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Asthma: An Evolving Challenge in Respiratory Health

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ABSTRACT :

Asthma is a chronic inflammatory airway disease characterized by variable airflow obstruction, bronchial hyperresponsiveness, and airway remodeling. It involves a complex interplay between genetic and environmental factors, triggering inflammatory responses mediated by mast cells, eosinophils, and various chemical mediators. Clinical manifestations include coughing, wheezing, chest tightness, and shortness of breath, often exacerbated by allergens, infections, physical activity, and environmental pollutants.

Diagnosis is based on a thorough history, physical examination, and confirmatory lung function tests such as spirometry. Management strategies include avoidance of triggers, pharmacological therapy, and patient education. Anti-asthmatic medications are categorized into bronchodilators (β2-agonists, anticholinergics, and methylxanthines), anti-inflammatory agents (inhaled and systemic corticosteroids, mast cell stabilizers, leukotriene antagonists), and targeted biologics such as anti-IgE monoclonal antibodies.

Bronchodilators provide rapid symptom relief by relaxing airway smooth muscles, while antiinflammatory agents are essential for long-term control. Corticosteroids remain the cornerstone of asthma management due to their potent anti-inflammatory effects. Leukotriene receptor antagonists and mast cell stabilizers serve as adjuncts for mild to moderate cases. Prevention focuses on early intervention, regular monitoring, adherence to action plans, and lifestyle modifications including vaccination and exercise. Although asthma is not curable, appropriate and timely treatment significantly improves quality of life and disease outcomes.

❖ Introduction:

Asthma is a chronic disease that affects the airways of lungs. Air-ways are the breathing tubes that carry the air in &out of lungs. When Patient is suffering from Asthma, airways become swollen[1].

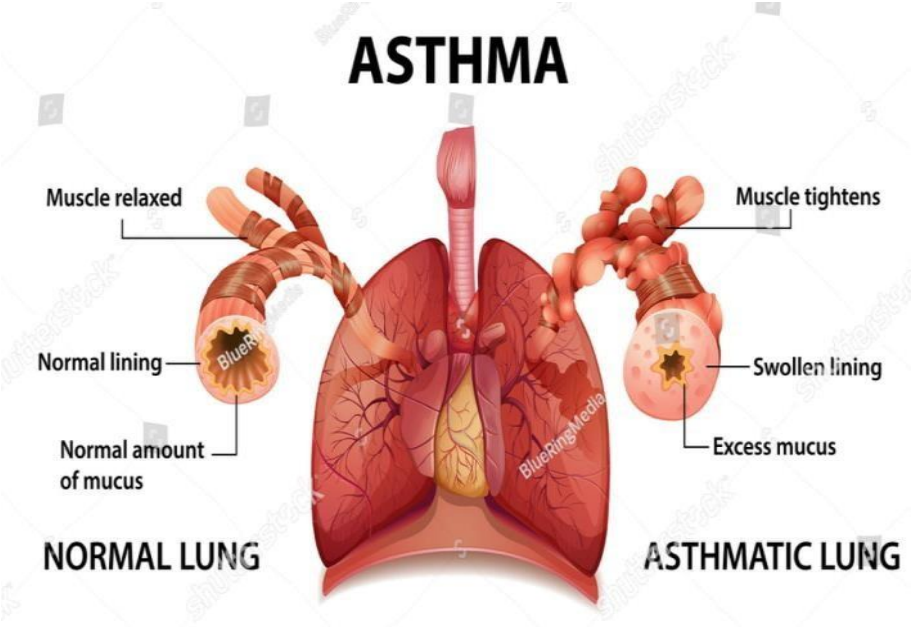
This swelling (inflammation) causes the airways to make thick, sticky secretions called Mucus. Asthma also causes the muscles in and around airways to get very tight or constrict. The swelling, mucus and tight muscles can make air ways narrower than normal and it becomes very hard for to get air into and out of lungs [2].

An “asthma attack” describes very severe symptoms. During an Asthma attack, may breathe so fast that may have a hard time talking. Coughing, wheezing and chest tightness can cause to feel anxious or scared. This may make feel even more short of breath [3].

Asthma is characterized by:

- Airway inflammation: The airway lining becomes red, swollen and narrow.
- Airway obstruction: The muscles encircling the airway tighten causing the airway to narrow making it difficult to get air in and out of the lungs.
- Airway hyper-responsiveness: The muscles encircling the airway respond more quickly and vigorously to small number of allergens and irritants.

It is a condition in which a person's airways become inflamed, narrow, swell and produce extra mucus, which makes it difficult to breathe. It is defined as a chronic inflammatory disease of the airways. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and/or coughing that can vary overtime and in intensity [6].



