Asthma

- Asthma is a chronic inflammatory disease of the airways (interaction between many cells and inflammatory mediators).
- Inflammatory mediators are mast cells, eosinophils, T lymphocytes, neutrophils, epithelial cells, LTs, PGs, and histamine.
- It is characterized by periodic attacks of wheezing, shortness of breath, chest tightness, and coughing.
- During very severe attacks, an asthma sufferer can turn blue from lack of oxygen, and can experience chest pain or even loss of consciousness. Severe asthma attacks may lead to respiratory arrest and death.

Epidemiology

- Asthma creates a clear burden on the patient relating to quality of life, but also on society in terms of emergency department (ED) visits, hospitalizations, and decreased productivity due to missed work and school.
- More than 27 million North Americans (300 million people worldwide) are affected with asthma.
- It is the most common chronic disease in American children. The highest percentage of prevalence is among children aged younger than 15 years especially boys. Adults and children miss most of the school days and work.
- Individuals aged 65 years and older represent the highest overall rate of death from asthma.

Risk Factors

- Precipitating factors are allergens (pollens, house dust, animal dander, mold, and cockroach), change in weather or season, exercise, hormonal change in women, irritants (tobacco smoke, air pollution), food, medications (aspirin, NSAIDs, nonselective BB), viral respiratory tract infection, and strong emotional expression (laughing or crying hard or stress).
- Current research suggests that genes coding various aspects of immune development are involved, and that there are numerous phenotypic expressions for these genes, each eliciting different inflammatory responses.
- Symptoms are often worse at nighttime or early in the morning and in the spring and fall when pollen levels are high.
- Gastroesophageal reflux disease (GERD), allergic rhinitis, obstructive sleep apnea, and obesity may also exacerbate asthma symptoms.

Diagnosis

- The medical history should address symptoms, pattern of symptoms (eg, time of day or season), specific triggers, family and social history, and history of exacerbations.
- Diagnosis and confirmation of asthma include peak flow measurement (FEV1), chest X ray, lung function tests, arterial blood gases and eosinophil count.
- Mucosal swelling, wheezing during normal breathing, and atopic dermatitis or eczema increase the probability of asthma.
- Signs of an asthmatic episode include wheezing, rapid breathing (tachypnea), prolonged expiration, a rapid heart rate (tachycardia), rhonchous lung sounds (audible through a stethoscope), and over-inflation of the chest.
- Spirometry is an objective tool used to measure airflow limitation and establish the reversibility of airflow obstruction, an important feature that distinguishes asthma from other chronic respiratory diseases like chronic obstructive pulmonary disease (COPD).
- It measures the volume of air that can be forcibly blown out after maximal inhalation (forced vital capacity) and the volume of air that can be forcibly blown out in 1 second (forced expiratory volume in 1 second FEV1).
- Measurements are taken before and after inhalation of a bronchodilator, and reversibility is determined by an increase in FEV1 after its use.
- Normal FEV1 value is 75% to 80% and is measured in volume in liters.

Pathophysiology

- Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, neutrophils, T lymphocytes, macrophages, and epithelial cells.
- In susceptible individuals, this inflammation causes recurrent episodes of coughing (particularly at night or early in the morning), wheezing, breathlessness, and chest tightness.
- These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.
- Airflow through the lungs is severely limited by inflammation, obstruction, hyper-responsiveness, and, eventually, airway remodeling. Inhaled allergens or irritants initiate an immunoglobulin E (IgE) response with activation of pro-inflammatory cells and mediators.
- Inflammation leads to leakage of plasma and cellular debris into the bronchial lumen, reduced mucus clearance, and formation of mucus plugs.
- While acute inflammation is a normal and beneficial response of tissues to injury, chronic inflammation leads to repeated repair of tissue with eventual scarring.
Smooth muscle surrounding the bronchioles may become thickened and develop an exaggerated bronchoconstriction in response to stimuli that would have little or no effect in normal airways.

Exacerbations of asthma are episodic, but underlying airway inflammation is continuously present.

