بسم الله الرحمن الرحيم

TREATMENT OF ASTHMA

Armin Sadeghi M.D.
Pulmonologist

Goals of Asthma Therapy

1) Reduction in symptom frequency to ≤2 times/week
2) Reduction of nighttime awakenings to ≤2 times/month
3) Reduction of reliever use to ≤2 times a week (except before exercise)
4) No more than 1 exacerbation/year
5) Optimization of lung function
6) Maintenance of normal daily activities
7) Satisfaction with asthma care with minimal or no side effects of treatment

Treatment approach

a) avoiding and reducing **asthma triggers**

b) if necessary, the adjunctive use of **medications**

➢Asthma medications are primarily divided into

1) those that **relax smooth muscle** and produce a fairly rapid relief of acute symptoms (reliever)

2) those that **target inflammation or mediator production**. (controller)

REDUCING TRIGGERS

- Mitigation
  - Occupational exposures, removal from the offending environment
  - Second hand smoke exposure and frequent exposure to combustion products of cannabis
  - The removal of pets
  - Pest control at home and in the school
  - The effect of dust or mold control in reducing asthma symptoms has been more variable
- There is moderate evidence that dust control may be effective in reducing symptoms

❑Allergen Immunotherapy

- It clearly reduces the symptoms of allergic rhinitis and thus may be helpful in reducing this comorbidity
- The evidence for its effectiveness in isolated asthma in those who are sensitized and have clinical symptoms is variable.
- Due to the risk of anaphylaxis, guidelines generally recommend immunotherapy only in patients whose asthma is under control and who have mild to moderate asthma.

❑Vaccination

- Respiratory infections are a major cause of asthma exacerbations.
- Patients with asthma are strongly advised to receive both types of currently available **pneumococcal vaccines** and yearly **influenza vaccines**.
- **COVID-19 vaccination** is advised

BRONCHODILATOR THERAPIES

- Bronchodilators act primarily on airway **smooth muscle** to reverse the bronchoconstriction of asthma
- **rapid relief** of symptoms but has little or **no effect on the underlying inflammatory** process.
- bronchodilators **are not sufficient to control asthma** in patients with persistent symptoms.
- There are three classes of bronchodilator in current use:

➢ **B2-adrenergic agonists**, **anticholinergics**, and **theophylline**

➢ B2-agonists are by far the most effective.

β2-Agonists

- β2-adrenergic receptors are widely expressed in the airways.
- Such receptors are also present on mast cells, but they contribute little to the efficacy of these agents in asthma.
- β2-receptors are G protein–coupled receptors that activate adenyl cyclase to produce cyclic AMP, which results in relaxation of smooth muscle.

β2-Agonists

- **Use:**

➢ β2-Agonists are primarily used in inhaled forms to provide **relief of bronchospasm** or to **reduce the degree of bronchospasm** anticipated in response to **exercise** or **other provocative stimuli**.

➢ **Regular use** has been associated with **tachyphylaxis** of the bronchoprotective effect and possible increased airway reactivity.

➢ **Frequent short-acting β-2 agonist** use has been associated with **increased asthma mortality** resulting in decreased enthusiasm for use in isolation **without inhaled corticosteroids.**

β2-Agonists

- Short-Acting β2-Agonists :

➢ **Albuterol** (also known as salbutamol) is the most commonly used agent.

➢ Bronchodilation begins within **3–5 min** of inhalation, and effects generally last **4–6 h.**

➢ It is most commonly administered by **metered-dose inhaler**.

➢ **Solutions for nebulization** are also used, especially for relief of bronchospasm in **children.**

➢ Oral forms are available but are not commonly used.

β2-Agonists

- Long-Acting a2-Agonists

- **Salmeterol** and **formoterol** are the two available LABAs. They have an ~**12-h** duration of action.
- **Formoterol** has a **quick onset** comparable to the short-acting β2-agonists.
- Salmeterol has a slower onset of action.
- These agents can be used **for prophylaxis of exercise-induced bronchospasm**.
- In contrast to COPD, these agents **are not recommended for use as monotherapy in the treatment of asthma**.
- Their use in asthma is generally restricted to use in **combination with an ICS.**

β2-Agonists

- Ultra-Long-Acting a2-Agonists

➢These agents (indacaterol, olodaterol, and vilanterol) have a 24-h effect.

