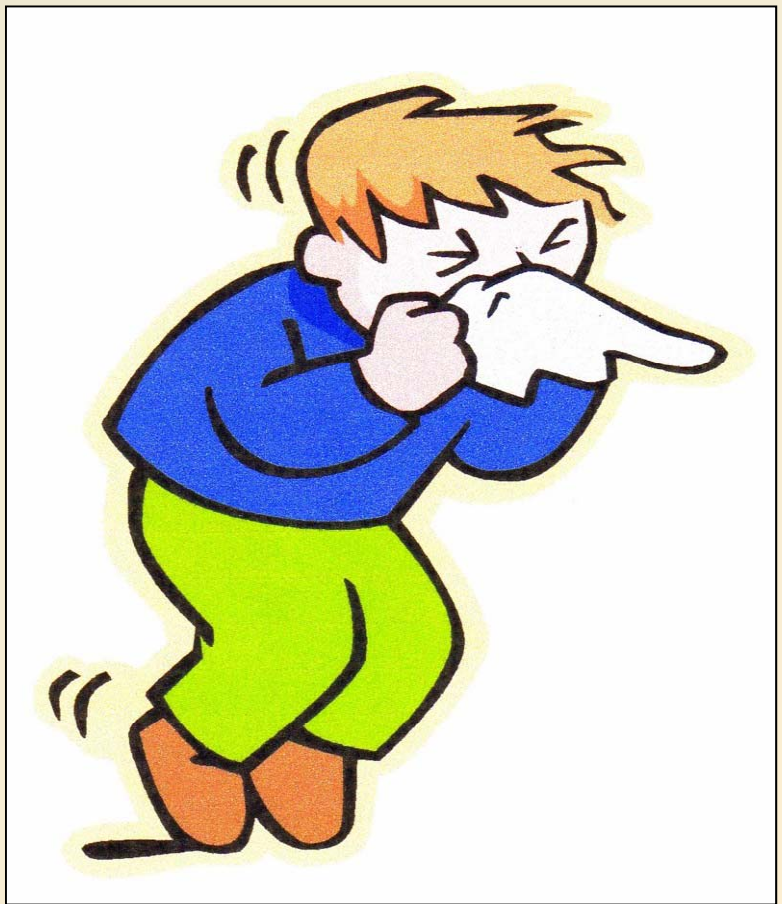
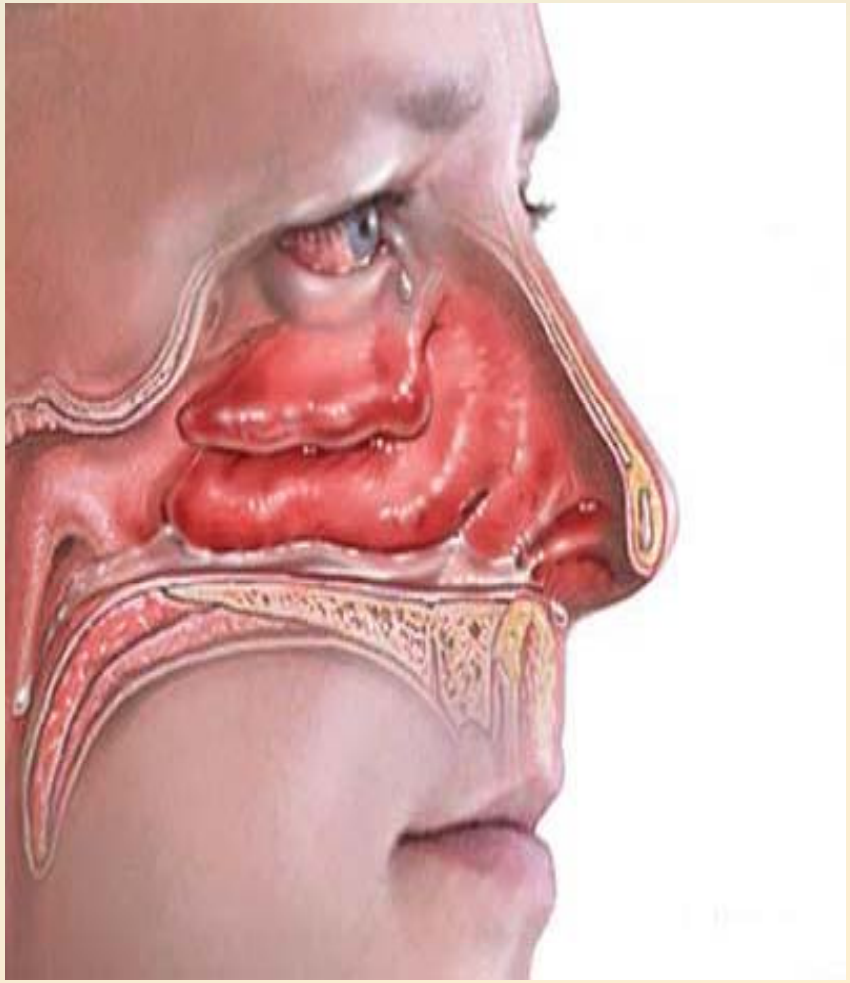
Pharmacological treatment of acute & chronic Rhinitis



