Respiratory Pharmacology

Inhaled Drugs

- Metered Dose Inhalers (MDIs)
  - Spacer
- Dry-Powder Inhalers
- Nebulizers

Drugs for Asthma

- Bronchodilators
  - Alpha-adrenergic Agonists
    - Nonspecific adrenergic agonists
    - Beta-2 agonists
  - Anticholinergics
  - Methylxanthines
- Anti-inflammatory
  - Steroids
  - Cromolyn
  - Leukotriene Inhibitors

Adrenergic Agonists

- Older non-selective drugs
  - Ephedrine
  - Epinephrine (still used for status asthmaticus)
  - Isoproteronol
- Newer selective Beta-2 adrenergic Agonist
  - Fewer systemic side effects
  - Promote bronchodilation
  - Suppress lung histamine
  - Increase ciliary motility

Adverse Events

- Tachycardia
- Nervousness, Irritability, Tremor
- Angina
- Inhaled preparations: less common
- Oral preparations: More common
  - Tachydysrhythmias
- Usually dose related
- May also be related to additives

Beta-2 Pharmacokinetics

- Duration
  - Short acting (begin immediately, 3-5 hour dur)
  - Long acting (begin 2-30 min, 10-12 hour dur)
- Routes
  - Inhaled
  - Oral
- Use
  - Short acting: PRN for symptoms
  - Long acting: Fixed schedule (NOT PRN EVER)

Agents

- Short acting
  - Albuterol (Proventil, Ventolin): MDI, neb
  - Levalbuterol (Xopenex): neb only
  - Bitolterol (Tornalate): neb only
  - Pirbuterol (Maxair): neb only
- Long Acting
  - Salmeterol (available only in combination)
  - Formoterol (Foradil Aerolizer): DPI
- Oral
  - Albuterol: Tablets, Extended tabs, syrup
  - Terbutaline: Tablets

Dosing

- Albuterol MDI: usually 1-2 puffs Q 4-6 hrs
  - Deep exhale
  - Inhale and puff
  - Hold breath for slow ten count
  - Exhale slowly
  - Wait one minute before second puff
  - Use spacer
- Dry Powder
  - Usually one inhalation, not a puff
  - One smooth continuous inhalation

Anticholinergics

- Anticholinergics (atropine derivative)
- Approved only for COPD bronchospasm but used in asthma also
- Reduces bronchospasm and mucus
- Few systemic side effects

Anticholinergics

- Ipratropium (Atrovent)
  - Onset 30 minutes; lasts 6 hours
  - MDI, Neb
  - Combivent MDI: combo with albuterol
  - Also available intranasally for allergic rhinitis
- Tiotropium (Spiriva)
  - Newer, lasts longer
  - Dry Powder Inhaler (Handi-haler)

Methylxanthines

- Primary actions
  - CNS excitation
  - Bronchodilation
- Other actions
  - Cardiac stimulation
  - Vasodilation
  - Diuresis
- Usually considered third line
  - High side effect profile
  - Narrow therapeutic range

Methylxanthines

- Theophylline and Aminophylline
  - Oral
  - IV (dangerous, usually aminophylline)
  - Longer duration
  - Metabolized in liver, variable half-life
  - Requires periodic blood level monitoring
  - Toxicity: NVD, restlessness, dysrhythmias, seizures
  - Interactions: caffeine, Tagamet, fluoroquinolones, other CNS drugs

Glucocorticoids

- Decrease release of inflammatory mediator
- Decrease infiltration and action of WBCs
- Decrease airway edema
- Decrease airway mucus production
- Increase number of beta-2 receptors
- Increase sensitivity of beta-2 receptors

