**Pharmacologic Management of Asthma**

**Objectives:**
1. Review the physiological basis for asthma therapy
2. Discuss the differences between SABA and LABA
3. Discuss the role of inhaled and oral systemic corticosteroids
4. Review Mast Cell Stabilizers, Leukotriene Modifiers, Anticholinergics and Immunomodulators.

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**Foundations of Pharmacology**

- Acetylcholine & Norepinephrine
- SLUD vs. Flight or Fight
- Parasympathomimetics
- Parasympatholytics
- Sympathomimetics
- Sympatholytics
Adrenal Gland and Hormones

Corticosteroids are secreted by the adrenal cortex.

Epinephrine produced by medulla.

Beta Agonists

SABAs (also called relievers, rescue meds, fast acting bronchodilators, etc)
Beta Agonist: SABA

- **Albuterol** (Ventolin & Proventil)
- Beta₂ specific
- Onset 3-5 minutes with duration 4-6 hours
- 200 puffs per canister
- Also in other forms (see chart) including syrup for 2-6 year olds
- **Levalbuterol** (Xopenex)
- 200 puffs per canister
- Also in solution 0.31, 0.63 and 1.25 mg (see chart)
- **Pirbuterol** (Maxair)
- 400 puffs (see chart)

Ultra Short Acting Bronchodilators

- **Epinephrine** (Bronchaid, Primatene Mist)
- Available in parenteral and aerosol solutions
- Not for routine asthma tx (rather anaphylaxis and angioedema)
- Stimulates Beta₁, Beta₂ & Alpha receptors
- MDI available OTC and can cause severe side effects if combined with prescribed bronchodilator
- **Racemic Epinephrine** (Vaponefrin, Asthmanefrin)
- Commonly used to address post extubation stridor
- Stimulates Beta₁, Beta₂ & Alpha receptors
- (see chart)
Long Acting Beta 2 Agonists (LABA)

- Duration of 12 hours so appropriate for nocturnal asthma
- Should be used with Inhaled Corticosteroids (ICS)
- May be used for EIB, but not routinely
- **Salmeterol** (Serevent) indicated for patients 4 years and older
- **Formoterol** (Foradil) indicated for patients 5 years and older
- See chart
- Brovana and Perforomist nebulizer solutions are not approved for asthma.

Side Effects of SABA and LABA

- Tachycardia
- Tremors
- Palpitations
- Hypokalemia
- Nausea / Vomiting
- Headache
Methylxanthines

- Theophylline considered a controller med, not for acute relief
- Short acting 6-12 hour duration / long acting 24 hours
- Consider an alternative for those >5 yrs old
- Therapeutic range 5-20 mcg/ml, monitor blood levels
- Take one to two hours after a meal with glass of water
- Cigarette smoking hampers effectiveness, caffeine side effects

Trade names: Theodur, Slo-Bid

Theophylline

Untoward effects:
- nausea
- headache
- nervousness
- Vomiting
- arrhythmias if >30 ug/ml
- Seizures if > 40 ug/ml
Anticholinergic Agents

Parasympathetic stimulation may increase Cyclic GMP. Increased Cyclic GMP causes smooth muscle contraction and Mast cell mediator release. **Anticholinergics** block parasympathetic stimulation.

Anticholinergic

- Used to treat bronchospasm due to beta blockers
- Indicated for moderate to severe exacerbations in the ED setting
- Ipratropium Bromide (Atrovent) is the most common in this class.
- 200 puffs in MDI
- Tiotropium (Spiriva) is a long acting agent (QD) approved for COPD

Anticholinergic agents (Atrovent) block the action of acetylcholine and result in smooth muscle relaxation.
**Anticholinergics**

Untoward effects:
- dry mouth
- cough
- pharyngitis
- eye pain
- urinary retention
- nervousness
- headache

**Steroids and LTRA**

Steroids inhibit phospholipase A2 enzyme from converting phospholipids to arachidonic acid.
Inhaled Corticosteroids (ICS)

- The **most effective** control medications for asthma
- Not for quick relief
- May cause suppression of growth in children
- Steroids should be reduced to the lowest level that maintains control
- ICS have fewer untoward side effects than OCS
- ICS are associated with improved peak flow, lower severity of symptoms and decreased ED visits

Inhaled Corticosteroids (ICS)

- **Fluticasone (Flovent)**
  - MDI-120 puffs and (3) strengths: 44 mcg, 110 mcg and 220 mcg per puff
  - Usually 2 puffs twice daily
  - DPI (Diskus)- 60 inhalations and (3) strengths: 50 mcg, 100 mcg, 250 mcg.
- **Budesonide (Pulmicort, Rhinocort)**
  - DPI (Turbuhaler)-200 inhalations and 200 mcg per inhalation for patients 6 yrs and older
  - **Respules**- Administered via SVN for children >1 year old
    - 0.25mg, 0.5 mg, and 1 mg ampules
    - Improvement within 8 days, full effect within 6 weeks
Inhaled Corticosteroids (ICS)

- **Pulmicort Flexhaler (DPI)**
  - Two strengths: 90 mcg with 60 inhalation and 180 mcg with 120 inhalations
  - ≥6 yrs starting dose 180 mcg twice daily
  - ≥18 yrs starting dose 360 mcg twice daily

- **Triamcinolone (Azmacort)**
  - No spacer/holding chamber needed
  - 240 actuations per inhaler
  - Optimization within two weeks
  - Must be reprimed after 3 days of non-use

- **Mometasone (Asthmanex Twisthaler) DPI**
  - Two strengths: 220 mcg and 110 mcg with 30 inhalations