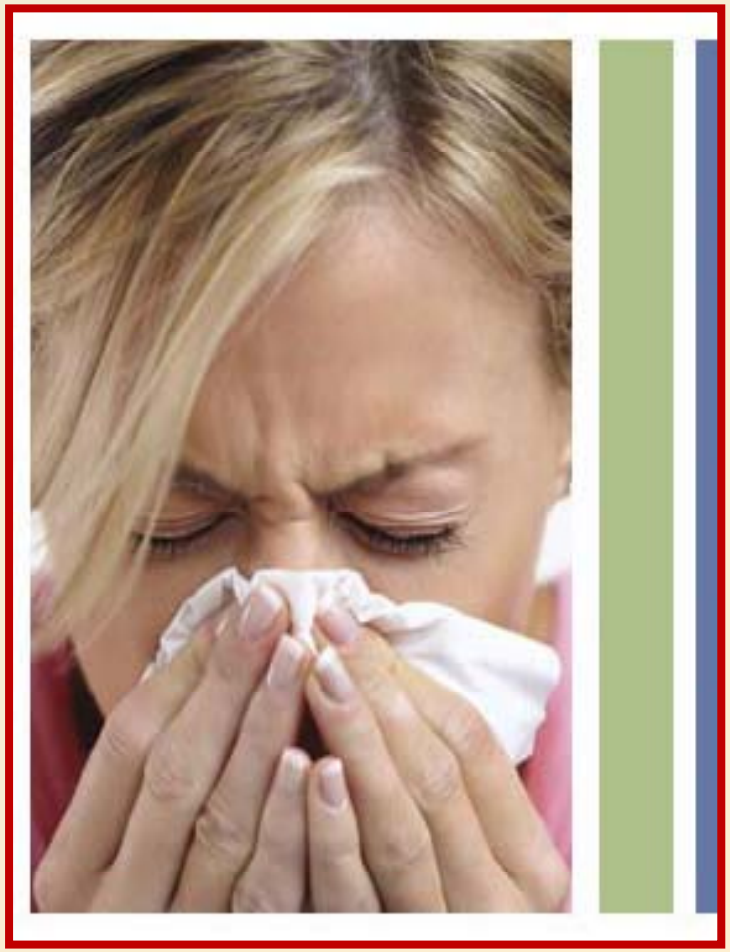
RHINITIS

- **An inflammation & swelling of mucous membrane of the nose**



Symptoms of Rhinitis

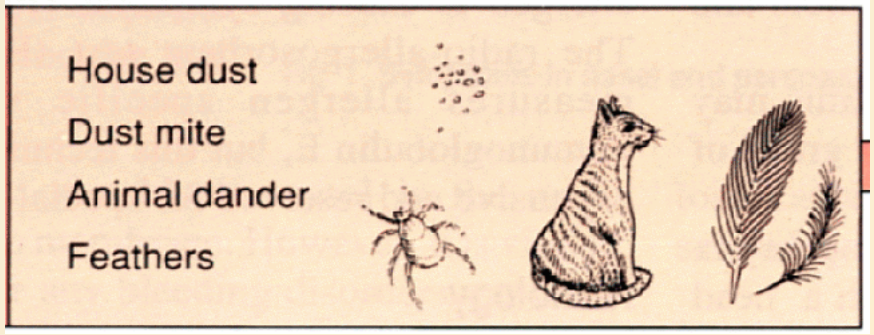
- **Runny nose, sneezing, itchy nose/eyes & stuffiness**



Causes of Rhinitis

Most common

- **Cold & allergies ---**