**Severity VS Control**
- The Expert Panel Report 3 recommends a stepwise approach to the treatment of asthma. An assessment of asthma severity is used to initiate therapy, whereas an assessment of asthma control is used to monitor and adjust therapy.
- Severity describes the underlying disease process and the extent of limitation to a patient's normal functioning.
- Control, on the other hand, is an assessment of how well therapeutic interventions have affected the clinical manifestations of the disease.
- An assessment of impairment and risk is initially used to classify asthma as intermittent, mild persistent, moderate persistent or severe persistent.
- **Lung function is not a component of the severity assessment** for children aged 0 to 4 years because of the inherent difficulty in attaining this measure.
- Asthma control is defined as symptoms and/or use of quick-relief medicines no more than twice a week, nighttime awakenings no more than twice a month, no interference with normal activities, and nearly normal lung function. If asthma is not well controlled, treatment should be stepped up by one step.
- Daily use of quick-relief medications is a warning that asthma control is deteriorating and treatment should be reevaluated.

**Therapeutic Goals**
- Goals of therapy in asthma are to prevent chronic symptoms (coughing, breathlessness at night, early morning, after exertion), maintain near normal pulmonary function, physical activities, prevent recurrent hospitalization and provide optimal drug therapy with little or no adverse drug effects.

**COPD**
- Chronic obstructive pulmonary disease (COPD) is a common condition characterized by dyspnea and airflow limitation due to progressive and irreversible structural changes in the lung. It is currently the fourth leading cause of death in the United States, has a higher prevalence in men, and accounts for 10% of bed occupancy in hospitals and 8% Americans have COPD.
- Historically, COPD has been defined in terms of either chronic bronchitis or emphysema. This led to multiple definitions and diagnostic criteria. To standardize, the World Health Organization and the National Heart, Lung, and Blood Institute joined to create the Global Initiative for Chronic Obstructive Lung Disease (GOLD).
- It is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.
- The GOLD guidelines not only provide us with a good definition for COPD, they also provide guidelines for diagnosis, management, and prevention as well.
- Clinical diagnosis of COPD is considered anytime a patient presents with dyspnea, chronic cough (or sputum production), and/or a history that relates exposure to known risk factors.
- Confirmation of COPD requires inhaled spirometry, with presence of a post-bronchodilator forced expiratory volume in 1 second (FEV1)/forced vital capacity ratio of less than 0.7.
- Second, the airflow limitation is measured from a post-bronchodilator FEV1. This will classify the patient as GOLD level 1 to 4, with 1 being the mildest and 4 being the most severe.
- One of the key elements of COPD is that it is considered a preventable disease. Inhaled cigarette smoke and other noxious particles, such as indoor and outdoor air pollution, occupational dust, and chemicals, cause lung inflammation.
- The pathologic changes occurring from chronic inflammation include parenchymal tissue destruction and disruption of normal tissue repair, and are irreversible. Therefore, smoking cessation is the cornerstone for all COPD treatment regimens regardless of disease stage.
- Cigarette smoking is the primary etiologic factor for the development of COPD, and alpha 1 antitrypsin is the genetic factor.
- Bronchodilators and corticosteroids are the mainstays of treatment for COPD. In both categories, inhaled therapy is the preferred route of administration. In bronchodilators, the choice of specific class depends on a combination of patient response, side effects, and availability.
- Chronic bronchitis is characterized by excessive mucus production and chronic productive cough is the hallmark.
- Emphysema is the complete alveolar destruction of lung walls.
- Influenza and pneumococcal vaccines annually are effective in patients with lung diseases in preventing COPD and asthma.
- Start with high dose and then step down therapy is preferred.
Developing a patient–centered treatment plan

- All symptomatic COPD patients should have a prescription for a short-acting bronchodilator for breakthrough symptoms.
- Although short-acting therapy may help with intermittent and breakthrough symptoms, long-acting, scheduled bronchodilator therapy is generally preferred in the majority of patients, because it reduces exacerbations and hospitalizations and improves the effectiveness of pulmonary rehabilitation.
- Routine use of corticosteroids may help with systemic and airway inflammation. Long-term treatment with oral corticosteroids is absolutely contraindicated.
- Long-term oxygen therapy (more than 15 hours per day) is one of the only treatment options shown to improve survival in patients with severe COPD.
- Developing a patient–provider relationship is at the core of effective asthma management.
- The discussion and development of goals should be a collaborative effort that uses the provider's recommendations and the patient's preferences to guide a personalized treatment plan.
- An asthma action plan helps a patient know what to do when his or her symptoms change or worsen.
- This plan should address each medication prescribed (both controller and quick-relief), symptoms that may occur with worsening control, changes in medications or doses if symptoms worsen, and whom to call in an emergency.
- Inhaler technique should be assessed at every visit. A patient may reasonably be using 2 or 3 different delivery devices for his controller and quick-relief medications.
- Many patients may benefit from using a valved holding chamber (ie, spacer) with their inhaler. The efficiency of drug delivery for an inhaled medication depends on proper administration, and pharmacists play a crucial role in ensuring that the patient understands the specific inhalation technique for each device.
- Patients should be educated on the differences between long-term control medications and quick-relief medications.
- Controller medications prevent symptoms and must be taken daily on a regular basis, not just when symptoms occur; they should not be used for quick relief during an asthma exacerbation.
- Rescue medications relax the airway smooth muscle to quickly increase airflow and relieve symptoms. They do not provide long-term control of asthma.

