Asthma

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Plan of lecture

- **Asthma**: etiology and pathogenesis;
- **Asthma**: diagnosis;
- **Asthma**: treatment.

Asthma

- Asthma is a disease of diffuse airway inflammation caused by a variety of triggering stimuli resulting in partially or completely reversible bronchoconstriction. Symptoms and signs include dyspnea, chest tightness, cough, and wheezing. The diagnosis is based on history, physical examination, and pulmonary function tests. Treatment involves controlling triggering factors and drug therapy, most commonly with inhaled beta-2 agonists and inhaled corticosteroids. Prognosis is good with treatment. (By **Victor E. Ortega** , MD, PhD, Center for Genomics and Personalized Medicine Research, Wake Forest School of Medicine; **Frank Genese** , DO, Wake Forest School of Medicine. Last full review/revision Jul 2019| Content last modified Jul 2019 - MSD Manual Professional Version [1])

Asthma etiology [1]

- Development of asthma is multifactorial and depends on the interactions among multiple susceptibility genes and environmental factors.
- More than **100 asthma susceptibility genes** have been reported. Many are thought to involve the broad category of T-helper cells type 2 (TH2) and may play a role in inflammation. Examples include the *FCER1B* gene, which encodes the beta chain of the high-affinity IgE receptor; the genes encoding certain interleukins (IL) such as IL-4, IL-13, and the IL-4 receptor; genes responsible for innate immunity (HLA-DRB1, HLA-DQB1, CD14), and genes participating in cellular inflammation (eg, genes encoding granulocyte-monocyte colony-stimulating factor [GM-CSF] and tumor necrosis factor-alpha [TNF-α]). Also, the *ADAM33* gene may stimulate airway smooth muscle and fibroblast proliferation and remodeling; it was the first asthma risk locus found with whole-genome family linkage studies.
- More recent the most replicated is at the chromosome 17q21 locus. This locus contains the *ORMDL3* gene, which is an allergen and cytokine (IL-4/IL-13)-inducible gene implicated in epithelial cell remodeling and sphingolipid metabolism to affect bronchial hyperreactivity.

Environmental risk factors for Asthma [1]

Environmental risk factors for asthma may include the following:

- Allergen exposure
- Diet
- Perinatal factors
- Evidence clearly implicates household allergens (eg, dust mite, cockroach, pet) and other environmental allergens in disease development in older children and adults. Diets low in vitamins C and E and in omega–3 fatty acids have been linked to asthma, as has obesity; however, dietary supplementation with these substances does not appear to prevent asthma. Asthma has also been linked to perinatal factors, such as young maternal age, poor maternal nutrition, prematurity, low birthweight, and lack of breastfeeding.
- On the other hand, endotoxin exposure early in life can induce tolerance and may be protective. Air pollution is not definitively linked to disease development, although it may trigger exacerbations. The role of childhood exposure to cigarette smoke is controversial, with some studies finding a contributory and some a protective effect.

Environmental risk factors for Asthma [1]

- Genetic and environmental components may interact . Infants may be born with a predisposition toward proallergic and proinflammatory TH2 immune responses, characterized by growth and activation of eosinophils and IgE production. Early childhood exposure to bacterial and viral infections and endotoxins may shift the body to TH1 responses, which suppresses TH2 cells and induce tolerance. Trends in developed countries toward smaller families with fewer children, cleaner indoor environments, and early use of vaccinations and antibiotics may deprive children of these TH2-suppressing, tolerance-inducing exposures and may partly explain the continuous increase in asthma prevalence in developed countries (the hygiene hypothesis).

Reactive airways dysfunction syndrome (RADS) and irritant-induced asthma [1]

Reactive airways dysfunction syndrome (RADS) is the rapid onset (minutes to hours, but not > 24 hours) of an asthma-like syndrome that:

- Develops in people with no history of asthma
- Occurs following a single, specific inhalation exposure to a significant amount of an irritating gas or particulate
- Persists for ≥ 3 months
- Numerous substances have been implicated, including chlorine gas, nitrogen oxide, and volatile organic compounds (eg, from paints, solvents, adhesives). The exposure event is usually obvious to the patient, particularly when symptoms begin almost immediately.

