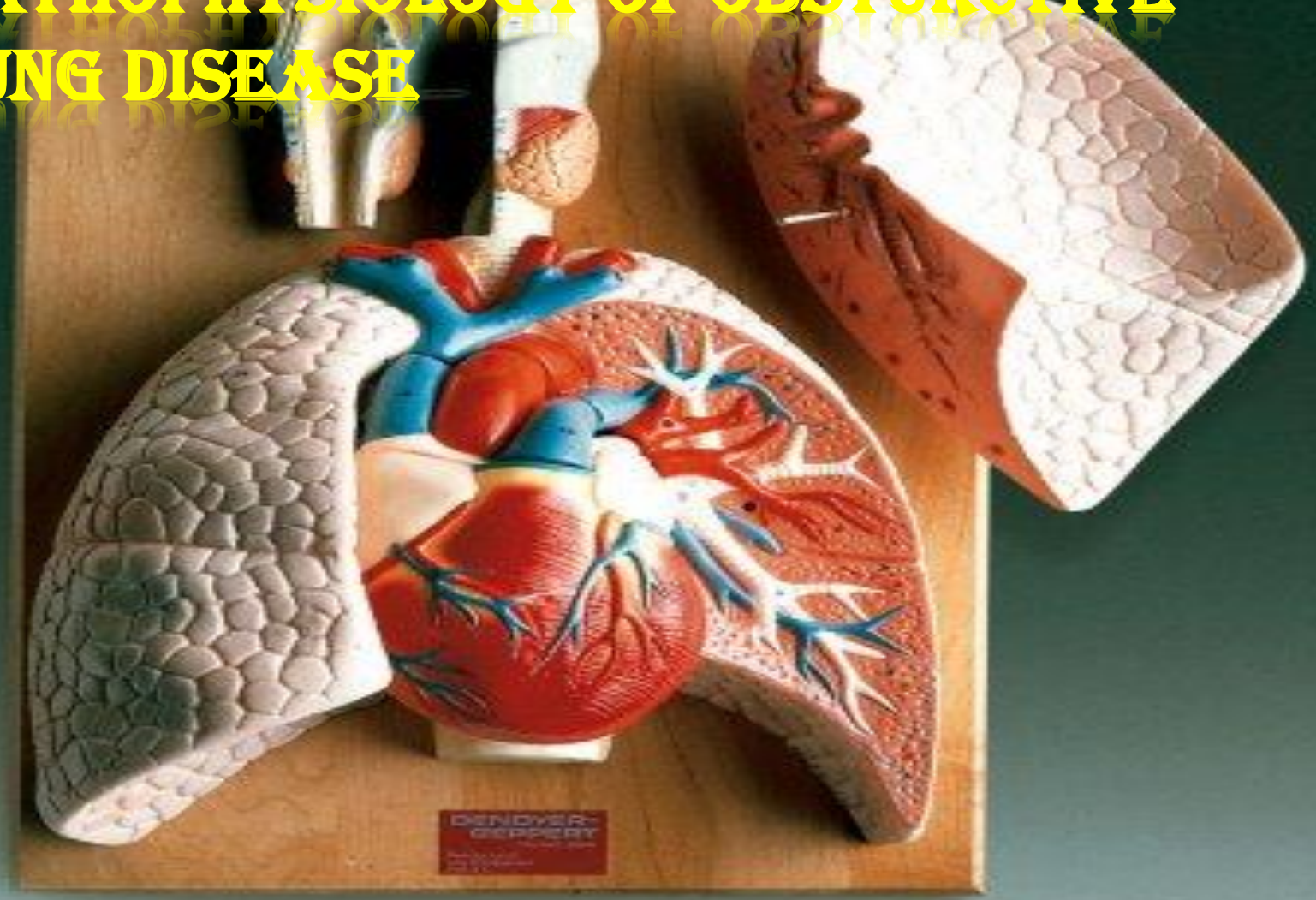
PATHOPHYSIOLOGY OF OBSTURCTIVE LUNG DISEASE



HINA VAISH

- Respiratory disease can be broadly divided into 2 type ;

- **Obstructive lung disease**
- **Restrictive lung disease**

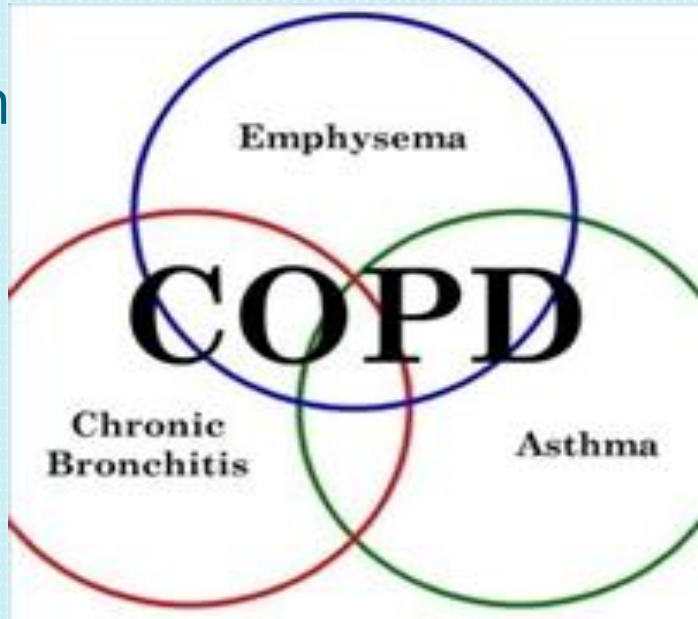
- Chronic obstructive lung disease is a term that refers to a group of disease that effect the ability of a person to breath.
- Combination of multiple condition
- Each of condition have their own symptoms , which do not normally become noticeable until damage to the lung become severe.

- Include condition in which ;

- Resistance to air flow -
  - Reversible factor such as bronchospasm or inflammation
  - Irreversible factor such as airway fibrosis or loss of elastic recoil owing to damage to the airway & alveoli.

They are ;

