

Asthma

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Asthma is one of the most frequent chronic respiratory diseases worldwide, with an increase in its prevalence in the last decade. Ongoing studies continue to search for better diagnostic tools and advanced treatment options in an effort to decrease the morbidity and mortality associated with it. Unfortunately, many asthmatic patients still suffer from poorly controlled asthma, which may lead to life-threatening situations. This article reviews the basics of asthma and highlights the current guidelines in making accurate diagnosis and initiating therapeutic plan. **Key words:** *asthma, asthma exacerbation, clinical management, obstructive lung disease, pharmacologic agents, risk factors*

ASTHMA is one of the most common chronic lung diseases that affects persons of all ages and ethnic groups.^{1,2} Estimates suggested that about 300 million people suffer from this disease worldwide,³ with potential increase to 400 million by 2025.⁴ It was also estimated that asthma is responsible for approximately 250 000 annual asthma-related deaths worldwide.⁵

In the United States, more than 22 million persons suffer from asthma.⁶ In 2012, the current and overall lifetime prevalence rates of asthma were found to be 8.3% and 13%, respectively.⁷ The current prevalence was noted to be higher among some subgroups in the United States such as Puerto Rican heritage (18.8%), black non-Hispanic (11.9%), and those who are under poverty level (12.4%).⁷ Moreover, asthma affects children more than adults (9.3% vs 8%), and fe-

males more than males (9.5% vs 7%), although the gender predominance is inverted in children younger than 18 years (boys 10% vs girls 8.6%).⁷ Although asthma prevalence has been increasing, the death rates have significantly declined during the last decade.^{1,8,9} The mortality rate is found to be higher among Puerto Rican heritage and black Americans than among other ethnic groups.^{9,10} Furthermore, the cost of asthma disease in the United States has been computed to be around \$18 billion every year.¹¹ Besides the financial burden of asthma, it negatively affects the patients, their families, and their quality of life.⁶ This article is an overview of asthma disease, with scientific understanding of the pathophysiology, risk factors, diagnosis, and management based on the current guidelines.

DEFINITION

Asthma is a chronic lung disease induced by an inflammation in the airways that leads to bronchial hyperresponsiveness and reversible airflow obstruction.⁶ This results in recurrent symptoms of shortness of breath, chest tightness, wheezing, and coughing, with a dramatic response to bronchodilator therapy.¹²

Asthma is a very old disease and the term “asthma” is originally derived from an ancient Greek word *aazein*, which means “to pant.”¹³ However, it was only acknowledged as a public health problem 4 decades ago.¹²

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PATHOPHYSIOLOGY

Asthma is triggered by either allergic stimuli (eg, pollens, molds, animals, and dust mites) or nonallergic triggers (eg, cold air, exercise, and tobacco smoke).¹⁴ The immune-mediated reaction takes place when type 2 T-helper lymphocytes (Th2) get activated by the stimulus and start producing interleukins (IL-4, IL-5, IL-9, and IL-13), which lead to significant inflammation in the airways by recruiting eosinophils and promoting immunoglobulin E (IgE) production. The results are the cardinal features of asthma (bronchospasm, mucus secretion, and airflow obstruction).^{14,15}

RISK FACTORS

Allergy

The family history of atopy increases the risk of developing asthma more than 3 times, and it is considered to be the most potent risk factor for asthma.^{16,17} However, there is a strong correlation between asthma and both total serum IgE level and the degree of positive skin allergy test.^{18,19} Thus, allergen control is essential in asthma management.²⁰

Air pollution

Polluted air can trigger asthma and increase the risk of exacerbation.²¹ In addition, air pollution, measured by particulate matter and nitrogen dioxide, might be associated with the development of asthma.^{22,23} A large prospective cohort study conducted by Young et al²⁴ showed that air pollution exposure significantly increases the risk of developing wheeze in US women. Moreover, a recent study by Leon Hsu et al²⁵ has linked children's asthma development with prenatal exposure to polluted air during mid-pregnancy.