Reactive airways dysfunction syndrome (RADS) and irritant-induced asthma [1]

- Irritant-induced asthma refers to a similar, persistent asthma-like response following multiple or chronic inhalational exposure to high levels of similar irritants. Manifestations are sometimes more insidious, and thus the connection to the inhalational exposure is clear only in retrospect.
- RADS and chronic irritant-induced asthma have many clinical similarities to asthma (eg, wheezing, dyspnea, cough, presence of airflow limitation, bronchial hyperresponsiveness)and respond significantly to bronchodilators and often corticosteroids. Unlike in asthma, the reaction to the inhaled substance is not thought to be an IgE-mediated allergy; low-level exposures do not cause RADS or irritant-induced asthma. However, repeated exposure to the initiating agent may trigger additional symptoms.

Asthma pathogenesis [1]

Asthma involves

- Bronchoconstriction
- Airway edema and inflammation
- Airway hyperreactivity
- Airway remodeling
- In patients with asthma, TH2 cells and other cell types—notably, eosinophils and mast cells, but also other CD4+ subtypes and neutrophils—form an extensive inflammatory infiltrate in the airway epithelium and smooth muscle, leading to airway remodeling (ie, desquamation, subepithelial fibrosis, angiogenesis, smooth muscle hypertrophy). Hypertrophy of smooth muscle narrows the airways and increases reactivity to allergens, infections, irritants, parasympathetic stimulation (which causes release of pro-inflammatory neuropeptides, such as substance P, neurokinin A, and calcitonin gene-related peptide), and other triggers of bronchoconstriction.

Asthma pathogenesis [1]

Additional contributors to airway hyperreactivity include loss of inhibitors of bronchoconstriction (epithelium-derived relaxing factor, prostaglandin E2) and loss of other substances called endopeptidases that metabolize endogenous bronchoconstrictors. Mucus plugging and peripheral blood eosinophilia are additional classic findings in asthma and may be epiphenomena of airway inflammation. However, not all patients with asthma have eosinophilia.

Asthma pathogenesis [1]

- **Asthma triggers**
- Common triggers of an asthma exacerbation include
- Environmental and occupational allergens (numerous)
- Cold, dry air
- Infections
- Exercise
- Inhaled irritants
- Emotion
- Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs)
- Gastroesophageal reflux disease (GERD)

Asthma pathogenesis [1]

- Infectious triggers in young children include respiratory syncytial virus, rhinovirus, and parainfluenza virus infection. In older children and adults, URIs (particularly with rhinovirus) and pneumonia are common infectious triggers. Exercise can be a trigger, especially in cold or dry environments, and cold air alone can also trigger symptoms. Inhaled irritants, such as air pollution, cigarette smoke, perfumes, and cleaning products can also trigger symptoms in patients with asthma. Emotions such as anxiety, anger, and excitement sometimes trigger exacerbations.
- Aspirin is a trigger in up to 30% of patients with severe asthma and in < 10% of all patients with asthma. Aspirin-sensitive asthma is typically accompanied by nasal polyps with nasal and sinus congestion, which is a condition also known as Samter's triad (asthma, nasal polyps, and sensitivity to aspirin and NSAIDs).

Asthma pathogenesis [1]

- GERD is a common trigger among some patients with asthma, possibly via esophageal acid-induced reflex bronchoconstriction or by microaspiration of acid. However, treatment of asymptomatic GERD (eg, with proton pump inhibitors) does not seem to improve asthma control.
- Allergic rhinitis often coexists with asthma; it is unclear whether the two are different manifestations of the same allergic process or whether rhinitis is a discrete asthma trigger.