Pharmacotherapy

- The Expert Panel Report recommends a stepwise approach to the treatment of asthma. Medication should be initiated based on an assessment of asthma severity and then stepped up if necessary and stepped down if possible based on asthma control.
- When available, inhaled medications are preferred because they deliver a higher concentration of medication to the lungs with a much lower risk of systemic side effects.
- The preferred therapy is similar among all age groups, but there have been very few studies of asthma treatment for young children, and many of the recommendations are extrapolated from data in older children and adults.
- In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.

<table>
<thead>
<tr>
<th>Components of severity</th>
<th>Persistent</th>
<th>Moderate</th>
<th>Mild</th>
<th>Intermittent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 – 19 yr 85% 80%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 – 30 yr 80% 75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 – 59 yr 75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60 – 80 yr 70%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td>≤ 2 days/week</td>
<td>≤ 2 days/week</td>
<td>Daily</td>
<td>Throughout the day</td>
</tr>
<tr>
<td>Nighttime Awakenings</td>
<td>≤ 2 times/month</td>
<td>3 – 4 times/month</td>
<td>&gt;1 time/week but not nightly</td>
<td>Often 7 times/week</td>
</tr>
<tr>
<td>SABA use for symptoms control</td>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week but not daily and not more than 1 time on any day</td>
<td>Daily</td>
<td>Several times per day</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor Limitation</td>
<td>Some limitation</td>
<td>Extremely limited</td>
</tr>
<tr>
<td>Lung function</td>
<td>Normal FEV₁ between exacerbations</td>
<td>FEV₁ &gt; 80% predicted</td>
<td>FEV₁ &gt; 60% but &lt; 80% predicted</td>
<td>FEV₁ &lt;60% predicted</td>
</tr>
<tr>
<td>Risk</td>
<td>0 – 1 year</td>
<td>≥ 2 year</td>
<td>Consider severity and interval since last exacerbation.</td>
<td></td>
</tr>
</tbody>
</table>
**Oral systemic corticosteroids**

Frequency and severity may fluctuate over time for patients in any severity category.

**Recommended step for Initiating Treatment**

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3 (± PO systemic corticosteroids)</th>
<th>Step 4 or 5 (± PO systemic corticosteroids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Step 2</td>
<td>Step 3 (± PO systemic corticosteroids)</td>
<td>Step 4 or 5 (± PO systemic corticosteroids)</td>
</tr>
</tbody>
</table>

### STEPWISE APPROACH TO TREATMENT IN YOUTHS ≥ 12 YEARS OF AGE AND ADULTS

<table>
<thead>
<tr>
<th>Intermittent</th>
<th>Persistent Daily Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Step 2</td>
</tr>
<tr>
<td>SABA PRN</td>
<td>Preferred: Low dose ICS</td>
</tr>
<tr>
<td>Alternative: Cromolyn, LTRA, Nedocromil Theophylline</td>
<td>Alternative: Low dose ICS + either LTRA, theophylline or zileuton</td>
</tr>
</tbody>
</table>