  -Attack may be precipitated by inhalation of an allergen (dust, pollen, animal dander)



Types of Rhinitis

i) Acute Rhinitis

Short lived; results from viral infections + other causes (allergies)

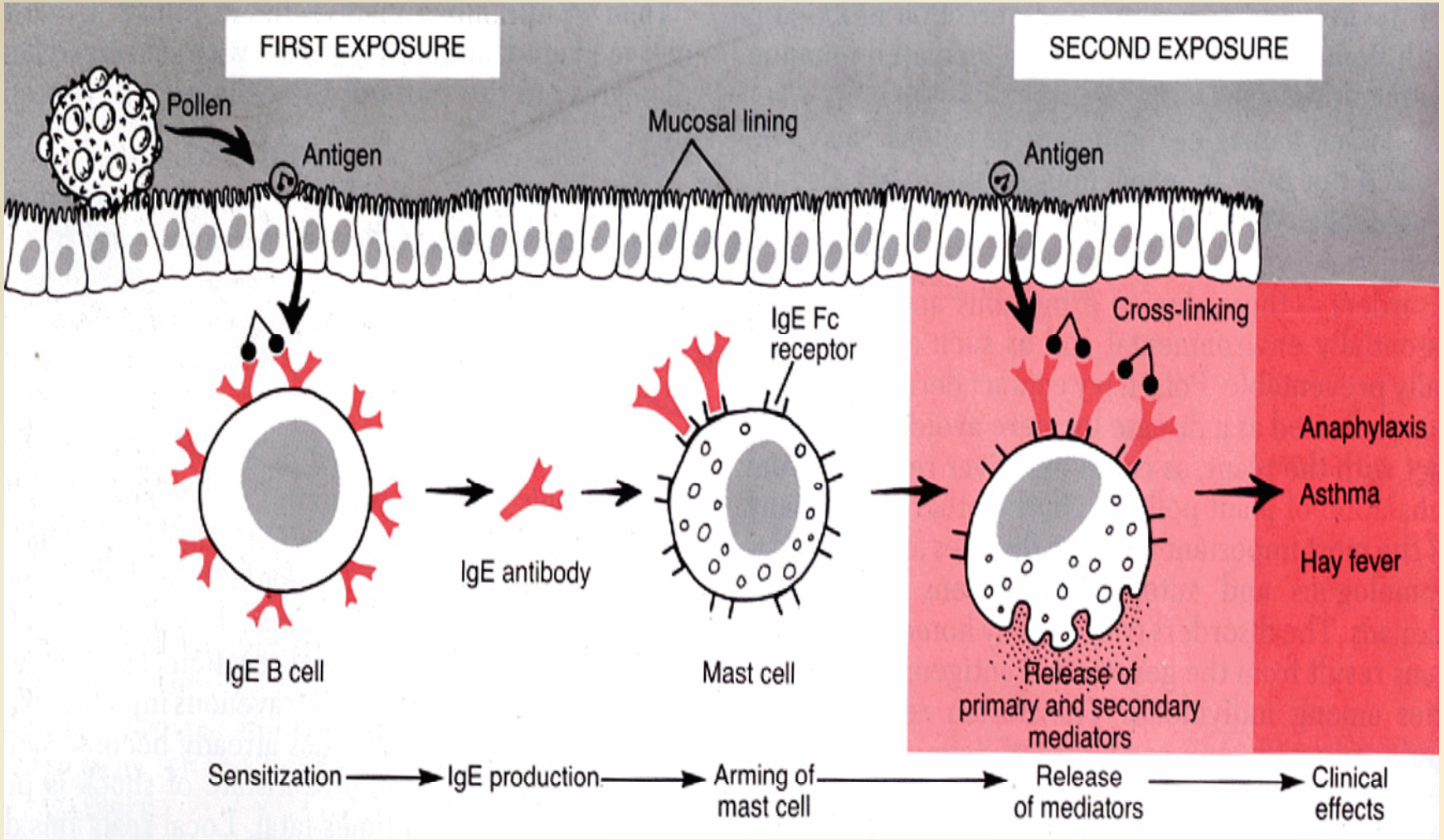
Symptoms= runny nose, sneezing, congestion, post nasal drip, cough & low grade fever

