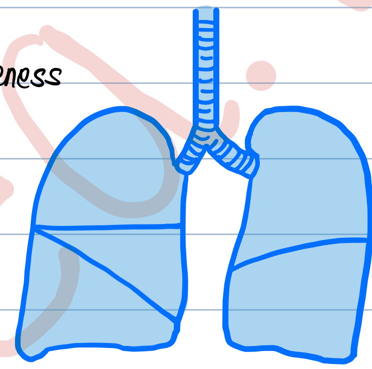
Asthma:

chronic inflammatory condition of the respiratory passage, particularly the mucosa, that cause narrowing of respiratory passages causing difficulty in breathing & is sometimes, fatal [obstructive lung disease]

PREDISPOSING / EXACERBATING FACTORS:

I **Atopic Triad:**
- Asthma
- Atopic dermatitis / eczema
- Allergic rhinitis

} genetic predisposition to hyper-responsiveness to allergens



II **SAMTER'S TRIAD:**
- Asthma
- Nasal polyps
- Aspirin sensitivity [excessive inhibition of COX enzyme leading to shunting of arachidonic acid to lipoxygenase pathway which causes increased leukotriene production]
  - → ↑ bronchospasm
  - → ↑ mucus production

III Dust, smoke

IV pet dander / hair

V Cockroaches

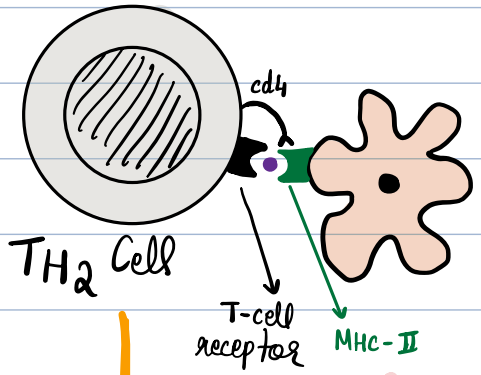
VI Cold / exercise

VII Viral upper respiratory tract infection

VIII β-blockers (β_2 action)

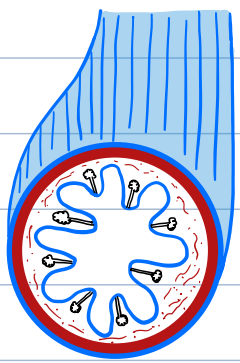
Hygiene hypothesis – people who have had reduced exposure to pathogenic microbes in early childhood are more susceptible to develop asthma later in life
↓
for late onset asthma

Allergen → comes in contact with → Dendritic cell (an APC) → phagocytosis & antigen presentation via MHC II to TH_2 cell



Production of
- IL-13 → Stimulates mucus secretion from bronchial submucosal glands & promotes IgE production by B cells.
- IL-4 → activates → Plasma cell → to produce → IgE (Y) → binds to → FCεRI → Mast cell → degranulation of mast cells → Production of
  - histamines
  - leukotrienes
- IL-5 → activates → eosinophil → releases → Leukotrienes & Proteases (produced in chronic cases ⇒ these cause tissue damage)

Bronchioles
* Bronchoconstriction
* increased mucous production
* inflamed mucosa (due to fluid collection & immune cell infiltration)
* increase in vascular permeability



⇒ narrowing of airway
- * ↓ reversible
- over chronic periods of exacerbation of asthma
  - tissue becomes fibrotic
  - thickening of the basement membrane

⇓ permanently narrowed * ↓ irreversible

Asthma is reversible *

Steps in Pathogenesis: Sensitization

[Inhaled allergens are taken up by APCs & elicit a T_H2-dominated response favouring IgE production & eosinophil recruitment]

↓

On Re-exposure, antigens bind to IgE bound on mast cells & release preformed mediators

↓

Early phase reaction: (produced directly by mediators from mast cells or by stimulation of vagal receptors in subepithelium)
- bronchoconstriction
- increased mucous production
- vasodilation with increased vascular permeability (causing edema)

↓

Late-phase Reaction:
- inflammation (leading to further narrowing of airways)
- airway remodelling.