- COPD (chronic bronchitis & emphysem
- bronchectasis
- asthma
- cystic fibrosis

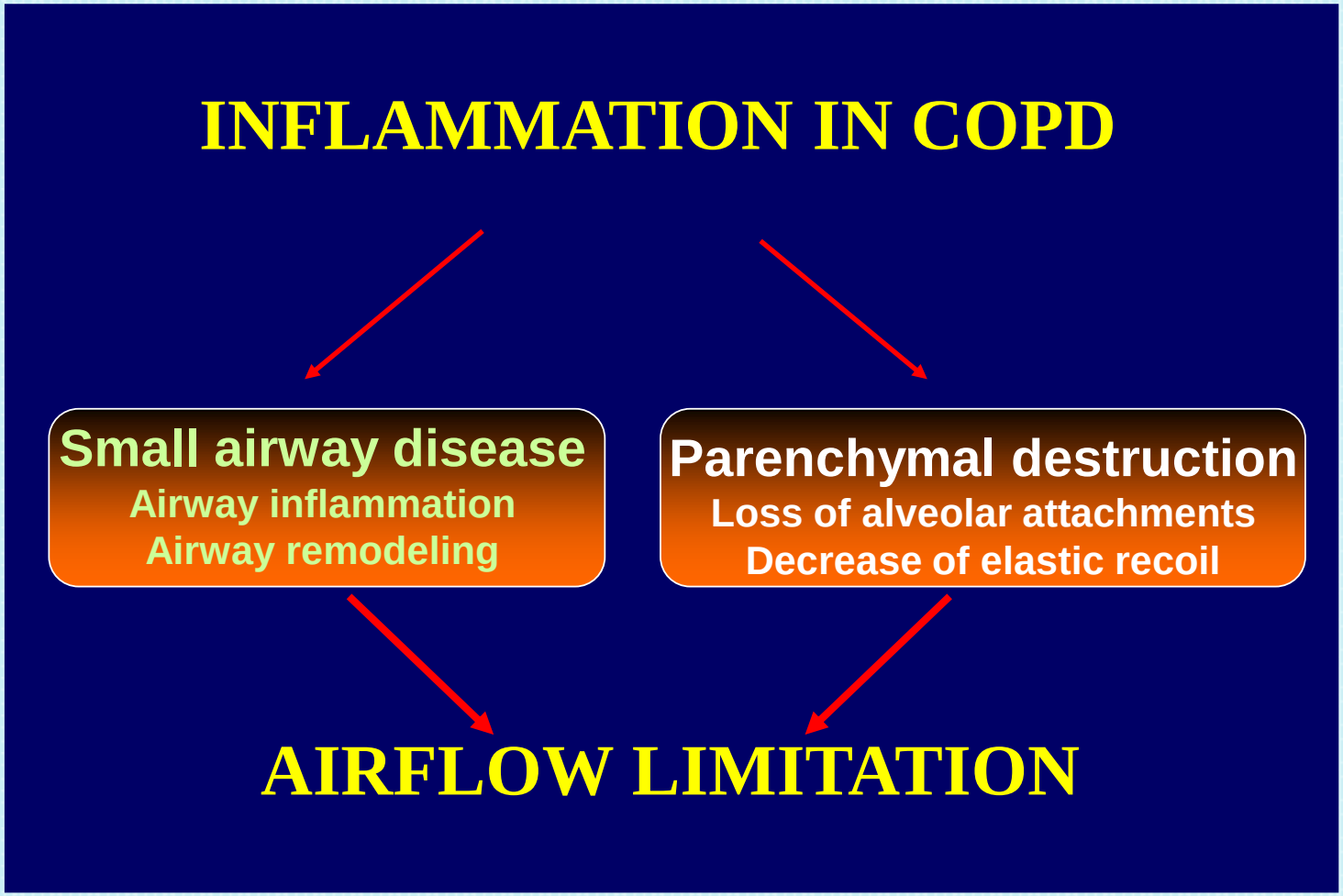


DEFINITION OF COPD

- COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients.
- Its pulmonary component is characterized by airflow limitation that is not fully reversible.
- The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.

RISK FACTORS FOR COPD

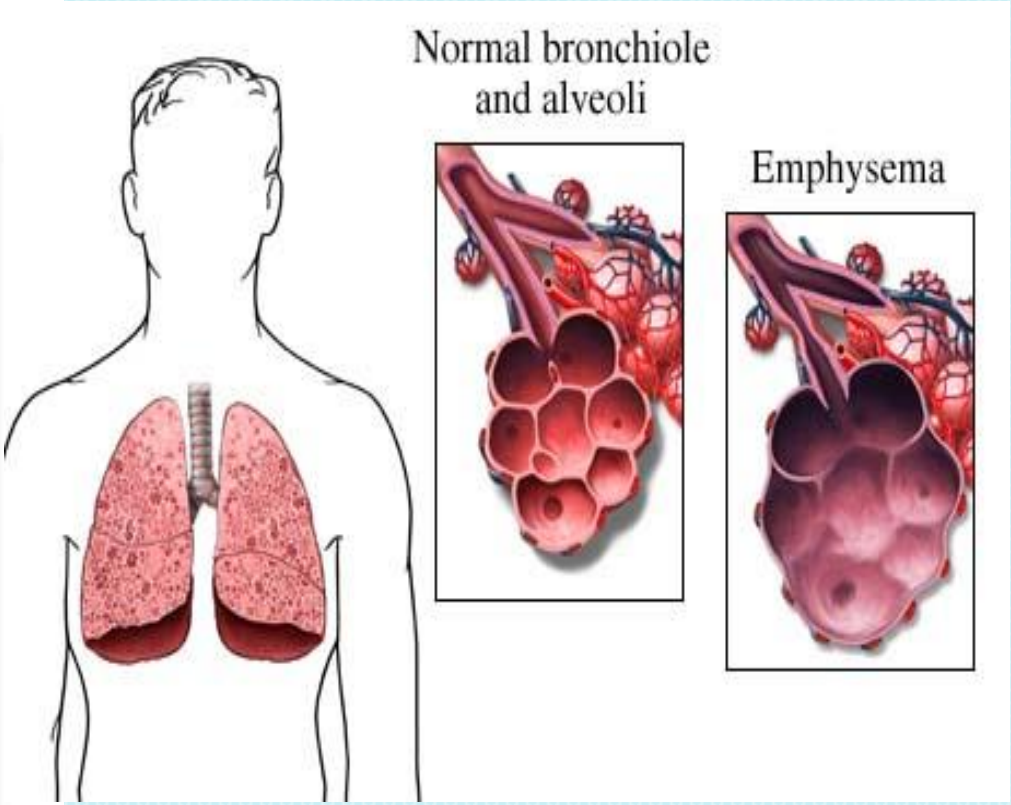
- Genes
- Exposure to particles
  - Tobacco smoke
  - Occupational dusts, organic and inorganic
  - Indoor air pollution from heating and cooking with biomass in poorly ventilated dwellings
  - Outdoor air pollution
- Lung growth and development
- Oxidative stress
- Gender
- Respiratory infections
- Socioeconomic status
- Nutrition
- Comorbidities


INFLAMMATION IN COPD
Small airway disease
Airway inflammation
Airway remodeling
Parenchymal destruction
Loss of alveolar attachments
Decrease of elastic recoil
AIRFLOW LIMITATION

- AIRFLOW limitation is caused by mixture of small airways disease (obstructive bronchilities) & parenchyma destruction.(emphysema)
- **INFLAMATION** caused structural changes & narrowing of airways .
- **DESTRUCTION OF LUNG PARANCHYMA** also by inflammatory process lead to the small airways & decrease elastic recoil.

- Many previous definition of COPD have emphasized a term **emphysema** & **chronic bronchitis**, which are not included on definition of GOLD report.
- Emphysema or destruction of gas exchange surface of lung(alveoli) is a pathological term that is often used clinically.
- Chronic bronchitis or the presence of cough & sputum production for at least 3 months in each of two consecutive years, remains a clinically & epidemiological useful term.