### β2 Agonists (SABA and LABA)

- Quick-relief medications should be provided at all steps of treatment.
- Short acting β2-agonists are the preferred choice for relief of acute symptoms.
- They relax the smooth muscle surrounding the airways, providing symptom relief within 3 to 5 minutes.
- Patients may use up to 3 treatments at 20 - minute intervals depending on the severity of their symptoms.
- Nonselective inhaled β2-agonists (eg, epinephrine, isoproterenol, metaproterenol) are not recommended because their beta1 activity can increase cardiovascular side effects.
- A 2 week trial period is necessary before increasing or changing the drug.
- A short-acting anticholinergic (ipratropium) is occasionally used in EDs because it provides an additive benefit to SABAs in moderate-to-severe exacerbations.
- Ipratropium may be considered as the primary reliever medication in patients who do not tolerate SABAs.
- Tiotropium, a long acting anticholinergic, is not approved for asthma.
- Use with corticosteroids provides improve symptoms and ↓ incidence of exacerbation.
- Inhaled long-acting β2-agonists have the same, mechanism of action as SABAs, but with duration of effect of at least 12 hours, which allows for twice-daily administration.
- Adding an LABA to low-dose ICSs improves multiple domains of asthma control more than doubling the dose of the ICS and spares dose-dependent side effects of glucocorticoids.
- For this reason, they are the preferred add-on therapy to ICSs.

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose, Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA</td>
<td>Albuterol/Salbutamol (Ventolin, Proair, Airomir)</td>
<td>Beta2 mediated are</td>
<td>Short acting are safe in pregnancy</td>
</tr>
<tr>
<td></td>
<td>Fenoterol (Berotec)</td>
<td>Tremor</td>
<td>Shake well MDIs before use and prime</td>
</tr>
<tr>
<td></td>
<td>Terbutaline (Bricanyl) (Ventolin/Proair/Airomir/Berotec/Fenoterol (100 mcg puff/actuation): 1 to 2 puffs qid prn (max of 8 puffs/day)</td>
<td>Palpitations</td>
<td>Wait at least one minute before inhaling the next puff of medicine</td>
</tr>
<tr>
<td></td>
<td>Terbutaline (0.5 mg/puff): 1 puff q 4 to 6 h prn (max of 6 puffs/day)</td>
<td>Restlessness</td>
<td>Exhale slowly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nervousness</td>
<td></td>
</tr>
</tbody>
</table>
### LABA

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose, Efficacy and Indications</th>
<th>Adverse effects</th>
<th>Interactions/Precautions/Monitoring/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipratropium Br</td>
<td>Ipratropium acts in lungs, especially larger airways and doesn’t dry out airflow obstruction.</td>
<td>Dry mouth</td>
<td>Shake well MDIs before use and prime</td>
</tr>
<tr>
<td></td>
<td>Blocks ACh, reduces cholinergic tone and produce bronchodilation.</td>
<td>Metallic taste</td>
<td>Wait at least one minute before inhaling the next puff of medicine</td>
</tr>
<tr>
<td></td>
<td>ASTHMA:</td>
<td>Blurred vision</td>
<td>Exhale slowly</td>
</tr>
<tr>
<td></td>
<td>Not protective VS early/late responses or exercised induced COPD:</td>
<td></td>
<td>Avoid contact with eyes</td>
</tr>
<tr>
<td></td>
<td>First line agent</td>
<td></td>
<td>Spiriva capsules are intended for use in the inhaler provided. Do not swallow the capsules.</td>
</tr>
<tr>
<td></td>
<td>High dose acceptable if tolerable</td>
<td></td>
<td>Do not use the inhaler device to administer any medication other than Spiriva.</td>
</tr>
<tr>
<td>Tiotropium Caps</td>
<td>Long-acting muscarinic antagonist (LAMA), produces bronchodilation by inhibiting acetylcholine’s</td>
<td>Headache</td>
<td>If monotherapy does not reach goal, may add 2nd agent and if goal still not met, add 3rd agent and if no</td>
</tr>
<tr>
<td>Sprira and daily</td>
<td>effect on muscarinic receptors in the airway smooth muscle.</td>
<td>Nasopharyngitis and cough</td>
<td>significant improvement then discontinue treatment.</td>
</tr>
<tr>
<td></td>
<td>Breath-activated dry powder inhaler indicated for long-term maintenance treatment of bronchospasm</td>
<td></td>
<td>Benefits maintained with continued therapy</td>
</tr>
<tr>
<td></td>
<td>associated with COPD including chronic bronchitis and emphysema 400 mcg actuation BID</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Inhaled Corticosteroids (ICS)

- ICSs are the **preferred long-term control** medication for initiating therapy in all age groups and at all steps of therapy. They target the primary pathophysiologic manifestation of asthma-chronic inflammation.
- Most of the benefit is seen in the low- to medium-dose range, but because of the variability in response among patients, higher doses are often needed.
- Add - on therapy with a medication from another class is often preferred over increasing the dose of ICSs in order to minimize side effects.
- Once a patient has maintained asthma control for 3 months, a **dose reduction by 25% to 50% in the ICS** should be considered.
### Theophyllines
- Sustained-release theophylline is the most commonly used methylxanthine.
- It is a nonselective phosphodiesterase inhibitor with bronchodilator and modest anti-inflammatory activity.
- It is generally considered an alternative, not preferred, monotherapy or add-on therapy in patients 5 years of age and older with persistent asthma and it is not recommended at any step of therapy for children younger than 5 years of age.

