

Lecture 2 respiratory pathology

4th year MBBS

OBSTRUCTIVE AIRWAY DISEASE

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During this lecture

- Obstructive airways disease
 - Asthma
 - Bronchiolitis
 - COPD
- Patho physiology and morphology

During this lecture

- Obstructive airways disease
 - *Asthma*
 - *Bronchiolitis*
 - COPD6th may at 9am
- Patho physiology and morphology

- **ASTHMA**

ASTHMA

- Asthma is a chronic inflammatory disorder of the airways that causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night and in the early morning.

ASTHMA

The hallmarks of the disease

- 1. Increased airway responsiveness to a variety of stimuli, resulting in episodic bronchoconstriction; inflammation of the bronchial walls; and***
- 2. Increased mucus secretion.***

ASTHMA

- **STATUS ASTHAMTICUS**

–Acute exacerbation of asthma that remains **unresponsive to initial treatment** with bronchodilators.

–It can vary from a mild form to a severe form with bronchospasm,

ASTHMA

- **INCIDENCE AND PREVALENCE**

- Common in younger

- Peak age 5-10 years

- Common in industrialized areas

- In UNITED STATES

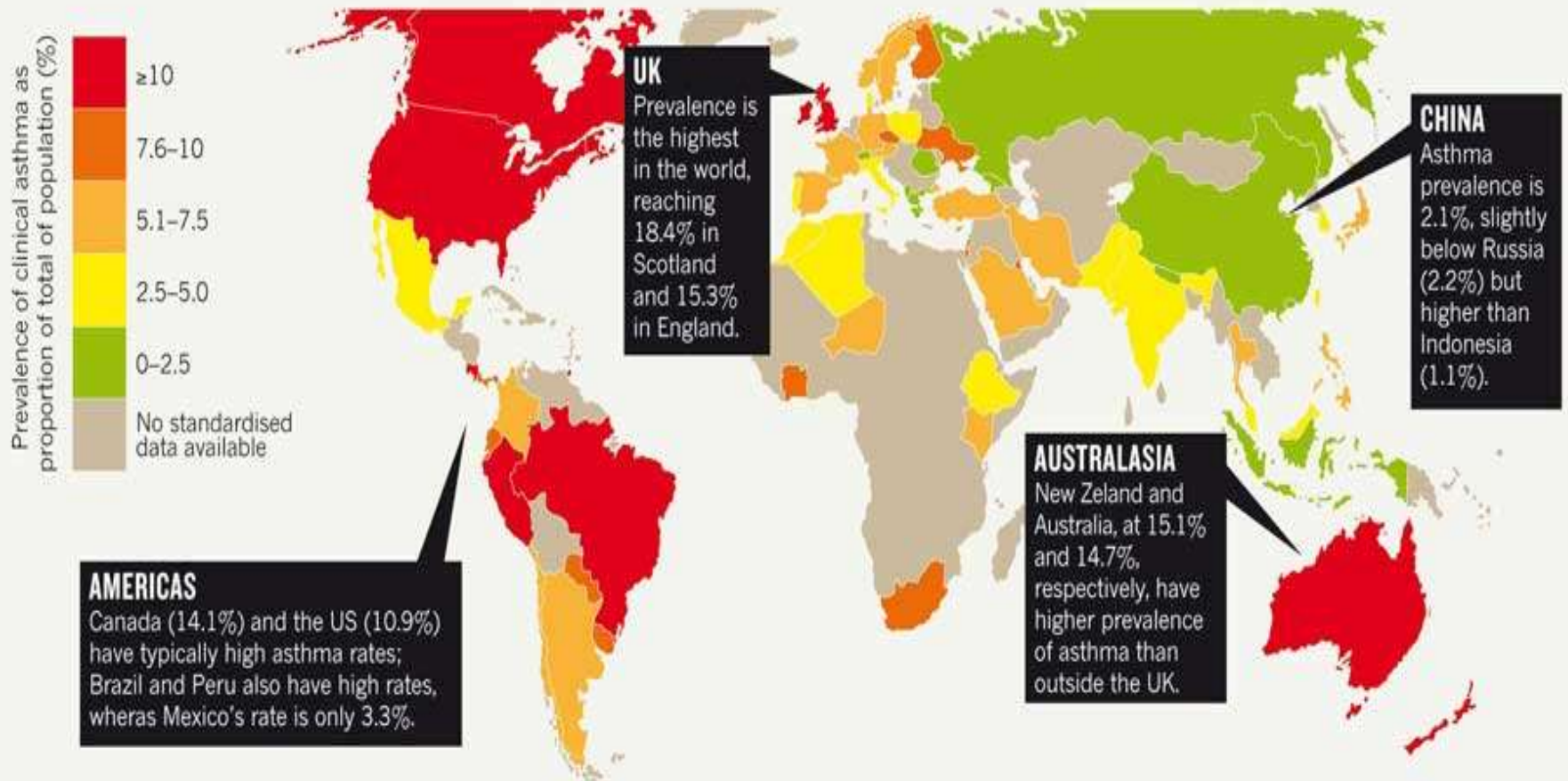
- Incidence 10 %

- Asthma prevalence is higher among children, women, blacks, and persons

Geographical prevalence of asthma

ASTHMA AROUND THE WORLD