Obesity

Childhood obesity is considered one of the risk factors for developing asthma in adults.²⁶ Chen et al²⁷ found that sedentary lifestyle and decreased physical fitness level during childhood lead to central obesity, which, in turn, increases the risk of asthma. Therefore,

weight reduction is suggested for obese patients with asthma due to its impact in improving the lung functions.^{28,29}

Respiratory viral infections

Getting infected by respiratory syncytial virus during infancy increases the risk of asthma and recurrent wheeze by more than 4-fold.³⁰ Also, rhinovirus-induced wheeze during early childhood was found to be a predictor of subsequent asthma.³¹

Occupational exposure

Approximately 16% of adult-onset asthma is secondary to occupational exposure.³² Occupational asthma can be induced immunologically by a sensitizer (eg, animal allergens, plants, and insects) or nonimmunologically by an irritant (eg, high concentration of gas, fume, or irritating dust).³³

DIAGNOSIS

The diagnosis of asthma requires a comprehensive medical history and physical examination along with assessing the lung functions. Classic recurrent respiratory symptoms with evidence of reversible expiratory airflow obstruction are pathognomonic features of asthma.³⁴ However, sometimes we might need to proceed with further testing to confirm the diagnosis of asthma or to rule out other diseases that may present with symptoms that mimic asthma (Figure 1).^{12,34}

Medical history

Personal history

Obtaining a detailed medical history is the most valuable step in approaching patients with asthma-like symptoms. Diagnosis of asthma is likely to be made for the first time during childhood and adolescence.³⁵ Asthmatic patients are generally asymptomatic until they get exposed to the trigger, which can be cold air, exercise, weather change, allergens, environmental irritants, or infections; hence, flares occur.³⁶ The key symptoms of asthma include shortness of breath, wheeze, cough, and chest tightness.

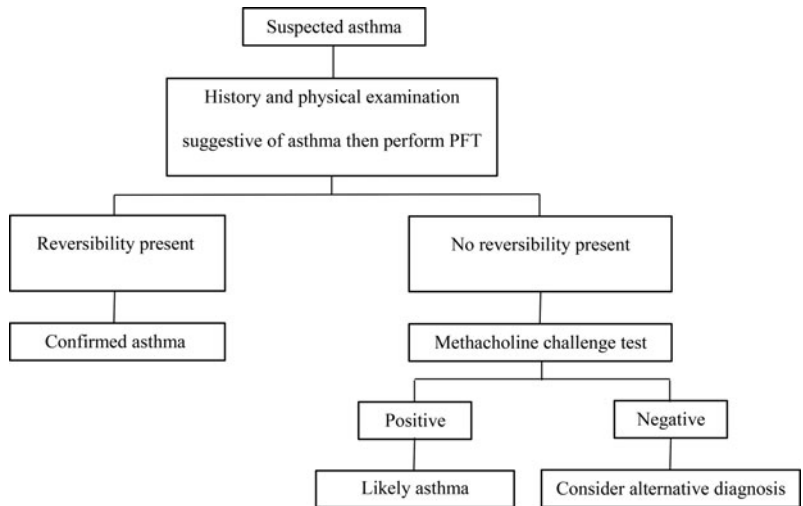


Figure 1. Diagnostic algorithm for patients with asthma-like symptoms. PFT indicates pulmonary function testing.

