DRUGS ACTING ON RESPIRATORY SYSTEM

Mr. D. Raju
M. Pharm., Lecturer
Upper respiratory tract includes: nares, nasal cavity, pharynx, and larynx.

Lower respiratory tract includes: trachea, bronchi, bronchioles, alveoli, and alveolar-capillary membrane.

Air enters the upper resp. tract & travels to the lower tract where gas exchange takes place.
Respiration = the process whereby gas exchange occurs at the alveolar-capillary membrane. 3 phases:

1. Ventilation - movement of air from the atmosphere through the upper & lower airways to the alveoli
2. Perfusion - blood from the pulmonary circulation is adequate at the alveolar-capillary bed
3. Diffusion - molecules move from area of higher concentration to lower concentration of gases - O2 passes into the capillary bed to be circulated & CO2 leaves the capillary bed & diffuses into the alveoli for vent. excretion
RESPIRATORY TRACT

- **Perfusion** - influenced by alveolar pressure. For gas exchange, the perfusion of each alveoli must be matched by adequate ventilation. Mucosal edema, secretions, & bronchospasms increase the resistance to airflow & dec. ventilation & diffusion of gases

- **Bronchial Smooth Muscle** - In the tracheobronchial tube is smooth muscle whose fibers spiral around the tube → contraction → constriction of airway
  - Parasympathetic Nervous system → releases acetylcholine → bronchoconstriction
  - Sympathetic Nervous system → releases epinephrine → stimulates beta-2 receptors in bronchial smooth muscle → bronchodilation
Upper Respiratory Infections (URI’s) = common cold, acute rhinitis, sinusitis, acute tonsillitis, acute laryngitis

- The common cold = most expensive > $500 million spent on OTC preparations

Common Cold & Acute Rhinitis -
- Common cold caused by the rhinovirus & affects primarily the nasopharyngeal tract.
- Acute rhinitis (inflammation of mucus membranes of nose) usually accompanies the common cold
- Allergic rhinitis - caused by pollen or a foreign substance
DRUGS FOR UPPER RESPIRATORY INFECTIONS

- Incubation period of a cold = 1 to 4 days before onset of symptoms & first 3 days of the cold
  - Home remedies = rest, chicken soup, hot toddies, Vitamins
  - 4 groups of drugs used to manage symptoms =
    - antihistamines (H-1 blocker), decongestants (sympathomimetic amines), antitussives, expectorants
Antihistamines or H-1 blockers - compete w/ histamine for receptor sites → prevents a histamine response.

2 types of histamine receptors - H-1 & H-2

H-1 stimulation = extravascular smooth muscles (including those lining nasal cavity) are constricted

H-2 stimulation = an inc. in gastric secretions = peptic ulcer disease

Do not confuse the 2 receptors - antihistamines decrease nasopharyngeal secretions by blocking the H-1 receptor
Histamines - A compound derived from an amino acid histadine. Released in response to an allergic rxn (antigen-antibody rxn) - such as inhaled pollen
- When released it reacts w/ H-1 receptors = arterioles & capillaries dilate = inc. in bld flow to the area = capillaries become more permeable = outward passage of fluids into extracellular spaces = edema (congestion) = release of secretions (runny nose & watery eyes)
- Large amts. of released histamine in an allergic rxn = extensive arteriolar dilation = dec. BP, skin flushed & edematous = itching, constriction & spasm of bronchioles = SOB & lg. amts. of pulmonary & gastric secretions
DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTIHISTAMINES

- Astemizole (Hismanal), Cetirizine (Zertec), Loratadine (Claritin), Chlorpheniramine (Chlortrimeton), Diphenhydramine (Benadryl)

- Actions = competitive antagonist at the histamine receptor; some also have anticholinergic properties

- Uses = Treat colds; perennial/seasonal allergic rhinitis (sneezing, runny nose); allergic activity (drying & sedation); some are also antiemetic

- SE = Drowsiness, dizziness, sedation, drying effects

- CI = glaucoma, acute asthma
Nasal congestion results from dilation of nasal bid. vessels d/t infection, inflammation, or allergy. With dilation there’s transudation of fluid into tissue spaces → swelling of the nasal cavity

Decongestants (sympathomimetic amines)
- stimulate alpha-adrenergic receptor → vasoconstriction of capillaries w/in nasal mucosa → shrinking of the nasal mucus membranes & reduction in fluid secretion (runny nose)
DRUGS FOR UPPER RESPIRATORY INFECTIONS - DECONGESTANTS

- Naphazoline HCL (Allerest), Pseudoephedrine (Actifed, Sudafed), Oxymetololazine (Afrin), Phenylpropanolamine HCL (Allerest, Dimetapp)
- Use - Congestion d/t common cold, hayfever, upper resp. allergies, sinusitis
- SE = Jittery, nervous, restless, Inc BP, inc. bld. sugar
- CI = Hypertension, cardiac disease, diabetes
- Preparations = nasal spray, tablets, capsules, or liquid
- Frequent use, esp. nasal spray, can result in tolerance & rebound nasal congestion - d/t irritation of nasal mucosa
DRUGS FOR UPPER RESPIRATORY INFECTIONS - INTRANASAL GLUCOCORTICOIDs

