The **cough** is particularly likely to be **productive in chronic bronchitis**
- The sputum is typically mucoid and white
- **In episodes of acute bronchitis** the sputum becomes **purulent** and yellow
- **Type A** *„pink puffer”* patients shows rapid shallow breathing and near normal blood gases (hyperventilation in **emphysema**). Cachectic appearance.
- **Type B**: *„blue bloater”* (blue: **cyanosis**) patients are hypoxic. It may lead to **cor pulmonale** and cardiac failure. They are usually obese (**chronic bronchitis**).

Chronic bronchitis

Definition

persistent or recurrent excess of secretion in the bronchial tree on most days for at least 3 months in the year, over at least 2 years

Causes

- **Cigarette smoking** (the most frequent cause)
- General **air pollution**
- Indoor air pollution combustion of biomass
- Occupational **dust exposure**, fog, and a damp, cold climate
- Infections by respiratory viruses and bacteria

Mechanism

- inflammation, mucus secretion ↑
- upregulation of the mucin (MUC) genes, Epidermal Growth Factor (EGF) is a key mediator in the mucous cell hyperplasia

Chronic bronchitis

Gross appearance

- Bronchi are filled with mucus (+/- pus). The mucosa is dusky red.
- The distal bronchi characteristically are slightly dilated

Microscopic appearence

- Inflammation: lymphocates, macrophages (+/- neutrophils)
- The submucosal glands are enlarged (reactive process to irritation)
- Shift in gland type from mixed seromucous to pure mucous.
- Measurement of **Reid index**: ratio of the thickness of the gland layer to the thickness of the wall between the base of the surface epithelium and the internal surface of the cartilage.
- **Reid index may double** from the normal value of 0.3
- Increased number of goblet cell
- Sulphomucin↓
- Sialomucin ↓

Chronic Bronchitis, Acute Exacerbations (AECB)

Pathogens:

Bacterial infection in 50% of cases: Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis

Viruses: **influenza**, **rhinovirus**, parainfluenza, RSV and others

Additional offenders: allergens, smoking, toxic fumes, etc.

Significant AECB flare:

Increased sputum production, Increased cough, Increased dyspnea

Morphology of chronic bronchitis with superadded infection:

mucus has accumulated in the bronchial lumen

pus in the lumen and chronic inflammation of the bronchial wall.

Emphysema

Emphysema is a **pathological inflation** of the affected tissue.

Definition: **abnormal, permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls.**

Morphology: The lungs have a doughy feel, pit on pressure, do not collapse when the chest is opened and overlap the heart because of their great size.

Centriacinar emphysema

- The **lesion involves the centre of the acinus** (the alveolar walls are lost)
- The changes are pronounced **in the upper lobes**
- Severe centriacinar emphysema may be difficult to distinguish from the panacinar
- Spaces that exceed 1 cm in size are known as bullae (in severe cases).

Panacinar emphysema

- Panacinar emphysema **involves all the air spaces beyond the terminal bronchiole**
- Severe **parenchymal destruction**

Paraseptal emphysema

- affects **air spaces adjacent to septa or to the pleura**

(periphery of the lung lobules)

- it may result from forces pulling on the septa and perhaps also from inflammation. (it may be associated to other forms of emphysema).

Interstitial emphysema

- emphysema like conditions
- air enters tissues that are normally airless
- **air reaches the interstitial tissues of the lung** when abnormal pressure ruptures the alveolar walls. (barotrauma).
- caused by excessively high pressure caused by artificial respiration, exposure to the blast of explosions, sudden decompression, or tearing of alveolar walls by fractured ribs or by instruments.

Etiology and pathogenesis of emphysema

Centriacinar emphysema is a result of **airway inflammation** related to **cigarette smoking** .

Elastases released by neutrophil leukocytes during episodes of acute inflammation **have central role**.

Panacinar emphysema, is associated with an **inherited deficiency of α_1-antitrypsin**. Deficiency of this protein results in **elastases acting unopposed on the connective tissues** of the lungs.

Patomechanism of emphysema

- **Reduced amount of elastic tissue** of lung parenchyma results in premature **closure of terminal bronchioles during expiration**
- The resultant air trapping is responsible for the **overinflation of the lungs** and **'barrel chest'** that are characteristic of emphysema.
- By the time air spaces measure about 4 mm in diameter, the alveolar surface is less than 10% of normal
- Symptoms: **dyspnoe**, impaired expiratory flow, **weight loss,**
- **blood gas value may be normal at rest - „pink puffer"**
- **Cor pulmonale – right sided heart failure, respiratory failure, pneumothorax**

Bronchiectasis (dilation of the bronchi)

Clinical features

- **chronic productive cough** of abundant foul sputum
- **dyspnoe** (orthopnoe and cyanosis may occur)

Etiology

- Infection: **measles, pertussis, adenovirus**
- Chemical damage: gastric acid, toxic gases
- Obstruction: **tumour, foreign body**, enlarged hilar nodes
- Impaired local defence: **cystic fibrosis, ciliary dyskinesia**
- Allergy: allergic bronchopulmonary aspergillosis

Pathogenesis

Injury of bronchial epithelium

inhibition of ciliary clearance

secondary bacterial colonisation

continued infection and inflammation

inflammatory weakening of the walls of the bronchi resulted from proteolytic enzymes and oxygen radicals released by neutrophils.