Global studies confirm an association with westernized lifestyles



ASTHMA

- **Genetic analysis**
 - **Chromosome 5q**, near the gene cluster encoding the cytokines
 - IL-3, IL-4, IL-5, IL-9, and **IL-13** and the IL-4
 - LPS (CD14) & the β 2-adrenergic receptors are mapped here

- Types of asthma

ASTHMA

- Types
 - Atopic asthma
 - Non atopic asthma
 - Occupational asthma
 - Drug induced asthma

ASTHMA

1. atopic asthma

- Occurs in patients prone to develop allergic manifestation like rhinitis,eczema
- Usually children and younger adult suffer
- They develop asthma after exposure to dust ,smoke and other allergin

ASTHMA

2. Non atopic asthma

- Occurs in patient with little history of allergic reaction
- They have sensitive respiratory epithelial that develop asthma symptoms in response to cold ,flue and emotional stress
- *It is thought that virus-induced inflammation of the respiratory mucosa lowers the threshold of the subepithelial vagal receptors to irritants.*

ASTHMA

3. Occupational

- Individuals in certain professions develop asthma on **chronic exposure to small amount** of inhaled particles .
- stimulated by
 - **fumes** (epoxy resins, plastics)
 - **organic and chemical dusts** (wood, cotton, platinum), gases (toluene)
 - **other chemicals** (formaldehyde, penicillin products)