Glucocorticoids

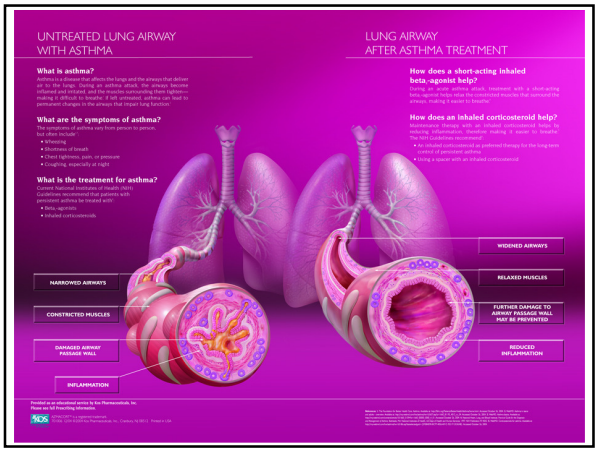
- Systemic
  - Stronger effects
  - Action unaffected by lung restriction
  - More side effects, esp with long term therapy
- Inhaled
  - Localized action
  - Fewer side effects: some absorption occurs
  - Disease may prevent penetration of drug to affected areas

Adverse Events

- Inhaled: gargle and use spacer
  - Oral candidiasis
  - Dyphonia
- General
  - Adrenal suppression
  - Bone loss: exercise, Vit D, calcium
  - Slow growth in children, but not ultimate height
  - Increase risk of cataracts and glaucoma
  - PUD

Inhaled Corticosteroids

- Fluticasone (Flovent) MDI
  - Advair Diskus DPI (combo with salmeterol)
- Flunisolide (Aerobid) MDI
- Budesonide (Pulmicor Turbohaler) DPI,neb
- Beclomethasone QVAR (MDI)
- Triamcinolone (Azmacort) MDI
- Almost all of these also have intranasal preparations for allergic rhinitis



Mast Cell Stabilizers

- Used for prophylaxis, not acute treatment
  - Seasonal allergy
  - Exercise induced asthma
  - Can be used intranasally for allergic rhinitis
- Stabilizes mast cells
  - Prevents release of histamine, inflam mediators
  - Inhibits eosinophils, macrophages
- MDI
  - Cromolyn
  - Nedocromil

Leukotriene Modifiers

- Two approaches
  - Inhibit leukotriene synthesis
    - Zileuton
  - Inhibit leukotriene receptors
    - Zafirkulast (Accolate)
    - Montelukast (Singulair) (fewest drug interactions); also works for allergic rhinitis
- ↓inflammation, bronchoconstriction, edema, mucus, recruitment of eosinophils

Asthma Treatment

- Mild Intermittent
  - Albuterol MDI PRN
- Mild persistent
  - Add anti-inflammatory
- Moderate Persistent
  - Increase dose of anti-inflammatory
  - Multiple anti-inflammatory
  - Long acting beta-2 antagonist
- Severe persistent asthma
  - High inhaled steroids, or systemic steroids

COPD Treatment

- Similar to asthma, difference is damage is progressive and irreversible
  - Ipratropium
  - O2 in advanced disease

Allergic Rhinits Medications

- Antihistamines
- Intranasal Glucocorticoids
- Intranasal Cromolyn
- Montelukast (Singulair)
- Sympathomimetics (Decongestants)

Decongestants

- Pseudoephedrine
- Phenylephrine Neo-Synephrine (PO & spray)
- Oxymetazoline (Afrin) nasal spray
- Phenylpropanolamine (taken off market)
- Effects
  - Vasoconstriction of nasal arteries
  - Shrinkage of swollen membranes
  - Adverse: tachycardia, ↑BP (caution HTN), irritability, insomnia, rebound (topical)

Cough Suppressants (Antitussives)

- Opioid
  - Codeine and Hydrocodone
  - Reduce cough reflex centrally
- Non-opioid
  - Dextromethorphan (DM)
    - Codeine derivative
    - Reduces cough reflex centrally
    - Less euphoria, inhibits Cytochrome P-450
  - Benzonatate (Tessalon pearls)
    - Local anesthetic
    - Decreases stomach receptor sensitivity; do not chew

Expectorants

- Only one is effective: Guaifenasin
  - Need higher doses than usally present in OTC
  - 100-200mg OTC (q12 hours)
  - 600-1200mg RX (q12 hours)
- Mucolytics: thin mucus
  - Hypertonic saline & Acetylcysteine
    - Both can cause bronchospasm
- Normal saline (inhaled)
  - Used to hydrate lung