➢They are only used in combination with ICSs in the treatment of asthma.

β2-Agonists

- Safety

➢ In some patients and especially at higher doses → they can produce **tremor**, **tachycardia**, **palpitations**, and hypertension.

➢ They promote potassium reentry into cells, and at high doses, they can produce **hypokalemia**.

➢ Type B (nonhypoxic) **lactic acidosis**

➢ Increased asthma mortality was associated with high potency β2-agonists

Anticholinergics

- Cholinergic nerve–induced smooth-muscle constriction **plays a role in asthmatic bronchospasm.**
- Anticholinergic medications can produce smooth-muscle relaxation by antagonizing this mechanism of airway narrowing.
- Agents that have been developed for asthma have been pharmacologically designed to be less systemically absorbed so as to minimize their systemic anticholinergic effects.
- The long-acting agents in this class are known as long-acting muscarinic antagonists (**LAMAs**).

Anticholinergics

- **Use**

➢The short-acting agents in this class can be used alone for acute bronchodilation.

➢They appear to be somewhat less effective than β2-agonists and have a slower onset of action as well.

- **Safety**

➢Dry mouth may occur.

➢At higher doses and in the elderly, acute glaucoma and urinary retention have been reported..

Theophylline

- Theophylline, an oral compound that increases cyclic AMP levels by inhibiting phosphodiesterase,
- now rarely used for asthma due to its narrow therapeutic window, drug-drug interactions, and reduced bronchodilation as compared to other agents.

CONTROLLER THERAPIES

- They reduce **asthma exacerbations** and **improve long-term control**, **decreasing the need for intermittent use of bronchodilator therapies**.
- None of these therapies have yet been shown to prevent progression of airway remodeling or the more rapid decline in lung function that can occur in a subset of asthma patients.

Corticosteroids

- Use

➢ Corticosteroids **reduce airway hyperresponsiveness**, **improve airway function**, **prevent asthma exacerbations**, and **improve asthma symptoms**.

➢ Corticosteroid use by inhalation (ICSs) minimizes systemic toxicity and represents a **cornerstone of asthma treatment.**

ICS and ICS/LABA

- ICSs are the cornerstone of asthma therapy.
- Their use is associated with decreased asthma mortality.
- They are generally used regularly twice a day as first-line therapy for all forms of persistent asthma.
- **Doses are increased**, and they are **combined with LABAs** to control asthma of **increasing severity.**
- Combining them with LABAs permits effective control at lower ICS dose.
- Longer-acting preparations permitting once-a-day use are available.
- Their effects can be noticeable in several days, but **continued improvement may occur over months** of therapy, with the **majority of improvement evident within the first month of regular use**.

ICS and ICS/LABA

- Not all patients respond to ICS.

➢ Increasing evidence suggests that the most responsive patients are those with significant type 2–mediated asthma

Oral Corticosteroids

- Chronic oral corticosteroids (OCSs) at the lowest doses possible (due to side effects) are used in patients who cannot achieve acceptable asthma control without them.
- Alternate- day dosing may be preferred, and pneumocystis pneumonia prophylaxis should be administered for those maintained on a daily prednisone dose of ≥20 mg.
- OCSs are also used to treat asthma exacerbations, frequently at a dose of 40–60 mg/d of prednisone or equivalent for 1–2 weeks.
- Since they are well absorbed, they may also be used for managing hospitalized patients.

Intravenous & Intramuscular Corticosteroids

- **Intravenous** preparations are frequently used in hospitalized patients.

➢Patients are rapidly transitioned to OCS once their condition has stabilized.

- **Intramuscular** Corticosteroids In **high-risk**, **poorly adherent** patients, intramuscular ***triamcinolone acetonide*** has been used to achieve asthma control and reduce exacerbations

Corticosteroids

- **Safety**

➢ Chronic administration of systemic corticosteroids is associated with a plethora of side effects including **diabetes**, **osteoporosis**, **cataracts and glaucoma**, **bruising**, **weight gain**, **truncal obesity**, **hypertension**, **ulcers**, **depression**, and **accelerated cardiac risk**, among others.

➢ Appropriate monitoring and infectious (**pneumocystis pneumonia prophylaxis** for those treated chronically with ≥20 mg prednisone/d) and bone health prophylaxis are necessary.