History of Asthma:

The earliest recorded reference to respiratory distress – a disorder characterized by "noisy breathing" is found in china in 2600 BC. The Babylonian "Code of Hammurabi" recorded symptoms of breathlessness: "if a man's lungs pant with his work."(1792-1750BC). Hippocrates (~400BC) was the first to use the term "Asthma" (Greek for "wind" or "to blow") for panting and respiratory distress. He is considered to be the physician who identified the relationship between the environment and respiratory disease correlating climate and location with illness. Some suggest he was the first allergist. When Alexander the Great invaded India, smoking the herb stramonium (an anticholinergic agent related to ipratropium and tiotropium currently used in inhalers) was used to relax the lungs. Roman doctors described asthma as gasping and the inability to breathe without making noise. "If the breath becomes difficult from running or any other work, it is called asthma," they stated. Pliny the Elder (c. 50 AD) noted that pollen caused respiratory problems and suggested using "ephedra," the precursor to ephedrine, in red wine as a treatment for asthma. Unfortunately, he also said that eating 21 millipedes steeped in honey and drinking the blood of wild horses might be beneficial. As a treatment for asthma, the Jewish Talmud (c. 200–500 AD) recommended "drinking three weights of hiltith," a resin belonging to the carrot family. The Egyptian's son was treated for asthma by Maimonides (1135–1204 AD), a Jewish philosopher and Saladin's physician. Rest, a clean environment and personal hygiene, avoiding opium, drinking a little wine, and following a particular diet were all recommended in his "Treatise on Asthma." Fruit, milk, nuts, chilly vegetables, and legumes (peanuts belong to this family) were prohibited, but "the soup of fat hens" was seen as healthy. In order to promote coughing and expectorate mucus, tobacco was brought to Europe from America in the 1500s [4].

The Incas in South America used a dried leaf that resembled cocaine to cure asthma, and the Aztecs in Central America consumed a plant that contained ephedra to remove phlegm. Arsenic was given for respiratory ailments in the 1800s. Allergy immunotherapy was first used to treat asthma in the early 1900s.

In the 1940s and 1950s, asthma medications included injections of epinephrine (adrenaline) and pills or suppositories of aminophylline. Oral combinations were the mainstay of long-term treatment in the 1960s. Rescue agents included inhaling isoproterenol (Isuprel) and epinephrine (Primatene). For severe conditions, oral prednisone has been and is still recommended.

There have been numerous advancements in treatment since the founding of the Allergy and Asthma Medical Group and Research Center in 1969. Both short- and long-acting versions of inhaled bronchodilators are available, and they are less likely to cause cardiac stimulation. By focusing on the underlying inflammation, inhaled corticosteroids reduce the possibility of cortisol side effects that are present in tablet and liquid form. New asthma treatments that could help patients even more are presently being intensively assessed by our clinical research department.

Asthma may also be more common in people with allergies. Although it can occur in adults as well, this kind of asthma usually starts in youngsters.

Pollen from grass, trees, and weeds, mildew, cockroach droppings, dog or cat fur, and dust mites are common allergens (items that cause allergies). These may result in runny nose, itchy eyes, wheezing, and sneezing.

If the lungs are, asthma may also result from recurrent sinus or lung infections. Wheezing or shortness of breath episodes caused by infections can last longer than those caused by allergies. Indeed, the most frequent cause of asthma attacks severe enough to prevent attendance at work or school is respiratory infections [5].

❖ Types of Asthma:

The different types of Asthma are:

(1)Adult-Onset Asthma:
While asthma typically developed during childhood, it can also develop as you get older in adulthood. Adult-onset asthma may occur because of certain chemicals and other irritants that you might be exposed to frequently in the workplace.

Even if you did not show any symptoms of asthma in your childhood, you can develop this disorder later in life. Unlike asthma in children, this disorder can be more grave in adults. The symptoms are more persistent and not easy to control. Asthma can also be fatal for adults.

Asthma happens to adults chiefly because of being exposed to harmful substances for long periods. Allergies too are responsible for adult-onset asthma.

(2)Childhood Asthma:
If a child is born premature, then the baby could contract asthma. The lungs do not develop completely and special treatment such as being put on ventilation to aid with breathing.

- Triggers of childhood asthma.
- Catching a cold, flu, sinus infections or pneumonia.
- Exposure to allergens like dust, mould, cockroach excreta, fur or feathers from pets.
- Coming into contact with irritants such as chemicals, pollutants, smoke, perfume spray.
- Stress or anxiety over exams and assignments.

(3)Allergic Asthma:
There exists a link between asthma and allergies. But research is ongoing to understand the relation between the two. Not everyone prone to allergies gets asthma. But very often, an asthma attack is preceded by a severe allergic reaction. Allergens such as pollens from flowers, dust particles, particulate matter present in the air can first trigger an allergy, which then progresses to an asthma attack.

(4)Non-Allergic Asthma:
This kind of asthma results from exposure to irritants and substances that do not provoke your immunity system to react to foreign bodies by producing antibodies. Objects like dust, pollutants, chemicals or a change in temperature or humidity can prompt the symptoms of asthma.