They last between few minutes to days and resolve spontaneously or with bronchodilator therapy. The variability in the intensity of those symptoms and the recurrent pattern of the exacerbations due to certain exposure are characteristics for asthma.³⁴ Identifying risk factors such as family history and atopic background (eg, seasonal sinusitis, eczema, and allergic conjunctivitis) is also suggestive of carrying the diagnosis of asthma. Furthermore, the comprehensive history might be helpful in diagnosing other diseases such as allergic sinusitis and gastroesophageal reflux, which can aggravate asthma and lead to poor symptom control.³⁷

Occupational history

Work history must be obtained for all patients with asthma. Work-related asthma (WRA) has to be considered when the asthma symptoms flare up during work hours and subside on holidays and vacations. It can be divided to 2 categories: work-exacerbated asthma (the patient has well-known preexisting asthma disease, but the symptoms are worsened by triggers in the workplace) and occupational asthma (the asthma is caused by work itself). In turn, the occupational asthma is classified into sensitizer-induced or irritant-induced asthma (Figure 2).³⁸

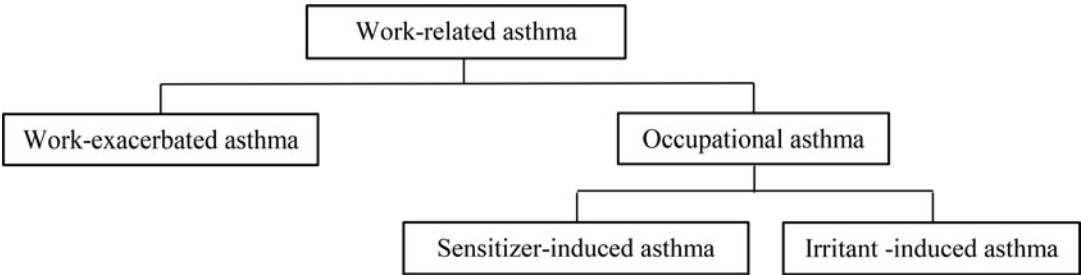


Figure 2. Work-related asthma classification.

Physical examination

Physical examination is very supportive in making diagnosis of asthma, although it can have completely normal findings. The presence of expiratory wheeze with prolonged exhalation suggests airflow obstruction. The maneuver of enhancing the wheezing with forced exhalation is neither sensitive nor specific for asthma.³⁹ HEENT (head, eyes, ears, nose, and throat) examination is essential in all asthmatic patients to look for signs related to asthma such as sinus tenderness, nasal polyps, and postnasal drip.³⁷ In addition, eczema and dermatitis can be seen in asthmatic patients as concurrent atopic conditions.¹⁴ On the contrary, diffuse crackles in chest auscultation, jugular venous distension, or clubbing suggest alternative diagnosis.³⁷

Pulmonary function testing

Spirometry

Expiratory airflow obstruction in asthma differs with time based on the exposure to the triggers and the effectiveness of the treatment. This variable airflow limitation is a characteristic of asthma.³⁴ Spirometry is the best available tool to objectively assess the airflow obstruction and to estimate the bronchial responsiveness to the treatment. Thus, this test is recommended for all asthmatic patients to confirm the diagnosis.³⁷ Spirometry has to be accomplished on the basis of proper protocols, which can be done either at the physician's office or in the pulmonary function laboratory.⁴⁰ Before performing the test, short-acting β_2 -agonists (SABAs) and long-

acting β_2 -agonists (LABAs) should be on hold for at least 4 and 12 hours, respectively.⁴⁰

The 2 most important measurements provided by spirometry are the forced vital capacity (FVC), which is the maximal amount of the exhaled air following deep breath, and the forced expiratory volume in 1 second (FEV₁), which is the portion of the expired volume in the FVC maneuver during the first second of exhalation.⁴⁰ To achieve accurate results, the expiration has to be forced and completed as possible. FEV₁ is by far the best and the most standardized measurement to assess the airflow limitation.¹² The calculated FEV₁/FVC ratio is normally above 0.75 to 0.8 in adults and above 0.9 in children. Thus, the airflow obstruction is suggested when this ratio drops below the lower normal limit.³⁴ The hallmark of the spirometry in asthma is the presence of the reversibility, which is characterized by a significant improvement in the airflow post-bronchodilator administration. Reversibility definition is an increase in FEV₁ and/or FVC from baseline by at least 12% and 200 mL after inhaling a bronchodilator or after 4 weeks of anti-inflammatory therapy.^{34,41}

