Drug Management of Bronchial Asthma

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Intended Learning Outcomes

Apply

- Apply the management principles of asthma to the mediators of airway inflammation involved in asthma.

Understand

- Understand the medications used in the treatment of asthma, their mechanisms of action, and adverse effects.

Know

- Know the difference between short-acting symptomatic treatments and long-acting preventive therapies.

Pathophysiology Of Asthma

Asthma is characterized by acute episodes of **bronchoconstriction** from airway inflammation.

Characterized by:

- Increased responsiveness of the bronchi and trachea to exogenous or endogenous stimuli.
- Inappropriate contraction of smooth muscle in the airway
- Production of thick viscid mucus
- Mucosal thickening from edema and cellular infiltration.

Asthma Management Principles

Avoid Trigger factors

Inhaled medications are the basis of treatment. Two types of drug treatment:

- Preventors (also called controllers) e.g. corticosteroids, to reduce the inflammation
- Relievers, e.g. salbutamol, to produce bronchodilation when symptoms occur.

Acute disease episodes: high concentrations of oxygen as required.

Classes Of Antiasthma Drugs

- There are **six classes of drugs** used to treat asthma:
  1. **β-adrenoreceptor agonists**
  2. **Glucocorticoids**
  3. **Acetylcholine antagonists**
  4. **leukotriene modifiers**
  5. **Xanthines**
  6. **Chromones**
  7. **Anti-IgE monoclonal antibodies**

Short-acting β2-agonist

Bind specifically to the β2-adrenergic receptor

- Activation of β2-receptors causes bronchodilation
- Avoid cardiovascular effects of β1 activation

Indication: Quick relief with short-acting inhaled β2-agonist in all patients regardless of severity.

- One to three times per acute episode
- Using short-acting β2-agonists more than two times a week indicates initiating long-term therapy.

E.g., albuterol, terbutaline, metaproterenol, and pirbuterol.

Pharmacology of Short-acting B2-agonists

Onset of action occurs in **minutes and lasts for 4– 6 hours**

Albuterol and terbutaline can be administered orally; terbutaline is available for subcutaneous injection for emergency treatment

Regular use can cause **transient hypokalemia** manifesting as muscle cramping

Excessive use of the oral preparations may result in **cardiovascular effects such as tachycardia**

Long-acting Inhaled β2 -Agonists

E.g, salmeterol and formoterol

Longer half-life (up to 12 hours).

Available in metered-dose inhalers

Fewer side effects than systemic administration

MOA: Produce relaxation in airway smooth muscles

Decrease release of mediators from mast cells and lymphocytes

Long-acting Inhaled B2 -Agonists

Should not be used to reverse an acute attack

- Should never be prescribed as monotherapy

Cross tolerance with albuterol

- Limiting their efficacy in acute exacerbations, and increased mortality

Inhaled β-agonists may cause tremor, tachycardia, and cough

Glucocorticoids

Glucocorticoids are an important treatment for mild persistent and more severe asthma.

Potent anti-inflammatory agents

- Reduce the production of inflammatory mediators
- Cause apoptosis of leukocytes
- Decrease vascular permeability

Indication: Prophylactic treatment of asthma; they have no effect on an acute event

- Do not cause relaxation of bronchial smooth muscle

Glucocorticoids Administration in Asthma

Administration by inhalation:

High concentration of drug where needed

Minimizes amount in the systemic circulation

Some drug is swallowed during inhalation or absorbed into the systemic circulation through the lungs

In emergency or non-responsive acute asthma episodes

Intravenous administration for short periods to reduce side effects

Oral for chronic poor control

Glucocorticoid: Adverse Effects

Local

- **Oral candidiasis**

Systemic

- Increased **loss of calcium from bone**
- Rarely, suppression of the **hypothalamic-pituitary-adrenal axis**.