(5)Exercise-induced Asthma:
Asthma attacks can come after a bout of exercise or any strenuous physical activity. This is called Exercise-induced Bronchoconstriction (EIB). This happen when there is a temperature change inlungs or loss of fluids triggered by Exercise. Person may begin to notice the symptoms of asthma within 3 or 4 minutes after starting your exercise routine and they may continue up to 15 minute after you finish. The symptoms can be worse in people who are out of shape. Moreover, if you exercise when the pollution level has shot up, or there is too much chlorine in the water where you are swimming, then your asthma could act up.

(6)Occupational Asthma:
Occupational asthma is another type of asthma that can be directly related to your working environment.

Something you are exposed to at your place of work can irritate your already sensitive airways to cause the symptoms of asthma to show up. People who breathe in industrial fumes, odor from chemicals, spices in spice packaging factories, wood shavings, paint particles or cleaning products for protracted periods can be victim of asthma. Here are some professions where people are at risk:-

- Bakers
- Manufactures of drugs
- Metalworkers

- Carpenters
- Manufacturers of detergents
- Millers
- People who produce objects made of plastic.

(7)Bronchial Asthma:
This is the commonest type of asthma. Bronchial asthma is just another term for asthma. And you get this disorder when your bronchial tubes get constricted because of the accumulation of mucous.

(8)Nocturnal Asthma:
Also called night-time asthma, this is another prevalent type of this disorder. People who have contracted nocturnal asthma witness the symptoms usually at night. Certain factors such as the airways cooling down once you settle in for the night, a reclining position that constricts the bronchial tubes, a change in your hormone secretion triggered by your circadian rhythm or heartburn in the aftermath of dinner can lead to an asthma attack.

It has been observed that most of the fatalities caused by asthma happen at night. So the people who have night-time asthma need to be extra cautious.

(9)Seasonal Asthma:
People with this kind of asthma suffer flare-ups only during certain times of the year such as during spring when pollen floats about in the air or winter when temperature plummets and a person contracts a head cold. Most people who have been diagnosed with seasonal asthma do not witness the symptoms during the rest of the year.

(10)Severe Asthma:
A very small percentage (nearly 4%)of all people who have asthmaarediagnosedwith severeasthma.This kind of asthma does not respond well to medication. They need a special kind of medicine called biologics to manage their symptoms.

Many different types of asthma are triggered by different factors. Once you identify your type, you can handle the symptoms and keep asthma in check with proper measures [7].

❖ Epidemiology of Asthma:

- In many countries the prevalence of asthma is increasing.
- This increase, with its accompanying allergy, is particularly in children and young adults where this disease may affect up to 15% of the population.
- Asthma being commoner in more developed countries [8].

The recent substantial increase in the reported prevalence of asthma worldwide has led to numerous studies of the prevalence and characteristics of this condition [9].

Foremost among these are 2 major international initiatives that have collected data using validated questionnaires, one among children, the International Study of Asthma and Allergies in childhoodand the other among young adults, the European Community Respiratory Health Survey. Follow-up investigations for both of these studieshave examined temporal trends within and across populations. During a mean of 7 years following phase 1 of the International Study of Asthma and Allergies in childhood, which in most participating countries was conducted between 1991 and 1993, the prevalence of asthmawas stable or decreased in some areas of the world but increased substantially in many other areas, especially among children 13-14 years of age [11].

Cross-sectional population-based studies such as these are highly dependent on recognition of symptoms, so they do not necessarily reflect the true heterogeneity of asthma. However, a wide variation inn prevalence rates has been documented: studies of both children and adults have revealed low prevalence rates (2%-4%) in Asian countries (especially China and India) and high rates (15%-20%) in the United Kingdom, Canada, Australia, New Zealand and other developed countries [12].

Local and national studies have also provided insights into the epidemiology of exacerbations of asthma. For example, epidemics of asthma exacerbations in Barcelona, Spain, were eventually linked to exposure to atmospheric soybean dust released during cargo handling at the local port [13].

Complementing these cross-sectional studies are longitudinal epidemiologic studies in a variety of populations and countries, which have allowed examination of risk factors predicting the development, persistence, remission or relapse of childhood asthma. One such population-based birth cohort study in Dunedin, New Zealand, which had a high retention rate, examined outcomes of childhood asthma at age 26 years [14].

Female sex, airway hyperresponsiveness in mid and later childhood, and sensitization to house dust mites were all significantly and independently related to the likelihood of persistence of childhood asthma to early adulthood. Early age of onset of wheezing symptoms was predictive of relapse after remission, as were airway hyperresponsiveness and allergy to house dust mites. That study and others have clearly demonstrated the tracking of characteristics of asthma from childhood to adulthood, including severity and impairment of lung function.