Asthma pathogenesis [1]

Response:

- In the presence of triggers, there is reversible airway narrowing and uneven lung ventilation. In lung regions distal to narrowed airways, relative perfusion exceeds relative ventilation; thus, alveolar oxygen tensions fall and alveolar carbon dioxide tensions rise. Usually, such regional hypoxia and hypercarbia trigger compensatory pulmonary vasoconstriction to match regional ventilation and perfusion; however, these compensatory mechanisms fail during an asthma exacerbation due to the vasodilatory effects of prostaglandins that are upregulated during an exacerbation. Most patients can compensate by hyperventilating, but in severe exacerbations, diffuse bronchoconstriction causes severe gas trapping, and the respiratory muscles are put at a marked mechanical disadvantage so that the work of breathing increases. Under these conditions, hypoxemia worsens and $PaCO_2$ rises. Respiratory acidosis and metabolic acidosis may result and, if left untreated, cause respiratory and cardiac arrest.

Asthma **Classification [1]**

- Unlike hypertension (eg, in which one parameter [blood pressure] defines the severity of the disorder and the efficacy of treatment), asthma causes a number of clinical and testing abnormalities. Also, unlike most types of hypertension, asthma manifestations typically wax and wane. Thus, monitoring (and studying) asthma requires a consistent terminology and defined benchmarks.
- The term status asthmaticus describes severe, intense, prolonged bronchospasm that is resistant to treatment.

Asthma **Classification [1]**

Severity

- Severity can usually be assessed directly only before treatment is started, because patients who have responded well to treatment by definition have few symptoms. Asthma severity is categorized as
- Intermittent
- Mild persistent
- Moderate persistent
- Severe persistent
- It is important to remember that the severity category does not predict how serious an exacerbation a patient may have. For example, a patient who has mild asthma with long periods of no or mild symptoms and normal pulmonary function may have a severe, life-threatening exacerbation.

Asthma **Classification [1]**

Control

- Control is the degree to which symptoms, impairments, and risks are minimized by treatment. Control is the parameter assessed in patients receiving treatment. The goal is for all patients to have well controlled asthma regardless of disease severity. Control is classified as
- Well controlled
- Not well controlled
- Very poorly controlled
- Severity and control are assessed in terms of patient impairment and risk (see tables Classification of Asthma Severity and Classification of Asthma Control).

Asthma **Classification [1]**

Impairment

- Impairment refers to the frequency and intensity of patients' symptoms and functional limitations. Impairment differs from severity by its emphasis on symptoms and functional limitations rather than the intrinsic intensity of the disease process. Impairment can be measured by spirometry, mainly forced expiratory volume in 1 second (FEV1), and the ratio of FEV1 to forced vital capacity (FVC), but is manifested as clinical features such as
- How often symptoms are experienced
- How often the patient awakens at night
- How often the patient uses a short-acting beta-2 agonist for symptom relief
- How often asthma interferes with normal activity

Asthma **Classification [1]**

- **Risk**
- Risk refers to the likelihood of future exacerbations or decline in lung function and the risk of adverse drug effects. Risk is assessed by long-term trends in spirometry and clinical features such as
- Frequency of need for oral corticosteroids
- Need for hospitalization
- Need for intensive care unit (ICU) admission
- Need for intubation

Asthma: Symptoms and Signs [1]

- Patients with mild asthma are typically asymptomatic between exacerbations. Patients with more severe disease and those with exacerbations experience dyspnea, chest tightness, audible wheezing, and coughing. Coughing may be the only symptom in some patients (cough-variant asthma). Symptoms can follow a circadian rhythm and worsen during sleep, often around 4 AM. Many patients with more severe disease waken during the night (nocturnal asthma).
- Signs include wheezing, pulsus paradoxus (ie, a fall of systolic blood pressure [BP] > 10 mm Hg during inspiration), tachypnea, tachycardia, and visible efforts to breathe (use of neck and suprasternal [accessory] muscles, upright posture, pursed lips, inability to speak). The expiratory phase of respiration is prolonged, with an inspiratory:expiratory ratio of at least 1:3. Wheezes can be present through both phases or just on expiration, but patients with severe bronchoconstriction may have no audible wheezing because of markedly limited airflow.

