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).

- _____
  _____
  _____

2 – Environmental factors(viruses,

occupational exposures, allergens, cold air, dust, smoking ,others…).

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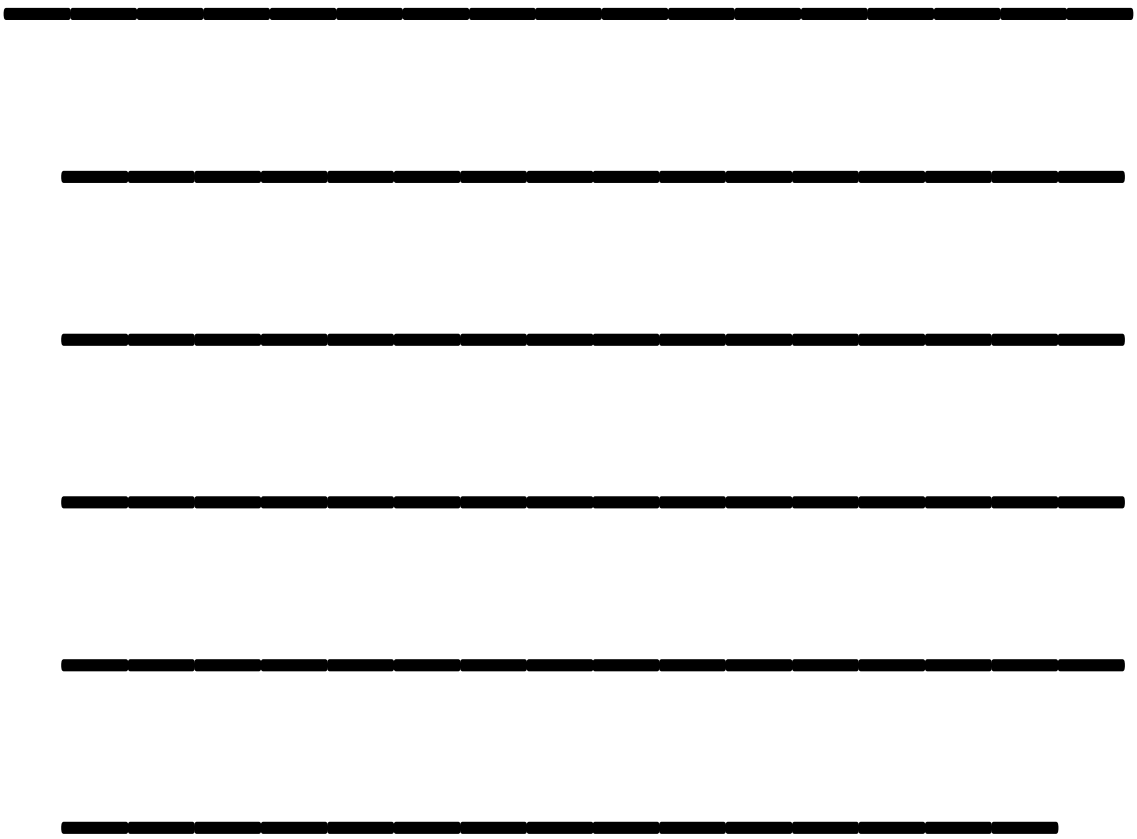
3- family history.



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others……

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Bronchial asthma Classifications

Asthma may be categorized into types

3- Bronchoconstriction triggering

agents - include

(a) Seasonal **asthma**

(b) Exercise-

induced **asthma.**

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

(d)

Occupational asthma

(e)

Eemotional asthma .

(f)

Asthmatic bronchitis **in smokers.**

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4-Recent studies added three subphenotypes of Asthma

, based on Airway inflammation pattern.

Asthma Types

- 1- **Atopic asthma**

(allergic

sensitization, 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 +…….
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- (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:**

- Non 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 worsened 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 T_H2 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 *T_H2 cells.*

2. T_H2 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