Sub: # Asthma

Defination:

Asthma is a chronic inflammatory disorder of the airways. The chronic inflammation causes an increases in the airway hyper-responsiveness that leads to recurrent episods of wheezing, breathlessness, chest tightness and cough particularly at night or early in morning.

⊙ The most frequent form has its onset in childhood between the ages of 3 and 5 years and may either worsen or improve during adolescence.

⊙ patient with asthma may experience symptom-free periods alternating with acute exacerbations, which last from minutes to hours or days.

Epidemiology:

⊙ In many countries the prevalence of asthma is increasing.

⊙ This increase, with its accompanying allergy, is particularly in children and young adults where this disease may affect up to 15% of the population.

⊙ Asthma being commoner in more developed countries.

⊙ In childhood asthma is more common in boys, but following puberty females are more frequently affected.

classification / Type:-

There are 5-type —

⊙ Atopic asthama.
⊙ Non-Atopic asthama.
⊙ Drug induced asthama
⊙ Occupational asthama.
⊙ Exercise induced asthama

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Hypersensitivity reaction

⊙ Atopic asthma:

When the Symptoms are induced by a hyperimmune response to the inhalation of specific allergen.

Type hypersensitivity reaction is the basis of the IgE positive history of asthma in family.

⊙ Non - Atopic asthma:

This is the type of asthma is triggered by the presence of irritants in the air that are not related to allergies.

This irritants stimulate parasympathetic nerven fibers in the airways causing broncho - constriction and inflammation.

⊙ Drug induced asthma:

Sensitive to certain drugs like aspirin, NSAIDS etc.

⊙ Occupational asthma:

Induced by triggers that exists in person's workplace including textiles, farming and wood working.

Stimulants such as fumes, organic and chemical ducts gas penicillin products etc.

⊙ Exercise induced asthma:

Beings after exercize and stops after 30 min, worsen in cold and dry climate.

Risk factors:

Endogenous factors.

Environmental factors.

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Endogenous factors → Genetic predisposition, Atopy, Airway, hyperresponsiveness, Gender, Ethnicity, obesity, viral infections.

Environmental factors → Indoor allergens, outdoor allergens, occupational sensitizens, passive smoking, Respiratory infections.

Symptoms:

- Wheezing
- breathlessness
- cough
- chest tightness prevalence 10-12% adults.
- 15% children developed country > Developing country.

Triggers:

Allergens → Dermatophagoides species (dust mite), environmental exposure, grass pollen, ragweed, tree pollen, fungal spores, pets furs, cockroaches etc.

Virus infection → upper respiratory tract virus such as rhinovirus, respiratory syncytial virus, corona-virus etc.

pharmacology agent → Beta blockers, AcE inhibitors, aspirin Exercise.

physical factors → cold air, hyperventilation, food.

Air pollutants → sulfur dioxide, irritant gases.

Irritants → household sprays paint fumes.

Occupational factors, Stress,

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Hormonal factors → fall in progesterone thyrotoxicosis
Gastrointestinal reflex.

Pathophysiology →

Exposure to allergens and irritants

⇓

IGE Stimulation.

⇓

Mast cell degradation.

↓ Histamine ↓ prostaglandins ↓ Bradikinins ↓ Leukotrienes

⇓

Airway hyperresponsiveness

↙ ⇓ ↘

Mucus Secretion — Inflammation — Bronchospasm

↓ ↓

Non-productive cough

Shortness of breath
Wheezing chest tightness
peakflow variability

Pathogenesis:

pathology
inflamanation.
inflammatory mediators.
Effects of inflammation.
Airway remodeling.

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pathology:

- chronic inflammation of lower airways.
- Mucosal infiltration of activated eosinophils and T-lymphocytes.
- Thickening of basement membrane.
- Goblet cell metaplasia.
- Smooth muscle hypertrophy and thickening.
- Shedding of epithelium.
- Occlusion of airway by mucosal plug.
- Vasodilatation and leakage.
- Angiogenesis.
- Lung parenchyma not affected.

Inflammation:

- Allergic type of inflammation occurs.
- From trachea to terminal bronchiole
- Predominately in bronchi
- Airway hyperresponsiveness.
- cell involved in inflammation - mast cell macrophages dendritic cell eosinophils neutrophils T lymphocytes and structural cells.
- Early phase reaction - mediated by granules release from mast cell, bronchoconstriction, vasodilation and increase permeability.
- Late phase reaction - inflammation with recruitment of eosinophils, T lymphocytes, neutrophils, macrophages etc and subsequent release of mediators.

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Inflammatory cells in Asthma:

- Eosinophils.
- Mast cells.
- Lymphocytes.
- Monocytes.
- Neutrophils

Eosinophils:

- Granulocytes derived from CD 34 cells.
- Exposure to allergen, recruited into airway by chemotactic signals chemokine EOTaxin.
- Migration into airway dependant on extravasation of peripheral blood eosinophils.

Lymphocytes:

- prominent source of cytokines.
- Increased no of activated T cells in airway.

Mast cells:

- Leukocytes that are effectors of inflammatory process
- Immature form in peripheral circulation, differentiate upon localisation to a tissue compartment.

Macrophage and Dendritic cells:

- phagocytic cells capable of antigen presenting.
- critical role in cleaning of microbes.
- Low affinity IgE receptors.

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Neutrophils:

- Increased in airways and sputum during acute exacerbations and in the presence of smoking.
- Determinant of lack of response to CS treatment.

Inflammatory mediators:

- chemokines.
- cytokines.
- Leukotrienes
- PROstanoids.
- IgE
- Nitric oxide.

chemokines:

- Recruitment or chemotaxis of inflammatory cells.
- Additional signaling function
- Attractive target for therapy.
- CCR5 inhibitor - currently in use.

cytokines:

- cross-linking of immunoglobulines in B lymphocytes Production of IgE and IgG.

IgE:

- Allergic inflammation prominent role in asthma.
- Mast cell mediators - major role in Asthma.
- IgE - Mast cell activation.

Leukotrienes:

- Arachidonic acid metabolites, Also incares mucus secretion.
- Rapidly synthesised within minutes following activation, LT, C4, D4, E4 potent.

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Smooth muscle cells:

- Excess accumulation of bronchial smooth muscle cells, prominent feature of airway wall remodeling.
- pro-activating signals for converting airway smooth muscle cells into a proliferative and secretory cell in asthma are unknown, but may include viruses and IgE.
- Another mechanism regulating smooth muscle proliferation is through production of metalloproteinas.
- Non specific BHR is a basic mechanism underlying the excessive smooth muscle contraction and airway narrowing.

Airway remodelling:

- Inflammation - thickening of sub BM.
- Mucus hypersecretion
- Subepithelial fibrosis.
- Airway smooth muscle hypertrophy.
- Angiogenesis.