In addition, the spirometry provides illustrated graphs (volume-time curve and flow-volume loop), which show the relationship between airflow, volume, and time. Typically, in asthma, there is scooping in the expiration curve of the flow-volume loop suggestive of airflow limitation, which is reversed after bronchodilator use (Figure 3).⁴²

Lung volumes and diffusing capacity

Measurements of lung volumes and diffusing capacity are advanced pulmonary

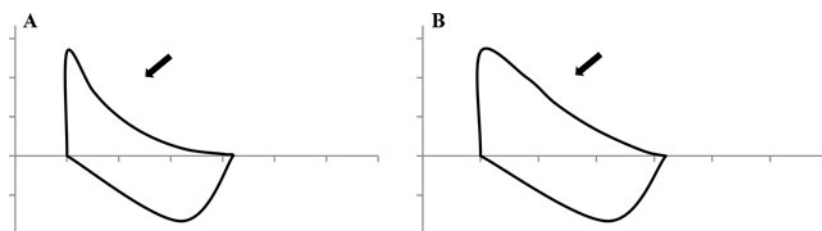


Figure 3. Flow-volume loop in asthma. A, Pre-bronchodilator administration. B, Post-bronchodilator administration.

function testing and not required for diagnosis of asthma. Lung volume test refers to measuring the volume of air inside the lungs by using body plethysmography, helium dilution, or nitrogen washout.⁴³ Total lung capacity, which is the total volume inside the lungs at the end of maximal inspiration, is usually normal in asthmatic patients. However, it can be elevated in severe asthma because of air trapping.¹² On the contrary, single-breath diffusing capacity of the lungs for carbon monoxide (DLCO) computes the ability to transfer gas from the air in the alveoli to the blood in the pulmonary capillaries. DLCO in general does not change in asthma, but it might increase in some cases.⁴⁴

Peak expiratory flow monitoring

Peak expiratory flow (PEF) is the highest expiratory flow that can be reached during forced exhalation.⁴⁰ It is measured during spirometry, but it also can be easily self-estimated by a small and portable device. PEF monitoring is very helpful in diagnosing the occupational asthma by asking the patient to track the PEF inside and outside the workplace. Diurnal PEF variation more than 20% or an increase from baseline at least 20% or 60 L/min post-bronchodilator administration supports the diagnosis of asthma. In addition, PEF monitoring can be used to assess the patient's response to the medical therapy. Yet, it is still not as reliable and effective as spirometry.^{14,42}

Challenge testing

Challenge testing is recommended to confirm the diagnosis of asthma for those patients who have a suggestive history of asthma but normal spirometry test. Asthma disease is characterized by airway hyperresponsiveness (AHR) to environmental stimuli. Hence, challenge test is conducted to assess the tendency of the airways to develop bronchoconstriction by exposure to a provocative trigger.¹² The test can be performed by either direct or indirect stimuli. The direct challenges (eg, methacholine or histamine) induce bronchospasm by directly affecting the

smooth muscles in the bronchi, whereas the indirect stimuli (eg, cold air, exercise, mannitol, or hypertonic saline inhalation) promote an inflammatory process in the airways, and, in turn, smooth muscles get affected and contracted.^{12,45-48}

Methacholine challenge testing

Methacholine challenge testing (MCT) is the most common provocative method to assess bronchial hyperresponsiveness. It must be performed on the basis of a strict protocol in a well-equipped pulmonary laboratory.¹⁴ The test is considered positive when FEV₁ drops by more than 20% post-nebulized methacholine administration. The dose of methacholine should be administered in doubling concentrations until FEV₁ decreases at least 20% or the dose has reached the maximum of 16 mg/mL. Then, the severity of AHR is determined on the basis of the provocative concentration of methacholine (PC₂₀), which leads to 20% decrease in FEV₁ (Table 1).⁴⁸