Route Of Administration: B2 -Agonists And Glucocorticoids

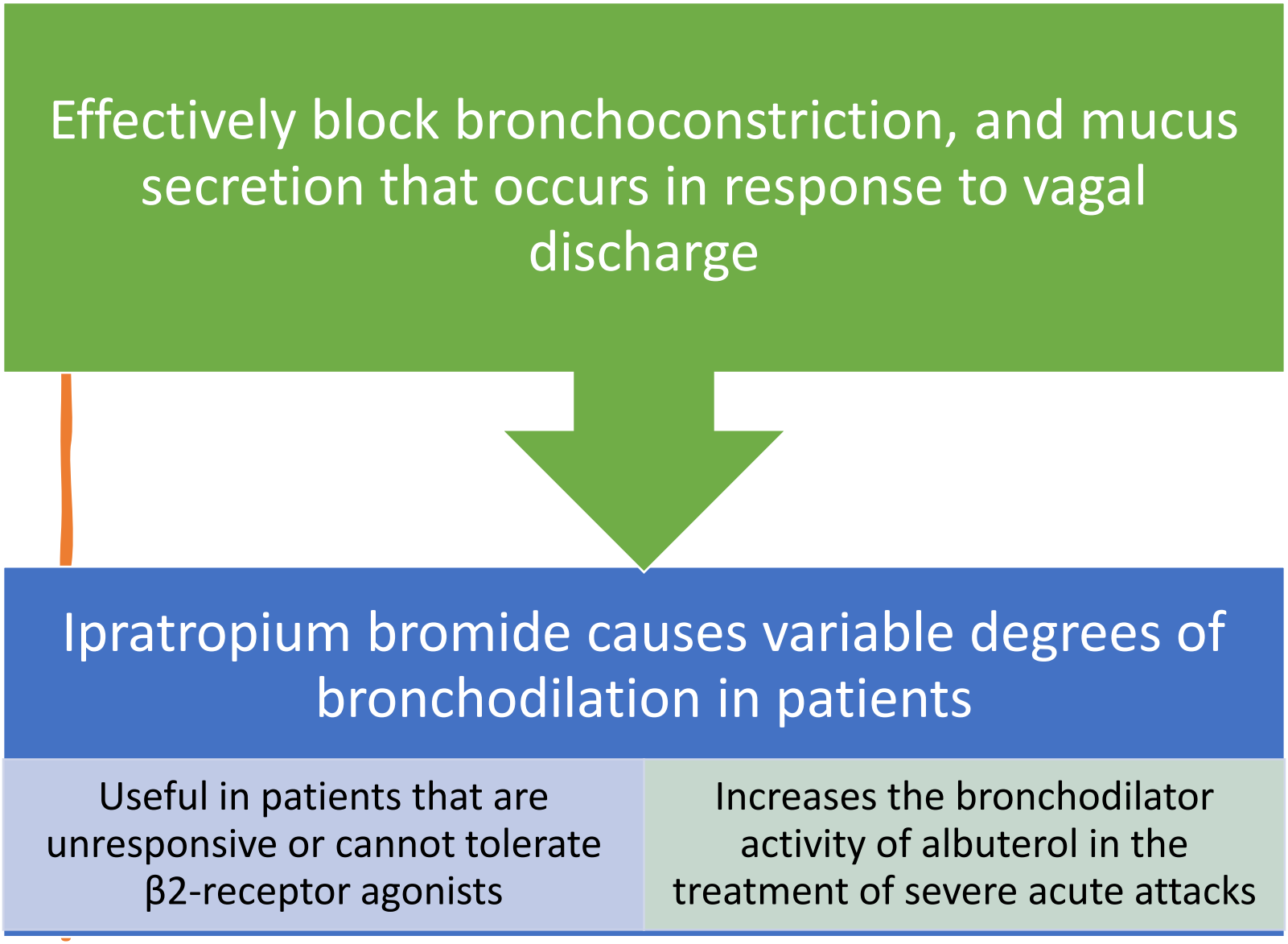
Metered dose inhaler (MDI)

Spacer dramatically increase the amount of medication delivered

Nebulizer for emergencies

Systemic use is recommended in patients with severe persistent asthma

Acetylcholine Muscarinic Cholinoreceptor Antagonists



Leukotrienes

Leukotrienes play an important role in the pathogenesis of asthma.