- Beclomethasone (Beconase, Vancenase, Vanceril), Budesonide (Rhinocort), Dexamethasone (Decadron), Fluticasone (Flonase)
- Action - steroids used to dec. inflammation locally in the nose
- Use - Perennial/seasonal allergic rhinitis (sneezing, runny nose) - May be used alone or w/ antihistamines
- SE - rare, but w/ continuous use dryness of the nasal mucosa may occur
DRUGS FOR UPPER RESPIRATORY INFECTIONS - ANTITUSSIVES

- Action - Acts on the cough control center in the medulla to suppress the cough reflex
- Use - Cough suppression for non-productive irritating coughs
  * Codeine - Narcotic analgesic to control a cough d/t the common cold or bronchitis
  * Dextromethorphan - nonnarcotic antitussive that suppresses the cough center in the medulla, widely used - syrup, liquid, chewable & lozenges
  - SE = drowsiness, sedation
DRUGS FOR UPPER RESPIRATORY INFECTIONS - EXPECTORANTS

- Action - Loosens bronchial secretions so they can be eliminated w/ coughing
  * A nonproductive cough becomes more productive and less frequent
- Uses - Nonproductive coughs
- Guaifenesin (Robitussin) = Most common
  * Use alone or in combo w/ other resp. drugs
- Hydration is the best expectorant
Lung Compliance - Lung volume based on the unit of pressure in the alveoli
* Determines the lung’s ability to stretch (tissue elasticity)
* Determined by: connective tissue; surface tension in the alveoli controlled by surfactant
  - surfactant lowers surface tension in alveoli & prevents interstitial fluid from entering
* Inc. (high) lung compliance in COPD
* Dec. (low) lung compliance in restrictive pulmonary disease = lungs become “stiff” & need more pressure
DRUGS FOR LOWER RESPIRATORY DISORDERS

- Chronic obstructed pulmonary disease (COPD) & restrictive pulmonary disease = 2 major lower resp. tract diseases
- **COPD** = airway obstruction w/ inc. airway resistance to airflow to lung tissues - 4 causes
  - Chronic bronchitis
  - Emphysema
  - Bronchiectasis
  - Asthma
* Above frequently result in irreversible lung tissue damage. Asthma reversible unless frequent attacks and becomes chronic.
DRUGS FOR LOWER RESPIRATORY DISORDERS

- **Restrictive lung disease** = a dec. in total lung capacity as a result of fluid accumulation or loss of elasticity of the lung.
  
  * Causes: Pulmonary edema, pulmonary fibrosis, pneumonitis, lung tumors, scoliosis

- **Bronchial Asthma** = 10-12 million people of all ages affected - a chronic obstructive pulmonary disease characterized by periods of bronchospasm resulting in wheezing & difficulty in breathing
**DRUGS FOR LOWER RESPIRATORY DISORDERS**

- **Asthma** - Bronchospasm or bronchoconstriction results when the lung tissue is exposed to extrinsic or intrinsic factors that stimulate a bronchoconstrictive response.
  - Causes: humidity, air pressure changes, temp. changes, smoke, fumes, stress, emotional upset, allergies, dust, food, some drugs.

* Pathophys = Mast cells (found in connective tissue throughout the body) are directly involved in the asthmatic response - esp. to extrinsic factors.
  - Allergens attach themselves to mast cells & basophils = antigen-antibody rxn.
DRUGS FOR LOWER RESPIRATORY DISORDERS - ASTHMA

- Mast cells stimulate release of chemical mediators (histamines, cytokines, serotonin, ECF-A (eosinophils))
- These chemical mediators stimulate bronchial constriction, mucous secretions, inflammation, pulmonary congestion
- Cyclic adenosine monophosphate (cAMP) - a cellular substance responsible for maintaining bronchodilation - When inhibited by histamines & ECF-A → bronchoconst.
- Sympathomimetic (adrenergic) bronchodilators inc. amt. of cAMP & promote dilation → first line drugs used
DRUGS FOR LOWER RESPIRATORY DISORDERS

- **Sympathomimetics: Alpha & Beta-2 Adrenergic Agonists**
- Increase cAMP → dilation of bronchioles in acute bronchospasm caused by anaphylaxis from allergic rxn give nonselective **epinephrine (Adrenalin)** - SQ in an emergency to promote bronchodilation & inc. BP
  
  SE = tremors, dizziness, HTN, tachycardia, heart palpitations, angina
- For bronchospasm d/t COPD - selective beta-2 adrenergic agonists are given via aerosol or tablet
**DRUGS FOR LOWER RESPIRATORY DISORDERS**

- **Metaproterenol (Alupent, Metaprel)** - some beta-1, but primarily used as a beta-2 agent - PO or inhaler/nebulizer
  - For long-term asthma Rx beta-2 adrenergic agonists frequently given by inhalation
    * more drug delivered directly to constricted bronchial site
    * Effective dose less than PO dose & less side effects
  - Action = relaxes bronchial smooth muscle - onset = fast
  - SE = Nervousness, tremors, restlessness, insomnia & inc. HR
**DRUGS FOR LOWER RESPIRATORY DISORDERS**