Asthma: Symptoms and Signs [1]

- Patients with a severe exacerbation and impending respiratory failure typically have some combination of altered consciousness, cyanosis, pulsus paradoxus > 15 mm Hg, oxygen saturation <90%, $PaCO_2$ > 45 mm Hg, or hyperinflation. Rarely, pneumothorax or pneumomediastinum is seen on chest x-ray.
- Symptoms and signs disappear between exacerbations, although soft wheezes may be audible during forced expiration at rest, or after exercise, in some asymptomatic patients. Hyperinflation of the lungs may alter the chest wall in patients with long-standing uncontrolled asthma, causing a barrel-shaped thorax. All symptoms and signs are nonspecific, are reversible with timely treatment, and typically are brought on by exposure to one or more triggers.

Asthma : Diagnosis [1]

- Clinical evaluation
- Pulmonary function testing
- Diagnosis is based on history and physical examination and is confirmed with pulmonary function tests. Diagnosis of causes and the exclusion of other disorders that cause wheezing are also important. Asthma and chronic obstructive pulmonary disease (COPD) are sometimes easily confused; they cause similar symptoms and produce similar results on pulmonary function tests but differ in important biologic ways that are not always clinically apparent.
- Asthma that is difficult to control or refractory to commonly used controller therapies should be further evaluated for alternative causes of episodic wheezing, cough, and dyspnea such as allergic bronchopulmonary aspergillosis, bronchiectasis, or vocal cord dysfunction.

Pulmonary function tests [1]

- Patients suspected of having asthma should undergo pulmonary function testing to confirm and quantify the severity and reversibility of airway obstruction. Pulmonary function data quality is effort-dependent and requires patient education before the test. If it is safe to do so, bronchodilators should be stopped before the test: 8 hours for short-acting beta-2 agonists, such as albuterol; 24 hours for ipratropium; 12 to 48 hours for theophylline; 48 hours for long-acting beta-2 agonists, such as salmeterol and formoterol; and 1 week for tiotropium.
- Spirometry should be done before and after inhalation of a short-acting bronchodilator. Signs of airflow limitation before bronchodilator inhalation include reduced FEV1 and a reduced FEV1/FVC ratio. The FVC may also be decreased because of gas trapping, such that lung volume measurements may show an increase in the residual volume, the functional residual capacity, or both. An improvement in FEV1 of > 12% or an increase ≥ 10% of predicted FEV1 in response to bronchodilator treatment confirms reversible airway obstruction, although absence of this finding should not preclude a therapeutic trial of long-acting bronchodilator

Pulmonary function tests [1]

- Flow-volume loops should also be reviewed to diagnose vocal cord dysfunction, a common cause of upper airway obstruction that mimics asthma. However, it should be noted that vocal cord dysfunction is intermittent and normal flow-volume loops do not exclude this condition.

Provocative testing, in which inhaled methacholine (or alternatives, such as inhaled histamine, adenosine, or bradykinin, or exercise testing) is used to provoke bronchoconstriction, is indicated for patients suspected of having asthma who have normal findings on spirometry and flow-volume testing and for patients suspected of having cough-variant asthma, provided there are no contraindications.

Pulmonary function tests [1]

- Contraindications include FEV1< 1 L or < 50% predicted, recent myocardial infarction or stroke, and severe hypertension (systolic BP > 200 mm Hg; diastolic BP > 100 mm Hg). A decline in FEV1 of > 20% on a provocative testing protocol is relatively specific for the diagnosis of asthma. However, FEV1 may decline in response to drugs used in provocative testing in other disorders, such as COPD. If FEV1 decreases by < 20% by the end of the testing protocol, asthma is less likely to be present.
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Asthma : Diagnosis [1]

Other tests may be helpful in some circumstances:

- Diffusing capacity for carbon monoxide (DLCO)
- Chest x-ray
- Allergy testing

DLCO testing can help distinguish asthma from chronic obstructive pulmonary disease. Values are normal or elevated in asthma and usually reduced in COPD, particularly in patients with emphysema. A chest x-ray may help exclude some causes of asthma or alternative diagnoses, such as heart failure or pneumonia. The chest x-ray in asthma is usually normal but may show hyperinflation or segmental atelectasis, a sign of mucous plugging. Infiltrates, especially those that come and go and that are associated with findings of central bronchiectasis, suggest allergic bronchopulmonary aspergillosis.