- Bronchoconstriction and overproduction of airway mucus.

Two classes of drugs interfere with leukotrienes

Inhibitor of 5-lipoxygenase decreasing the biosynthesis of leukotrienes. e.g. **Zileuton**

Specific, competitive Cys-LT1 **receptor antagonists. E.g., Zafirlukast and montelukast**

Pharmacology of Leukotrienes

The two classes of drugs are equally effective

In mild-to-moderate persistent asthma

As effective as low-dose inhaled glucocorticoids

All leukotriene modifiers are administered orally

Zileuton is associated with liver toxicity

Monitoring liver enzymes recommended

Methylxanthines

Examples: **theophylline, theobromine, and caffeine**

Theophylline is a second-line agent to treat asthma (reliever)

Theophylline MOA: Inhibiting cyclic nucleotide phosphodiesterase; increasing intracellular cAMP and cyclic guanosine monophosphate (cGMP)

- **Antagonist of adenosine receptors**
  - In asthma activation of pulmonary adenosine receptors results in bronchoconstriction

Pharmacology of Theophylline

Produces bronchodilation and improves long-term control of asthma

- Available for oral administration, suppository, and parenteral use

Plasma levels variability between patients

Narrow therapeutic window.

- Blood levels need to be monitored

Infants and neonates have the slowest rates of clearance

Chromones

Examples **cromolyn and nedocromil**

Indications: Prophylaxis of mild-to-moderate persistent asthma

Mechanism of action:

- Inhibition of mediator release from mast cells
- Suppression of activation of leukocytes
- Inhibition of various chloride channels responsible for mucous secretion and cellular activation

No effect on airway smooth muscle tone Cannot reverse bronchospasm (prevention/ controller)

Pharmacology of Chromones

Administered by inhalation

Poorly absorbed into the systemic circulation

Indications: Reducing antigen and exercise-induced asthma

Side effects: **throat irritation, cough, and nasal congestion**

Serious adverse reactions: anaphylaxis, anemia, and pulmonary infiltration

Anti-IgE monoclonal antibodies

IgE bound to mast cells plays an important role in antigen-induced asthma.

Omalizumab: monoclonal antibody that targets circulating IgE and prevents its interaction with mast cells