Cont…

ii) Chronic Rhinitis

- Long- standing
- Usually occur with chronic sinusitis
- Chronic rhinitis is usually an extension of rhinitis caused by inflammation or an infection
- It may also occur with disease (syphilis, tuberculosis, leishmaniasis & rhinosporidiosis)

Pathogenesis of Allergic Rhinitis



Treatment of Rhinitis

- **Non-pharmacological therapy**
  - Avoidance of irritants
  - Dusting/vacuuming; washing of bed sheets
  - Intake of fluids
  - Rest
  - Surgery (DNS, Polyp)

Cont….

Pharmacological therapy

1- Antihistamines (H_1 receptor antagonists)

2- α-Adrenergic agonists

3- Corticosteroids

4- Cromolyn

5- Antibiotics (not relieve symptoms of allergic rhinitis)

Antihistamines

- **Agents block the actions of histamines**
- **Classical antihistamines = H1 receptor antagonist**

Histamine

❖Biologically active amine functions as neurotransmitter; Synthesized from histidine

❖Distributed in mast cells, basophils, neurons of brain, cells of stomach

Histamine receptors

Three types

H_1-receptors= Smooth muscles, endothelial cells of blood vessels & brain

H_2-receptors= Parietal cells of stomach, heart muslces, mast cells, brain

H_3-receptors (presynaptic)= brain, myenteric plexus of GIT, other neurons

Effects of histamine

CVS

- Stimulation of heart (H_2)+dilatation of arterioles & precapillary sphincters ⇒ ⇓ SBP +DBP

GIT

- Acid production↑ (stimulation of H2)+↑intestinal secretion
- Contraction of sm muscles (H1 receptor stimulation)

Respiratory tract

- Bronchoconstriction (H1 receptors)

CNS

- Regulation of body temp., effects CVS system & sexual arousal, causes pain & itching by stimulation of peripheral nerve ending
- Cont…..

Triple response

- Histamine (i.d)⇒ **red spot + edema + flare** response

Reddening= caused by dilatation of small vessels followed by

Edematous wheal & irregular flare(surrounding wheal)=flare is caused by axon reflex ⇒sensation of itching

1- ANTIHISTAMINES

- **They block H1 receptors** (competitive antagonists) **of histamine**
- They do not influence the formation of or release of histamine, rather they block the receptor mediated response of a target tissue

Classification

A- First generation drugs

i) Ethanolamine

e.g., *Diphenhydramine, dimenhydrinate*

Cont…

ii) Piperazine derivatives

e.g., *Cyclizine, meclizine*

iii) Alkylamines

e.g., *Chlorpheniramine*

iv) Phenothiazine derivatives

e.g., *Promethazine*

v) Miscellaneous (other drugs)

e.g., *Cyproheptadin*e

B- Second generation drugs

1-Piperdine

e.g., fexofenadine

2-Miscellaneous

e.g., *Loratadine* (longer acting), *Cetrizine*

Properties of Antihistamines

First generation drugs = lipid soluble , easily cross into brain, produce sedation & drowsiness

