

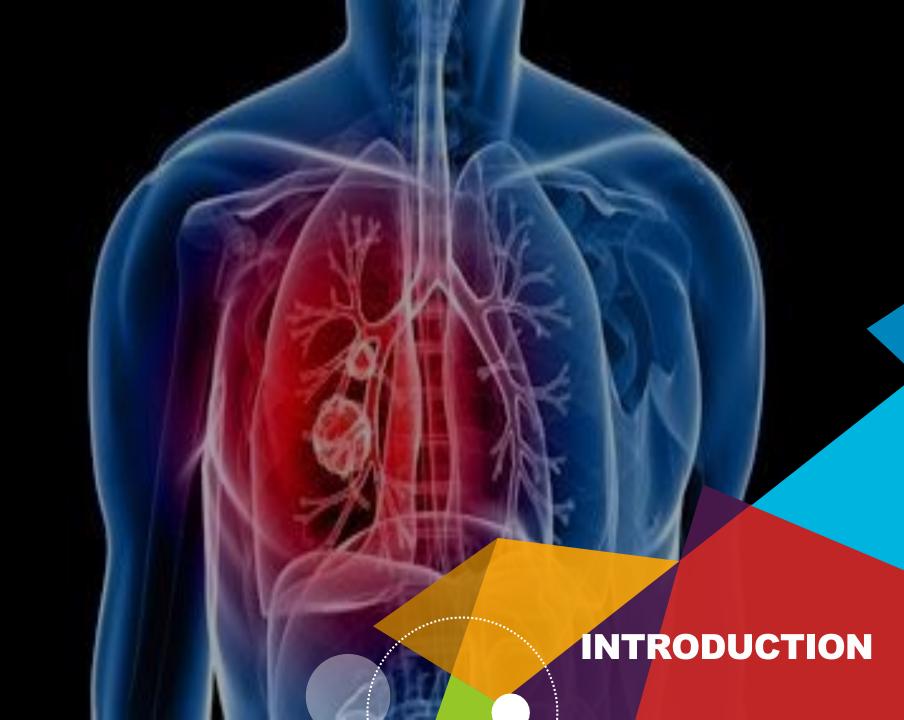
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CONTENTS



ASTHMA

- INTRODUCTION
- CLASSIFICATION
- RISK FACTORS
- Diagnosis
- **Treatment & Prevention**



Introduction

- Asthma is a chronic inflammatory disorder of the airways that is characterized:
- o *clinically* by recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night/early morning.
- physiologically by widespread, reversible narrowing of the bronchial airways and a marked increase in bronchial responsiveness.

Introduction

- In 2015, 358 million people globally had asthma, up from 183 million in .1990
- It caused about 397,100 deaths in 2015, most of which occurred in the developing world.



Classification

- > Extrinsic /allergic :70%
- Most common type
- Environmental agent: dust, pollen, food, animal dander
- Family history present
- Serum IgE levels increased

Classification

- ➤ Intrinsic /non-allergic(30%)
- > Triggered by respiratory tract infection
- Viruses most common cause
- Family history uncommon
- IgE level normal
- No associated allergy
- Cause- hyperirritability of bronchial tree

Classification

- > Drug induced asthma
- Several pharmacologic agents
- Aspirin sensitive asthma.
- o sensitive to small doses of aspirin.
- Inhibits COX pathway



Pathophysiology

- I. Chronic inflammation
- II. Airway Hyperresponsiveness

Pathophysiology

I. Inflammation

- Chronic inflammatory state
- Involves respiratory mucosa from trachea to terminal bronchioles, predominantly in the bronchi.
- Activation of mast cell, infiltration of eosinophils & T-helper type 2 (Th2) lymphocytes

Pathophysiology

I. Inflammation

- Exact cause of airway inflammation is unknown.
- Thought to be an interplay between endogenous and environmental factors.
- Endogenous factors
- Genetic predisposition to IgE mediated type I hypersensitivity
- The major risk factor for asthma

Pathophysiology

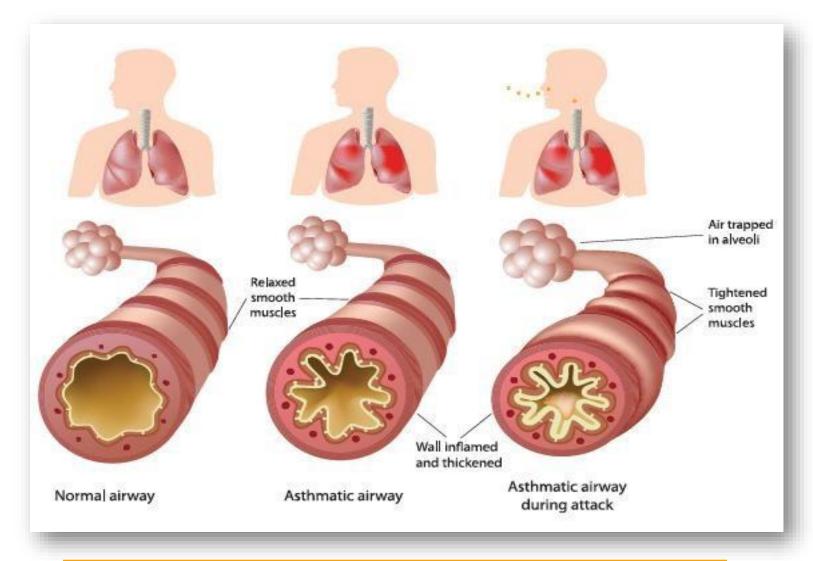
- I. Inflammation
- **■** Environmental factors
- Viral infections: Mycoplasma,
 Chlamydia
- > Air pollution
- > Allergens: house dust mite