Corticosteroids

- **Safety**

➢ICSs have **dramatically reduced side effects as compared to OCSs.**

➢At higher doses, **bruising** occurs and o**steoporosis** can accelerate.

➢There is a **small increase in glaucoma and cataracts**.

➢Local effects include **thrush**, which can be reduced by use of a **spacer** and **gargling.**

➢**Hoarseness** may be the result of a direct myopathic effect on the vocal cords.

➢Rare patients exhibit side effects even at moderate doses of ICS.

➢Children may experience **growth suppression**.

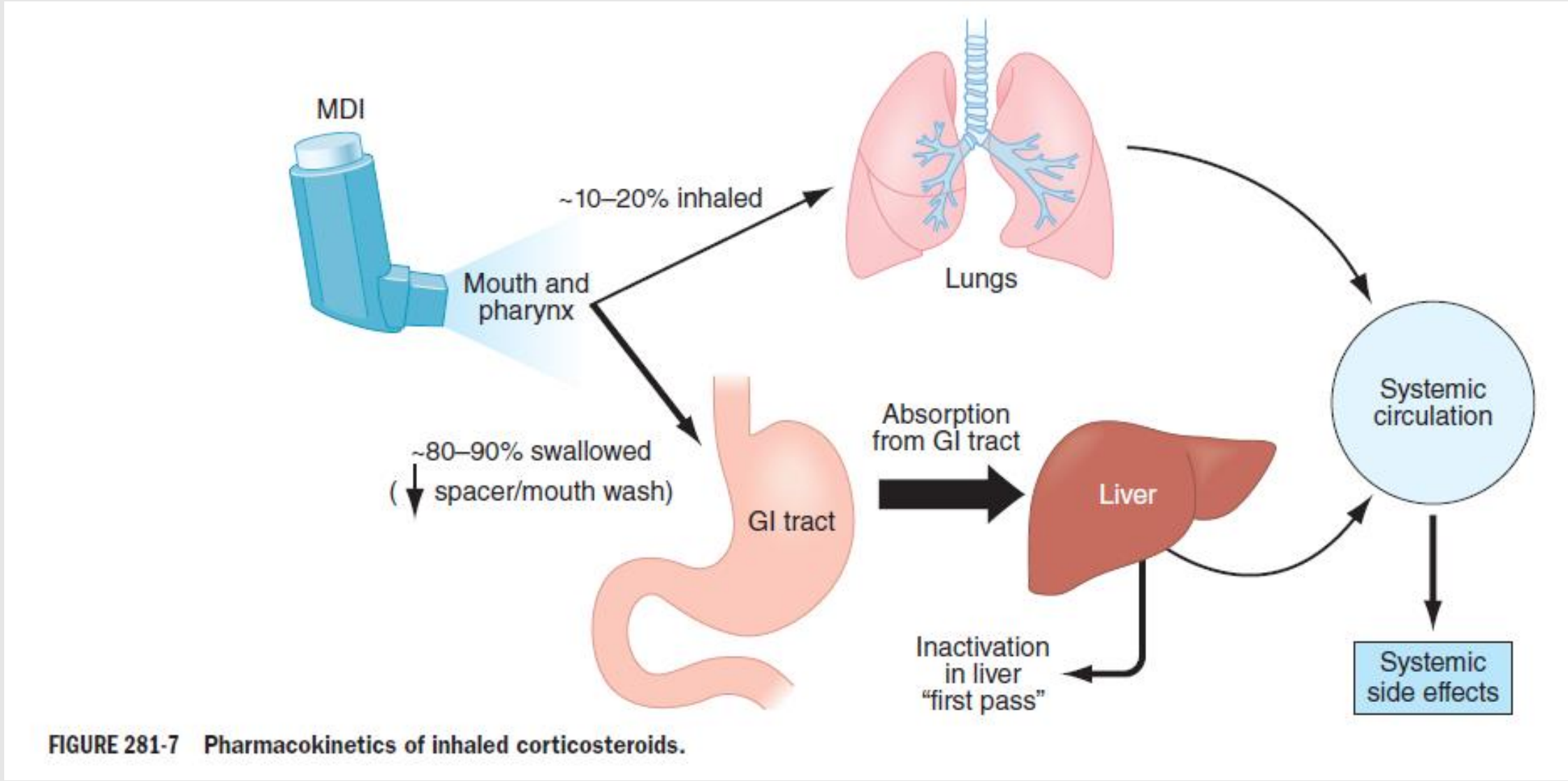

FIGURE 281-7 Pharmacokinetics of inhaled corticosteroids.