MCT has a very high sensitivity for asthma, but it might be falsely positive in certain diseases such as allergic rhinitis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and congestive heart failure.⁴² In addition, MCT should not be performed in the presence of any of the contraindications that are listed in Table 2.⁴⁸

Exercise challenge testing

Exercise challenge testing (ECT) is less common than MCT. However, it helps establish

Table 1. Methacholine Challenge Testing Interpretation

Test Interpretation	PC ₂₀ Level, mg/mL
Normal	>16
Borderline AHR	4-16
Mild AHR	1-4
Moderate to severe AHR	<1

Abbreviations: AHR, airway hyperresponsiveness; PC₂₀, provocative concentration of methacholine that causes 20% drop in FEV₁.

Table 2. Contraindications to Methacholine Challenge Testing

Absolute Contraindications	Relative Contraindications
Severe airflow obstruction (FEV ₁ <50% or <1.0 L)	Moderate airflow obstruction (FEV ₁ <60% or <1.5 L)
Myocardial infarction or stroke during the last 3 mo	Inability to perform acceptable spirometry
Uncontrolled hypertension (BP >200/100)	Pregnancy or breast-feeding
Aortic aneurysm	Use of cholinesterase inhibitor medication

Abbreviations: BP, blood pressure; FEV₁, forced expiratory volume in 1 second.

the diagnosis of exercise-induced bronchoconstriction (EIB) for asthmatic patients whose symptoms occur during or after the exercise. In addition, ECT is recommended to assess the work ability of those who have lifesaving jobs (eg, military, firefighting, and police) and complain of symptoms suggestive of EIB.⁴⁸ The test can be performed by either treadmill or bicycle ergometer, followed by serial spirometry during the next half an hour post-exercise cessation. EIB is suggested when FEV₁ drops more than 15%.⁴⁸ EIB might be further graded into mild, moderate, and severe, based on the decrease in FEV₁ (15%-25%, 25%-40%, and >40%, respectively).³⁷

Imaging

Chest radiography and chest computed tomography are not required for diagnosis of asthma; however, they may help in excluding asthma mimics such as congestive heart failure, bronchiectasis, vascular anomalies, and lung cancer.^{12,37} New technologies, turbo-inversion recovery-magnitude magnetic resonance imaging and nuclear imaging dependent on glutathione, have been recently studied to estimate the airway inflammation and measure the lung edema in asthma.^{49,50} Further studies are necessary to validate the role of such advanced technologies.

MANAGEMENT

The currently used medications for asthma are categorized into quick-relief and long-term control drugs, based on their overall role in asthma treatment. The quick-relief medications are SABAs, short-acting muscarinic

antagonists (SAMAs), and systemic corticosteroids. The long-term control drugs include inhaled corticosteroids (ICSs), combination of LABAs with ICSs, leukotriene modifiers (LTMs), anti-IgE therapy, methylxanthines, and oral corticosteroids (Table 3).^{6,51}

Pharmacologic agents

β₂-agonists agents

β₂-Agonists are the standard of care in treating asthma. This group of medications has been used for a long time. It started with nonselective β-adrenergic agonists such as isoproterenol, and subsequently selective β₂-agonists, such as albuterol and terbutaline, were introduced to minimize the side effects of β-agonists.⁵² By binding with β₂ receptors in the airways, β₂-agonists enhance the intracellular cAMP (cyclic adenosine monophosphate) production, which, in turn, leads to airway smooth muscle relaxation.⁵³ β₂-Selective agonists are either short-acting (onset of 5 minutes, peak of 30-60 minutes, and duration of 4-6 hours) or long-acting (onset of 5-20 minutes, peak of 3-5 hours, and duration of 12 hours); both of them are delivered by aerosol.^{51,54} Side effects of β₂-adrenergic agonists are minimal due to direct inhalation to the bronchi. Adverse events include tremor (stimulation of skeletal muscle β₂-receptors), tachycardia and arrhythmias (stimulation of cardiac β₂-receptors), transient minimal hypoxemia during severe asthma exacerbation (due to decompensation of vasoconstriction in the hypoventilated lung segments), and rarely hypokalemia, hypomagnesemia, and hyperglycemia. In addition, long-term use of