Classification of Asthma:

I According to type of antigen:

- **Atopic (allergic/extrinsic):** → most common type → Type I IgE-mediated HS Rx.
  - → usually begins in childhood
  - → family history of asthma / allergic diseases is common
  - → skin test with causative allergen ⇒ immediate wheal-&-flare reaction seen
  - → triggering allergens: dust, pollen, animal dander, foods
- **Non-atopic (intrinsic):** → no causative exogenous triggering factors can be identified
  - → skin tests are usually negative → may be due to hyper-irritability of bronchial tree
  - → family h/o asthma is less common
  - → triggering events – respiratory infections due to viruses
    - inhaled air pollutants

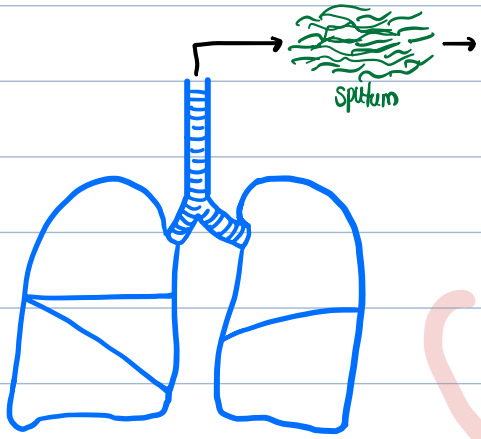
II According to Agents / Events that Trigger Bronchoconstriction:

- Seasonal
- Exercise-induced
- Drug-induced *
- Occupational
- Asthmatic bronchitis in smokers

* eg: aspirin

Clinical Signs & Symptoms:

- Cough
- chest tightness
- shortness of breath (SOB) [aka dyspnoea]
- difficulty in finishing their sentences
- use of accessory muscles of respiration
- hyper-resonance (on percussion)
- wheezing upon expiration



→ Sputum microscopy

- Curschmann Spirals – increased mucus production forms mucus plugs.
  - Mucus plugs contain desquamated epithelial cells & eosinophils & form spiral-shaped casts of the airways.
- Charcott-Leyden Crystals – crystalloids derived from an eosinophil lysophospholipase-binding protein called galectin-10.
- Creola Bodies – compact clusters or strips of columnar epithelial cells shed from the bronchus.

Airway Remodelling: → group of structural changes in bronchial wall due to repeated bouts of inflammation

1. Hypertrophy / hyperplasia of the submucosal glands
2. Hypertrophy / hyperplasia of bronchial wall smooth muscle
3. Increased vascularity
4. Deposition of subepithelial collagen accompanied by fibrosis & thickening of basement membrane.

Clinical Course:

- acute asthmatic attack usually lasts upto several hours.
- in some, mild degree of chest tightness, dyspnoea, wheezing & cough +/- sputum production may constantly present
- between asthmatic attacks, patients may be asymptomatic
- Status asthmaticus: → most severe form of asthma
  - ↳ severe acute paroxysm persists for days / weeks
  - → bronchoconstriction does not respond to drugs
  - → may cause severe airflow obstruction leading to severe cyanosis & death.

Diagnosis:

→ demonstration of an increase in airflow obstruction (from baseline levels)

→ difficulty with expiration [prolonged expiration, wheeze]

→ elevated eosinophil count in peripheral blood

Pulmonary Function Tests (PFTs)

can be done only in symptomatic patients

- FVC — decreased
- FEV_1 — markedly decreased
- FEV_1 : FVC ratio < 75% ⇒ indicates obstructive disorder

↓

SABA — short acting β_2 agonist

⇒ produces bronchodilation

↓

Repeat PFTs

- $FEV_1 \geq 12\%$ after SABA → confirms asthma
- $FEV_1 < 12\%$ after SABA → COPD

If patient is asymptomatic ⇒ Methacholine challenge test

Pulmonary Function Tests (PFTs)

- FVC — decreased
- FEV_1 — markedly decreased
- FEV_1 : FVC ratio < 75% ⇒ indicates obstructive disorder