Leukotriene Modifiers

- Agents that inhibit production of leukotrienes (zileuton, an inhibitor of 5-lipoxygenase) or the action of leukotrienes at the CysLT1 receptor (montelukast and zafirlukast) are moderately effective in asthma.
- They can improve airway function and reduce exacerbations but not to the same degree as bronchodilators or ICS, respectively.
- They are also effective in reducing symptoms of allergic rhinitis and, thus, can be used in patients with concomitant allergic rhinitis.
- **Montelukast**, in particular, is frequently used in **children** with **mild asthma** due to concerns of ICS-related growth suppression.

Leukotriene Modifiers

- **Montelukast** use may decrease due to **safety warnings regarding depression** with this compound.
- Leukotriene modifiers are effective in preventing **exercise-induced bronchoconstriction without the tachyphylactic effects** that occur with regular use of LABAs.
- Leukotriene modifiers are particularly effective in **aspirin-exacerbated respiratory disease**, which is characterized by significant leukotriene overproduction.
- They have also shown modest effect as add-on therapy in patients poorly controlled on high-dose ICS/LABA.
- Montelukast and zafirlukast are administered orally **once or twice daily**, respectively.

➢The onset of effect is rapid **(hours),** with the majority of **chronic effectiveness seen within 1 month**.

Leukotriene Modifiers

- Safety
- Montelukast is well tolerated, but an **association with suicidal ideation** has now resulted in a warning label from the U.S. Food and Drug Administration.

- Zileuton increases liver function tests (transaminases) in 3% of patients.

➢Intermittent monitoring is suggested.

Cromolyn Sodium

- Cromolyn sodium is an inhaled agent believed to stabilize mast cells.
- It is only available by nebulization and must be administered **two to four times a day**.
- It is **mildly to modestly effective** and appears to be helpful for **exercise-induced bronchospasm**.
- It is used primarily in **pediatrics** in those concerned about ICS side effects..

Anti-IgE

- **Omalizumab**, a monoclonal antibody to the Fc portion of the IgE molecule, prevents the binding of IgE to mast cells and basophils.
- Reduction in free IgE that can bind to effector cells blocks antigen-related signaling, which is responsible for production or release of many of the mediators and cytokines critical to asthma pathobiology.
- In addition, through feedback mechanisms, **reduction in IgE production occurs as well**.
- Anti-IgE has been shown to **increase interferon production in rhinovirus infections**, **decrease viral induced asthma exacerbations**, and **reduce duration and peak viral shedding**.

➢This effect is believed to be due to IgE's ability to reduce interferon γ production in response to viral infections.

Anti-IgE

- **Use**

- In asthma, anti-IgE has been tested in patients with a **circulating IgE ≥30 IU/mL** and a **positive skin test or RAST to a perennial allergen**.
- It is generally used in patients **not responsive to moderate- to high-dose ICS/LABA**.
- It **reduces exacerbations by 25–50%** and can **reduce asthma symptoms** but has **minimal effect on lung function.**
- Anti-IgE is dosed based on **body weight** and **circulating IgE** and is administered **subcutaneously every 2–4 weeks**.
- the maximum dose is **300 mg every 2 weeks.**
- Most effects are generally seen in 3–6 months.

Anti-IgE

- Retrospective studies have suggested that patients with an **exhaled nitric oxide approximately ≥20 ppb** or **circulating eosinophils ≥260/µL** have the greatest response as ascertained by reduction in exacerbations.
- FeNO is slightly reduced by treatment, but circulating IgE, as measured by available clinical tests, is not affected since these tests measure total circulating IgE, not free IgE.

◦ Safety

- The incidence of side effects is low. Anaphylaxis has been reported in 0.2% of patients receiving the drug.

Anti-IL-5 and Anti–IL-4/13

- Antibodies that block IL-5 (**mepolizumab, reslizumab**) or its receptor (**benralizumab**) markedly **reduce blood and tissue eosinophils** and **reduce exacerbations** in patients who have persistently increased sputum eosinophils despite maximal ICS therapy.

