PATHOLOGY OF BRONCHIAL ASTHMA

Bronchial Asthma

 Define bronchial asthma.

o Describe types of bronchial asthma.

o Discuss etiopathogenesis of asthma.

o Describe morphological features.

Obstructive and restrictive lung diseases

* Obstructive lung diseases
* (i.e. increased resistance to air flow) include:-
* 1. **Bronchial** **Asthma.**
* 2. Emphysema.
* 3. Chronic bronchitis.
* 4. Bronchiectasis.
* 5. Cystic fibrosis and bronchiolitis.
* **Why should we care about asthma?**

**What is Asthma?**

* Definition:
* **Asthma is a chronic inflammatory disorder of the airways that causes recurrent spasmodic episodes, due to increased hyperirritability or responsiveness of the bronchial tree to various stimuli.**
* **This associated with these clinical manifestations:**
* ***1. Wheezing.***
* ***2. Breathlessness.***
* ***3. Chest tightness.***
* ***4. Cough, particularly at night and/or in the early morning.***

**It is manifested physiologically** by a widespread **narrowing of the air passages**, which may be relieved spontaneously or as a result of **therapy**. Can not cure but can **controlled**.

**Life threatening disease**

**How long this episodes taking place? (Mild, severe) (Min\hr)**

**Bronchial asthma risk factors**

* **1- Atopy** (allergic asthma- largest risk factor- genetic).
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 **2 – Environmental factors( viruses, occupational exposures, allergens, cold air, dust, smoking ,others…** ).

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 **3- family history.**

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 **4- others……………..**

**Bronchial asthma Classifications**

 **Asthma may be categorized into types**

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 **3- Bronchoconstriction triggering agents - include**

 **( a)** Seasonal **asthma ( b)** Exercise-induced **asthma.**

 **(c)** Drug-induced **asthma (e.g.,** aspirin & NSAID**).**

 **(d) O**ccupational **asthma**

 **(e) Eemotional asthma .**

 **(f ) A**sthmaticbronchitis **in smokers.**

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 **4-Recent studies added three subphenotypes of Asthma , based on Airway inflammation pattern.**

**Asthma Types**

* **1- Atopic asthma (**allergicsensitization, Extrinsic) :
* ***Classic example of*** *type I IgE-mediated hypersensitivity reaction.*
* Usually encountered in patient known case of **rhinitis, eczema.**
* **Genetic predisposition.**
* **A positive family history of asthma is common.**
* **Begins in childhood.**
* Triggered by **environmental allergens, such as dusts, pollens, roach or animal dander, and certain types of foods., etc…**
* Diagnosis: clinical diagnosis is essential +…………………………….
* (a) Skin test : **Using the offending antigen 🡪 immediate wheal-and-flare reaction.**
* (b) Serum radioallergosorbent tests (called RAST): TO  **identify the presence of IgE specific for a panel of allergens.**

**Asthma Types**

 2. **Non-atopic asthma:**

 **- N**on allergic.

 - Triggered commonly 🡪  **by Respiratory infection due to viruses (e.g., rhinovirus, parainfluenza virus).**

 - Family history: less common.

 - Skin test: reveals negative reaction.

- Mechanism:

 ***It is thought that virus-induced inflammation of the respiratory mucosa 🡪 lowers the threshold of the subepithelial vagal receptors to irritants*.**

**Asthma Types**

**3**- **Bronchoconstriction triggering agents**

**(a) Drug-Induced Asthma.**

***- Aspirin-sensitive asthma* + NSAID occurring with *recurrent rhinitis and nasal polyps.***

-Others examples: adrenergic antagonists, coloring agents .