### Chromoglycates
- Cromolyn (Intal) 1 mg/puff 2 puffs QID
- Nedocromil (Tilade) 2 mg/puff 4 puffs QID

#### Dosing
- **Cromolyn**:
  - (Intal) 1 mg/puff
  - 2 puffs QID
- **Nedocromil**:
  - (Tilade) 2 mg/puff
  - 4 puffs QID

#### Efficacy and Indications
- **Mast cell stabilizers**
- **ASTHMA**: Inhibits early/late response and exercise induced asthma
- Effective prophylactically in children with mild to moderate asthma
- Must be used regularly in order to provide significant protection

#### Adverse effects
- Rare

#### Interactions/Precautions/Monitoring/Comments
- Nedocromil is an effective anti-inflammatory agent, especially for mild persistent asthma and is similar to cromolyn in efficacy and in low incidence of side effects.

### Additional Notes
- **Fluticasone/Salmeterol** (Advair Diskus) 100/50, 250/50, 500/50
- **Asthma maintenance for patients 4 – 11 years**: use, 100/50 mcg INH bid for pts not controlled on inhaled steroid
  - Adults: 100/50-250/50 mcg INH bid if not on inhaled steroid.
  - COPD adults: 250/50 mcg INH bid
- **Upper respiratory infection**
- **Pharyngitis**
- **Dysphonia**
- **Candidiasis**
- **Cataract**
- **Decrease immune system**
- **Muscle weakness**
- **Oral thrush can be reduced by rinsing mouth or using spacer**
- If using bronchodilator and steroid then use bronchodilator first and use bronchodilator after few minutes.
- Absorption from lungs in most likely contributor to possible HPA suppression of other systemic effects.
- Delivery system affects pulmonary system.
- **Addition of spacer also increases pulmonary deposition**.
- Low dosages are accepted as quite safe.
- Favor starting at high and stepping down.
- Patient education may have greater effectiveness.
- Administration of ICS is preferred BID.
- More than 3 – 4 puffs at each dosing should be avoided.
- Compliance is major determinant of success with aerosol corticosteroids and education is essential.
- Prime dulera before first time by releasing 4 test sprays in the air, shaking well for 5 seconds before each spray; repeat if unused for > 5 days or if inhaler has been dropped.
- After inhalation, rinse mouth with water without swallowing.

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**Theophyllines**

- **Ednum**
- **US/CANADIAN PHARMACY EXAM**
- **ALLAH O AKBAR**

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**Page 6**
### Systemic Corticosteroids
- **Dexamethasone, hydrocortisone, methylprednisolone, prednisolone, and prednisone** are used for moderate- to-severe exacerbations, because they speed resolution of symptoms and prevent recurrent exacerbations.
- Onset of anti-inflammatory activity occurs within 4 to 6 hours, and treatment should continue for 5 to 10 days depending on the severity of the exacerbation.
- Possible side effects include hyperglycemia, increased appetite, fluid retention, weight gain, changes in mood, and peptic ulcer. Refer to the section on inhaled corticosteroids (ICSs) for a discussion of potential long-term effects of glucocorticoids.

### Immunomodulators

### Antileukotrienes

- **Zileuton (Zyflo) tab 10 mg**
- **Zileuton, (Zyflo) tab 225 – 350 mg po BID**
- **Aminophylline (Phyllocontin) Inj, LIq, (Theodur, Uniphyl)**
- **Theophylline**
- **Montelukast**
- **Zafirlukast**

#### Adverse effects
- Nausea
- Nervousness
- Headache
- Signs of toxicity
- Vomiting
- Palpitations
- Tremor
- Seizures
- Hypokalemia
- Hypotension
- Dizziness
- Tremor