Table 3. Pharmacologic Agents for Asthma Treatment

Quick-Relief Medication			Long-term Control Medication				Phosphodiesterase Inhibitor
SABA	SAMA	ICS	LABA	LTM	Anti-IgE		
Albuterol Levalbuterol Pirbuterol	Ipratropium	Beclomethasone Budesonide Ciclesonide Flunisolide Fluticasone Mometasone Triamcinolone	Salmeterol Formoterol Vilanterol Arformoterol	Zileuton Montelukast Zafirlukast Pranlukast	Omalizumab	Theophylline	

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; LTM, leukotriene modifier; SABA, short-acting β_2 -agonist; SAMAs, short-acting muscarinic antagonist.

LABAs might cause receptor desensitization and lesser bronchodilator response.⁵⁴

SABAs are the fastest rescue therapy for bronchoconstriction; therefore, they are the cornerstone in treating exacerbations of asthma. It is recommended to be administered on as-needed basis or prior to known trigger exposure such as exercise.⁵¹ Albuterol, lev-albuterol, and pirbuterol are common SABA medications. However, albuterol is most frequently used worldwide (named as salbutamol outside the United States). The formulation of albuterol contains both *R*-isomer and *S*-isomer; the latter is the culprit for the side effects. Hence, levalbuterol, only the *R*-isomer part of albuterol, was developed to decrease the adverse reactions.^{55,56}

LABAs are characterized with prolonged activity of more than 12 hours. The LABA group includes salmeterol, formoterol, arformoterol, and vilanterol. Formoterol has a faster onset of action than salmeterol, 5 minutes versus 15 to 20 minutes, respectively.⁵¹ Despite being potent bronchodilators, LABAs must not be used as monotherapy for asthmatic patients because of increased asthma-related deaths with prescribing LABA alone, especially in the African American subpopulation.⁵⁷ For this reason, the US Food and Drug Administration is adding a black box warning on all medications that include LABAs. On the basis of that, it is recommended to prescribe LABA alone with concomitant ICSs to achieve long-term asthma control.⁶ Combinations of ICSs and LABAs are available in the market under different brand names such as Symbicort (budesonide with formoterol), Advair (fluticasone with salmeterol), BREO (fluticasone with vilanterol), and Dulera (mometasone with formoterol) (Table 4). This combination therapy should be considered when ICS alone fail to control asthma.⁶

Inhaled corticosteroids

ICSs are considered to be the first-line treatment in the long-term control of asthma. They suppress the airway inflammation by reversing histone acetylation and recruiting histone deacetylase and, in turn, inhibiting the

Table 4. Inhaled Corticosteroids and Their Combinations

Generic Names	Brand Names of ICS and LABA Combination			
	Alone	With Formoterol	With Salmeterol	With Vilanterol
Beclomethasone	QVAR			
Budesonide	Pulmicort	Symbicort		
Ciclesonide	Alvesco			
Flunisolide	AeroBid			
Fluticasone	Flovent		Advair	BREO
Mometasone	Asmanex	Dulera		
Triamcinolone	Azmacort			

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist.

inflammatory gene transcription.^{58,59} Besides improving the pulmonary functions and asthmatic symptoms, ICSs lower asthma exacerbations and asthma-related hospitalizations by approximately 50% compared with placebo or SABA alone.⁶⁰⁻⁶² In addition, the regular use of low-dose ICSs was found to decrease the risk of asthma-related deaths.⁶³ Moreover, airway inflammatory markers such as sputum eosinophils and exhaled nitric oxide levels were noted to fall post-ICS course; results of which might be helpful to assess the response to ICS treatment.^{64,65}