**Commonly occurs in adult.**

**Mechanism*:***

***A*spirin inhibiting the *cyclooxygenase pathway* of arachidonic acid metabolism without affecting the lipoxygenase route, thus tipping the balance toward *elaboration of the bronchoconstrictor leukotrienes*.**

**Asthma Types**

**(b) Occupational Asthma.**

**Caused or worsene**d by breathing in irritants on the job.

* **Triggered\stimulated by:**
* 1) Fumes (epoxy resins, plastics)
* 2) Metal and dusts (platinum, wood, cotton)
* 3) Chemicals and Gases (formaldehyde, penicillin products, toluene, enzymes).
* 4) Animal substances (5) Plants

* **- Minute quantities & Repeated exposure.**

* **- Mechanisms:**
* **According to stimulus include:-**
* **Type I hypersensitivity reactions .**
* **Liberation of bronchoconstrictor substances.**
* **Hypersensitivity responses of unknown origin.**

**Bronchial asthma**

* **4- Pattern of the Airway inflammation :**
* **1) Eosinophilic asthma.**
* **2) Neutrophilic asthma.**
* **3) Mixed inflammatory asthma.**
* **4) Pauci-granulocytic asthma.**
* **These subgroups may differ in their:**
* **(a) Etiology.**
* **(b) Immunopathology.**
* **(c ) Response to treatment.**

Asthma Pathogenesis-1

**GENETIC CONSIDERATIONS**

**Genetic predisposition**

**In case of Atopic asthma- type I hypersensitivity**

**Inheritance of susceptibility genes (postulation) that makes individuals prone to develop strong TH2 reactions against environmental antigens (allergens)**

Asthma Pathogenesis-2

**1. The airway epithelium and submucosa contain dendritic cells that capture &process antigen \allergens.**

**Initial sensitization 🡪 stimulate induction of *TH2 cells.***

***2.* TH2 cells secrete cytokines e.g.(IL-4, IL-5,IL-13) that promote allergic inflammation and stimulate B cells to produce IgE and other antibodies.**

**3. Action of Cytokins**

**(a) IL-4 🡪Production of IgE by B cells.**

 **(b)IL-5 🡪 Activates recruited eosinophils.**

**(c ) IL-13🡪 Mucus secretion(bronchial submucosal glands)**

 **🡪 also Promotes IgE production by B cells.**

 **Asthma Pathogenesis-3 (Early & Late reaction)**

**3. IgE coats submucosal mast cells.**

**4. Repeat exposure triggers the mast cells to release granule contents and produce cytokines and other mediators🡪 induce the *early-phase (immediate hypersensitivity) reaction and the late-phase reaction***

 **Asthma Pathogenesis-4 (Early reaction- Minutes)**

- **Antigens🡪Th2+ IgE production🡪IgE binding to mast cells leads to Eosp. recruitment& release of primary mediators=**

 (Histamine, chemotactic factors, and secondary mediators i.e. leukotriens, prostaglandins, cytokines and neuropeptides). This results in:

* **(A) Bronchospasm-** triggered by direct stimulation of **subepithelial vagal (parasympathetic) receptors** through both **central** and **local** reflexes .
* **(B) Secretion of mucus**.
* **(C) Variable degree of vasodilatation&** increase permeability.
* **(D) Accumulation of leukocytes.**

 **Asthma Pathogenesis-5 (Late reaction- Hours)**

 - **6- 10 hr later,** produces a continued state of airway

 hyperresponsiveness with eosinophilic and neutrophilic infiltration. (steroid helpful to treat this stage)

**Components**: **consists largely of inflammation with recruitment of leukocytes= ( Eosinophils, neutrophils, and more T cells).**

 **- Leukocyte recruitment is stimulated by chemokines produced by mast cells, Epithelial cells (eotaxin *)* and T cells, and by other cytokines.**

 **- Outcome: persistent bronchospasm, edema, and necrosis of epithelial cells by *The major basic protein of eosinophils.***

**Cellular sources of inflammatory mediators& their effects**

 **Morphology of Asthma**

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***Airway remodeling.***

* Overall thickening of airway wall . Reduction of diameter
* Basement membrane fibrosis(BM thickening).
* Increases muscle mass (Hypertrophy and/or hyperplasia).
* Increased in size and number of blood vessels.
* Increase number of the submucosal glands.
* Mucus metaplasia of epithelium.
* Increased fibrogenic factors🡪 collagen type I,II “scar”
* **Irreversible Airflow obstruction.**

Bronchial asthma, microscopic

Curschman’s spirals

**Charcot-Leyden crystals**

THE END