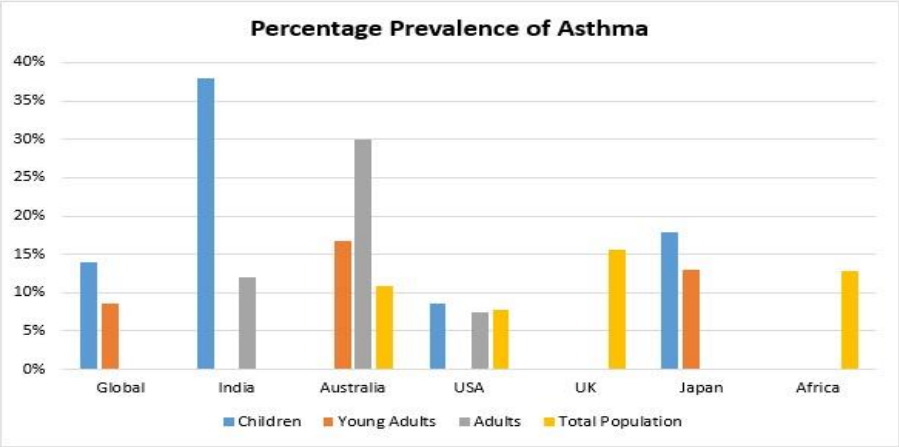


Fig 2. Asthma Prevalence by Region and Age Group

- In the United States Asthma affects an estimated 15-18 million persons.
- Of these 5 million are children less than 18years.
- Over 10 million days are missed from school due to asthma.
- Over 200,000 hospitalizations resulting in 1.9 million days of inpatient care.
- 1.7 times increase risk of learning disability.

❖ Classification of Anti-Asthmatic Drugs:

(1)Bronchodilators:

a) Beta-sympathomimetics:

- Salbutamol (Albuterol)
- Terbutaline
- Salmeterol
- Formoterol

b) Methylxanthines:

- Theophylline
- Aminophylline
- Cholinetheophyllinate

c) Anticholinergics:

- Ipratropium bromide
- Tiotropium bromide

(2)Leukotriene Antagonists:

- Montelukast
- Zafirlukast

(3)Mast cell Stabilizers:

- Sodium cromoglycate
- Ketotifen **(4)Corticosteroids:**

a) Inhalational:

- Beclomethasone
- Budesonide
- Fluticasone

b)Systemic:

- Hydrocortisone
- Prednisolone

(5)Anti-IgE antibody:

- Omalizumab

(6) Mast cell stabilizers:

- Cromoglycate [15]

❖ Pathophysiology of Asthma:

Asthma is a complex condition where interaction of genetics and environment occurs involving many inflammatory cells which release a wide range of variety of mediators [16].

These mediators act on the cells of the airway leading to smooth muscle contraction, mucus hyper secretion, plasma leakage, edema, activation of cholinergic reflexes and activation of sensory nerves, which lead to amplification of the continuing inflammatory response.
The chronic inflammation leads to structural changes, including sub-epithelial fibrosis and smooth muscle hypertrophy and hyperplasia. This late process is less easily reversed than the acute changes and might end up with airway remodeling [16].

Bronchoconstriction:

In asthma, the dominant physiological event leading to clinical symptoms is airway narrowing and a subsequent interference with airflow. In acute exacerbations of asthma, bronchial smooth muscle contraction (bronchoconstriction) occurs quickly to narrow the airways in response to exposure to a variety of stimuli including allergens or irritants [17]. Allergen-induced acute bronchoconstriction results from an IgE-dependent release of mediators from mast cells that includes histamine,tryptase, leukotrienes, and prostaglandins that directly contract airway smooth muscle[18].

Airway edema:

As the disease becomes more persistent and inflammation more progressive, other factors further limit airflow. These include edema, inflammation, mucus hypersecretion and the formation of inspissated mucus plugs, as well as structural changes including hypertrophy

Ss

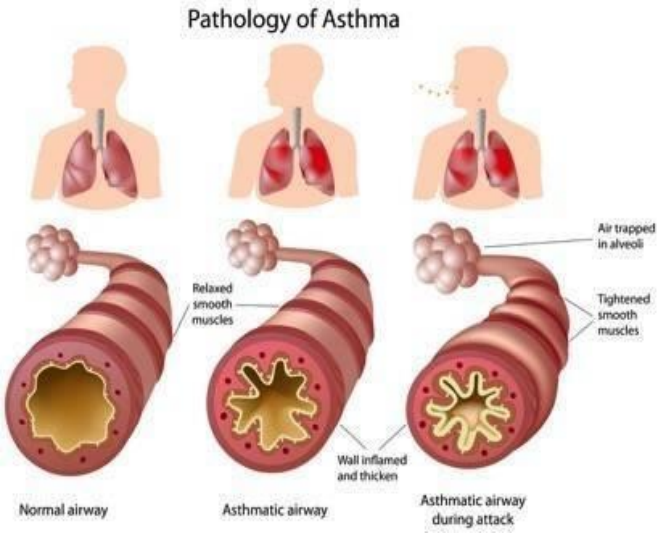


Fig 3. Asthma Pathology and Airway Changes

and hyperplasia of the airway smooth muscle. These latter changes may not respond to usual treatment [19].