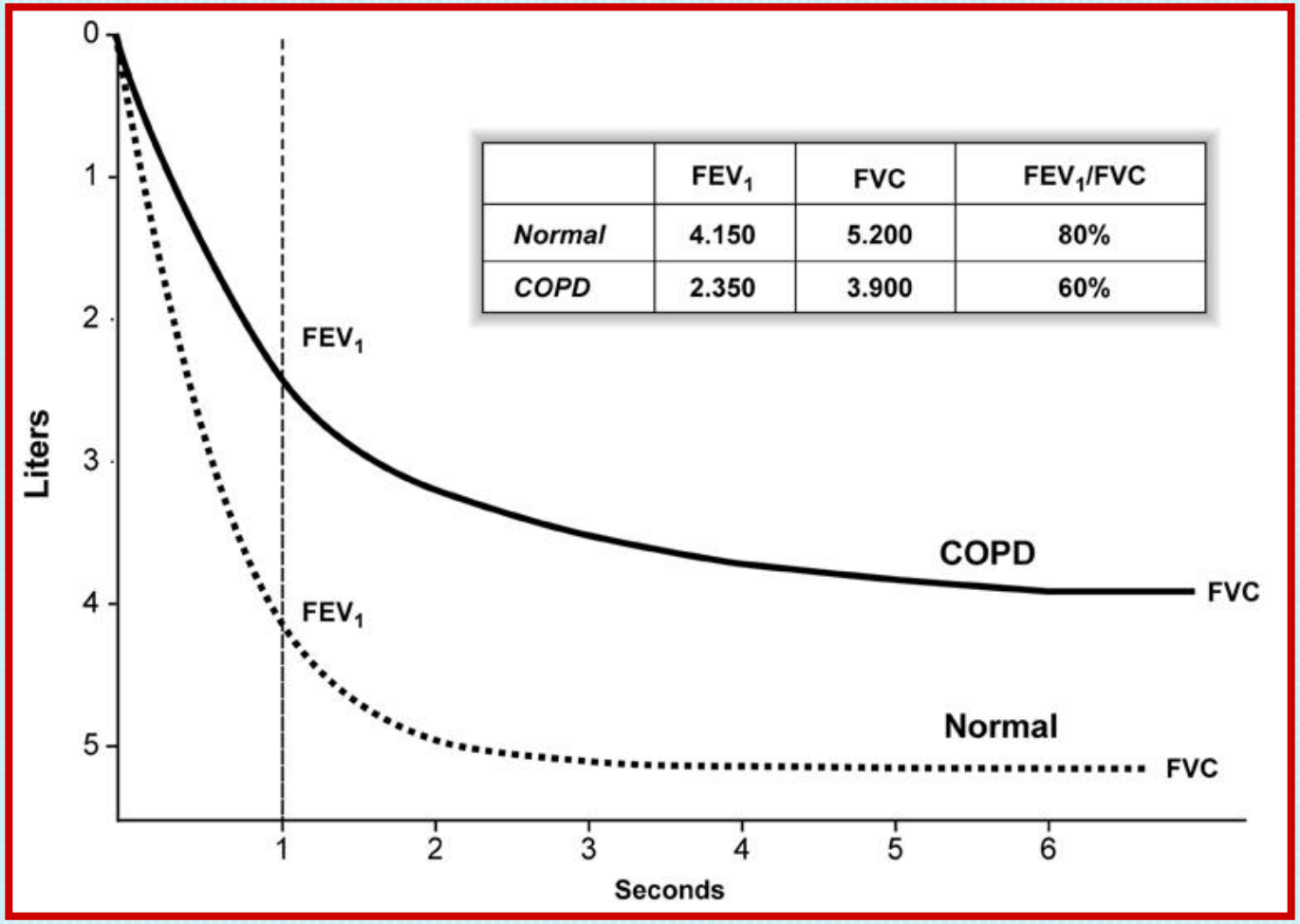

Normal bronchi
Bronchitis
A.D.A.M.


Normal bronchiole
and alveoli
Emphysema

Classification of COPD Severity by Spirometry

- Stage I: Mild — $FEV_1/FVC < 0.70$; $FEV_1 \geq 80\%$ predicted
- Stage II: Moderate — $FEV_1/FVC < 0.70$; $50\% \leq FEV_1 < 80\%$ predicted
- Stage III: Severe — $FEV_1/FVC < 0.70$; $30\% \leq FEV_1 < 50\%$ predicted
- Stage IV: Very Severe — $FEV_1/FVC < 0.70$; $FEV_1 < 30\%$ predicted *or* $FEV_1 < 50\%$ predicted *plus* chronic respiratory failure