#### Interactions/Precautions/Monitoring/Comments
- Increases levels of Cimetidine, erythromycin, verapamil, quinolones, fluvoxamine
- **Decreases levels of**
  - Rifampin, Carbamazepine, Phenytoin, Smoking
  - Contraindicated in CHF
- Liver disease decrease theophylline clearance
- **Theophylline LA oral preparation should be taken with full glass of water, swallowed whole or cut into half if scored, do not crush.**
- Monitor heart rate, CNS effects and respiratory rate
- Aminophylline injection contains 79 – 88 % theophylline content
- Therapeutic levels are 10 – 20 mcg/ml and adverse reactions are noticed when serum concentration is 25 mcg/ml
- Levels > than 35mcg/ml are fatal

#### Theophylline
- (Theodur, uniphyl)
- Caps, elixir, Soln, Tab, Inj
- 200 – 300 mg po BID in divided dose
- S/C
- HS

#### Theophylline Dosing
- **Inhibit phosphodiesterase activity and increase cAMP**
- **Mild anti-inflammatory activity**
- **Theophylline anhydrous oral solid form contains 100% theophylline content**
- **Theophylline monohydrate oral solution contains 91% theophylline content**
- **ASTHMA:** Not for early response Not first line
- **COPD:**
  - Improves FEV1, and dyspnea
  - Improve respiratory muscle fatigue, mucociliary clearance, and gas exchange

#### Aminophylline Dosing
- **HS**
- **Zileuton requires 4 daily dosing and has more side effects and drug interactions.**
- **Take zafirlukast on empty stomach 1 hr before or 2 hr after meals**
- **children 2 – 5 years can take one 4 mg chewable tab of montelukast q hs or evening time**
- **children 6 – 14 years can take one 5 mg chewable tab q hs**
- Zileuton is contraindicated in hepatic impairment
- Monitor closely in patients who consume large quantities of alcohol. Montelukast has been shown to result in reduction of ICS dose. Zileuton requires 4 daily dosing and has more side effects and drug interactions.

#### Montelukast
- Selective cysteinyl leukotriene receptor antagonist anti-inflammatory effects
- Zileuton blocks 5 lipoxygenase

#### Zafirlukast
- Early response and exercise
- When steroids can't be use and ASA induced asthma
- Determine 6 – 8 week trial to see effects
Proper Selection and Utilization of Devices for COPD

The primary method for medication delivery for COPD treatment is via respiratory devices. The current delivery systems are MDIs (with or without a spacer device), DPIs, SMIIs, and nebulized solutions. Each of these systems has its own combination of steps, coordination, and inspiratory capacity for utilization.

Selecting a delivery system will depend on several factors, including cognitive function, lung function, dexterity and strength, lifestyle, and medication availability. Overall, the patient must be able to understand, demonstrate, and remember all of the steps necessary for medication delivery. Dexterity and strength will limit some patients from using certain delivery systems (such as MDIs), whereas lung function will limit others (such as DPIs).

Some inhalers have a running count of doses left and the patient's vision must be good enough to read it or they risk getting no dose. Patients with cognitive issues will need inhalers that have a minimal number of steps. More active patients will want an inhaler that is not bulky and can be used quickly. Patients with more advanced disease, or those with difficulty using other respiratory devices due to significant cognitive and/or physical impairment, may require use of nebulized treatments. Finally, insurance coverage (such as the addition of a spacer device for use with MDIs) and medication availability will be the deciding factor for many patients.

The first step is to determine the devices in which the medication is available along with the cost to the patient. The manufacturers and clinicians recommend that if a patient has “sufficient inspiratory flow or an effective vital capacity,” the patient be given a DPI if available, followed by an MDI with spacer device. Additionally, in most patients it is preferred to use the same type of device for inhalation, because continuity across their inhalers will increase medication adherence. If different combinations are required, multiple DPIs are preferred.

The patient should be very involved in the selection process because it fosters a sense of ownership, which will encourage regular and proper use. Given the specific attributes of each inhaler, good initial counseling as well as ongoing reinforcement education is required to ensure patients receive maximum benefit from their chosen therapy.

Metered Dose Inhaler (MDI):

- It is aerosol canister with actuation device valve that controls precise release of a premeasured amount. Drug in the canister is a suspension or solution mixed with propellant.
- The MDI is one of the most common types of inhaler. Once activated, the medication is dispensed as a fine mist or spray.
- This mist is immediately but slowly inhaled into the lungs and held there for a few seconds before exhaling.
- There is a certain amount of coordination required in activating the canister and inhaling in a timely manner. An attachment, called a spacer device, is available for most MDIs to assist with this process.
- The spacer serves 2 purposes: to overcome difficulties with timing of the inhaler and to slow down the speed of delivery of the aerosol so less of it impacts the throat and more is made available to the lungs.
- One limitation of the MDI is that it does require some compression strength in the fingers and hand that may not be present in certain patients (such as those with arthritis).

