PATHOLOGY OF THE REPIRATORY SYSTEM

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Respiratory system divided into two parts:

1- **Upper respiratory tract**
2- **Lower respiratory tract**

THE UPPER RESPIRATORY TRACT INFECTIONS:

- Upper respiratory tract infection represents the most common acute illness evaluated in the outpatient setting.
- Range from the common cold, a mild self-limited catarrhal syndrome of the nasopharynx to life-threatening illnesses such as epiglottitis.
- It includes: rhinitis, sinusitis, pharyngitis, laryngitis, epiglottitis.
- **Most of these inflammatory conditions are viral in origin, but they are often complicated by superimposed bacterial infections.**

Nasal Polyps:

- It is focal protrusion of the mucosa, secondary to recurrent attacks of rhinitis.
- Not true neoplasms, they are associated with inflammation and allergy. Generally, they are multiple, and nearly always bilateral.
- **Microscopically:** 1- edematous stroma with 2-hyperplastic or cystic mucous glands, 3-Infiltrated by variety of inflammatory cells including neutrophils, eosinophils, and plasma cells with occasional clusters of lymphocytes.
- **Complication:** 1-When multiple or large it may obstruct the airway or impair sinus drainage. 2-it may become ulcerated or infected.

Tumors of nasal cavity:

NASOPHARYNGEAL CARCINOMA

- This rare neoplasm has a strong epidemiologic links to EBV & a high frequency in China.
- These facts raise the possibility of viral oncogenesis on a background of genetic susceptibility.
- It is usually clinically occult until they present at advanced stages with nasal obstruction, epistaxis, and metastases to the cervical lymph nodes in up to 70% of patients.
- The histological subtypes:
  1- Squamous cell carcinoma (keratinizing or nonkeratinizing)
  2- **Undifferentiated carcinoma: is the most common and the one most closely linked with EBV**, characterized by syncytial growth with prominent eosinophilic nuclei
- Nasopharyngeal carcinomas invade locally, spread to cervical lymph nodes, and then metastasize to distant sites.

LARYNGEAL TUMORS:

Benign Lesions:

❖ Vocal cord nodules (Reactive nodules)

- Vocal cord nodules are NOT a neoplasm but smooth protrusions (usually less than 0.5 cm in diameter) located, most often, on the true vocal cords.
- The nodules are composed of fibrous tissue and covered by stratified squamous mucosa.
- These lesions occur chiefly in heavy smokers or singers (singer's nodes), suggesting that they are the result of chronic irritation or voice abuse.
- Because of their strategic location and accompanying inflammation, they characteristically change the character of the voice and often cause progressive hoarseness.

❖ Laryngeal papilloma (squamous papilloma) of the larynx:

- It is a benign neoplasm, usually on the true vocal cords, that forms a soft, raspberry-like mass rarely more than 1 cm in diameter.
- Microscopically, it consists of multiple, slender, finger-like projections supported by central fibrovascular cores and covered by benign, stratified squamous epithelium.
- Papillomas are usually solitary in adults but are often multiple in children, a condition referred to as **juvenile laryngeal papillomatosis**.
- These lesions are caused by human papillomavirus (HPV) types 6 and 11**.**
- **They do not become malignant**, but frequently recur and often spontaneously regress at puberty.

Malignant Lesions

Carcinoma of the Larynx

- Most commonly occurs within the **sixth decade** of life and is more common in **men** than in women.
- Nearly all cases occur in **smokers**. alcohol, asbestos exposure, irradiation, and infection with HPV may also play roles.

Morphology.

Grossly: fungating mass, focal thickenings, or ulcerated lesions.

- Types according to the **sites**:
  1- **Glottic carcinoma:** (on the vocal cord), 60-70% 0f cases.
  2- **supraglottic carcinoma**: above the vocal cord 25%
  3- **subglottic:** below the vocal cord less than 5% of cases.

Mic.: the vast majority (95%) are squamous cell carcinomas, which started as mucosal hyperplasia, dysplasia & carcinoma in situ.

Clinically The initial manifestation is often persistent hoarseness of voice, dysphagia, and dysphonia.

Prognosis: is directly related to **clinical stage** and **tumor site**.

- ✓ **Glottic carcinomas** are **confined to the larynx (good prognosis),** this is due to the fact that this area has sparse lymphatic supply.

- ✓ **Supraglottic carcinomas** in one third of cases showing cervical lymph nodes metastases.
- ✓ The usual cause of death is infection of the distal respiratory passages or widespread metastases and cachexia.

LUNGS

Congenital Anomalies

1- Agenesis or hypoplasia of both lungs, one lung, or single lobes.
Pulmonary hypoplasia. is the defective development of both lungs resulting in: Decreased weight, volume, and acini compared to the body weight and gestational age
2-Tracheal and bronchial anomalies (atresia, stenosis, tracheoesophageal fistula)
3- Vascular anomalies 4- Congenital pulmonary airway malformation.
5-Lung cyst 6- cystic fibrosis

Cystic fibrosis:

- Cystic fibrosis (CF) is **inherited disorder**, **autosomal recessive,** Defect in gene on **chromosome 7.**
- Disorder of exocrine gland function that involves **multiple organ systems** but chiefly results in chronic respiratory infections, pancreatic enzyme insufficiency, and associated complications in untreated patients.
- End-stage lung disease is the principal cause of death.
- **Pathogenesis:**

*Gene defect ……. defect in cystic fibrosis transmembrane conductance regulator (CFTCR) …. reduced chloride permeability across epithelial membrane …. Increase intracellular chloride…. increase in sodium …increase in water inside the cells …. increase viscosity of mucus secretion …… obstruction of ducts …… atrophy & infection.