SPIROMETRY : NORMAL & COPD



	FEV_1	FVC	FEV_1/FVC
Normal	4.150	5.200	80%
COPD	2.350	3.900	60%

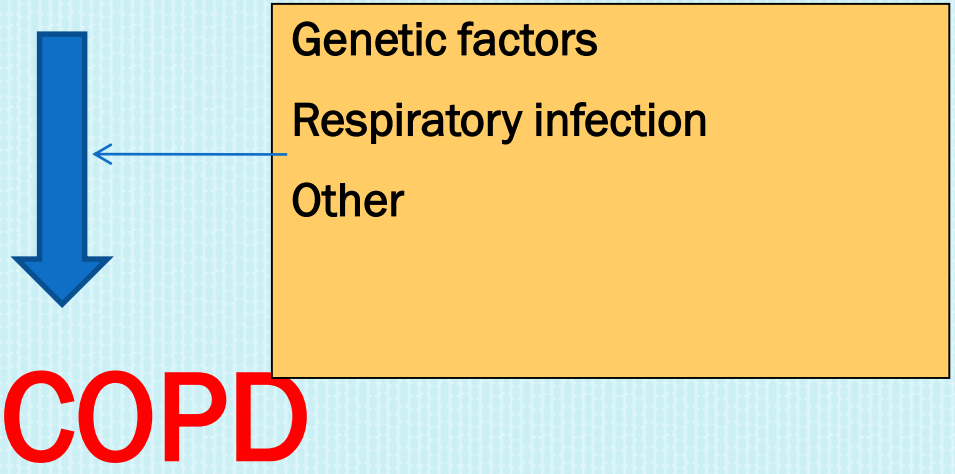
STAGES

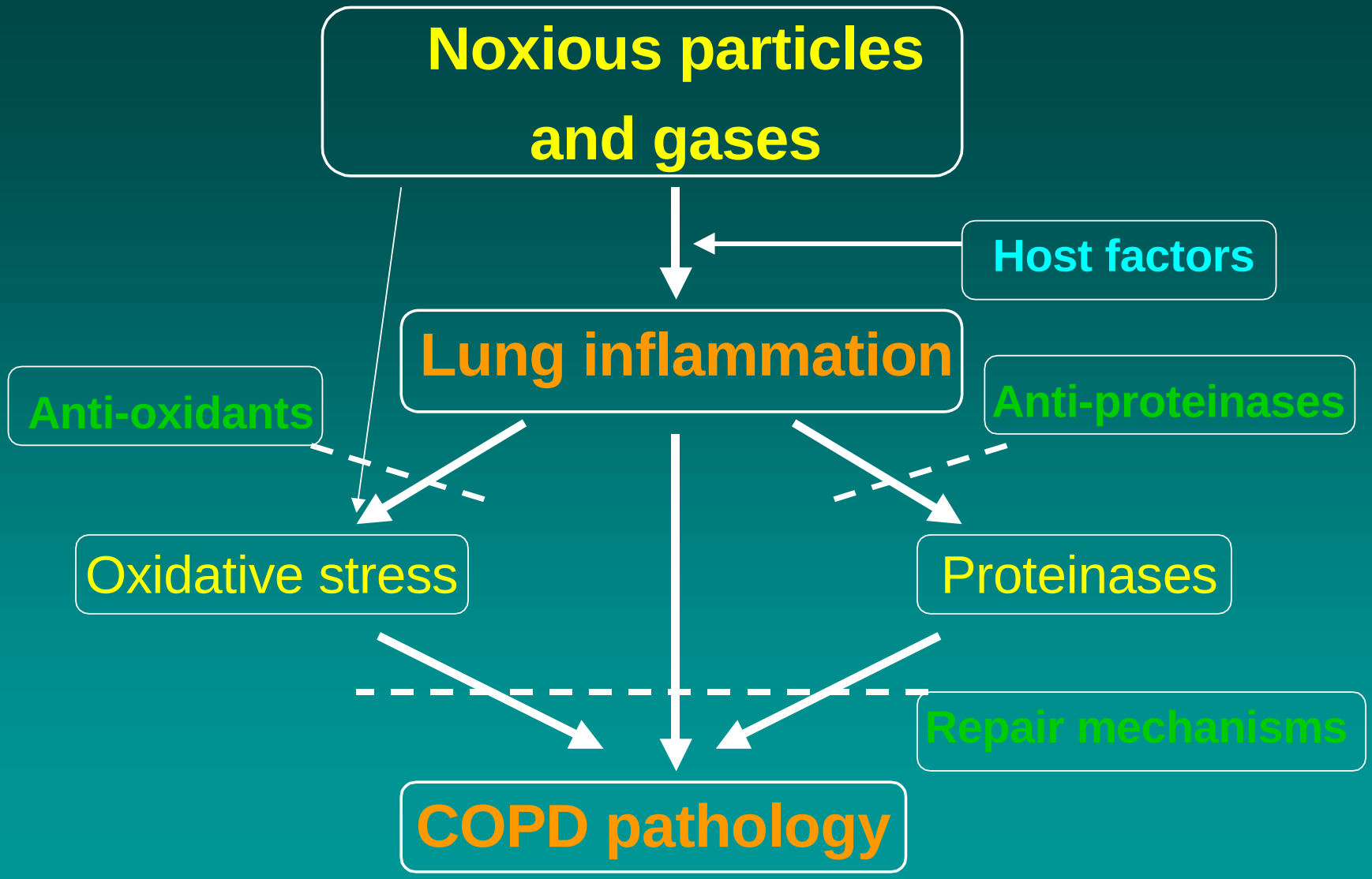
Stage	Characterstics
0: At risk	Normal spirometry Chronic symptoms (cough, sputum)
I: Mild	FEV1/FVC < 70%; FEV1 80% predicted, With or without chronic symptoms (cough, sputum) (pt.is unaware that he has lung abnormality)
II: Moderate	FEV1/FVC < 70%; 50% £ FEV1 < 80% predicted, With or without symptoms (cough, sputum,dyspnea)
III: Severe	FEV1/FVC < 70%; 30% £ FEV1 < 50% predicted With or without chronic symptoms (cough, sputum, dyspnea)
IV: Very Severe	FEV1/FVC < 70%; FEV1 < 30%

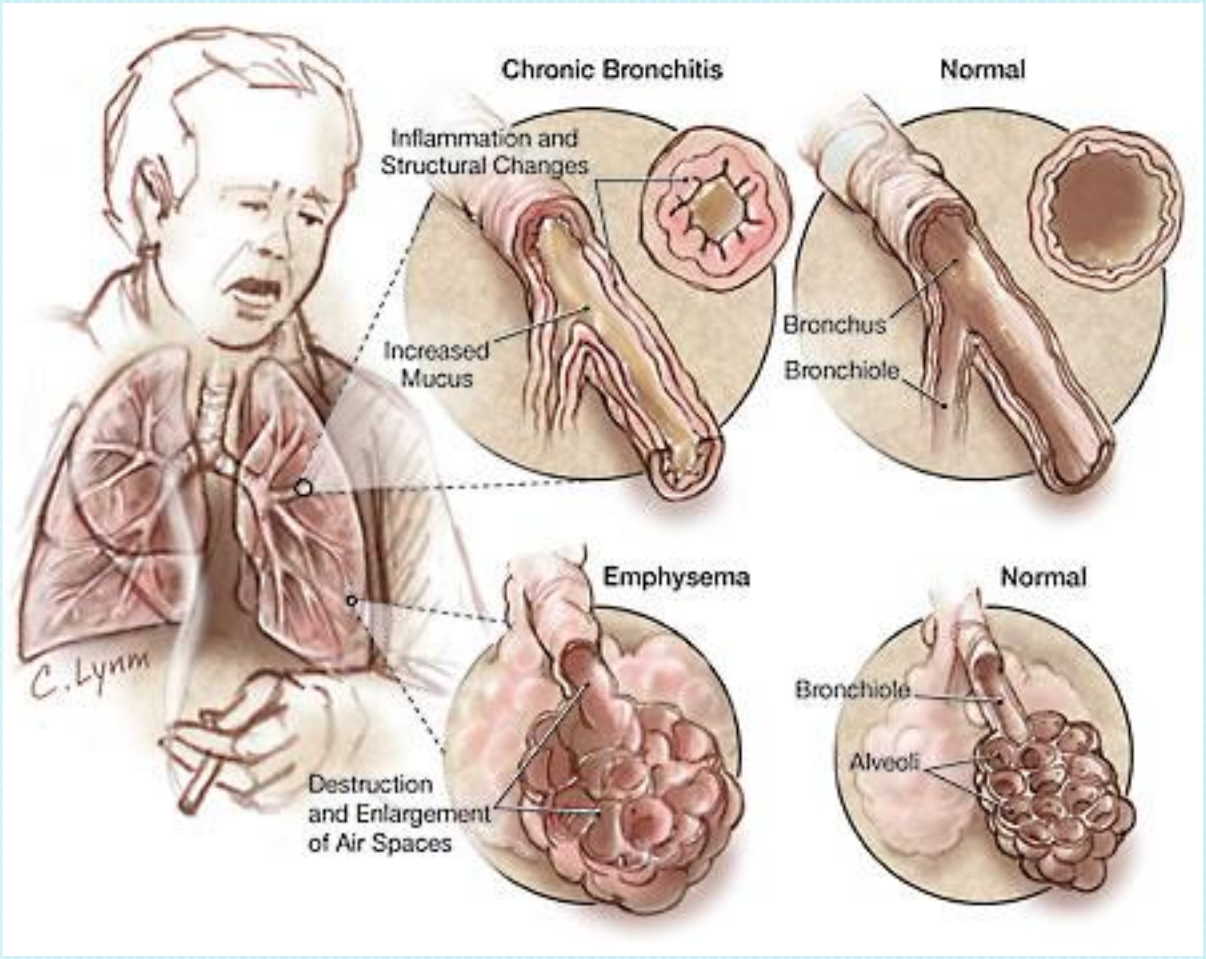
PATHOGENESIS OF COPD

- **NOXIOUS AGENT**

(tobacco smoke, pollutants, occupational agent)




Noxious particles and gases
Host factors
Lung inflammation
Anti-oxidants
Anti-proteinases
Oxidative stress
Proteinases
Repair mechanisms
COPD pathology


Chronic Bronchitis
Normal
Inflammation and
Structural Changes
Increased
Mucus
Bronchus
Bronchiole
Emphysema
Normal
Destruction
and Enlargement
of Air Spaces
Bronchiole
Alveoli
C. Lynn

PATHOLOGY

Bronchial glands / cells inflame

Increased secretions

Inflammation spreads to smooth muscle (bronchiole)

Airway obstruction, decreased ciliary action

Air trapping / Collapse of small airways

Further air trapping

Hyperventilation

Increased pressure in airways

Weakened airway walls / wall destruction

Alveolar destruction

PATHOPHYSIOLOGY

- How the underlying disease process in COPD leads to characteristic physiologic abnormalities and symptoms.
- Dec FEV1 results from inflammation and narrowing of peripheral airways
- Dec gas transfer arise from parenchymal destruction of emphysema