↓ methacholine (muscarinic agonist)

bronchoconstriction

↓

Repeat PFTs

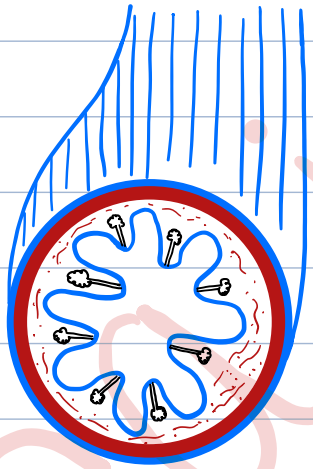
↓

If FEV_1 drops 20% or more from the original ⟹ confirms Asthma

CBC: → elevated eosinophils in DLC

Serology: → elevated levels of IgE antibodies

Chest X-ray: → showing hyper-inflation
↳ for ruling out pneumonia

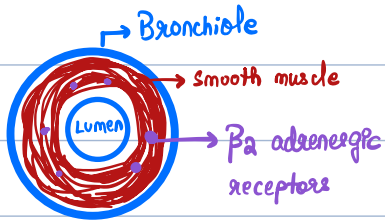


Type	Frequency of day-time symptoms	Frequency of night-time symptoms	FEV_1
Intermittent	< 2 times / week	< 3 times / month	$> 80\%$
Mild	> 2 times / week	3-4 times / month	$\geq 80\%$
Moderate	7 times / week	≥ 1 time / week	60 - 80 %
Severe	Everyday, throughout the day	everynight, throughout the night	$< 60\%$

Type	Medication Protocol
Intermittent	• SAB_2A (PRN)
Mild	• SAB_2A (PRN) • Inhaled corticosteroid (ICS) - low dose
Moderate	• SAB_2A (PRN) • Medium-dose ICS (or) Low-dose ICS with LAB_2A
Severe	• $SA\beta_2A$ (PRN) + medium dose ICS + $LA\beta_2A$ →refractory→ • $SA\beta_2A$ (PRN) + high dose ICS + $LA\beta_2A$ →refractory→ • $SA\beta_2A$ (PRN) + high dose ICS + $LA\beta_2A$ + oral corticosteroids

* PRN = Pro re nata ⇒ as the need arises

SAβ_2A:
- Albuterol
- Levalbuterol



→ Bronchodilation

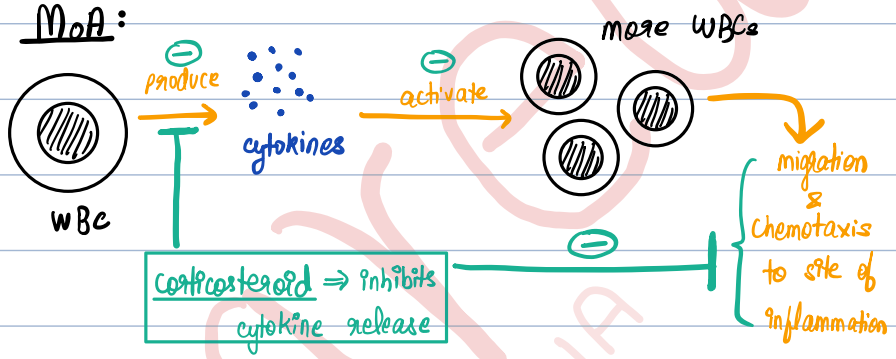
Adverse effects:
- Tachyarrhythmias
- Tremors
- Dizziness

C/I:
- heart block
- narrow angle glaucoma

Corticosteroids:
- fluticasone
- Budenoside
- Mometasone

} ICS

MoA:



Adverse effect: Candidiasis

LAβ_2A: same MoA as SAβ_2A

same adverse effects as SAβ_2A
- Formoterol
- Salmeterol

Black box warning:
- → never use for acute exacerbations
- → never give without an ICS

Oral Corticosteroids (P.O.):
- Methyl prednisolone
- prednisone
- prednisolone

} P.O. or I.V.

Adverse effect: ++++++

∴ use only for short-term.

Other drugs:

Mast cell stabilizers	LT receptor antagonist	Omalizomab ⇒ anti-IgE antibody
• Cromolyn sodium	• Montelukast	