Bronchial asthma
ASTHMA

- Asthma is a chronic relapsing inflammatory disorder of the airways characterized by paroxysmal reversible bronchospasm due to smooth muscle hyper-activity.

- There is increased responsiveness of the tracheobronchial tree to a variety of stimuli.
The major hallmarks of the disease are:

- **Increased airway responsiveness** to a variety of stimuli, resulting in episodic bronchoconstriction or spasm.

- **Inflammation** of the bronchial walls.

- Increased **mucus production**.
Clinical manifestation

1. Episodic expiratory wheezing (Inspiratory as well when severe).
2. Nocturnal cough.
3. Increased anteroposterior diameter of chest due to air trapping and residual volume.

- Severe and unremitting form of the disease is termed as **status asthmaticus** that may be fatal.

- It affects all age group but nearly 50% of cases develop it before the age of 10 years.
Types of asthma

1. Extrinsic asthma/atopic or allergic type

- Immune mediated disease
- Most common type
- Begins in childhood or early adult life
- Caused by a classic type I hypersensitivity (i.e. IgE mediated)
- Triggered by environmental antigens (e.g. pollen, certain foods etc.)
Most patients of this type have personal or family history of preceding allergic diseases such as rhinitis, urticaria or infantile eczema. Most of these allergens cause ill effects by inhalation like house dust, pollens, animal danders, moulds etc. There is increased level of IgE in the serum and positive skin test with inhaled antigen representing an IgE–mediated type I hypersensitivity reaction.
2. Intrinsic (Non-atopic) asthma

- Non immune type and acts by stimulating the nerves of the airway passage.

- This type of asthma mainly develops later in adult life with negative personal or family history of allergy, negative skin test and normal serum levels of IgE.

- Association with nasal polyp and chronic bronchitis.
Causative agents of intrinsic asthma are:

- Aspirin
- Pulmonary infections, especially caused by viruses (e.g. Rhinovirus, parainfluenza virus, respiratory syncytial virus)
- Cold
- Psychological stress
- Exercise
- Inhaled irritants (Cigarette smoke)
- Ozone induced asthma
3. Mixed type

- Many patients do not clearly fit into either of the above two categories and have mixed features of both.

- Those patients who develop asthma in early life have strong allergic component, while those who develop the disease late tend to be non-allergic.

- Either type of asthma can be precipitated by cold, exercise and emotional stress.
Pathogenesis of Extrinsic asthma 
(Atopic/Allergic type)

It is a Type I Hypersensitivity reaction with exposure to extrinsic allergens & develops in children with an atopic family history to allergies.

1) Initial sensitization to an inhaled allergen

- Stimulate induction of subset 2 helper T cells (CD4TH2) that release interleukin (IL)-4 and IL5
  - IL-4 stimulates isotype switching to IgE production.
  - IL-5 stimulates production and activation of eosinophils.
II) Inhaled antigens cross-link IgE antibodies on mast cells on mucosal surfaces.

a. Release of histamine and other preformed mediators.
b. These mediators stimulate bronchoconstriction, mucus production, influx of leukocytes.

III) Late phase reaction (4-8 hours later)

a. Exotaxin is produced which is Chemotactic for eosinophils and activates eosinophils.
b. Eosinophils release major basic protein (MBP) and cationic protein that Damage epithelial cells and produce airway constriction.
Other mediators involved in pathogenesis

- **Leukotrienes** LTC-D-E4 causes prolonged bronchoconstriction.
- **Acetylcholine** causes airway muscle contraction.
Genetic association of Asthma

Genetic associations have been made with:

- certain HLA alleles
- polymorphisms in IL-13, CD14, ADAM-33
- polymorphism in β2-adrenergic receptor, and the IL-4 receptor.
Morphology

Gross:

- Lungs are overinflated with patchy atelectasis.
- Mucus plugging of airways.
- The cut surface shows characteristic occlusion of the bronchi and bronchioles by viscid mucus plugs.
Microscopy

- There is hypertrophy of submucosal glands as well as of the bronchial smooth muscle.
- The bronchial wall shows thickened basement membrane of the bronchial epithelium, submucosal oedema and inflammatory infiltrate consisting of lymphocytes and plasma cells with prominence of eosinophils.
- Subepithelial fibrosis.
- The mucus plugs contain normal or degenerated respiratory epithelium forming twisted strips called Curschmann’s spirals (Whorled mucus plugs).
- The sputum usually contains numerous eosinophils and diamond-shaped crystals derived from eosinophils called Charcot–Leyden crystals.
Laboratory findings

Pulmonary function test:
1. Initially develop *respiratory alkalosis*
   - Patients work hard at expelling air through inflamed airways.
   - May progress into *respiratory acidosis* if bronchospasm is not relieved.

**FEV1** is the best measure of severity.

**Others:**
Eosinophilia, Positive skin test for allergens.
Status asthmaticus

- Acute severe asthma (also referred to as *status asthmaticus*) is an acute exacerbation of asthma that does not respond to standard treatments of bronchodilators and steroids.

- Life threatening condition.