ASTHMA

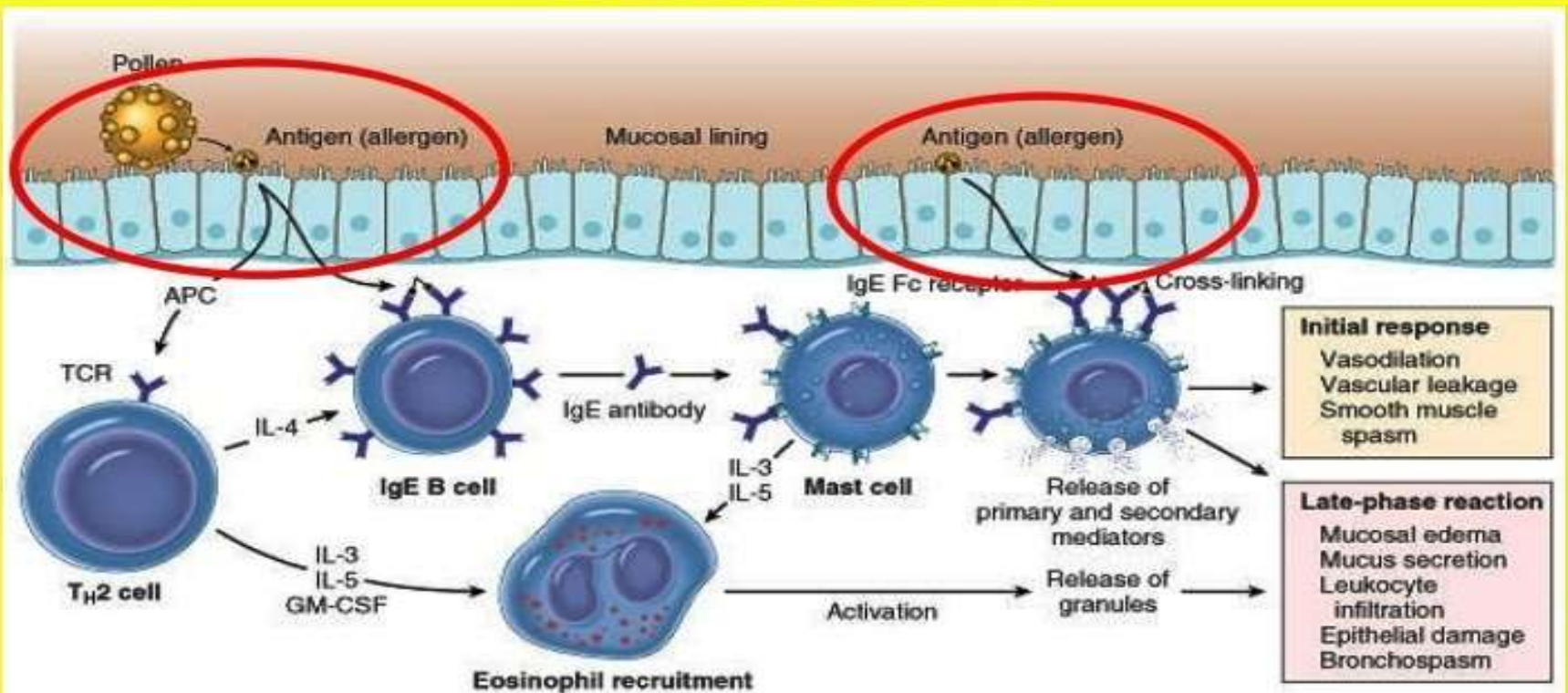
4. Drug induced asthma

- These patient develop asthma symptoms due to intake of drugs.
- Aspirin and NSAIDS
- Beta blockers

- Increased synthesis of leukotrienes or blockage of sympathetic fibres.

Pathophysiology of atopic asthma

Type I Hypersensitivity A sequence of Events



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Pathophysiology of atopic asthma

- Genetic predisposition to type I hypersensitivity (“atopy”)
- Exposure to environmental triggers ..poorly understood

Pathophysiology of atopic asthma

- Ig E coats submucosal mast cells
- Repeat exposure to the allergen triggers the mast cells to release granule contents and produce cytokines and other mediators,
 - *Early -phase (immediate hypersensitivity) reaction*
 - *the late-phase reaction.*

Pathophysiology of atopic asthma

- **The early reaction** is dominated by
 - Bronchoconstriction , via sub epithelial vagal fibres
 - Increased mucus production
 - Vasodilatation with increased vascular permeability.
- **The late-phase reaction**
 - consists largely of inflammation with recruitment of leukocytes, notably eosinophils, neutrophils, and more T cells

Pathophysiology of atopic asthma

- **Type 1 hypersensitivity reaction**
 - Sensitive individuals inherit genes that code for strong TH-2 reaction to allergen
- **Airways**
 - TH 2 are formed in response to allergen
 - They secrete cytokine
 - IL_4.....Ig E
 - IL_5.....eosinophils
 - IL-13.....mucous production

Pathophysiology of atopic asthma

- **Early phase mediators**

strong effect

- *Leukotrienes C4, D4, and E4,*

- bronchoconstriction as well as increased vascular permeability and increased mucus secretion,

- *Acetylcholine*

- released from intrapulmonary motor nerves,

Pathophysiology of atopic asthma

- **Early phase mediators**
- *less important*
 - *Histamine*
 - *Potent bronchoconstrictor, increased vascularity*
 - *Prostaglandin*
 - *bronchoconstriction*
 - *Serotonin*
 - *Bronchoconstriction and mucous secretion*
 - *Platelet activating factor*