Asthma : Diagnosis [1]

- Allergy testing may be indicated for children whose history suggests allergic triggers (particularly for allergic rhinitis) because these children may benefit from immunotherapy. It should be considered for adults whose history indicates relief of symptoms with allergen avoidance and for those in whom a trial of therapeutic anti-IgE antibody therapy is being considered. Skin testing and measurement of allergen-specific IgE via radioallergosorbent testing (RAST) can identify specific allergic triggers.
- Blood tests may be done. Elevated blood eosinophils (> 400 cells/mcL [> 0.4×10^9 /L]) and elevated nonspecific IgE levels are suggestive but are neither sensitive nor specific for a diagnosis of allergic asthma.

Asthma : Diagnosis [1]

- Sputum evaluation for eosinophils is not commonly done; finding large numbers of eosinophils is suggestive of asthma but is neither sensitive nor specific.
- Peak expiratory flow (PEF) measurements with inexpensive handheld flow meters are recommended for home monitoring of disease severity and for guiding therapy.

Asthma : Evaluation of exacerbations [1]

- Patients with asthma with an acute exacerbation are evaluated based on clinical criteria but should sometimes also have certain tests:
- Pulse oximetry
- Sometimes peak expiratory flow (PEF) measurement

The decision to treat an exacerbation is based primarily on an assessment of signs and symptoms. PEF measures can help establish the severity of an exacerbation but are most commonly used to monitor response to treatment in outpatients. PEF values are interpreted in light of the patient's personal best, which may vary widely among patients who are equally well controlled. A 15 to 20% reduction from this baseline indicates a significant exacerbation. When baseline values are not known, the percent predicted PEF based on age, height and sex may be used, but this is less accurate than a comparison to patient's personal best.

Asthma : Evaluation of exacerbations [1]

- Although spirometry (eg, FEV1) more accurately reflects airflow than PEF, it is impractical in most urgent outpatient and emergency department settings but may be used for office-based monitoring of treatment or when objective measures are required (eg, when an exacerbation appears to be more severe than perceived by the patient or is not recognized).
- Chest x-ray is not necessary for most exacerbations but should be done in patients with symptoms or signs suggestive of pneumonia, pneumothorax, or pneumomediastinum.
- Arterial or venous blood gas measurements should be done in patients with marked respiratory distress or symptoms and signs of impending respiratory failure.

Asthma : Prognosis [1]

- Asthma resolves in many children, but for as many as 1 in 4, wheezing persists into adulthood or relapse occurs in later years. Female sex, smoking, earlier age of onset, and sensitization to household dust mites, are risk factors for persistence and relapse.
- Although a significant number of deaths each year are attributable to asthma, most of these deaths are preventable with treatment. Thus, the prognosis is good with adequate access and adherence to treatment. Risk factors for death include increasing requirements for oral corticosteroids before hospitalization, previous hospitalization for acute exacerbations, and lower PEF values at presentation. Several studies show that use of inhaled corticosteroids decreases hospital admission and mortality rates.
- Over time, the airways in some patients with asthma undergo permanent structural changes (remodeling) and develop to baseline airflow obstruction that is not completely reversible. Early aggressive use of anti-inflammatory drugs may help prevent this remodeling.

Asthma: treatment **[1]**

Treatment :

- Control of triggers
- Drug therapy
- Monitoring
- Patient education
- Treatment of acute exacerbations

Treatment objectives are to minimize impairment and risk, including preventing exacerbations and minimizing chronic symptoms, including nocturnal awakenings; to minimize the need for emergency department visits or hospitalizations; to maintain baseline (normal) pulmonary function and activity levels; and to avoid adverse treatment effects.