- **Airflow limitation & air trapping :-**
- Reduction in FEV1 & FEV1/FVC ratio
- Peripheral airways obstruction progressively traps air during expiration resulting in hyperinflation
- **Gas exchange abnormalities :-**emphysema is more often associated with gas exchange abnormalities
- Hyperinflation reduces inspiratory capacity such that FRC increases , particularly during ex.(dynamic hyperinflation), this results in dyspnea & limitation of ex. Capacity.
- Results in hypoxemia & hypercapnia

- **Mucus hypersecretion :-**
- Results in chronic cough
- Due to increase no. of goblet cell & enlarge submucosal glands in response to chronic airway limitation by cigarette smoke & other noxious agent
- **Pul. Hypertension :-**
- Due to hypoxic vasoconstriction of small arteries
- Resulting in structural changes include intimal hyperplasia & smooth muscle hypertrophy
- Loss of pul.capillary bed in emphysema may also contribute to increased pressure in pul. Circulation .
- Leads to - pul hypertension - rt. Ventricular hypertrophy - right sided cardiac failure. (core pulmonale)

KEY INDICATORS FOR CONSIDERING DIAGNOSIS OF COPD

- Consider COPD & perform spirometry, if any of the indicators are present in individual above 40 yrs of age

1. dyspnea : progressive, persistent, inc with exercise
2. chronic cough : intermittent, may be unproductive
3. Chronic sputum production
4. History of exposure to risk factors

ADDITIONAL INVESTIGATIONS (FOR PATIENTS WITH STAGE II DISEASE OR BEYOND.)

- Alpha1 antitrypsin deficiency screening.
- ABG analysis- in advanced COPD measurement of ABG while patient breathing room air is important. The test should be performed in stable patient with FEV1<50% predicted or with clinical signs suggest of respiratory failure or right heart failure.
- Bronchodilator reversibility testing-an increase in FEV1 that is greater than 200 ml and 12% above the pre bronchodilator FEV1 is considered significant.

- Chest X-ray- is seldom diagnostic until bullous changes are present.
- Valuable in excluding alternative diagnosis.
- Radiological changes associated with COPD are-

Signs of hyperinflation- flattened diaphragm, increase in volume of retrosternal space.

Hyperlucency of lung. Rapid tapering of the vascular markings.

ASTHMA

- Definition :- asthma is a clinical syndrome characterized by attack of wheezing and breathlessness due to narrowing of the intrapulmonary airways. The severity of the narrowing varies over short periods and is reversible either spontaneously or as a result of treatment.(Hargreave et al 1990)

- In asthma there is increase responsiveness of trachea & bronchi to various stimulus ..
- The changes causing airway obstruction include ;

- Hypertrophy & hyperplasia of smooth muscle
- Thickening of the epithelial basement membrane of airways
- Edema & eosinophilic infiltration of the bronchial wall & hypertrophy of mucus gland.

- EXTRINSIC ASTHMA
- Excessive IGE in response to allergent
- Affect young person
- Family history positive
- Attack related to specific antigen
- Intermittent attack
- Acute but self limiting

- INTRINSIC ASTHMA
- IGE production can not be demonstrated
- Common in adult over age 35.
- -ve family history
- Attack related to infection or exercise
- Persistent attack
- Attack are severe

PATHOLOGY

- AIRWAYS - dynamic structure
- Dilate - when large amount of air need to be moved - during ex.
- Constrict - when need to be protected - during exposure to irritant gases.

Ability of airway to alter their diameter in response to both external & internal stimuli is called airway reactivity.

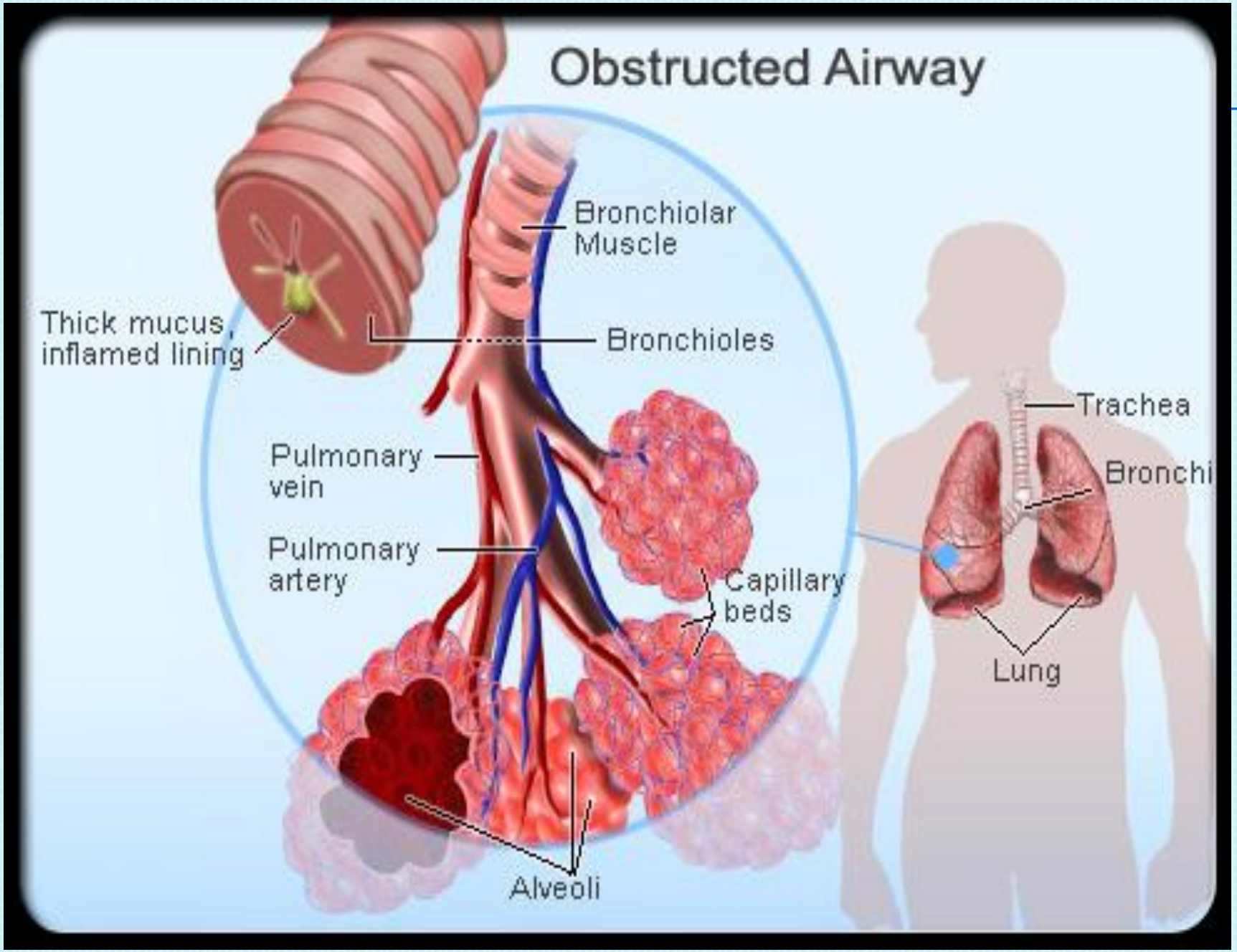
Asthamatics → airway reactivity increased and so that develop more intense broncho constriction.