Pathophysiology

II. Airway Hyperresponsiveness (AHR)

The excessive bronchoconstrictor response to multiple inhaled triggers that would have no effect on normal airways.

Pathophysiology





Risk factors

- **Host factors:**
- predispose individuals to, or protect
 them from, developing asthma
- i. Genetic
- ii. Gender
- iii. Obesity

Risk factors

- > Environmental factors:
- Indoor allergens, Outdoor allergens
- Occupational sensitizers
- Tobacco smoke, Air Pollution
- Respiratory Infections
- o Diet

Triggers

- **☐** Asthma Triggers
- Allergens
- Virus Infections
- Drugs
- Exercise
- Food
- Air pollutants
- Physical factors
- Stress



Clinical manifestations

- > Symptoms
- Wheezing, dyspnea and cough.
- Variable both spontaneously and with therapy.
- Symptoms worse at night.
- Nonproductive cough
- Limitation of activity

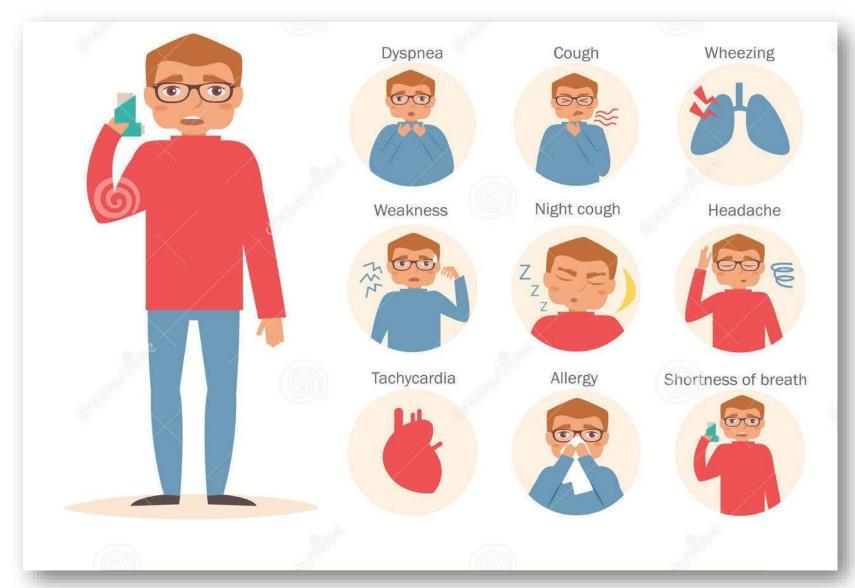
Clinical manifestations

- > Signs
- †respiratory rate, with use of accessory muscles
- Expiratory sounds
- No findings when asthma is under control

Classification for asthma severity

Grade	Symptoms	Night-time Symptoms
Mild intermittent متقطع	Symptoms ≤ 2 times/week	2 ≥times/month
Mild persistent متواصل	Symptoms ≥ 2 times/week but $\leq 1/\text{day}$	2 ≤times/month
Moderate persistent	Daily Symptoms	/1 ≤week
Severe persistent	Continued Symptoms Limited physical activity	Frequent

Clinical manifestations



Laboratory diagnosis

- > Pulmonary function tests:
- Using Spirometry
- Estimate degree of obstruction.



Laboratory diagnosis

- > Chest X- ray
- > Arterial blood-gas analysis
- hypoxia & hypocarbia
- > Sputum & blood eosinophilia
- > Elevated serum IgE levels



Management

I. Non-Pharmacological

II. Pharmacological



Non-Pharmacological

- Reduce exposure to indoor allergens
- Avoid tobacco smoke
- Avoid vehicle emission
- Identify irritants in the workplace



Non-Pharmacological

- Influenza Vaccination
- Should be provided to patients with asthma when vaccination of the general population is advised

- ☐ Classification of drugs
- > Bronchodilators : rapid relief, by relaxation of airway smooth muscle
- β2 Agonists
- Anticholinergic Agents
- Methylxanthines
- **Controllers**: inhibit the inflammatory process
- Glucocorticoids
- Leukotrienes pathway inhibitors
- Cromones
- Anti-IgE therapy

- \triangleright β 2 Agonists in asthma
- Potent bronchodilators.
- Usually given by inhalation route.
- Effects:
- Relaxation of airway smooth muscle
- Inhibition of mast cell mediator release
- Increased mucociliary transport
- Inhibition of sensory nerve activation
- No effect on airway inflammation

- > β2 Agonists in asthma
- a) Short-Acting β2 Agonists
- E.g salbutamol
- Rapid onset, without significant systemic side effect
- Bronchodil. of choice in acute severe asthma
- Used for symptomatic relief
- Only treatment required for mild, intermittent asthma.
- Use >2 times a week indicates need of a regular controller therapy.

