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RESPIRATORY SYSTEM

***Chronic Obstructive Pulmonary Diseases***

1. Emphysema
2. Chronic bronchitis
3. Asthma
4. Bronchiectasis

***1-Emphysema***

It is an abnormal **permanent** enlargement of the air space distal to the terminal bronchiole with **destruction** of their wall, there is **NO** fibrosis.

**Overinflation**: dilatation of the airspace without **destruction** of their walls.

***Types of emphysema***

**1-Centriacinar emphysema**

-It is the **most common** type.

-Occur in heavy smokers.

-The dilatation includes the **respiratory bronchiole only,** while the distal alveoli are spared

-Affects the upper lobe mostly.

**2-Panacinar emphysema**

* The **Whole acinus** is uniformly dilated.
* Affects the lower zones mostly.
* Associated with anti elastase deficiency e.g. α-1 atni-trypsin deficiency.

**3-distal acinar (paraseptal) emphysema**

-Only the **distal part of the acinus** is involved

-The common site is that adjacent to the **pleura** and lobular connective tissue septa.

-It causes the formation of multiple cysts (0.5cm- 2 cm) that may rupture and 🡪 spontaneous **pneumothorax** in young adult.

**4-IRREGULAR EMPHYSEMA**

-The acini are **irregularly** involved.

-Associated with scaring following a healed inflammatory process.

***Pathogenesis***

The key role in the whole process is:

**PROTEASE --- ANTIPROTEASE** imbalance.

Proteases: are enzymes which digest the tissue.

Anti-proteases: are the counteracting enzymes that **stop** the action of digestion.

* Normal persons have a balance between the two enzymes.
* The main **cellular elastase** (protease) is secreted from the **NEUTROPHILS**, it is capable to digest human lung if not inhibited by the anti-elastase enzyme e.g. (α-1 anti-trypsin).
* The **free radicals** released from the neutrophils can inhibit the release of this α-1 atni-trypsin.

**Other sites that release proteases:**

Macrophages, Bacteria, Mast cell, Pancreas.

***So the Development of emphysema occurs:***

1-When there is ***🡹 elastase activity*** as in smoking.

2-When there is ***🡫 anti-elastase activity*** as in :

**-Hereditary** α-1 anti- trypsin deficiency.

**-Acquired** as in smokers due to the effect of nicotine, O2 free radicals that inhibit the release of anti-elastase.

**The effect of smoking in the development of emphysema**

1-It ***🡹*** the no. of **neutrophils,** macrophages within the alveoli through its direct nicotine chemoattractant effect and through the reactive oxygen species contained in it. This will activate synthesis of TNF and IL-8 which intern attract and activate more neutrophils. The accumulated active neutrophils release their granules which are rich in elastase and proteinase.

2- Smoking **stimulates** the elastase activity in macrophages; this elastase is not inhibited by α-1 anti- trypsin additionally it can digest this antiprotease.

3-The smoke contains abundant reactive oxygen free radicals which deplete the antioxidant mechanisms leading to tissue damage. Also the oxidative injury inactivates antiproteases resulting in functional α-1 anti- trypsin deficiency even in patients without enzyme deficiency.

Complications (prognosis):

1. Patient become barrel chested and dyspneic
2. Hyperventilation is prominent with adequate gas exchange
3. Loss of elastic tissue in the surrounding alveolar septa in advanced emphysema may lead to collapse during expiration.
4. The eventual outcome of emphysema is development of pulmonary shypertension due to loss of capillary surface area from alveolar destruction and stretching.

***2- Chronic bronchitis***

***Clinically:***

 It is a clinical term characterized by productive cough (cough +sputum) for at least 3 months in at least 2 consecutive years.

***Complications:***

**1-**

***Pathogenesis:***

1. **Chronic irritation** by smoking leading to **hyper secretion of mucous** in the **large** airways (trachea & bronchus). Prolong irritation leads to hypertrophy of mucous gland a**nd marked increase** in mucin secreting goblet cells of small airways (small bronchi & bronchioles).
2. The irritants cause inflammation with infiltration of CD8 T lymphocytes, macrophages and neutrophils
3. **Microbial infection**: which is often present but has a secondary role and responsible for maintaining the inflammation.