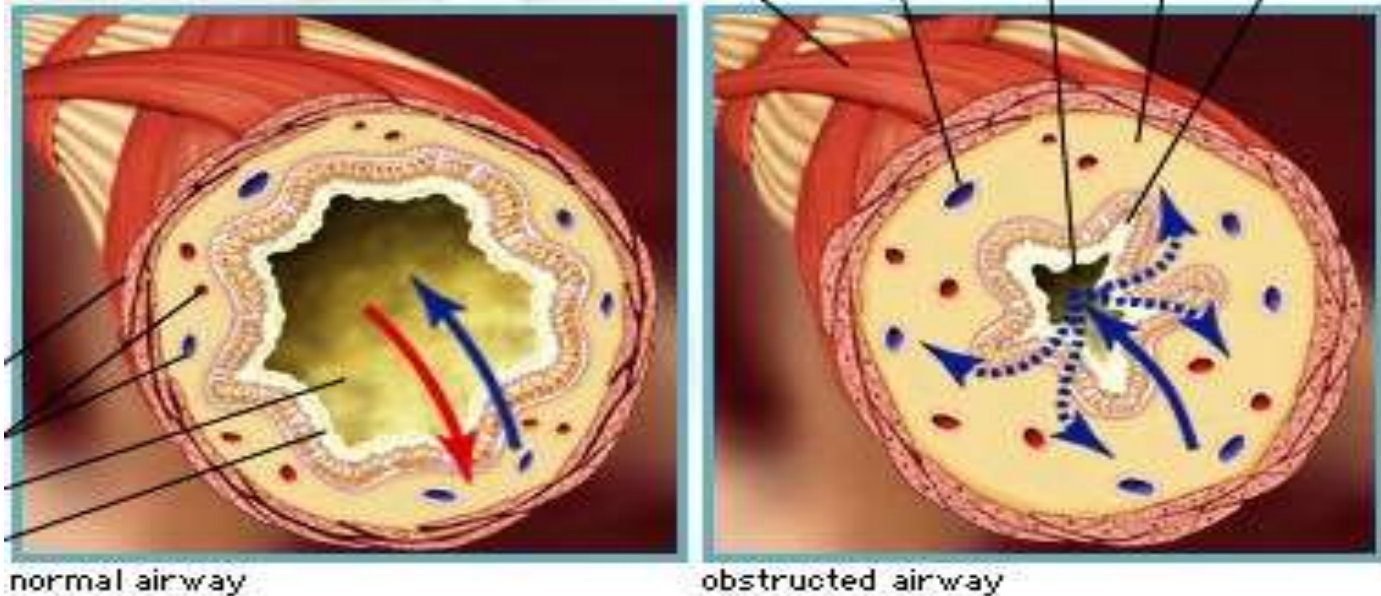
Pathophysiology of atopic asthma

- **Late phase mediators**
 - Important
 - IL-1, TNF, and IL-6 chemokines (e.g., eotaxin), neuropeptides, nitric oxide, bradykinin, and endothelins.

Morphology of asthma

ASTHMA

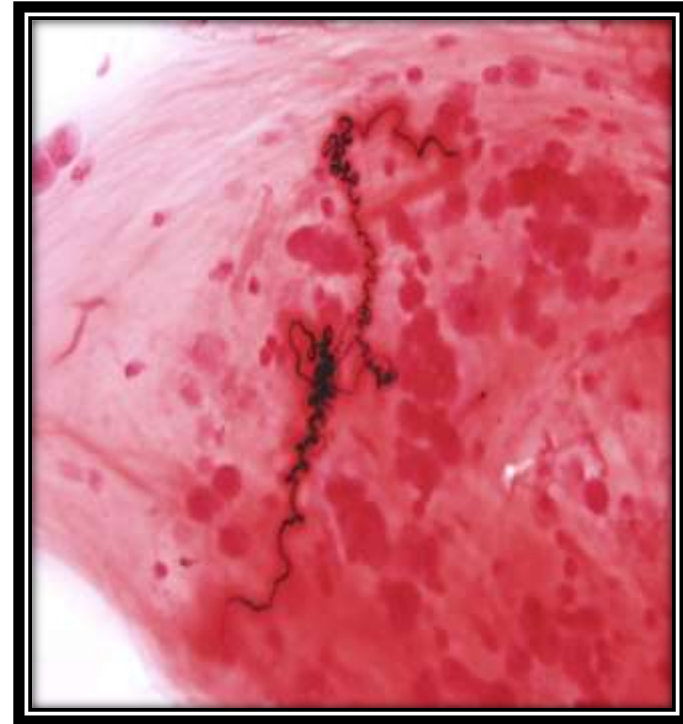
- Gross Morphology
 - Occlusion of bronchi and bronchioles by thick, tenacious mucus plugs.