- 3 main pathological changes ;

1. spasm of smooth muscle .
2. Edema of mucus membrane.
3. Excessive mucus production.

- Bronchial wall become infiltered with eosinophil & thickening of epithelial basement membrane.
- If attack persistent - long standing changes - hypertrophy of smooth muscle.
- Increase no of goblet cell and mucus gland- over distention of alveoli.- air trapping.

- Allergic reaction - antigen mediated broncho constriction.
- Antigen (allergens) binds to 2 IGE molecule on the membrane of mast cell (present in bronchial lining)
- Binding releases mediator which acts on receptor site on smooth muscle cells
-
- Causing changes in intracellular cyclic AMP level
- results in smooth muscle contraction
- This antigen antibody reaction is part of bodies immune response , previous exposure to the antigen results in greater broncho - constriction.


Obstructed Airway
Bronchiolar Muscle
Thick mucus, inflamed lining
Bronchioles
Pulmonary vein
Pulmonary artery
Capillary beds
Alveoli
Trachea
Bronchi
Lung

PATHOGENESIS

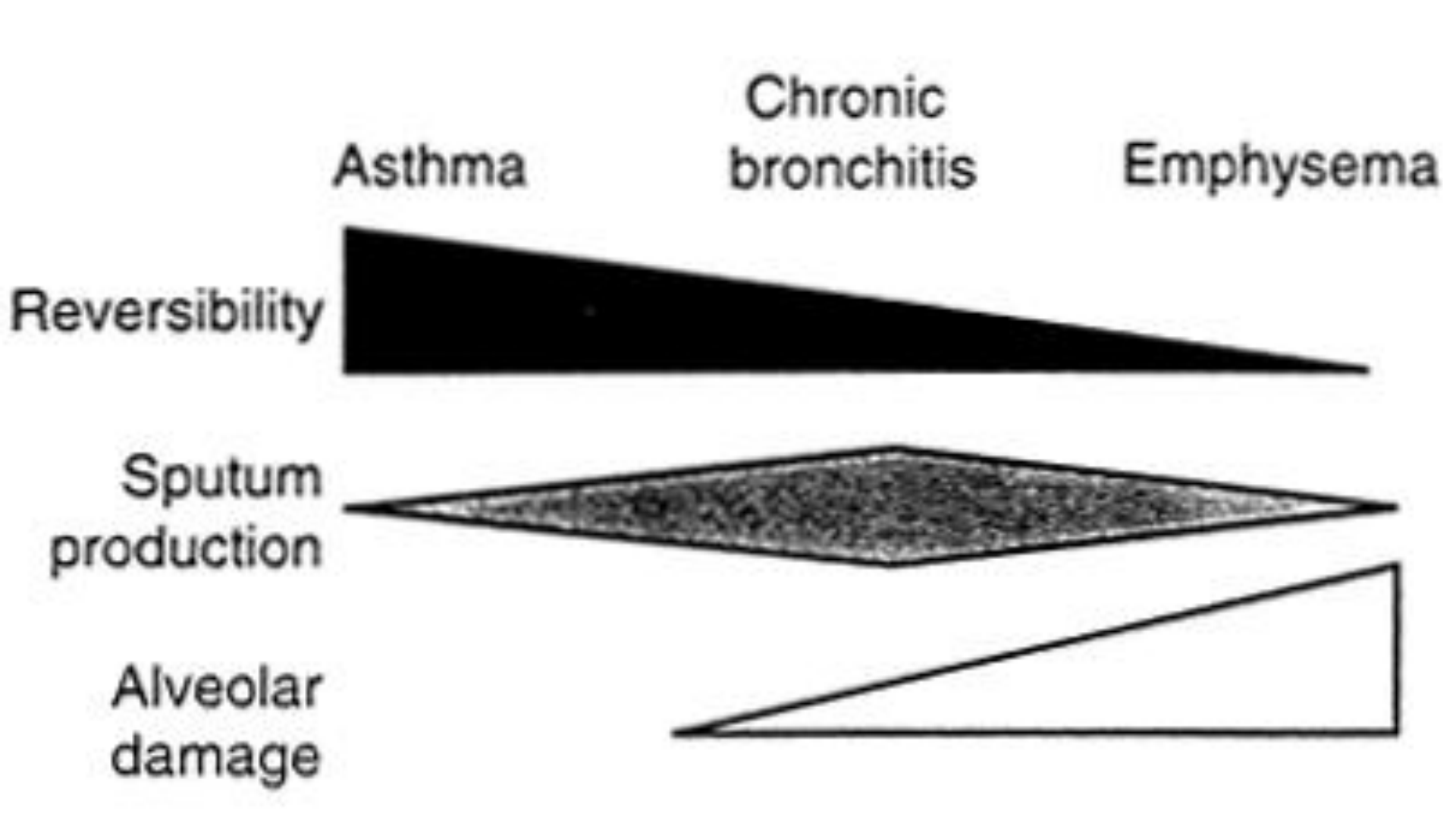
- Allergens
- Exercise
- Infections
- Occupational stress
- Environmental stress
- Pharmocological stress
- Emotional stress

PATHOPHYSIOLOGY

- OBSTRUCTION - either episodic or continuos
- FEV1 & FEV1/FVC ratio reduced.(ratio<75% - obstruction +ve)
- Abnormality in closing volune
- V.C. reduced , FRC & RV increase
- If PFT shows - Asthma
  - Repeat test after the administration of bronchodilator.
  - an improvement in 15% or more in FEV1 is considered reversibility of obstruction .
- In asthma attack severity of obstruction is non uniform.

- initially perfusion is diverted ,
- later on V/Q mismatch.

- Minute ventilation increased


Asthma
Chronic bronchitis
Emphysema
Reversibility
Sputum production
Alveolar damage

DIFFERENTIAL DIAGNOSIS: COPD AND ASTHMA

COPD

- Onset in mid-life
- Symptoms slowly progressive
- Long smoking history
- Dyspnea during exercise
- Largely irreversible airflow limitation

ASTHMA

Onset early in life (often childhood)

- Symptoms vary from day to day
- Symptoms at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma
- Largely reversible airflow limitation

BRONCHIECTASIS

- **Definition** :- Bronchiectasis is a permanent, an abnormal dilatation & distortion of one or more bronchi that is caused by destruction of the elastic & muscular component of bronchial wall.
- Dilatation - associated with obstruction & infection .
- Common cause - damage to bronchial tree after infection .