Bronchial Thermoplasty

- This procedure involves radiofrequency ablation of the airway smooth muscle in the major airways administered through a series of three bronchoscopies for patients with severe asthma.
- There is some evidence that it may reduce exacerbations in very select patients.
- The procedure may be accompanied by significant morbidity, and most guidelines do not recommend it other than in the context of clinical trials or registries..

Alternative Therapies

- Nonpharmacologic treatments, including **hypnosis**, **acupuncture**, **chiropraxis**, **breathing control, yoga**, and **speleotherapy**, may be popular with some patients.
- However, placebo-controlled studies have shown that each of these treatments lacks efficacy and cannot be recommended.
- However, they are not detrimental and may be used as long as conventional pharmacologic therapy is continued.

APPROACH TO THE PATIENT

- guidelines advise a **symptomatic approach** to asthma treatment assuming that appropriate measures have been taken to address **asthma triggers**, **exposures**, and **comorbidities**.
- Additionally, adherence and inhaler techniques need to be addressed.
- **Poor adherence** or **poor inhaler technique** has been identified as the cause of poor asthma control in **up to 50% of patients** referred for poorly controlled asthma.

The stepwise approach

- It involves "stepping" therapy up or down based on assessment of whether asthma is controlled by the criteria listed in Table 287-4.
- Assuming **comorbidities** have been addressed, **adherence** has been evaluated, **education regarding avoiding triggers** has been performed, and **inhaler technique** is verified

➢ **cornerstone of preferred therapy is the intensification of ICS therapy in conjunction with the use of a LABA to achieve greater control at lower ICS doses.**

The stepwise approach

TABLE 287-4 Goals of Asthma Therapy

1. Reduction in symptom frequency to ≤2 times/week
2. Reduction of nighttime awakenings to ≤2 times/month
3. Reduction of reliever use to ≤2 times a week (except before exercise)
4. No more than 1 exacerbation/year
5. Optimization of lung function
6. Maintenance of normal daily activities
7. Satisfaction with asthma care with minimal or no side effects of treatment

The stepwise approach

TABLE 287-5 Step Therapy for the Treatment of Asthma Ages 12+ (modified from GINA and NAEPP)

	Address exposures and comorbidities (see Tables 287-2 and 287-3) Confirm inhaler technique and optimize adherence Move up or down steps based on control (see Table 287-3)					
	STEP 1	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
Preferred regular therapy	None	None[a] or low-dose ICS[b]	Low-dose ICS/ formoterol	Medium-dose ICS/formoterol	Medium to high-dose ICS/LABA, + add-on LAMA	Anti-IgE or anti–IL-5 or anti–IL4-Rα; step 5 therapy as required
Alternative regular therapy	None	LTRA	Medium-dose ICS	High-dose ICS	Anti-IgE or anti–IL-5 or anti–IL4-Rα	OCS[c]
Adjunctive therapy			LTM and/or LAMA (especially LAMA at Step 5)			
As-needed reliever therapy	ICS/formoterol (low dose) or SABA[b]	ICS/formoterol (low dose), or PRN concomitant ICS and SABA[b] or SABA[e]	ICS/formoterol (low dose)[d]			

[a]If using as-needed ICS/formoterol or PRN concomitant ICS & SABA, this is an option. [b]National Asthma Education and Prevention Program (NAEPP) recommendation. [c]To be avoided as much as possible. [d]PRN ICS/formoterol only suggested for steps 3 and 4 by NAEPP. [e]If using low-dose ICS as regular therapy.

Abbreviations: ICS, inhaled corticosteroid; IL, interleukin; LABA, long-acting β-agonist; LAMA, long-acting muscarinic antagonist; LTM, leukotriene modifier; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid; PRN, as needed; SABA, short-acting β-agonist.

The stepwise approach

- A major change in the stepwise approach, advocated for more than two decades, has occurred.
  - **As-needed ICS** can be used instead of regular ICS **in milder asthma** and that the trigger for such use could be patient perception of the need to use a reliever inhaler.
  - Since **formoterol is a LABA with a rapid onset**, combination **ICS/formoterol** has been used as a single agent in multiple studies:
- as needed without background therapy in **milder asthma**, and as needed in addition to twice daily ICS/formoterol in more **severe asthma**.