ASTHMA

histological morphology

- Large mucus plugs contain spirals of shed epithelium called Curschmann spirals
- Numerous eosinophils and Charcot-Leyden crystals made up of neutrophil remnants



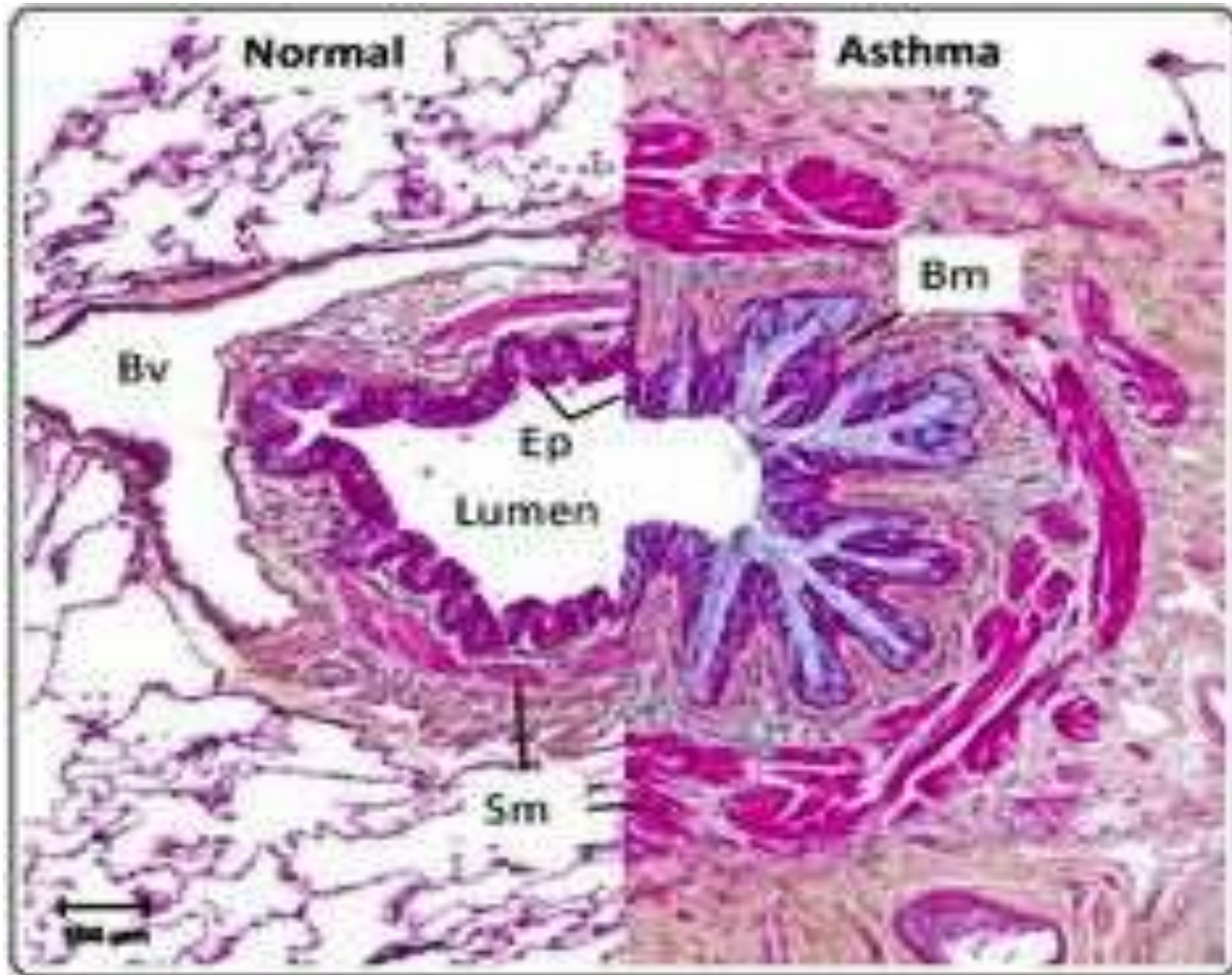
ASTHMA

histological morphology,

- **Airway remodeling**

- Overall thickening of airway wall
- Sub-basement membrane fibrosis (due to deposition of type I and III collagen)
- Increased vascularity
- Hyperplasia of submucosal glands and mucous metaplasia of airway epithelial cells
- Hypertrophy and/or hyperplasia of the bronchial wall muscle

ASTHMA



ASTHMA

Clinical presentation