- **Airway hyperresponiveness:**

Airway hyperresponsiveness-an exaggerated bronchoconstrictor response to a wide variety of stimuli-is a major, but not necessarily unique, feature of asthma. The degree to which airway hyperresponsiveness can be defined by contractile responses to challenges with methacholine correlates with the clinical severity of asthma. The mechanism influencing airway hyperresponsiveness are multiple and include inflammation appears to be a major factor in determining the degree of airway hyperresponsiveness. Treatment directed toward reducing inflammation can reduce airway hyperresponsiveness and improve asthma control [20].

- **Airway Remodeling:**

In some persons who have asthma, airflow limitation may be only partially reversible. Permanent structural changes can occur in the airway; these are associated with a progressive loss of lung function that is not prevented by or fully reversible by current therapy. Airway remodeling involves an activation of many of the structural cells, with consequent permanent changes in the airway that increase airflow obstruction and airwayresponsiveness and render the patient less responsive to therapy [21].

Features of Airway Remodeling:

- Inflammation
- Mucus hypersecretion
- Subepithelial fibrosis
- Airway smooth muscles hypertrophy Angiogenesis [22].

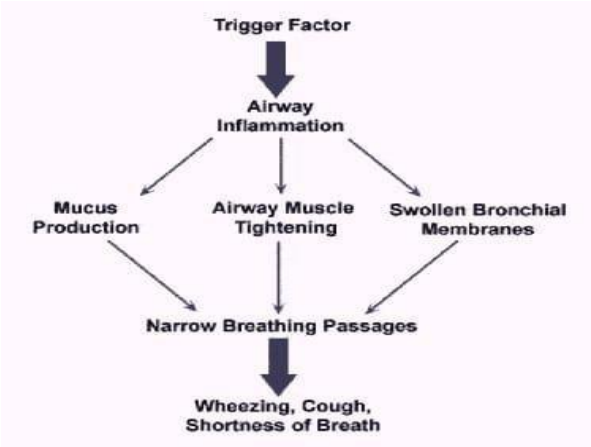


Fig 4. Asthma Pathway and Symptoms

❖ Signs & Symptoms:

Recognizing the sign and symptoms of asthma is an important part of managing asthma. Knowing when early warning signs or mild symptoms are occurring is helpful so that treatment and other interventions can begin early. Early treatment is most effective. If severe symptoms are present, it is vital to begin the appropriate treatment immediately.

Early Warning Signs:

Early warning signs are experienced before the start of an asthma episode. By recognizing these clues that occur before actual asthma symptoms, early treatment can be started.

These signs are unique to each person.

- Headache
- Stuffy or runny nose
- Sore throat
- Coughing
- Wheezing
- Difficulty in sleeping
- Mood Swings
- Tiredness or weakness during Physical activity
- Irritability

Asthma Symptoms:

- Chest pain
- Coughing, especially at night or when laughing
- Difficulty in breathing
- Shortness of breath
- Sleep problems resulting from Breathing issues
- A wheezing or whistling sound in the chest when exhaling
- Difficulty in talking
- Blue Lips and/or Fingernails[23].

❖ Causes:

Although the actual etiology of asthma is unknown, both hereditary and environmental factors appear to be important.

Sensitization to an allergen, for example, can be both a cause and a trigger. Other causes and triggers are listed in the sections below. [24].

Pregnancy: Although the actual etiology of asthma is unknown, both hereditary and environmental factors appear to be important.

Sensitization to an allergen, for example, can be both a cause and a trigger. Other causes and triggers are listed in the sections below. [24].

Obesity:

A 2018 study found that obesity affects asthma in both adults and children, acting as a disease modifier and risk factor.

Obesity can lower a person's quality of life and cause more frequent and severe symptoms. Additionally, they might not react as well to drugs [26].

Allergies:

When a person's body becomes sensitive to a particular substance, an allergy occurs. The individual will be vulnerable to an allergic reaction every time they come into touch with the substance once the sensitization has taken hold.

The most prevalent kind of asthma is allergic asthma. Asthma symptoms are usually brought on by inhaling an allergen [27].

Smoking tobacco:

: The American Lung Association states that smoking cigarettes can aggravate asthma symptoms.

Additionally, breathing in secondhand smoke can harm the lungs. This can impair lung airflow and a person's reaction to treatment [28].

Environmental factors:

Air pollution, both at one's home and outdoors, can affect the development and triggers of asthma.