**\* Smoking🡪 irritation🡪 stimulate mucous secretion🡪 sputum** **overproduction.**

Although other environmental irritant may provoke irritation, smoking still the single most common one

**Prognosis of chronic bronchitis:**

1. It may end up with pulmonary hypertension and cardiac failure (core pulmonale).
2. It causes atypical metaplasia &dysplasia.
3. Recurrent infection and respiratory failure are constant threats.

***3- Bronchial Asthma***

It is a chronic **relapsing** inflammatory disorder of the airways that cause recurrent attacks of breathlessness. It is characterized by **hyper-reactive airways**🡪 episodic (recurrent attacks) **of reversible** bronchoconstriction due to 🡹 responsiveness of the trachiobronchial tree to various stimuli.

**Types of Asthma**

**1-Extrinsic :**

* Is the most common type.
* Initiated by type one hypersensitivity reaction (**type** **I HSR)**.
* Caused by exposure to external allergens (dust, pollens, food).
* It starts at childhood.
* Associated with Atopy (increase total serum IgE and reactive T helper lymphocytes type 2 TH2).
* +ve family history.

**2-Intrinsic :**

Initiated by non immune mechanism e.g. aspirin ingestion, pulmonary infection, stress, exercise.

Not associated with Atopy.

Starts at adulthood.

The attack is severe may🡪 status asthmaticus.

***Pathogenesis***

The major components of asthma are:

**1-** Chronic airway **inflammation** with many types of inflammatory cells and mediators.

**2-** Bronchial **hyper-responsiveness.**

3- Genetic predisposition to **type I HSR (atopy) in extrinsic asthma.**

**Details of the pathogenesis are elicited in the following model:**

**1-Sensitization phase**: inhaled allergen🡪 **IgE** formation on the mast cell & eosinophil recruitment.

On re- exposure to the antigen there will be:

**2-Immediate (acute) reaction**: there is **cross linking** of the IgE situated on the mast cell🡪 **degranulation** of the mast cell🡪 release of mediators🡪 open the junction between the epithelial cells 🡪so the Ag can enter the mucosa& activate the eosinophils & mast cell 🡪more mediator secretion. (occur within minutes of re-exposure)

These mediators lead induction of:

* Bronchospasm🡪 breathlessness.
* Increase vascular permeability🡪 edema🡪breathlessness .
* Mucous production.
* Brings more mediators releasing cells from the blood e.g. neutrophil, basophil, lymphocyte, preparing for the late phase.

**3-Late phase**: occur after hours, initiated by the accumulated leucocytes from the previous stage with another round of mediator release.

**Course and prognosis:**

1. **Sever dyspnea and wheezing durin attack**
2. **Obstruction of the airways during expiration🡪 hyper inflated lung**
3. **Bronchi are constricted and filled with mucus and debris**
4. **Attack last from 1 to several hours subsided either spotanously or with drugs**
5. **Sever paroxysm occurs that does not respond to therapy and persist for days and even weeks (status asthmaticus) and the associated hypoxia, hypercapnia and acidosis may be fatal (cause of death)**

 ***4- Bronchiectasis***

Is a chronic **necrotizing infection** of the bronchi &bronchioles leading to or associated with **abnormal permanent dilatation** of these airways.

***Clinically:***

**Cough** + fever (when a powerful microorganism present) + **copious foul smell purulent sputum.**

Dyspnea & orthopnea in sever cases.

***Bronchiectasis may be associated with*:**

1. Bronchial obstruction by a tumor, foreign body, or a mucous plug as in cases of asthma & chronic bronchitis.
2. Congenital & hereditary conditions e.g. cystic fibrosis, immotile cilia syndrome, Kartegner syndrome (bronchiectasis+ sinusitis+ situs inversus).
3. Necrotizing pneumonia caused by staph. Or T.B.

***Etiology &pathogenesis***

Two important factors should be present:

**1-Obstruction.**

**2-Infection.**

So either the condition starts with:

**A- Bronchial obstruction**🡪 atelactasis🡪 bronchial wall inflammation + accumulated bronchial secretion🡪 dilatation which is reversible.

**If** The obstruction persists or there is a superadded infection, the **dilatation** will be irreversible.

**B- Bronchial infection**🡪 bronchial wall inflammation & weakening 🡪 further **dilatation.**