Indications: treatment of asthma, if allergies exacerbate asthma

MOA: Decreasing the amount of IgE antibodies available to bind mast cells

Reducing mast cell release of mediators

- In early- and late-phase responses to antigen

Indications For Omalizumab

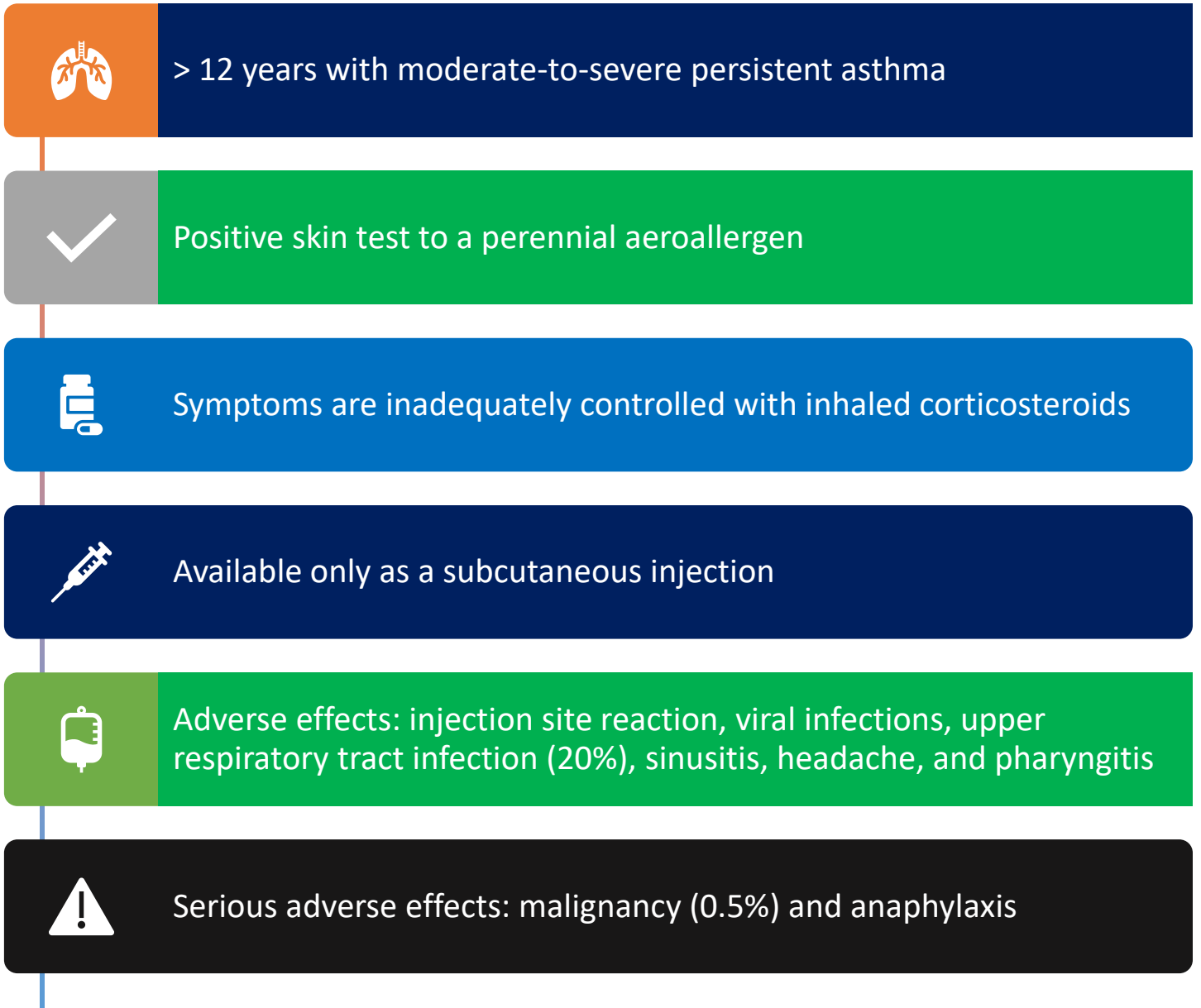


Table 37–1 • RECOMMENDATIONS FOR PHARMACOLOGIC MANAGEMENT OF ASTHMA IN ADULTS AND CHILDREN OLDER THAN 5

Asthma Severity	Symptom Frequency	Medications
Mild intermittent	<2 days/week, <2 nights/month	No regular therapy; short-acting β_2-agonists as needed for symptom relief
Mild persistent	>2 per week but <once per day >2 nights/month	Low-dose inhaled glucocorticoids. Alternate: cromolyn, nedocromil, leukotriene modifier, *or* sustained release theophylline
Moderate persistent	Daily, >1 night/week	Low- to medium-dose glucocorticoids and long-acting inhaled β_2-agonists. Alternate: leukotriene modifier or theophylline
Severe persistent	Continual during day, frequent at night	High-dose glucocorticoids *and* long-acting inhaled β_2-agonist *and* (if needed) systemic glucocorticoids. Consider omalizumab for allergy sufferers

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THE END

Thank You For Your Participation