Some allergens inside the house include:

- Mold
- Dust
- Animal hair and dander
- Fumes from household cleaners and paints
- Cockroaches

Other triggers in the home and outdoors include:

- Pollen
- Air pollution from traffic and other sources
- Ground-level ozone [29].

Stress:

Like a number of other emotions, stress can trigger asthma symptoms. An asthma attack can be brought on by a variety of emotional responses, including joy, rage, excitement, laughter, tears, and more. According to some research, there may be a connection between asthma and mental health issues including anxiety and depression. Chronic asthma may be caused by epigenetic changes brought on by prolonged stress, according to other studies [30].

Genetic factors:

The American Lung Association states that a person's lifelong risk of developing asthma may be influenced by their genetic makeup.
An individual is at a higher risk of developing asthma if one or both of their parents have the ailment [31].

Hormonal factors:

About 9.8% of women and 6.1% of men suffer from asthma. Furthermore, symptoms can alter based on a person's menstrual cycle and throughout life transitions like menopause.
For example, a person's symptoms may be worse during menstruation than at other times of the month during their reproductive years because of a drop in progesterone and estrogen levels. Physicians refer to phenomenon as perimenstrual asthma.
Hormones and asthma have a complicated and individual-specific interaction. Menopause-related hormone drops may exacerbate asthma symptoms or even trigger asthma in certain individuals. Conversely, some people may experience an improvement in their asthma symptoms following menopause. Additionally, hormonal activity may influence immunological function, leading to airway hypersensitivity. Additionally, people with intermittent asthma could only occasionally experience symptoms [32].

❖ Diagnosis:

Your doctor will talk to you about your medical and personal history in order to diagnose asthma. Additionally, they will do a physical examination. It is possible that you will require a lung function test, which is easily performed in the clinic. Additional diagnostics, including a blood test or a chest and sinus X-ray, can be required. Don't wait if you or your child frequently experience breathing difficulties! See a physician (or other healthcare professional, such as a nurse practitioner) right away [33].

Personal and medical history:

To learn more about your symptoms and their causes, your doctor will ask you questions. To assist you in responding to your doctor's inquiries, bring notes. Be prepared to respond to inquiries regarding your lifestyle, medications, and family history of allergies and asthma. Be prepared to discuss any current medical ailments, problems, or worries. All prior medical conditions are also included in this.
Any exposure to environmental variables that can exacerbate asthma at work or at home should be reported to your doctor. Pet dander, pollen, dust mites, mold, cockroaches, and certain meals in some individuals are a few examples. Asthma can be brought on by environmental irritants such as tobacco smoke and cleaning agents.
The doctor may also ask if you get chest symptoms when you:

- Get a head cold
- Exercise
- Use specific medicines (such as NSAIDs) • Are under increased amounts of stress [34].

Physical examination:
The doctor will likely focus on the upper respiratory tract, the chest, and the skin. They will likely listen for signs of wheezing, which can indicate an obstructed airway and asthma.

They may also check for:

- Runny nose
- Swollen nasal passages
- Any growths on the inside of the nose

They will also check the skin for signs of eczema or hives[35] .

Asthma tests:
: To determine how well the lungs are functioning, the physician may do a lung function test.
The most popular lung function test used by medical practitioners to diagnose asthma is a spirometry test. Inhaling deeply and exhaling strongly into a tube will be required. The tube connects to a device known as a spirometer, which displays the rate at which air is expelled from the lungs.

Other tests:
Other tests for diagnosis include:

- **Challenge test:**

Additional diagnostic tests include the challenge test, which looks at your lifestyle, medications, and history of allergies and asthma. Be prepared to discuss any current medical ailments, problems, or worries. All prior medical conditions are also included in this.
Any exposure to environmental variables that can exacerbate asthma at work or at home should be reported to your doctor. Pet dander, pollen, dust mites, mold, cockroaches, and certain meals in some individuals are a few examples. Asthma can be brought on by environmental irritants such as tobacco smoke and cleaning agents.
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Physical examination:

The doctor will probably concentrate on the skin, chest, and upper respiratory tract. They will probably listen for wheezing, which can be an indication of asthma and a blocked airway.
They might also look for any growths on the inside of the nose, a runny nose, or swollen nasal passages. Additionally, they will examine the skin for indications of hives or eczema [35].

Asthma tests:

To determine how well the lungs are functioning, the physician may do a lung function test.
The most popular lung function test used by medical practitioners to diagnose asthma is a spirometry test. Inhaling deeply and exhaling strongly into a tube will be required. The tube connects to a device known as a spirometer, which displays the rate at which air is expelled from the lungs.
Other tests:

Other tests for diagnosis include:

- **Challenge test:**
- Covering their nose and mouth during exercise in cold weather
- Making sure they adequately warm up first
- Taking time to properly cool down afterward

- Avoiding activities outside when air quality is poor [38].

❖ Prevention

While there's no way to prevent asthma, you and your doctor can design a step-by-step plan for living with your condition and preventing asthma attacks [39].