Asthma : treatment **[1]**

Control of triggering factors

- Triggering factors in some patients may be controlled with use of synthetic fiber pillows and impermeable mattress covers and frequent washing of bed sheets, pillowcases, and blankets in hot water. Ideally, upholstered furniture, soft toys, carpets, curtains, and pets should be removed, at least from the bedroom, to reduce dust mites and animal dander. Dehumidifiers should be used in basements and in other poorly aerated, damp rooms to reduce mold. Steam treatment of homes diminishes dust mite allergens. House cleaning and extermination to eliminate cockroach exposure is especially important. Although control of triggering factors is more difficult in urban environments, the importance of these measures is not diminished. High-efficiency particulate air (HEPA) vacuums and filters may relieve symptoms, but no beneficial effects on pulmonary function and on the need for drugs have been observed.
- Sulfite-sensitive patients should avoid sulfite-containing food (eg, certain wine and salad dressings).

Asthma : treatment **[1]**

- Nonallergenic triggers, such as cigarette smoke, strong odors, irritant fumes, cold temperatures, and high humidity should also be avoided or controlled when possible. Limiting exposure to people with viral upper respiratory infections is also important. However, exercise-induced asthma is not treated with exercise avoidance because exercise is important for health reasons. Instead, a short-acting bronchodilator is given prophylactically before exercise and as needed during or after exercise (rescue inhaler); controller therapy (step 2 and above in Table Steps of Asthma Management) should be started if exercise-induced symptoms are not responsive to rescue inhalers or occur daily or more frequently.
- Patients with aspirin-sensitive asthma can use acetaminophen, choline magnesium salicylate, or celecoxib in place of NSAIDs.
- Asthma is a relative contraindication to the use of nonselective beta-blockers (eg, propranolol, timolol, carvedilol, nadolol, sotalol), including topical formulations, but cardioselective drugs (eg, metoprolol, atenolol) probably have no adverse effects.

Asthma : treatment **[1]**

Drug therapy:

Major drug classes commonly used in the treatment of asthma and asthma exacerbations include

- Bronchodilators (beta-2 agonists, anticholinergics)
- Corticosteroids
- Leukotriene modifiers
- Mast cell stabilizers
- Methylxanthines
- Immunomodulators

Asthma : treatment **[1]**

- **Bronchial thermoplasty**
- Bronchial thermoplasty is a bronchoscopic technique in which heat is applied through a device that transfers localized controlled radiofrequency waves to the airways. The heat decreases the amount of airway smooth muscle remodeling (and thus the smooth muscle mass) that occurs with asthma. In clinical trials in patients with severe asthma not controlled with multiple therapies, there have been modest decreases in exacerbation frequency and improvement in asthma symptom control. However, some patients have experienced an immediate worsening of symptoms, sometimes requiring hospitalization immediately after the procedure.

Asthma : treatment **[1]**

- Criteria for consideration of bronchial thermoplasty include severe asthma not controlled with inhaled corticosteroids and long-acting beta agonists, intermittent or continuous use of oral corticosteroids, FEV1 ≥ 50% of predicted, and no history of life-threatening exacerbations. Patients should understand the risk of post-procedure asthma exacerbation and need for hospitalization before proceeding with the procedure. The long-term efficacy and safety of bronchial thermoplasty is not known. There are no data in patients with > 3 exacerbations per year or an FEV1 < 50% of predicted because these patients were excluded from the clinical trials.

Asthma : treatment **[1]**

Monitoring response to treatment:

Guidelines recommend office use of spirometry (FEV1, FEV1/FVC, FVC) to measure airflow limitation and assess impairment and risk. Spirometry should be repeated at least every 1 to 2 years in patients with asthma to monitor disease progression, and a step-up in therapy might be required if lung function declines or becomes impaired with evidence of airflow obstruction. Outside the office, home PEF monitoring, in conjunction with patient symptom diaries and the use of an asthma action plan, is especially useful for charting disease progression and response to treatment in patients with moderate to severe persistent asthma. When asthma is quiescent, one PEF measurement in the morning suffices. Should PEF measurements fall to <80% of the patient's personal best, then twice/day monitoring to assess circadian variation is useful. Circadian variation of > 20% indicates airway instability and the need to re-evaluate the therapeutic regimen.

