Pathophysiology

Dr. Baydaa Hameed LEC: 6

RESPIRATORY SYSTEM

***Chronic obstructive pulmonary diseases***

1. Emphysema
2. Chronic bronchitis
3. Asthma
4. Bronchiectasis
5. ***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.**

-Affects the upper lobe mostly.

1. **PANACINAR EMPHYSEMA**

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

1. **PARASEPTAL EMPHYSEMA**

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

-The common site is adjacent to the **pleura**, near a fibrotic, scaring, atelactic area.

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

1. **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:**

1. Macrophages.
2. Bacteria.
3. Mast cell.
4. 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, in the alveoli.

2-Nicotine is a **chemotactic** substance for neutrophils.

3-It **stimulates** the elastase activity.

4-The oxidants in the smoke and the free radicals from the accompanying neutrophils 🡪 **inhibit** the secretion of anti-elastase.

***Other types of over inflation (hyperinflation)***

1. **Compensatory hyperinflation:** dilatation of the alveoli without destruction of their walls. e.g. surgical removal of a lobe.
2. **Senile hyperinflation:** due to the changes in the geometry of the lung in old persons. Also there is No destruction of the alveolar wall.
3. **Obstructive hyperinflation:** air gets trapped in the lung and the obstructive agent act as a (ball valve) i.e. air can get in &can’t get out.🡪 Emergency.
4. **Bullous emphysema:** includes any form of emphysema that produces a large sub-pleural bullae > 1 cm in diameter.
5. **Interstitial emphysema:** due to the presence of an alveolar tear (occur when there is cough +bronchial obstruction)🡪 air will escape into the connective tissue stroma of the lung, mediastinum & subcutaneous tissue.

***2- Chronic bronchitis***

***Clinically:***

It is characterized by (cough +sputum) production for at least 3 months in at least 2 consecutive years.

***Complications:***

**1-** It may end up with corepulmonale.

**2-** It causes atypical metaplasia &dysplasia.

***Pathogenesis:***

***Two important things should be present:***

1. **Chronic irritation** which may interfere with the ciliary action of the respiratory epithelium. e.g. Smoking.
2. **Microbial infection**: which is usually secondary and responsible for maintaining the condition?

***These two factors will initiate the earliest features which are:***

1. **Hyper secretion of mucous** in the **large** airways (trachea & bronchus) due to hypertrophy of mucous gland.
2. **Marked** 🡹**in goblet cells** of **small** airways (small bronchi & bronchioles).

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

***Microscopically:***

1. ***Enlarged mucous secreting glands*** in the trachea &bronchus, this is best estimated by the increase in the Reid Index.

2-Marked narrowing of the bronchioles due to ***goblet cell metaplasia***, mucous plug, inflammation & fibrosis.

3-The bronchial epithelium may show ***squamous metaplasia and dysplasia.***

***Reid Index*:** It is the **ratio** of the thickness of the **mucous gland** layer / thickness of the **wall** between the epithelium and the cartilage.

**Normally it is 0.4, it increases in chronic bronchitis.**

***3- Bronchial Asthma***

It is a chronic **relapsing** inflammatory disorder characterized by **hyper-reactive airways**🡪 episodic, **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 **I HSR**.

Caused by exposure to external allergens (dust, pollens, food).

It starts at childhood.

Associated with Atopy.

+ve family history.

1. **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 Two major components of asthma are:

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

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

**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:

1. **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.
* Increase vascular permeability.
* Mucous production.
* Brings more mediators releasing cells from the blood e.g. neutrophil, basophil, lymphocyte, preparing for the late phase.

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

***Morphology:***

**Grossly:**

* Lungs are over inflated.
* There are foci of **atelactasis**.
* The most striking is the **occlusion** of the airways by thick, mucous plugs.

**Microscopically:**

* The plugs composed of sheded epithelium forming the so called **Curschmann spirals.**
* **Charcot Leyden crystals** which are collections of the eosinophils membrane protein.
* Thickening of the **basement membrane** of the bronchial epithelium.
* **Edema & inflammatory** cells in the Br. Wall.
* Increase in the no. of **submucosal glands.**
* Hypertrophy of the bronchial wall **muscle** as a reflection of prolonged bronchoconstriction.

***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.

**Complications:**

Corepulmonale.

Amyloidosis



***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.**

***Grossly:***

* Affects the **lower lobes** bilaterally.
* The affected airways are **dilated** & may take the shape of tube (cylindroid bronchiectasis). Others may show fusiform or sharp saccular distention.
* The dilatation produce **cystic pattern** on cut surface.

***Microscopically:***

The full blown picture will show:

1. **Ulceration** of the **lining epithelium** with desquamation.
2. Pseudo-stratification of the columnar cells or **squamous metaplasia**.