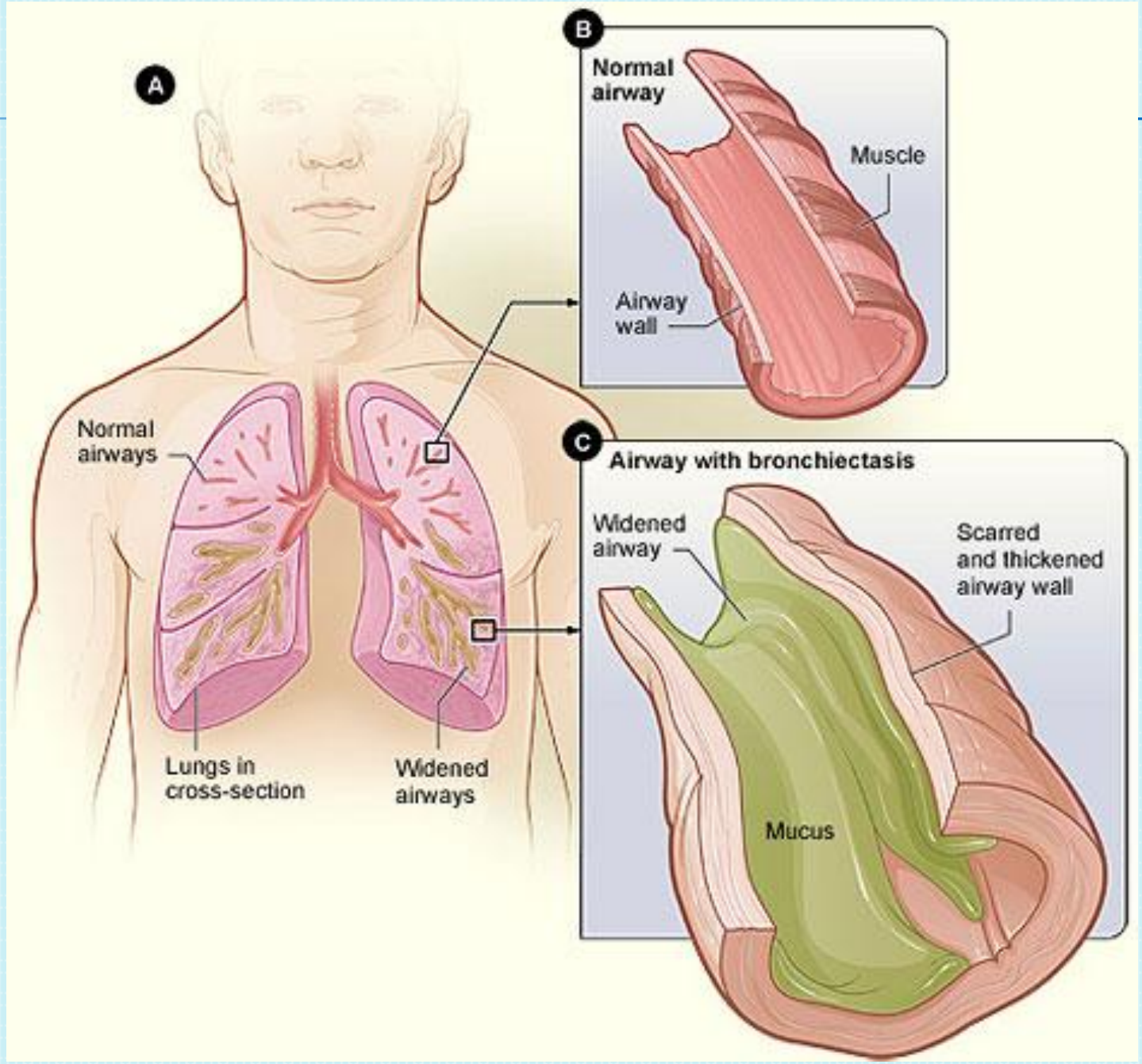
CAUSES....

- **Congenital :-**
- kartagener's syndrome (Immotile cilia syndrome)
- immune defect (Hypogammaglobulinaemia)
- **Acquired :-**
- Infection :- childhood infection - measles , whooping cough, influenza, pnemonia, lung dz like T.B.
- Obstruction :- foreign body
  bronchial stinosis
  pressure from lymphnode
  T.B bronchial carcinoma

- **Prevalence :-**
  - Incidence of broncheictasis is decreasing
  - Common in preantibiotic era.
- **C/F :-**
  - Cough
  - Copious mucopurulant sputum
  - Fetid breath
  - Recurrent pul. Infection
  - Recurrent hemoptysis

PATHOLOGY

- Bronchial obstruction → air can't reach upto distal obstruction → collapse of lung part → traction force exerted to proximal airway * → collection of secretion distal to obstruction * → secretion become infected → inflammation of bronchial wall with destruction of elastic & muscular tissue → if dz spreads - bronchi become dilated & pocket containing pus formed → more destruction of elastic tissue


A
Normal airways
Lungs in cross-section
Widened airways
B
Normal airway
Muscle
Airway wall
C
Airway with bronchiectasis
Widened airway
Scarred and thickened airway wall
Mucus

PATHOPHYSIOLOGY

- PFT :- depends on extent of dz
  - mild bronchiectasis - normal results
  - diffuse involvement - FVC , FEV1 , FEV1 /FVC reduced.
    R.V increased
  - pt with atelectasis & fibrosis - reduced FRC
- ABG :- arterial hypoxemia due to V/Q mismatch.
  - co2 retantion
- Laboratory findings :- H. Influenzae & staphylococcu pnemonia

CYSTIC FIBROSIS

- Definition :- Cystic fibrosis is a hereditary disorder of exocrine glands with a high sodium chloride content in sweat & pancreatic insufficiency resulting in mal absorption.
- Most common hereditary disorder being transmitted by recessive gene
- Hypertrophy & hyperplasia of mucus secreting gland - excessive mucus production - lead to chronic broncho pul . Infection .

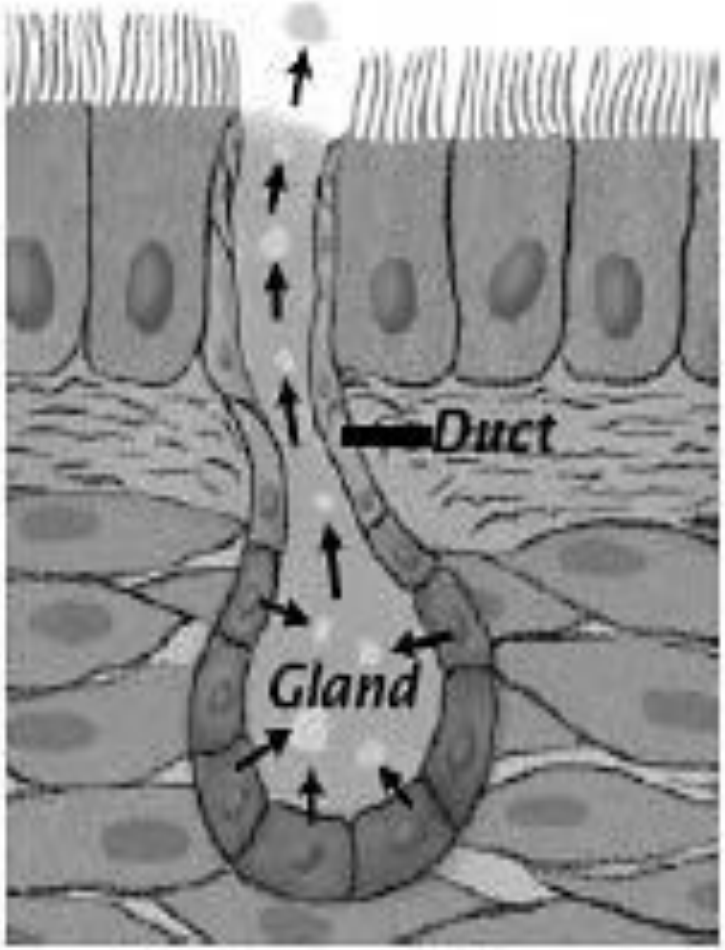
- Caused by .....
- Mutations in a single gene on the long arm of chromosomes 7 , that encode the cystic fibrosis transmembrane conductive regulation (CFTR).
- Diagnosis of .....
- high level of chloride in sweat
- Sweat test - quantitiative pilo-carpine ionotophoresis method (sweat chloride >60 m Eq/l)

PATHOGENESIS

- Block in chloride permeability at the epithelial surface is a common factor in all tissue affected by CF.
- Abnormality in ion transport explains the increased sweat chloride concentration found in perspiration of children with CF.