Treatment of acute asthma exacerbation [1]

- The goal of asthma exacerbation treatment is to relieve symptoms and return patients to their best lung function. Treatment includes
- Inhaled bronchodilators (beta-2 agonists and anticholinergics)
- Usually systemic corticosteroids
- Details of the treatment of acute asthma exacerbations, including of severe attacks requiring hospitalization, are discussed elsewhere.

Treatment of chronic asthma [1]

- Current asthma guidelines recommend treatment based on the severity classification. Continuing therapy is based on assessment of control. Therapy is increased in a stepwise fashion until the best control of impairment and risk is achieved (step-up). Before therapy is stepped up, adherence, exposure to environmental factors (eg, trigger exposure), and presence of comorbid conditions (eg, obesity, allergic rhinitis, GERD, COPD, obstructive sleep apnea, vocal cord dysfunction, inhaled cocaine use) are reviewed. These factors should be addressed before increasing drug therapy. Once asthma has been well controlled for at least 3 months, drug therapy is reduced if possible to the minimum that maintains good control (step-down).

Exercise-induced asthma [1]

- Exercise-induced asthma can generally be prevented by prophylactic inhalation of a short-acting beta-2 agonist or mast cell stabilizer before starting the exercise. If beta-2 agonists are not effective or if exercise-induced asthma causes symptoms daily or more frequently, the patient requires controller therapy.

Aspirin-sensitive asthma [1]

- The primary treatment for aspirin-sensitive asthma is avoidance of aspirin and other NSAIDs. Celecoxib does not appear to be a trigger. Leukotriene modifiers can blunt the response to NSAIDs. Alternatively, desensitization can be done in either the inpatient or outpatient clinic setting depending on the severity of aspirin sensitivity and asthma severity; desensitization has been successful in the majority of patients who are able to continue desensitization treatment for more than one year.

Future therapies [1]

Multiple therapies are being developed to target specific components of the inflammatory cascade. Therapies directed at interleukin 6 (IL-6), thymic stromal lymphopoietin, tumor necrosis factor-alpha, other chemokines, and cytokines or their receptors are all under investigation or consideration as therapeutic targets.

Asthma : treatment **Pregnant women [1]**

- About one third of women with asthma who become pregnant notice relief of symptoms, one third notice worsening (at times to a severe degree), and one third notice no change. GERD may be an important contributor to symptomatic disease in pregnancy. Asthma control during pregnancy is crucial because poorly controlled maternal disease can result in increased prenatal mortality, premature delivery, and low birth weight.
- Asthma drugs have not been shown to have adverse fetal effects, but safety data are lacking. In general, uncontrolled asthma is more of a risk to mother and fetus than adverse effects due to asthma drugs. During pregnancy, normal blood PCO_2 level is about 32 mm Hg. Therefore, carbon dioxide retention is probably occurring if PCO_2 approaches 40 mm Hg.