All patients who have persistent asthma should be prescribed at least ICSs on daily basis. In general, it is recommended to start ICSs for any patient with one of the following symptoms: asthmatic symptoms more than twice a month, nighttime symptoms more than once a month, and high risk of exacerbations (eg, low FEV₁, intensive care unit admission for asthma attack, or use of oral corticosteroids in the previous year).³⁴ The ICS group includes budesonide, fluticasone, mometasone, beclomethasone, ciclesonide, and triamcinolone (Table 4).⁵¹

The side effects of ICSs are very minimal compared with systemic corticosteroids. The risk of glaucoma and cataract might rise with the use of ICSs.^{66,67} Although one observational study by Israel et al⁶⁸ showed an elevated risk of bone loss with ICS use, a meta-analysis of several studies revealed

no association between ICSs and changes in bone mineral density.⁶⁹ On the contrary, laryngeal and pharyngeal adverse reactions (eg, sore throat, oral candidiasis, hoarseness, and coughing) are not uncommon with the use of ICSs.⁷⁰ Rinsing the mouth post-ICS delivery and using a valved-holding chamber can minimize those side effects.

Anticholinergic agents

Anticholinergic agents are not as effective in asthma as they are in COPD. They work as bronchodilators by blocking the action of acetylcholine in airway smooth muscles and leading to bronchial muscle relaxation. They are categorized into SAMAs such as ipratropium and long-acting muscarinic antagonists (LAMAs) such as tiotropium.

Unlike COPD, SAMAs are not recommended as a rescue therapy for asthmatic patients. This is likely because SAMAs take longer (20-30 minutes) to launch than SABAs, besides the decreased role of cholinergic tone in asthmatic bronchospasm.^{12,51} However, SAMAs might be considered in moderate to severe asthma exacerbations in the emergency department settings, β_2 -agonists intolerance, and β -blocker-induced asthma attack.^{6,51,71} On the contrary, randomized trials failed to show any benefits of combining SAMAs with SABAs compared with SABA alone for chronic asthma.⁷² Yet, the use of LAMAs was found to be beneficial in chronic uncontrolled asthma as

an add-on treatment, but further studies are needed before they become approved.⁷³⁻⁷⁵

Leukotriene modifiers

LTMs have a weak bronchodilator effect and result in some reduction in symptoms and exacerbations of asthma.⁷⁶ They are less effective than ICSs or LABA and rarely used as monotherapy.¹² LTMs include 5-lipoxygenase inhibitors (eg, zileuton), which impair leukotriene synthesis, and cysteinyl leukotriene-1 receptor antagonists (LTRAs) (eg, montelukast, zafirlukast, and pranlukast), which block the final destination of leukotriene.⁶ LTMs are administered orally and can be considered in treating aspirin-sensitive asthma, mild persistent asthma, and exercise-induced asthma.⁷⁷⁻⁷⁹ Liver function testing has to be monitored with the use of zileuton.

Phosphodiesterase inhibitors

Sustained-release theophylline has a moderate bronchodilator effect with mild anti-inflammatory properties. Theophylline is not commonly used because of its narrow ther-

apeutic range. It is administered orally for poorly controlled asthma. Side effects include arrhythmia, seizure, anorexia, and palpitation.^{6,12}

Anti-IgE therapy

Omalizumab is an anti-IgE monoclonal antibody that prevents the effect of IgE on immune cells. Thus, it reduces asthma exacerbations and provides better control.⁸⁰ It is given subcutaneously every 2 to 4 weeks for moderate to severe uncontrolled asthma with elevated IgE level.⁵¹ Anaphylaxis can occur post-first doses; for this reason, short-term observation is recommended after the first 3 injections.