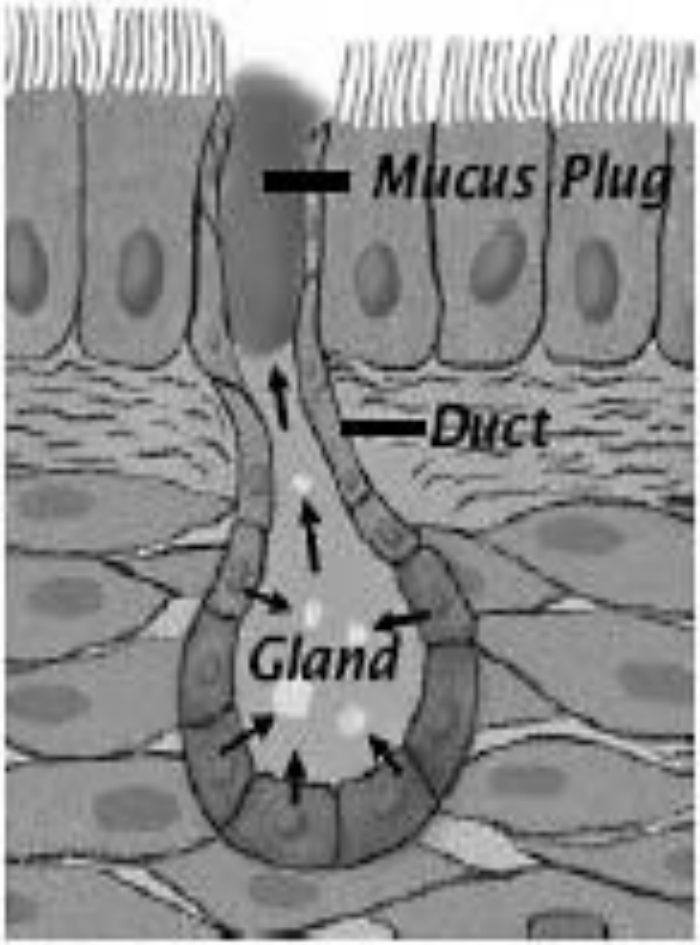
Lung Cells

Normal



In a healthy mucus gland, secretions exit the gland.

CF



CF causes the gland to be plugged with mucus.

PATHOLOGY

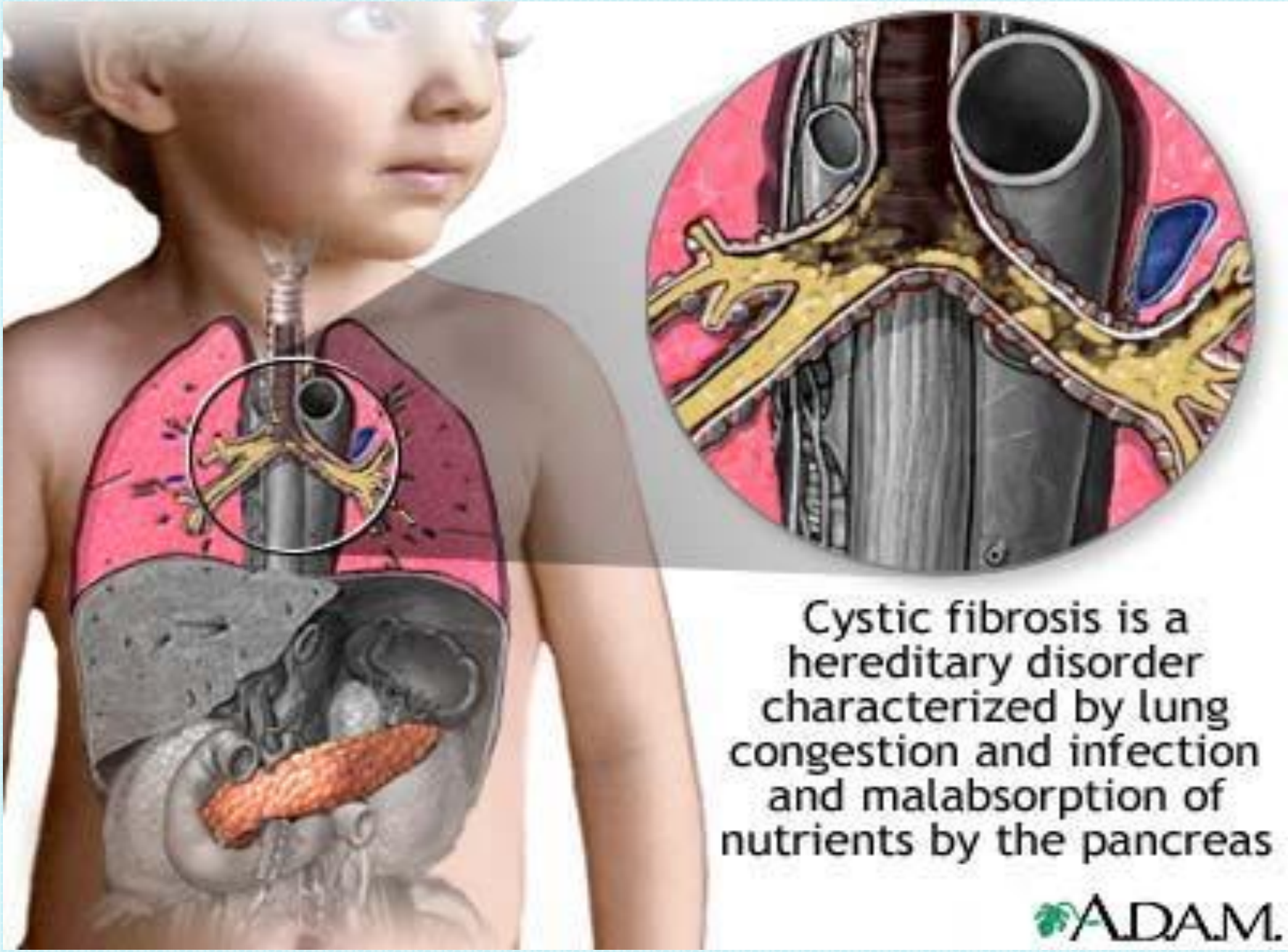
- Mutation in CFTR gene → defective chloride transport →decrease sodium & water transport in epithelium → dehydration→ hence increase viscosity of secretion→ children with CF have persistent endobronchial bacterial infection inflammatory response continues inflammation with thickened secretion obstruction & hyperinflation alt pul.mech. →

PATHOPHYSIOLOGY

- Excessive mucus :- specially in small bronchi & bronchioles
- Impaired mucocilliary clearance of secretion
- Viscid mucus :- abnormalities in mucus gland which produce viscid mucus with reduced water content
- PFT :-
- FEV1/FVC reduced
- FVC reduced
- R.V. increased
- ABG :-

Low po2 with or without co2 retention

- by auscultation - aspiratory & expiratory wheezes with added coarse crepitation.


Cystic fibrosis is a hereditary disorder characterized by lung congestion and infection and malabsorption of nutrients by the pancreas
A.D.A.M.


THINK