The stepwise approach

- Since asthma **mortality can occur even in mild asthma** (albeit at lower rates than more severe asthma), **GINA**, as part of a comprehensive strategy of asthma management, recommends **ICS/formoterol be used as the reliever in all steps of asthma severity**, including intermittent asthma (Step 1).
- **NAEPP** guidelines recommend that **ICS/ formoterol** be used as the reliever medication in patients requiring **step 3 and 4 therapy** and that **as-needed concomitant ICS and short-acting β-agonist (SABA)** can be used as a therapy in **step 2.**

The stepwise approach

- **Leukotriene receptor antagonists (LTRAs)** are alternative medications in **step 2**, which may be used in those concerned about the minimal ICS side effects.
- However, recent warnings about **suicidal ideation** associated with **montelukast** may make this approach less appealing.
- **Leukotriene modifiers** and **long-acting anticholinergics** are possible add-on (adjunctive) therapies in those requiring **step 4 and/or 5 therapies**.
- **Biologics** are incredibly effective in their **specific endotypes** (**type 2 with exacerbations and specific biomarkers**), but their high cost currently relegates them to **step 5 therapy or beyond**.

Asthma Attacks

- Asthma deteriorations of **mild to moderate severity** can be initially treated with a **β2-agonist administered up to every 1 h**.
- Increasing the dose of **ICSs by four- to fivefold** may be helpful as well.
- If patients fail to achieve adequate control and continue to require β2-agonists hourly for several hours, they should be referred for urgent care.
- In the urgent care setting, PEFR or FEV1 should be assessed, and patients are usually treated with **nebulized β2-agonists** up to **every 20 min**.

Asthma Attacks

- Those with **PEFR >60%** of predicted will frequently respond to **β2-agonists alone**.
- If they fail to respond in 1–2 h, **intravenous corticosteroids** should be administered.
- **Supplemental oxygen** is usually administered to correct hypoxemia.
- An **LTRA** and **magnesium** are sometimes given as well.
- **Nebulized anticholinergics** can be administered to produce additional bronchodilation.
- **Failure to achieve PEFR >60% or persistent severe tachypnea over 4–6 h** should prompt consideration of **admission to the hospital**.

Asthma Attacks

- In-hospital treatment may include **continuous bronchodilator nebulization**.
- **Noninvasive positive-pressure ventilation** to assist with respiratory exhaustion is sometimes used to prevent a need for intubation, and **helium-oxygen mixtures** may be used to decrease the work of breathing.
- Antibiotics should be administered only if there are signs of infection.
- Mechanical ventilation may be difficult in patients with status asthmaticus due to high positive pressures in the setting of high resistance to airflow due to airway obstruction.

Asthma Attacks

- Most patients with asthma attacks present with hypocapnia due to a high respiratory rate.
- Normal or near-normal Pco2 in a patient with asthma in respiratory distress should raise concerns of impending respiratory failure and need for mechanical ventilation.
- Mechanical ventilation should aim for **low respiratory rates and/or ventilation volumes** to decrease peak airway pressures.
- This can frequently be achieved by "**permissive hypercapnia**"—allowing the Pco2 to rise and, if necessary, temporarily correcting critical acidosis with administration of fluids to increase the pH.

Asthma Attacks

- Neuromuscular paralysis may sometimes be beneficial.
- Bronchoscopy to clear mucus plugs has been described but may be dangerous in the setting of difficulties with mechanical ventilation..

SPECIAL CONSIDERATIONS

HIGH-RISK ASTHMA PATIENTS

These characteristics should be considered in evaluating and treating patients who present with asthma

TABLE 287-6 Patients at Greater Risk for Asthma Mortality

1. History of intensive care unit admission for asthma
2. History of intubation for asthma
3. Illicit drug use
4. Depression
5. New diagnosis
6. ≥2 emergency unit visits in past 6 months
7. Severe psychosocial problems
8. Lower socioeconomic status
9. On daily prednisone prior to admission

EXERCISE-INDUCED SYMPTOMS

- In many cases, the degree of exercise intolerance may reflect poor asthma control.
- Treatment involves step therapy of asthma.
- In other cases, however, asthma may be well controlled in all other respects, but patients may report that they cannot undertake the level of exercise they desire.
- Some increase in exercise capacity can be achieved by starting at lower levels of exercise (warming up) and by using a mask in colder weather to condition the air.
- Pretreatment with an SABA can increase the threshold of ventilation required to induce bronchoconstriction.
- LABAs may extend the period of protection, but their use alone in asthma is to be discouraged.