- These symptoms of chest tightness, dyspnea, wheezing, and cough with or without sputum production,
- Status asthmaticus, the severe acute paroxysm persists for days and even weeks, and under these circumstances airflow obstruction might be so extreme as to cause severe cyanosis and even death.

ASTHMA

Clinical presentation

- increase in airflow obstruction (from baseline levels)
- difficulty with exhalation (prolonged expiration, wheeze)
- elevated eosinophil count in the peripheral blood

Asthma

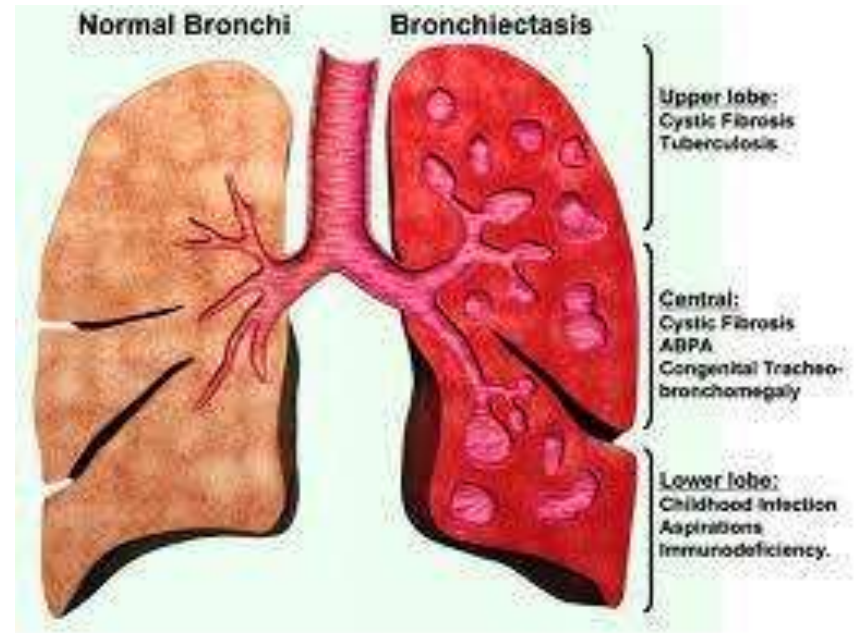
Outcome and long term complications

- Reduced physical ability
- Raised pulmonary pressures
- Right heart failures
- Increased risk of respiratory tract infection