- **Follow your Asthma action plan:**
- Create a thorough plan for taking your meds and handling an asthma attack with your doctor and medical team. Then, make sure you stick to your plan.
  Asthma is a chronic illness that requires constant care and observation. You may feel more in charge of your life if you take charge of your treatment [40].
- **Get vaccinated for Influenza and Pneumonia:**

Staying current with vaccinations can prevent flu and pneumonia from triggering asthma flare-ups [41].

- **Identify and avoid asthma triggers:**

A number of outdoor allergens and irritants ranging from pollen and mold to cold air and air pollution — can trigger asthma attacks. Find out what causes or worsens your asthma, and take steps to avoid those triggers [42].

- **Monitor your breathing:**

You may learn to recognize warning signs of an impending attack, such as slight coughing, wheezing or shortness of breath.

- **Identify and treat attacks early:**

If you act quickly, you're less likely to have a severe attack. You also won't need as much medication to control your symptoms.When your peak flow measurements decrease and alert you to an oncoming attack, take your medication as instructed. Also, immediately stop any activity that may have triggered the attack. If your symptoms don't improve, get medical help as directed in your action plan [43].

- **Take your medication as prescribed.**

Don't change your medications without first talking to your doctor, even if your asthma seems to be improving. It's a good idea to bring your medications with you to each doctor visit. Your doctor can make sure you're using your medications correctly and taking the right dose.

- **Pay attention to increasing quick-relief inhaler use:**

If you find yourself relying on your quick-relief inhaler, such as albuterol, your asthma isn't under control. See your doctor about adjusting your treatment [44].

❖ Drugs for Asthma:

Anti-asthmatic drugs

Bronchodialators **(Quick relief medications)** Treat acute attack of asthma. • Short acting β_2-agonists • Anticholinergics • Xanthine preparations	**Anti-inflammatory agents** **(Prophylactic therapy)** Reduce the frequency of attacks. • Corticosteroids • Mast cell stabilizers • Leukotrienes antagonists • Anti-IgE monoclonal antibody

1. <u>Bronchodialators:</u>

Mechanism of action:

- Direct β_2 stimulation➋stimulate adenyl cyclase➋increase cAMP➋bronchodilation Increase mucus clearance by (increasing ciliary activity).
- Stabilization of mast cell membrane.

• Short acting drugs:

- **Salbutamol**
- **Terbutaline**

- **Salbutamol**, inhalation, orally, I.V.

- **Terbutaline**, inhalation, orally, S.C.
- Have rapid onset of action (15-30min).
- Short duration of action (4-6hr).
- Used for acute attack of asthma (drugs of choice).

• Long-acting drugs:

- **Salmeterol**
- **Formoterol**

- Are given by inhalation
- Long-acting bronchodilators (12hours) due to high lipid solubility (creates depot effect).
- Are not used to relieve acute episodes of asthma
- Used for nocturnal asthma
- Combined with inhaled corticosteroids to control asthma (decrease the number and severity of asthma attacks) [45].

Advantages:

- Minimal CVS side effects
- Suitable for asthmatic patients with CV disorders as hypertension or heart failure.

Disadvantages:

- Skeletal muscle tremors.
- Nervousness
- Tolerance (β-receptors down regulation).

- Overdose may produce tachycardia due to β1stimulation.

• Anti-cholinergic antagonists

- **Ipratropium**
- **Tiotropium**

- Act by blocking muscarinic receptors.
- given by aerosol inhalation
- Have delayed onset of action.
- Quaternary derivatives of atropine (polar).
- Does not diffuse into the blood Does not enter CNS.

- Have minimal systemic side effects
- Ipratropium has short duration of action 3-5 hr Tiotropium has longer duration of action (24 h) [46].

Pharmacodynamics:

- Inhibit bronchoconstriction and mucus secretion

- Less effective than β2-agonists.
- No anti-inflammatory action only bronchodilator [47].

Uses:

1. Main choice in chronic obstructive pulmonary diseases (COPD).

2. In acute severe asthma combined with β2 agonists & corticosteroids.
3. Never use as a rescue medication.

• **Methylxanthines**

- Theophylline
- Aminophylline

 Mechanism of Action:

- are phosphodiestrase inhibitors
- increase cAMP➐ bronchodilation
- Adenosine receptors antagonists (A1)
- Increase diaphragmatic contraction Stabilization of mast cell membrane [48].