- For occasional exercise, ICS/LABA can be used, but regular use may expose the patient to unnecessary doses of ICS.
- If regular exercise is undertaken, then LTRAs may provide protection and can be used regularly.
- A SABA (or ICS/formoterol) should always be available for quick relief.
- Exercise-induced airway narrowing in elite athletes may be related to direct epithelial injury. In addition to the above, conditioning of incoming air may be of major assistance.
- Ipratropium has been reported to be of utility as well.

PREGNANCY

- Asthma may **improve, deteriorate**, or **remain unchanged** during pregnancy.
- Poor asthma control, especially exacerbations, is associated with poor fetal outcomes.
- The general principles of asthma management and its goals are unchanged. Avoidance of triggers, especially smoking environments, is critical.
- There is extensive experience suggesting the safety of **inhaled albuterol**, **beclomethasone**, **budesonide**, and **fluticasone**, with reassuring information on **formoterol** and **salmeterol** in pregnancy.
- Animal studies have not suggested toxicity for montelukast, zafirlukast, omalizumab, and ipratropium

- Chronic use of **OCS** has been associated with **neonatal adrenal insufficiency**, **preeclampsia**, **low birth weight**, and a **slight increase in the frequency of cleft palate**.
- However, it is clear that poorly controlled asthma during pregnancy carries greater risk to the fetus and mother than these effects.
- There should be no hesitancy in administering routine pharmacotherapy for acute exacerbations.
- Initiation of **allergen immunotherapy** or **omalizumab** during pregnancy is not recommended.
- In cases where prostaglandins are needed to manage pregnancy, **PGF2-α** should be avoided since it is associated with bronchoconstriction.

ASPIRIN-EXACERBATED RESPIRATORY DISEASE

- A subset of patients (5–10%) present in adulthood with difficult-to control asthma and type 2 inflammation with eosinophilia, sinusitis, nasal polyposis, and severe asthma exacerbations that are precipitated by ingesting inhibitors of cyclooxygenase, with aspirin being the most prominent of such inhibitors.
- Such patients, classified as having aspirin-exacerbated respiratory disease, overproduce leukotrienes in response to inhibition of cyclooxygenase-1, probably secondary to inhibition of PGE2.
- These patients should avoid inhibitors of cyclooxygenase-1, (aspirin and NSAIDs) but can generally tolerate inhibitors of cyclooxygenase-2 and acetaminophen.

- They should be treated with leukotriene modifiers.
- Aspirin desensitization can be undertaken to decrease upper respiratory symptoms and to allow chronic administration of aspirin or NSAIDs for those that require it.

SEVERE ASTHMA

- Severe and difficult-to-treat asthma, which composes ~5–10% of asthma, is defined as asthma that, having undergone appropriate evaluation for comorbidities and mimics, education, and trigger mitigation, remains uncontrolled on step 5 therapy or requires step 5 therapy for its control.
- A significant proportion of these patients have trouble with adherence and/or inhaler technique, and these factors need to be investigated vigorously.
- Almost half of these patients have evidence of persistent eosinophilic inflammation as evidenced by peripheral blood eosinophils and/or induced sputum.

- Those with recurrent exacerbations have a substantially increased likelihood of responding to the type 2 targeted biologics.
- Treatment for those with mixed inflammation, isolated neutrophilic inflammation, or pauci-granulocytic inflammation remains to be determined.
- Some data suggest that many of these patients may have aberrations in the pathways responsible for resolution of inflammation.

ELDERLY PATIENTS WITH ASTHMA

- Asthma may **present at or persist** into older age.
- The mortality of asthma in those >65 years old is **five times greater than that of younger** cohorts even when adjusting for comorbidities.
- Many of these patients had asthma as children, some with quiescent periods as they entered adulthood.
- Of those with new-onset asthma, almost **half were smokers** or are currently smoking.
- **One-quarter** of adult-onset asthma is believed to be due to **occupational exposure**.
- Patients presenting with **eosinophilic inflammation** appear to have more severe asthma.
- Besides investigations of comorbidities, these patients may require adjustment to step therapy based on intolerance of **β2-agonist** therapy due to **arrhythmia** or **tremulousness**.