Bronchiectasis

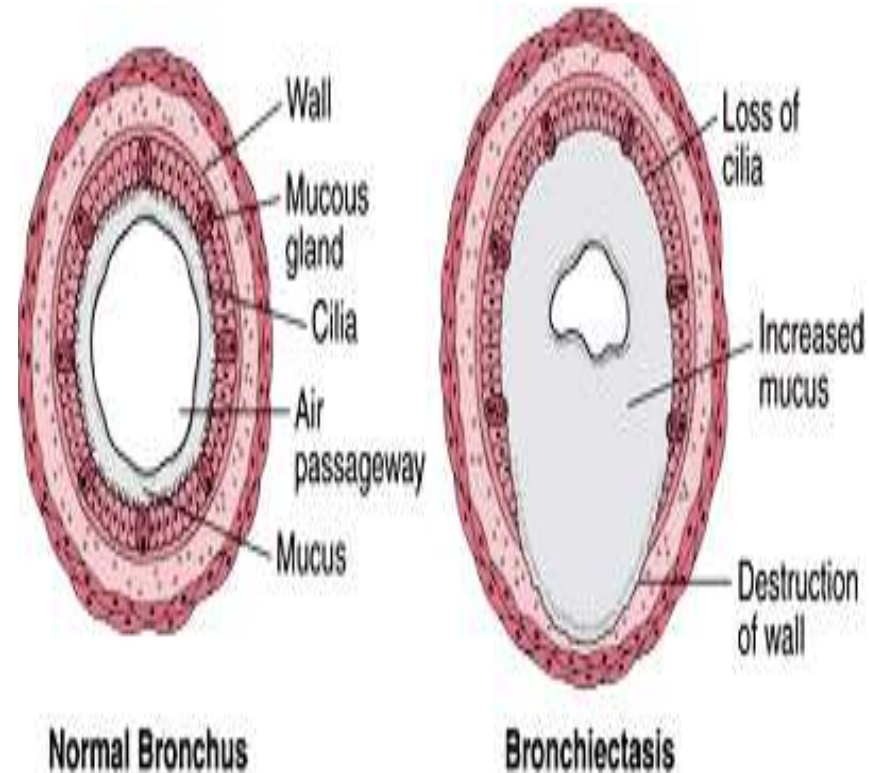
Bronchiectasis

- *Permanent dilation of bronchi and bronchiole caused by destruction of the muscle and elastic tissue, resulting from or associated with chronic necrotizing infections.*
- an uncommon condition.



Bronchiectasis

- ***Permanent dilation of bronchi and bronchiole caused by destruction of the muscle and elastic tissue, resulting from or associated with chronic necrotizing infections.***
- an uncommon condition.



Bronchiectasis

types

- **Congenital or hereditary conditions**
 - cystic fibrosis, intralobar sequestration of the lung, immunodeficiency states, and primary ciliary dyskinesia and Kartagener syndromes
- ***Post infectious conditions*** necrotizing pneumonia
 - Bacteria (*M. tuberculosis*, *S.aureus*, *H.influenzae*, *Pseudomonas*),
 - viruses (adenovirus, influenza virus, human immunodeficiency virus [HIV]),
 - fungi (*Aspergillus* species)

Bronchiectasis

types contd..

- ***Bronchial obstruction***
 - due to tumor, foreign bodies, and occasionally mucus impaction in which the bronchiectasis is localized to the obstructed lung segment
- **Other conditions**
 - rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease

Bronchiectasis

path physiology

- Infection and obstruction are major mechanism
 - **Obstruction**
 - leads to pooling of secretion due to mucocilliary dysfunction.
 - This leads to inflammation and destruction of walls
 - **Severe infections** of the bronchi lead to inflammation, often with necrosis, fibrosis, and eventually dilation of airways.

Bronchiectasis

Pathophysiology

- **Cystic fibrosis**

- the primary defect in ion transport leads to defective mucociliary action, and accumulation of thick viscid secretions that obstruct the airways.
- Severe repeated infection take place leading to destruction of supporting structure and result in bronchiectasis

Bronchiectasis

Pathophysiology

Ciliary dysfunction

Primary ciliary dyskinesia , an autosomal recessive syndrome with poorly functioning cilia contribute to the retention of secretions. There is an absence or shortening of the dynein arms that are responsible for the coordinated bending of the cilia.

Kartagener syndrome

The lack of ciliary activity interferes with bacterial clearance, predisposes the sinuses and bronchi to infection, and affects cell motility during embryogenesis, resulting in the situs inversus. Males with this condition tend to be **infertile**, as a result of sperm dysmotility.