Second generation drugs = less lipid soluble, not significantly pass into brain, do not cause sedation

Pharmacokinetics

- Rapidly absorb----after oral
- Wide distribution
- Some extensively metabolized by microsomal systems in liver (CYP3A4 system)—important drug interaction with Ketoconazole
- Most drugs-----4-6 duration
- Meclizine & 2nd generation drugs-----12-24 h

Pharmacological actions

1-Sedation

First generation drugs

- Common effect; Varies with drugs & with patients; (promethazine ↑)
- At ordinary dose=children---excitation; at ↑ toxic dose=marked stimulation, agitation, convulsion & coma

2nd generation drugs= little or no sedating effect

2- Antinausea & Antiemetic actions

- Some 1st generation drugs are effective antiemetic agents e.g., *promethazine, meclizine, cyclizine, dimenhydrinate diphenhydramine*

3- Antiparkinsonism effects

Some H1 antagonists (diphenhydramine) =suppressant effect on extrapyramidal symptom associated with antipsychotic drug ⇒ diphenhydramine given for acute dystonic reaction

4- Anticholinoceptor actions

- Many 1st generations agents (diphenhydramine & dimenhydramine) = atropine like effect --- beneficial for non allergic rhinorrhea (may cause urinary retention & blurred vision)

5- Adrenoceptor blocking actions

Phenothiazine sub group= cause orthostatic hypotension

6-Serotonin blocking actions

- E.g., Cyproheptadine—antiserotonin agent

7- Local anesthesia

- Several 1st generation agents have local anesthetic effects (by blocking Na+ channels in excitable membranes) e.g., *diphenhydramine & promethazine*

8- Other actions

- Some H1 antagonist (cetrizine) inhibit mast cell release of histamine + some other mediators of inflammation → treatment of allergies

Clinical Uses

1- Allergic reaction

- Urticaria & allergic rhinitis (histamine primary mediator)
- Pruritis & hay fever not in asthma

2- Nausea & vomiting

Many 1st generation = *promethazine, dimenhydrinate, cyclizine, meclizine* & ***Doxylamine*** (during pregnancy)→teratogenic= not used

3-Motion sickness

Many 1st generation = *promethazine, dimenhydrinate, cyclizine, meclizine & diphenhydramine*

Adverse Effects

1-Antimuscarinic effects

1st generation drugs= dryness of mouth, blurring of vision, retention of urine, constipation & ↓sweating

2-Alph Antagonist effects

1st generation drugs= blocking of α-receptors on blood vessels =postural hypotension

3-CNS

1st generation drugs=sedation but may cause mental agitation & convulsion (toxic doses).....cont....

4-Cardiac Arrhythmias

- Astemizole (older agent) & terfenadine (large doses)≅ cardiac arrhythmias

Drug Interactions

Ketoconazole, itraconazole & erythromycin = inhibit metabolism of astemizole & terfenadine → lethal cardiac arrhythmias

MOA of Arrhythmia

Blockade of K+ channels in heart → prolongation of action potential → arrhythmias

2- Alpha Adrenergic agonists

A- Short acting α-adrenergic agonist (nasal decongestants e.g., Phe) → constrict dilated areterioles in nasal mucosa & ↓airway resistance

B- Longer acting oxymetazoline

C- Alpha agonists + antihistamine

Alpha agonists should not be used for longer time b/c of rebound nasal congestion

3-Corticosteroids

A-Nasal sprays

e.g., beclomethasone, budesonide, fluticaosne, flunisolide & triamcinolone

Side effects

Localized to intranasal (nasal irritation, nose bleed, sore throat, candidiasis)

B- Topical steroids

More effective compared to systemic antihistamines for allergic & non allergic rhinitis

4- Cromolyn

- Mast cell stabilizer (prevent release of histamine & other mediators from mast cells)
- Intranasal cromolyn= useful particularly when given before (1 to 2 weeks) contact with allergen
- Multiple daily dosing of cromolyn = required

Effects:

- Reduces nasal pruritis, sneezing, rhinorrhea and congestion