Inhaled Corticosteroids (ICS)

- **Beclomethasone (Vanceril)**
  - CFC Preparation
  - 42 mcg per puff (two puffs 3-4 times daily)
  - ≥6 years old

- **Beclomethasone (QVAR)**
  - HFA Preparation
  - 40 or 80 mcg per dose
  - ≥5 years old
Inhaled Corticosteroids (ICS)

- Ciclesonide (Alvesco)
- Is a Prodrug
- Two strengths 80 mcg and 160 mcg
- Highest recommended daily dose 320
- Maximum effect usually achieved after 4 weeks
- MDI with 60 inhalations
- When dose indicator turns RED 20 puffs remain
- Not indicated for ≤ 12 years old

Combination Medications

- Advair (Fluticasone and Salmeterol) DPI
  - >4 years old
  - Three strengths 100/50, 250/50, 500/50
  - 60 doses
  - Cannot be used with another LABA
- Advair MDI
  - >12 years old
  - Three strengths 45/21, 115/21, 230/21
  - 120 doses
**Combination Medications**

- **Symbicort (Budesonide and Formoterol)**
  - Delivered via MDI with 60 or 120 inhalations; >12 yrs old
  - Two strengths 80/4.5 and 160/4.5
- **Dulera (Mometasone and Formoterol)**
  - Delivered via MDI with 120 inhalations; >12 yrs old
  - Two strengths 100/5 and 200/5
  - Built-in counter, change at # “20”

- **Combination Medications**
  - Albuterol and Ipratropium Bromide (DuoNeb)
    - Safety in patients < 18 not studied
    - SVN-4 times per day
  - Albuterol and Ipratropium Bromide (Combivent)
    - Not studied in Pediatrics
    - MDI- 2 inhalations, 4 times per day
Oral Systemic Corticosteroids

- Used to gain control in moderate to severe exacerbations
- Are used as an adjunct to SABA
- Untoward effects more pronounced than ICS and include:
  - Immunosuppression
  - Cushings syndrome
  - Growth suppression
  - Fluid retention
  - Weight gain
  - Muscle weakness
  - Increased glucose levels

Death due to adrenal insufficiency has occurred during transfer from systemic to inhaled corticosteroids.

Oral Systemic Corticosteroids

**Prednisone** (Deltasone, Orasone)

- Patients on oral corticosteroids should be slowly weaned off as indicated after starting ICS. The daily dose of prednisone may be reduced by 2.5 mg.
- Asthma symptoms must be closely monitored during withdrawal of oral steroids.

**Other oral steroids include:**

- Prednisolone
- Methylprednisolone (Medrol, SoluMedrol)
- Usually 3-10 day course
- See chart
Leukotriene Modifiers (LTRA)

- Used for **long term control** in mild persistent asthma or in combination with ICS for moderate asthma. Also blocks early response to allergen challenge.
- Not for quick relief
- **Montelukast (Singulair)**
  - Acts by blocking leukotrienes at the receptor sites
  - Approved for patients **>1 year** old
  - Once daily (QD)
- **Zafirlukast (Accolate)**
  - Indicated for patients **>7 yrs** old
  - Must monitor hepatic enzymes
  - Inhibits **aspirin** induced asthma
  - BID

Leukotriene Modifiers

(5-lipoxygenase inhibitor)

- **Zileuton (Zyflo)**
  - Indicated for patients **>12 yrs** old
  - Called 5-lipoxygenase inhibitor and stops production of leukotrienes
  - One 600 mg tablet 4 times per day (QID)
  - **Hepatic enzymes** checked at baseline, once per month for 3 months and every 2-3 months thereafter
  - Interacts with Theophylline and Warfarin
Leukotriene Modifiers

Untoward effects:
- headache
- nausea
- infections
- nervousness
- dizziness

Mast Cell Stabilizers
- Controller and alternative for mild persistent asthma, not quick relief
- May prevent EIA
- Inhibits the release of histamine and leukotrienes
Mast Cell Stabilizers

- **Cromolyn Sodium (Intal)**
- MDI: 2 puff 4 times/day
- 112 or 200 inhalations, 0.8 mg per puff
- Nebulizer: 20 mg in 2 ml ampule
- DPI: 20 mg capsule
- Max effect after (1) month of use
- Administer 15-30 minutes prior for EIB
- **Nedocromil Sodium (Tilade)** See Chart

**Untoward effects:**
- nasal congestion
- dermatitis
- gastroenteritis
- bad taste
Immunomodulator

- **Omalizumab (Xolair)**
  - Alternative for patients (≥12 yrs) with persistent asthma associated with **allergy** that is not controlled with high dose ICS.
  - Xolair blocks IgE antibodies from binding to receptor sites on mast cells and basophils.
  - Recommended if IgE level between 30-700 iu/ml and positive skin test for perennial allergen
  - Administered via injection every 2 to 4 weeks
  - Must monitor for anaphylaxis

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**Omalizumab**

**Untoward effects:**
- anaphylaxis
- bronchospasm
- hypotension
- syncope
- urticaria
- angioedema of throat and tongue
Test Your Knowledge

1. List 5 non-steroidal anti-asthmatic drugs used for control

2. Which immunoglobulin is associated with allergic asthma?

3. An intern wishes to order stat cromolyn for a pediatric pt in the ED in moderate distress. Do you agree?

4. Why is it important to protect pt’s eyes when administering Ipratropium?

5. State the generic name for each of the following:
   - Ventolin
   - Serevent
   - Foradil
   - Maxair
   - Advair
   - Combivent