Management of asthma exacerbation

Asthma exacerbation is defined by worsening in the patient's symptoms from baseline. It is likely caused by exposure to a known trigger. The patient can be treated as outpatient if the symptoms are mild, but acute care facility referral is required in case of outpatient treatment failure, recent severe exacerbation,

Table 5. Classification of Asthma Severity^a

Components of Severity	Intermittent Asthma	Persistent Asthma		
		Mild	Moderate	Severe
Impairment				
Symptoms	≤2 d/wk	>2 d/wk but not daily	Daily	Throughout the day
Nighttime awakenings	≤2×/mo	3 to 4×/mo	>1×/wk but not nightly	Often 7×/wk
SABA use for symptom control	≤2 d/wk	>2 d/wk but not daily	Daily	Several times per day
Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Lung function (between exacerbations)	FEV ₁ /FVC NL	FEV ₁ /FVC NL	FEV ₁ /FVC reduced 5%	FEV ₁ /FVC reduced >5%
	FEV ₁ >80%	FEV ₁ >80	FEV ₁ 60%-80%	FEV ₁ <60%
Risk				
Exacerbations	0-1/y	≥2/y	≥2/y	≥2/y

FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; NL, normal; SABA, short-acting β₂-agonist.

^aFrom Lugogo et al.¹²

Table 6. Stepwise Approach in Asthma Management^a

Step up if needed (first, check adherence, environmental control, and comorbid conditions)		
Step down if possible (and asthma is well controlled at least 3 mo)		
	Preferred	Alternative
Persistent asthma (daily medication)	Step 6 High-dose ICS + LABA + oral corticosteroid AND Consider omalizumab for patients who have allergies	
	Step 5 High-dose ICS + LABA AND Consider omalizumab for patients who have allergies	High-dose ICS + LABA + tiotropium
	Step 4 Medium-dose ICS + LABA	Medium-dose ICS + LTRA, theophylline, or zileuton Medium-dose ICS + tiotropium Low-dose ICS + LTRA, theophylline, or zileuton
	Step 3 Medium-dose ICS OR Low-dose ICS + LABA	
	Step 2 Low-dose ICS	Cromolyn, nedocromil, LTRA, or theophylline
Intermittent asthma	Step 1 SABA as needed	Quick-relief medication for all patients (SABA as needed)
Patient education and environmental control at each step		

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting β_2 -agonist; LTRA, leukotriene-1 receptor antagonist; SABA, short-acting β_2 -agonist.
^aFrom National Asthma Education and Prevention Program⁶ and Lugogo et al.^{1,2}

current oral corticosteroid use, noncompliance, or psychiatric disorder.¹²

SABAs and systemic corticosteroids are first-line treatment of asthma attacks. Patients can receive repeated or continuous SABA doses until symptoms improve. Adding ipratropium to SABAs at the initiation of management can be considered in moderate to severe cases. Systemic corticosteroids can be administered intravenously or orally with similar efficacy.^{81,82} Magnesium sulfate, a smooth muscle relaxant, can be used intravenously for severe asthma flares to decrease admission rates to the hospital.⁸³ Life-threatening exacerbations may require advanced treatments including heliox therapy, noninvasive positive pressure ventilation, and oral intubation with mechanical ventilation.

Treatment approach

The current guidelines recommend assessing the severity of asthma (Table 5)^{6,12} and then following a stepwise approach to adjust the medications for best control of symptoms. The treatment plan can be escalated or deescalated in case of deterioration or improve-

ment in the patient's condition, respectively (Table 6).^{6,34}

SUMMARY

Asthma is a chronic pulmonary disease characterized by recurrent respiratory symptoms due to a variable bronchospasm in response to a provocative trigger. History and physical examination are essential to raise the suspicion of asthma. Spirometry confirms the diagnosis by the presence of airflow obstruction pattern, which is significantly reversed after bronchodilator use. Challenge testing might be needed in case of normal spirometry. Management includes quick-relief and long-term control medications. SABAs and systemic corticosteroids are the cornerstone in managing the asthma attack, whereas ICSs are the first-line treatment option for long-term control. Stepwise approach is recommended to adjust the medical therapy, which includes LTMs, combinations of ICSs with LABAs, and anti-IgE. Patient's education, proper teaching to use inhalers, established follow-up plan, and compliance monitoring are the key features to achieve better asthma control.

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