Structural changes

- **Fibromuscular and elastic framework of the bronchial wall are partly destroyed**.
- Dilation (cylindrical or saccular) of airways up to four times in diameter (dilation may be localized in case of tumour or foreign body)
- Congestion in mucosa.
- The **dilated airways** are filled with a **purulent exudate.**
- The distal lung shows **absorption type collapse**.

Complications

- Lung abscess and empyema
- Metastatic abscesses, particularly in the brain, generalised amyloidosis and immune complex vasculitis, cor pulmonale is common in the generalised form
- Pseudomonas aeruginosa: it survives within a biofilm on the mucosal surface.
- Bronchiectatic cavities may be colonised saprophytically by fungi

Bronchial asthma

Definition:

periodically difficult breathing caused by widespread narrowing of the bronchi

Symptoms decrease in severity over short periods of time, either spontaneously or under treatment.

Symptoms:

episodic attacks of **wheezing, tightness of the chest**,

shortness of breath and cough.

the difficulty of breathing becomes **particularly apparent during expiration**

Extrinsic asthma (atopy):

Allergy to exogenous substances, begins in **childhood** and is generally paroxysmal. It is **often familial**.

Intrinsic asthma:

Onset is in adult life. It is chronic and tends to **worsen with age**.

Bronchial asthma

Extrinsic asthma can be provekd by dusts, pollen, animal dander, and foods.

Intrinsic asthma: provoked by rhinovirus, parainfluenza virus infection

Atmospheric pollution aggravates asthma.

Morphology

The **sputum is viscous and yellow.** Yellow color is due to myeloperoxidase.

Microscopic appearence of formed elements: Charcot–Leyden crystals, Curschmann's spirals. **Charcot–Leyden crystals**: consisted of lysophospholipase originating from the **cell membranes of eosinophils** (arrowhead).

A **Curschmann spiral** is a corkscrew-shaped twist of **condensed mucus** several millimetres long (arrow).

Morphology

Gross

Status asthmaticus: mucous plugging of airways and hyperinflation of the lungs.

Latin term: „volumen pulmonum auctum acutum”

Microscopic

Airway narrowing caused by **increased amounts of mucus**, inflammatory oedema and **muscular hypertrophy**.

Eosinophils infiltrate the walls of bronchi and proximal bronchioles.

Lymphocytes (mainly T-helper cells) are generally numerous in asthma.

Separation and detachment of superficial columnar epithelial cells from the underlying basal cells is observable.

The epithelial **basement membrane is often thickened** in asthma (not specific for this disease).

Pathogenesis of asthma

Inhaled antigens first react with immunoglobulin E bound to mast cells free in the bronchial lumen, and this causes **release of mediators from these mast cells**

Mast cell secretes a range of bioactive substances

Eosinophil secretes substances that are **injurious to** the integrity of the **respiratory epithelium**.

Cystic Fibrosis (Mucoviscidosis)

- **Disorder of ion transport**
- **Decreased fluid transport in exocrin glands and epithelial surfaces**
- Complications: **recurrent infections**, pancreatic insufficiency, steatorrhea, malnutrition, hepatic cirrhosis, **intestinal obstruction**, and male infertility
- Incidence: 1 in 2500 birth
- **autosomal recessive inheritence**
- even heterozygote carriers have a higher incidence of respiratory and pancreatic diseases as compared with the general population

<u>Different mutations with different consequences exist:</u>

Defective protein synthesis, abnormal protein folding, defective regulation, decreased conductance, reduced abundance, altered function in regulation of ion channels.
(**ΔF508** mutation – deletion of three nucleotides coding for phenylalanine –results in complete lack of CFTR. **70% of all cases**.)

Pathogenesis of cystic fibrosis

- Chloride channel defect **in the sweat duct** (top) causes **increased chloride and sodium concentration** in sweat.
- **In the airway** (bottom), patients have **decreased chloride secretion** and increased sodium and water reabsorption leading to **dehydration of the mucus layer** coating epithelial cells, **defective mucociliary action**, and **mucus plugging of airways**.

Morphological findings in cystic fibrosis

- **viscous mucus secretions** of the submucosal glands of the airways leads to **secondary obstruction and infection of the air passages**
- The **bronchioles are often distended with thick mucus** associated with marked hyperplasia and hypertrophy of the mucus-secreting cells.
- Superimposed (mainly bacterial) infections result in severe chronic bronchitis and bronchiectasis.
- lung abscesses frequently develop