- **Albuterol (Proventil, Ventolin)** - More beta-2 selective
  - PO or inhaler
  - Used for acute/chronic asthma
  - Rapid onset of action & longer duration than Metaproterenol
  - Fewer SE because more beta-2 specific, but high doses can still effect beta-1 receptors & cause nervousness, tremors & inc. pulse rate
**DRUGS FOR LOWER RESPIRATORY DISORDERS - ANTICHOLINERGICS**

- **Ipratropium bromide (Atrovent)** -
  - Action: competitive antagonist (inhibits) of cholinergic receptors in bronchial smooth muscle = bronchiole dilation - Inhaler
  - Use: In combination with beta agonist for asthma & for bronchospasm associated with COPD
  - Need to teach clients how to use properly: If using Atrovent with a beta-agonist, use beta-agonist 5 min. before Atrovent; If using Atrovent with an inhaled steroid or cromolyn, use Atrovent 5 min. before the steroid or cromolyn - bronchioles dilate & drugs more effective
DRUGS FOR LOWER RESPIRATORY DISORDERS - METHYLXANTHINE DERIVATIVES

- Aminophylline, Theophylline (TheoDur), Caffeine –
  * PO or IV -
  * Use - Treatment of asthma & COPD
  * Action - Inc. cAMP → bronchodilation; also - diuresis, cardiac, CNS & gastric acid stimulation
  * When given IV → a low therapeutic index & range -
    Monitor levels frequently
  * PO doses can be given in standard dosages
  * Avoid smoking, caffeine & inc. fluid intake
• Drug Interactions: Inc the risk of dig toxicity, decreases the effects to lithium, dec theophyllin levels with Dilantin, theophyllin and beta-adrenergic agonist given together - synergistic effect can occur ➔ cardiac dysrhythmias. Beta blockers, Tagamet, Inderal and e-mycin decrease the liver metabolism rate and inc. the half-life and effects of theophyllin

• SE: Anorexia, N&V, nervousness, dizziness, palpitations, GI upset & bleeding, HA, restlessness, flushing, irritability, marked hypotension, hyper-reflexia and seizures.

• CI: Severe cardiac dysrhythmias, hyperthyroidism, peptic ulcer disease (increases gastric secretions)
Leukotriene (LT) a chemical mediator that can cause inflammatory changes in the lung. The group cysteinyl leukotrienes promotes and inc in eosinophil migration, mucus production, and airway wall edema, which result in broncho-constriction.

LT receptor antagonists & LT synthesis inhibitors (Leukotriene modifiers) effective in reducing the inflammatory symptoms of asthma triggered by allergic & environmental stimuli - Not for acute asthma
LEUCOTRIENE RECEPTOR ANTAGONIST AND SYNTHESIS INHIBITORS

• Zafirlukast (Accolate), Zileuton (Zyflo), Montelukast sodium (Singulair) – PO

• Action - Decreases the inflammatory process    Use - prophylactic & maintenance drug therapy for asthma

• Accolate – 1st in group, leukotriene receptor antagonist    reduce inflammation & dec bronchoconstriction,  PO- BID-rapidly absorbed

• Singulair – New leukotriene receptor antagonist, short t1/2 (2.5-5.5)    Safe for children under 6yo.
DRUGS FOR LOWER RESPIRATORY DISORDERS - GLUCOCORTICOIDS (STEROIDS)

- Glococorticoids have an anti-inflammatory action and are used if asthma is unresponsive to bronchodilator therapy

- Given: inhaler- beclomethasone (Vanceril, Beclovent); tablet - triamcinolone (Amcort, Aristocory), dexamethasone (Decadron), prednisone; injection - dexamethasone, hydrocortisone

- SE significant w/ long-term oral use - fluid retention, hyperglycemia, impaired immune response

- Irritating to the gastric mucosa - take w/ food

- When d/c’ing taper the dosage slowly
DRUGS FOR LOWER RESPIRATORY DISORDERS - CROMOLYN & NEDOCROMIL

- **Cromolyn (Intal)** - for prophylactic Rx of bronchial asthma & must be taken on a daily basis - NOT used for acute asthma - Inhaler
  * Action - inhibits the release of histamine that can cause an asthma rxn
  * SE - mouth irritation, cough & a bad taste in the mouth
  ** Caution - rebound bronchospasm is a serious side effect do not d/c the drug abruptly

- **Nedocromil sodium** - action & uses similar to Intal - prophylactic usage - inhalation therapy - may be more effective than Intal
DRUGS FOR LOWER RESPIRATORY DISORDERS - MUCOLYTICS

- **Acetylcysteine (Mucomyst)** - nebulization
  * Action - liquefies & loosens thick mucous secretions so they can be expectorated
  * Use - dissolves thick mucous, acetaminophen overdose (bonds chemically to reduce liver damage)
  * SE - N & V, chest tightness, bronchoconstriction
  * Use w/ a bronchodilator

- **Dornase alfa (Pulmozyme)** - an enzyme that digests the DNA in thick sputum of cystic fibrosis (CF) clients