Breath Actuated MDIs:

- Breath-actuated MDIs (BA-MDIs) are a derivative of traditional MDIs.
- These inhalers incorporate a flow trigger that delivers the medication when an appropriate breath is inhaled by the patient. This takes care of the coordination between actuation and inhalation. Sufficient inspiratory flow is required for the actuation to occur. Getting the correct inhalation speed and force takes some practice for patients to master. However, in several studies these were the most preferred type of inhaler.
- The primary limitation of the BA-MDI delivery system is the minimal number of medications available utilizing it. Currently, only pirbuterol (MaxAir Autohaler) and beclomethasone (QVAR Autohaler) are available.

Dry Powder Inhalers (DPIs):

- DPIs were developed as an alternative to the aerosolized MDIs. There are multiple delivery systems within this class.
- Some hold the medication in the inhaler and require some procedure to prepare the medication. Others use a capsule that is placed in the inhaler and punctured during activation.
- Either way, once the medication has been actuated or loaded, the inhaler must be held level or the medication can fall out of the inhaler, resulting in no dose received.
- Holding the inhaler at a 45-degree angle or steeper is the most common mistake made with a DPI. The force of a sharply inhaled breath propels the medication out of the device and into the lungs.
- DPIs do have a minimum inspiratory flow rate required for proper dose delivery. As such, they may not be appropriate for patients with very advanced disease progression.

Omalizumab (Xolair) is a monoclonal antibody that prevents IgE from binding to basophils and mast cells.

Omalizumab is only indication is as adjunctive therapy in patients with severe allergic asthma who are not controlled on ICSs.

It is administered by subcutaneous injection every 2 to 4 weeks, with the dose depending on serum IgE levels and the patient's body weight.

Omalizumab has been shown to increase quality of life and decrease severe exacerbations and ED visits in patients already taking high-dose ICSs plus and LABA.
For any patient with adequate inspiratory flow, the dry powder devices are generally preferred due to the minimal need for coordination and wide number of medications available utilizing these delivery systems.

**Soft Mist Inhalers (SMIs):**
- This delivery system is a propellant-free inhaler that uses a fine, slow-moving mist to deliver the active ingredients.
- Prior to first use, a cartridge is inserted into the inhaler and the unit is primed using a very specific sequence of steps. Once priming is complete, use is very similar to an MDI.
- With a long aerosol generation time and low aerosol velocity, these devices would be best considered in patients who are not appropriate users of a DPI, but cannot manage the coordination of an MDI.
- The SMI delivery system does have several intricate steps required for priming the unit, especially prior to first use. This, combined with the limited number of medications available with this proprietary system, means extra education and reinforcement will definitely be required.

**Air Jet Nebulizer:**
- Drug is placed in a small volume of solute and placed in a small reservoir (nebulizer) connected to an air source such as a small compressor pump and an oxygen tank.
- Air travels from the relatively large diameter tubing of the air source into a pinhole-sized opening in the nebulizer, creating a negative pressure at the site of entry and causes the drug solution in the solution in the bottom of the nebulizer reservoir to be sucked up through a small capillary tube where it then encounters the rapid airflow.
- Drug solution is forced against a small baffle that causes mechanical formation of a mist.

**Diskus:** Hold the diskus in one hand and put the thumb of your other hand on the thumb grip. Push your thumb away from you as far as it will go until the mouthpiece appears and snaps into position. Hold the diskus in a level, flat position with the mouthpiece towards you. **Slide the lever away from you as far as it will go until it clicks.** It is ready to use. Every time the lever is pushed back, a dose is ready to be inhaled. This is shown by a **decrease in numbers** on the dose counter. Before inhaling your dose from the diskus, **breathe out (exhale) fully** while holding the diskus level and away from your mouth. Never breathe out into the diskus mouthpiece. Put the mouthpiece to your lips. Breathe in quickly and deeply through the diskus. Remove the diskus from your mouth. **Hold your breath for about 10 seconds,** or for as long as is comfortable. Breathe out slowly. **Never wash the mouthpiece** or any part of the diskus. **Keep it dry.** Rinse your mouth with water after breathing-in the medicine. Spit the water out. Do not swallow.