 Pharmacological effects:

- Bronchial muscle relaxation
- Increase contraction of diaphragm➐ improve ventilation

CVS: ↑ heart rate, ↑ force of contraction

GIT: ↑ gastric acid secretions

Kidney: ↑renal blood flow, weak diuretic action

CNS stimulation

* Stimulant effect on respiratory center.
* Decrease fatigue & elevate mood.
* Overdose (tremors, nervousness, insomnia, convulsion)

 Pharmacokinetics:

- Theophylline is given orally
- Aminophylline, is given as slow infusion
- metabolized by Cyt P450 enzymes in liver
- T ½= 8 hours
- has many drug interactions [49] **Enzyme inducers:**
- as phenobarbitone & rifampicin
- ↑ metabolism of theophylline → ↓ T ½[50].
- **Enzyme inhibitors:**
- as erythromycin

↓ metabolism of theophylline → ↑ T ½.

 Uses:

1. Second line drug in asthma (theophylline).
2. For status asthmatics (aminophylline, is given as slow infusion).

 Side Effects:

1. Low therapeutic index (narrow safety margin) monitoring of Theophylline blood level is necessary.
2. GIT effects: nausea & vomiting
3. CVS effects: hypotension, arrhythmia.
4. CNS side effects: tremors, nervousness, insomnia, convulsion.

2. <u>Prophylactic therapy:</u>

Anti - inflammatory drugs include:

- Glucocorticoids
- Leukotrienes antagonists
- Mast cell stabilizers
- Anti-IgE monoclonal antibody

e.g.Omalizumab

Anti - inflammatory drugs: (control medications / prophylactic therapy)

- ↓ bronchial hyper-reactivity.
- ↓ reduce inflammation of airways
- ↓ reduce the spasm of airways

• **Glucocorticoids**

 Mechanism of action

- **Anti-inflammatory action due to:**
- Inhibition of phospholipase A2
- ↓ prostaglandin and leukotrienes
- ↓ Number of inflammatory cells in airways.
- Mast cell stabilization →↓ histamine release.
- ↓ capillary permeability and mucosal edema. Inhibition of antigen-antibody reaction.
- Upregulate β2receptors (have additive effect to B2agonists).

 Routes of administration:

Inhalation:
e.g. Budesonide & Fluticasone, beclomethasone

- Given by inhalation (metered-dose inhaler).
- Have first pass metabolism
- Best choice in asthma, less side effects

Orally: Prednisone, methyl prednisolone Injection: Hydrocortisone, dexamethasone **Glucocorticoids in asthma:**

- Are not bronchodilators
- Reduce bronchial inflammation
- Reduce bronchial hyper-reactivity to stimuli
- Have delayed onset of action (effect usually attained after 2-4 weeks).
- Maximum action at 9-12 months.
- Given as prophylactic medications, used alone or combined with β2agonists.
- Effective in allergic, exercise, antigen and irritant-induced asthma. **Clinical Uses of Glucocorticoids:**
- Treatment of inflammatory disorders (asthma, rheumatoid arthritis).
- Treatment of autoimmune disorders (ulcerative colitis, psoriasis) and after organ or bone marrow transplantation as immunosuppressants.
- Antiemetics in cancer chemotherapy.

 Side effects due to systemic corticosteroids:

- Fat distribution
- Fluid retention
- Weight gain
- Hypertension

• **Mast cell stabilizers**

- Cromoglycate

- act by stabilization of mast cell membrane.
- given by inhalation (aerosol, nebulizer).
- Have poor oral absorption (10%)

 Pharmacodynamics:

- are not bronchodilators
- Not effective in acute attack of asthma.
- Prophylactic anti-inflammatory drug Reduce bronchial hyper-reactivity.

- Effective in exercise, antigen and irritant-induced asthma.
- Children respond better than adults.

 Uses:

1. Prophylactic therapy in asthma especially in children.
2. Allergic rhinitis.
3. Conjunctivitis. **Side effects:**

1. Bitter taste
2. Minor upper respiratory tract irritation (burning sensation, nasal congestion)

• **Leukotriene receptor antagonists**

- **Zafirlukast**

- **Montelukast**

- Taken orally.
- Are bronchodilators
- Have anti-inflammatory action
- Less effective than inhaled corticosteroids **Uses of leukotriene receptor antagonists:**
- Not effective in acute attack of asthma.
- Prophylaxis of mild to moderate asthma.
- Aspirin-induced asthma
- Antigen and exercise-induced asthma
- Can be combined with glucocorticoids (additive effects, low dose of glucocorticoids can be used).

 Side effects:

1. Elevation of liver enzymes
2. Headache [51]

Conclusion

Asthma is a multifactorial chronic respiratory condition that significantly impacts individuals across all age groups. Understanding its pathophysiology—including airway inflammation, bronchoconstriction, and remodeling—is essential for accurate diagnosis and effective management. A combination of environmental control, lifestyle modifications, and pharmacological interventions tailored to disease severity can provide substantial symptom relief and improve long-term outcomes. Anti-asthmatic drugs, ranging from quick-relief bronchodilators to long-term anti-inflammatory agents, form the cornerstone of asthma thera py. With proper education, adherence to treatment, and regular monitoring, most individuals with asthma can achieve good control of their symptoms and maintain a high quality of life.

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