- \triangleright β 2 Agonists in asthma
- b) Long-Acting β2Agonists
- E.g salmeterol,
- Duration of action >12 hrs.
- Used in combination with inhaled corticosteroid therapy.
- Improve asthma control
- Should not be used as monotherapy (increased mortality)
- Not effective for acute bronchospasm.

- > Anticholinergic agents
- E.g Ipratropium bromide, tiotropium.
- Prevent cholinergic nerve induced bronchoconstriction.
- Less effective than $\beta 2$ agonists.
- Use in asthma
- Intolerance to inhaled β2 agonist.
- Status asthmaticus –additive effect with β2 agonist

- > Anticholinergic agents
- Ipratropium:
- o Slow
- Tiotropium:
- longer acting
- Dryness of mouth



- > Methylxanthines
- Medium potency bronchodilator
- E.g Theophylline, theobromine, caffeine
- Recently interest has declined in this class of drugs:
- Still widely used drugs especially in developing countries due to their lower cost.

- > Methylxanthines
- Adverse effects
- Anorexia, nausea, vomiting, abdominal discomfort
- headache, and anxiety
- Seizures or arrhythmias
- Doxyphylline
- o long acting, or al



- > Corticosteroids in asthma
- Effective drugs for treatment of asthma.
- Development of inhaled corticosteroids is a major advance in asthma therapy.
- Used prophylactically as a controller therapy.
- Reduce the need for β 2 agonist.
- Benefit starts in 1week but continues up to several months.



- > Corticosteroids in asthma
- Effects: Broad anti-inflammatory effects:
- Marked inhibition of infiltration of airways by inflammatory cells.
- Modulation of cytokine and chemokine production

- > Corticosteroids in asthma
- Inhaled corticosteroids(ICS)
- Use of β2Agonists >2 times a week indicates
 need of a ICS
- o E.g Beclomethasone, Fluticasone

- > Corticosteroids in asthma
- Inhaled corticosteroids (ICS)
- Adverse effects:
- Oropharyngeal candidiasis, dysphonia
- Decreased bone mineral density.
- Skin thinning
- Growth retardation in children

- > Leukotrienes pathway inhibitors
- a) Inhibition of 5-lipoxygenase, thereby preventing leukotriene synthesis. Zileuton.
- b) Inhibition of the binding of LTD4 to its receptor on target tissues, thereby preventing its action. E.g Montelukast.
- Oral route.
- Adverse effects
- Liver toxicity

- > Leukotrienes pathway inhibitors
- They are less effective than ICSs in controlling asthma
- Use in asthma
- o Patients unable to manipulate inhaler devices.
- Aspirin induced asthma.
- Mild asthma alternative to ICS.
- Moderate to severe asthma may allow reduction of ICS dose

> Cromones

- E.g Cromolyn sodium
- On chronic use (four times daily) reduce the overall level of bronchial reactivity.
- They are only of value when taken prophylactically.
- Inhalation route

Pharmacological treatment

> Cromones

- May act by stabilization of Mast cells with inhibition of mediator release
- Uses
- Asthma Prevention of asthmatic attacks in mild to moderate asthma
- Adverse effects
- Well tolerated drugs
- Minor side effects- throat irritation, cough, and mouth dryness, rarely, chest tightness, and wheezing

- > Anti-IgE therapy:
- أوماليزوماب Omalizumab
- Antibody targeted against IgE.
- Action:
- IgE bound to omalizumab cannot bind to IgE receptors on mast cells and basophils, thereby preventing the allergic reaction

- > Anti-IgE therapy:
- Use in asthma
- Persons >12 years of age with moderate-tosevere asthma.
- Omalizumab is not an acute bronchodilator
- Expensive drug
- Has to be given under direct medical supervision due to the risk of anaphylaxis



Status asthmaticus (severe acute asthma)

- Severe airway obstruction
- Severe dyspnea & unproductive cough
- O Sweating, central cyanosis, tachycardia

Status asthmaticus (severe acute asthma)

- > Treatment of Status asthmaticus
- High conc. of oxygen through facemask
- Salbutamol in oxygen given immediately
- Ipratopium bromide + salbutamol in oxygen,who don't respond within 15-30 min

Status asthmaticus (severe acute asthma)

- > Treatment of Status asthmaticus
- Terbutaline s.c. or i.v.
- Hydrocortisone hemisuccinate i.v., followed by infusion.
- Endotracheal intubation & mechanical ventilation if above ttt fails

Prophylaxis

- Preservation of the environment, healthy life-style (smoking cessation, physical training) – are the basis of primary asthma prophylaxis.
- These measures in combination with adequate drug therapy are effective for secondary prophylaxis.