Bronchiectasis

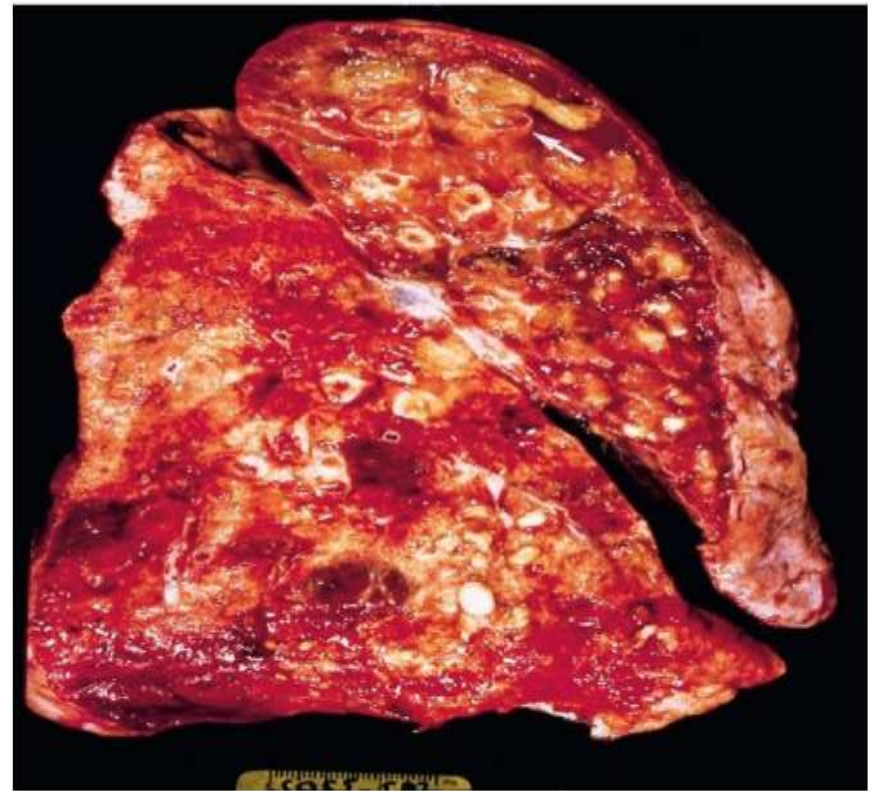
Gross morphology

- Lower lobes bilaterally, particularly vertical air passages
- Most severe in the more distal bronchi and bronchioles.
- Localized to single unit if obstruction is by tumor or foreign body
- **The airways are dilated, sometimes up to four times normal size.**
- Characteristically, the bronchi and bronchioles are sufficiently dilated that they can be followed almost to the pleural surfaces.

Bronchiectasis

Gross morphology

On the cut surface of the lung, the transected dilated bronchi appear as cysts filled with mucopurulent secretions .



Bronchiectasis

Histological findings

- Vary with the activity and chronicity of the disease.
- In active case there is an intense inflammatory exudation within the walls of the bronchi and bronchioles, associated with desquamation of the lining epithelium and extensive areas of necrotizing ulceration.
- Pseudo stratification of the columnar cells or squamous metaplasia of the remaining epithelium.
- lung abscess can be seen in severe cases

Bronchiectasis

Histological findings

- **Fibrosis**

- of the bronchial and bronchiolar walls and peribronchiolar fibrosis develop in the more chronic cases, leading to varying degrees of subtotal or total obliteration of bronchiolar lumens.

- **On CULTURE**

- a mixed flora can be seen from the involved bronchi, including staphylococci, streptococci, pneumococci, enteric organisms, anaerobic and microaerophilic bacteria, and (particularly in children) *Haemophilus influenzae* and *Pseudomonas aeruginosa*.

Bronchiectasis

clinical presentation

- Patient presents with productive cough with large amount of sputum that may be clear to turbid
- Sputum may contain blood
- Clinical examination ...wheezing reduced chest expansion and evidence of infection
- CT scan Chest can detect

End of the Lecture

GOOD LUCK