Asthma : treatment **Older patients [1]**

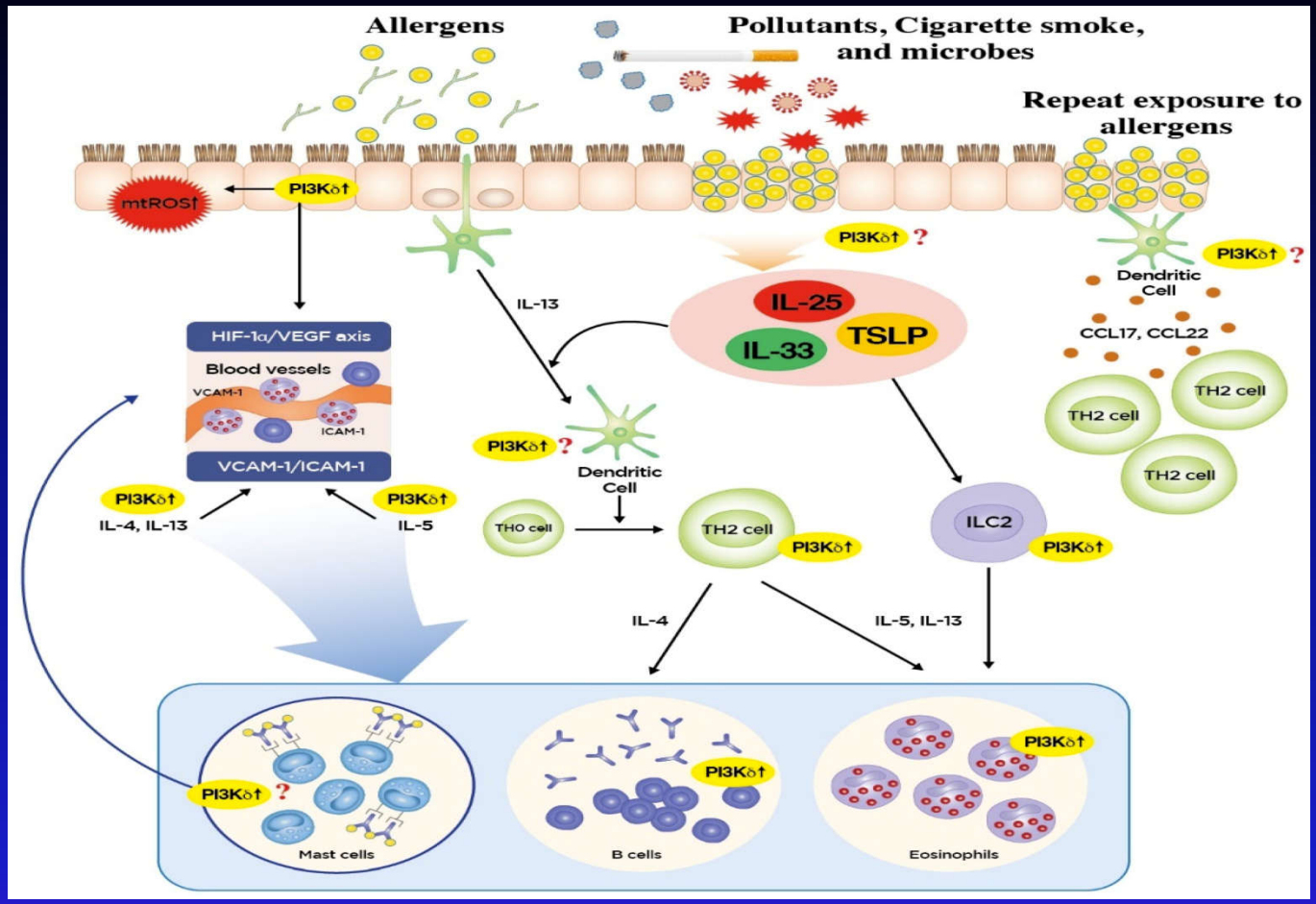
- Older patients have a high prevalence of other obstructive lung disease (eg, COPD), so it is important to determine the magnitude of the reversible component of airflow obstruction (eg, by a 2- to 3-week trial of inhaled corticosteroids or pulmonary function testing with bronchodilator challenge). Older patients may be more sensitive to adverse effects of beta-2 agonists and inhaled corticosteroids. Patients requiring inhaled corticosteroids, particularly those with risk factors for osteoporosis, may benefit from measures to preserve bone density (eg, calcium and vitamin D supplements, bisphosphonates).

Key Points of Asthma [1] :

- Asthma triggers range from environmental allergens and respiratory irritants to infections, aspirin, exercise, emotion, and gastroesophageal reflux disease.
- Consider asthma in patients who have unexplained persistent coughing, particularly at night.
- If asthma is suspected, arrange pulmonary function testing, with methacholine provocation if necessary.
- Educate patients on how to avoid triggers.
- Control chronic asthma with drugs that modulate the allergic and immune response—usually inhaled corticosteroids—with other drugs (eg, long-acting bronchodilators, mast cell stabilizers, leukotriene inhibitors) added based on asthma severity.
- Treat acute exacerbations with inhaled beta-2 agonists and anticholinergic drugs, systemic corticosteroids, and sometimes injected epinephrine.
- Treat asthma aggressively during pregnancy.

Bronchial Asthma morphology

Bronchial Asthma etiology



Bronchial Asthma pathogenesis