*The one exception to this is the **sweat ducts**, *CFTR* mutations; lead to formation of hypertonic fluid with high sodium chloride. This is the explanation for the “salty” sweat that mothers can often detect in their affected infants.

- **Diagnostic test: Sweat test:** excess sweat chloride, Na.

- **Complications:** abnormally viscous secretions that obstruct organ passages, resulting in most of the clinical features of this disorder:
  1. Bronchiolitis.
  2. **Recurrent pneumonia** (pseudomonas, staphylococci).
  3. Obstruction of bronchi……. Bronchiectasis
  4. Obstruction of biliary system ……. biliary cirrhosis.
  5. Viscid secretion in intestine…… meconium ileus. (Thick viscid plugs of mucus found in the small intestine of infants)
  6. Obstruction of seminal vesicles……. Male infertility

7. pancreatic duct obstruction …steatorrhea and malabsorption

ATELECTASIS (COLLAPSE):

- It is loss of lung volume caused by incomplete expansion of airspaces; this leads to shunting of inadequately oxygenated blood from pulmonary arteries into veins, thus giving rise to hypoxia.
- It is either;
  - **neonatal atelectasis**: Incomplete expansion of lungs (neonatal respiratory distress syndrome due to loss of surfactant substance), or
  - **acquired atelectasis:** Collapse of previously inflated lung producing area of relatively airless parenchyma
- Atelectasis is almost always secondary condition, usually unilateral involving part or entire lung.
- **The main types of acquired atelectasis**, which occur in adults, are the followings:

1. Resorption atelectasis: occurs when an **obstruction** prevents air from reaching distal airways. The air already present distally gradually becomes absorbed, followed by alveolar collapse. Depending on the level of airway obstruction, an entire lung, a complete lobe, or a segment may be involved. **The most common cause** of resorption collapse is obstruction of a bronchus, most frequently occurs postoperatively due to intrabronchial mucous or mucopurulent plugs, but also may result from foreign body aspiration (particularly in children), bronchial asthma, bronchiectasis, chronic bronchitis, or intrabronchial tumor, in which it may be the first sign of malignancy.

2. Compression atelectasis: is usually associated with accumulation of fluid, blood, or air within the pleural cavity. A frequent cause is pleural effusions occurring in the setting of congestive heart failure. Leakage of air into the pleural cavity (pneumothorax) also leads to compression atelectasis. **Basal atelectasis** resulting from a failure to breathe deeply commonly occurs in bedridden patients, in patients with ascites, and during and after surgery.

3. Contraction atelectasis occurs in the presence of focal or generalized pulmonary fibrosis or pleural fibrosis; in these situations, there is interference with normal expansion of lung during expiration.

- Atelectasis (except contraction type) is reversible and should be treated quickly to prevent hypoxemia and infection of the collapsed lung.

Acute Respiratory Distress Syndrome (ARDS)

- **A clinical syndrome of progressive respiratory insufficiency caused by diffuse alveolar damage**
- **Clinically: It is characterized by**

1. Acute onset of dyspnea.
2. Hypoxemia (refractory to O2 therapy).
3. Development of bilateral pulmonary infiltrates **on radiographs**.
4. Absence **of clinical evidence of primary** left-sided heart failure.

- The condition may progress to multisystem organ failure.

- Represent the most common cause of noncardiogenic pulmonary edema.

The clinical setting associated with ARDS include:

A. Respiratory

1. Diffuse infections (viral, bacterial) 2. Aspiration 3. Inhalation (toxic gases, near drowning) 4. O2 therapy

B. Non-respiratory

1. Sepsis (septic shock) 2. Trauma (with hypotension) 3. Burns 4. Pancreatitis
5. Ingested toxins

Pathogenesis

- The alveolar capillary membrane is formed by two separate barriers -the microvascular endothelium and the alveolar epithelium.
- **In ARDS** there is **damage to alveolar capillary membrane** by either endothelial or epithelial injury, or, more commonly, both. this leads to; Increased vascular permeability, loss of diffusion capacity of the gasses and widespread surfactant abnormalities caused by damage to type II pneumocytes.
- Most work suggests that ARDS stems from an inflammatory reaction initiated by a variety of pro-inflammatory mediators, which causes the endothelial damage.
- **Following the insult**, there is **increased synthesis of a potent neutrophil chemotactic and activating agents** IL-8 & TNF **by pulmonary macrophages**. The recruited activated neutrophils release oxidants, proteases, ect. That cause damage to the alveolar epithelium leading to loss of surfactant that interferes with alveolar expansion.

Morphology

- **Gross appearance** of lungs resembles the liver; **they are dark red, firm, airless.**
- **Microscopically:**

➢ **In acute exudative phase:**

- Capillary **congestion**,
- **Necrosis** of alveolar epithelial cells,
- Interstitial and intraalveolar **edema** and hemorrhage, and (particularly with sepsis) collections of neutrophils in capillaries.
- The most characteristic finding **is hyaline membranes formation, particularly lining the distended alveolar ducts** such membranes consist of protein-rich edema fluid admixed with remnants of necrotic epithelial cells.
- **In the organizing stage:**
- Marked regenerative proliferation of type II pneumocytes, organization of the fibrin exudates (this eventuates in intra- alveolar fibrosis) and marked fibrotic thickening of the alveolar septa.