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ASTHMA AND TREATMENT

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ABSTRACT

Asthma is a condition marked by chronic inflammation of the airways, increased sensitivity to various triggers, and airway obstruction. It is at least partially reversible, either spontaneously or with appropriate treatment. Asthma affects approximately 3-5% of the U.S. population and is more prevalent in children than in adults. Airway obstruction can result from smooth muscle spasms in the walls of the smaller bronchi and bronchioles, swelling (edema) of the airway lining, excessive mucus production, and/or damage to the airway's epithelial layer.

Currently, numerous medications are available for asthma treatment. A key strategy for managing this disease includes preventing exposure to triggering antigens, reducing airway inflammation and hypersensitivity, and using medications to dilate narrowed airways. This review explores the pathophysiological approaches to asthma management.

Asthma is also the most common respiratory disorder in Canada. Despite advancements in its

Diagnosis and management, many Canadians with asthma remain poorly controlled. However, for most patients, effective control can be achieved through avoidance measures and appropriate pharmacological treatments.

Inhaled corticosteroids (ICS) are the standard treatment for most patients. For adults who do not achieve adequate control with ICS alone, combination inhalers containing ICS and long-acting beta2-agonists (LABA) are preferred. Allergen-specific immunotherapy offers a potentially disease-modifying option for certain asthma patients but should only be administered by physicians trained in allergy management.

Regular monitoring of asthma control, adherence to prescribed therapies, and proper inhaler techniques are essential aspects of effective asthma management. This article reviews current literature and guidelines for the accurate diagnosis and optimal treatment of asthma.

KEYWORD : *Pathophysiological approaches, symptoms, causes and treatment of asthma*

INTRODUCTION

Individuals with asthma often react to concentrations of triggers that are too low to cause symptoms in those without the condition. Common triggers include allergens such as pollen, dust mites, mold, or specific foods.

Other frequent triggers of asthma attacks include emotional stress, aspirin, sulfiting agents (found in wine, beer, and salad bar greens), physical activity, exposure to cold air, or inhaling cigarette smoke.

In the early (acute) phase of an asthma response, smooth muscle spasms occur, accompanied by excessive mucus production that can clog the bronchi and bronchioles, worsening the attack.

The late (chronic) phase is marked by inflammation, fibrosis, swelling (edema), and the death (necrosis) of bronchial epithelial cells. Various mediator chemicals, such as leukotrienes, prostaglandins, thromboxane, platelet-activating factor, and histamine, play a role in this phase.

Symptoms of asthma include difficulty breathing, coughing, wheezing, chest tightness, rapid heart rate (tachycardia), fatigue, moist skin, and feelings of anxiety. Acute attacks are typically managed with inhaled beta2-adrenergic agonists, such as albuterol, which help relax the smooth muscles in the bronchioles and reopen the airways.

Long-term asthma treatment focuses on suppressing the underlying inflammation. The most commonly used anti-inflammatory drugs include inhaled corticosteroids (glucocorticoids), cromolyn sodium, and leukotriene blockers.

Asthma is a chronic (long-term) lung condition characterized by inflammation and narrowing of the airways. It causes recurrent episodes of wheezing

Asthma affects individuals of all ages but most commonly begins during childhood. In the United States, over 25 million people are diagnosed with asthma, including approximately 7 million children.

To understand asthma, it is helpful to know how the airways function. The airways are tubes that transport air into and out of the lungs. In individuals with asthma, the airways are inflamed, making them swollen and highly sensitive. This sensitivity causes them to react strongly to certain inhaled substances.

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When the airways react, the surrounding muscles tighten, narrowing the airways and reducing airflow to the lungs. The swelling may worsen, further restricting airflow. Additionally, cells in the airways may produce excessive mucus, a thick, sticky substance that can exacerbate the narrowing of the airways.

This series of reactions leads to asthma symptoms, which occur whenever the airways are inflamed.
Asthma is the most common chronic respiratory condition in Canada, affecting approximately 10% of the population. While it is often considered a lung-specific disord.

DEFINITION

Asthma is a chronic inflammatory condition of the airways. This inflammation is linked to airway hyperresponsiveness, which is an exaggerated narrowing of the airways in response to triggers like allergens or physical activity. It results in recurring symptoms, including wheezing, shortness of breath (dyspnea), chest tightness, and coughing.

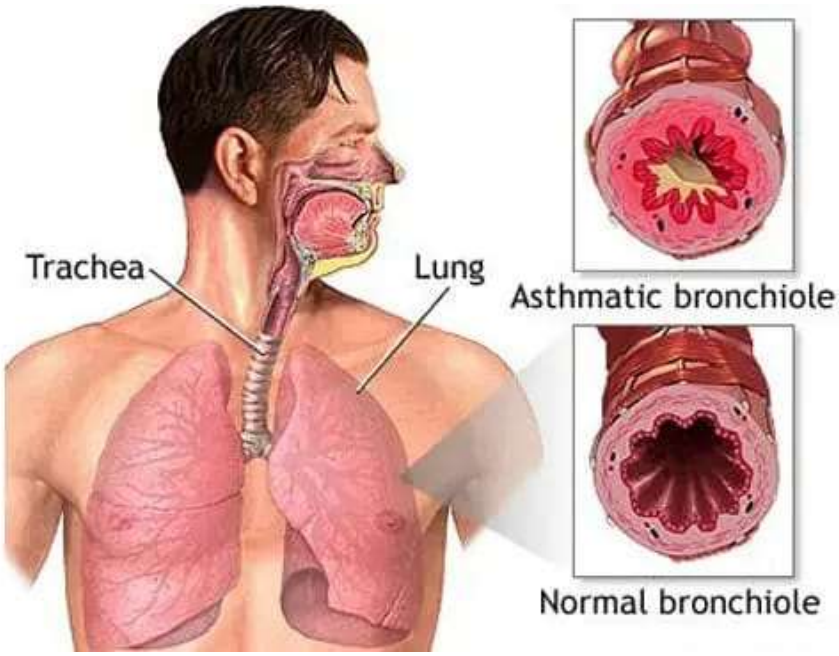
Symptom episodes are typically associated with widespread but variable airflow obstruction in the lungs. This obstruction is usually reversible, either spontaneously or with appropriate treatment.

Asthma symptoms can sometimes be mild, resolving on their own or with minimal medication. However, in other cases, symptoms may worsen over time. When symptoms become more severe or additional symptoms develop, it is referred to as an asthma attack, also known as a flare-up or exacerbation.

It is crucial to treat symptoms as soon as they appear to prevent them from escalating into a severe asthma attack. Severe attacks may require emergency medical care and can be life-threatening.

Asthma currently has no cure. Even when symptoms are absent, the condition persists and can flare up unexpectedly. However, with modern treatments and a better understanding of the disease, most individuals with asthma can effectively manage their condition. Many experience few, if any, symptoms and can lead normal, active lives, including uninterrupted sleep at night.

To manage asthma successfully, individuals should take an active role in their treatment. Building strong partnerships with healthcare providers is essential for effective, continuous, and personalized management of the disease.



SIGNS AND SYMPTOMS

Asthma is marked by recurring episodes of wheezing, difficulty breathing, chest tightness, and coughing. Coughing may produce sputum from the lungs, though it is often difficult to expel. During recovery from an asthma exacerbation (attack), the sputum may appear pus-like due to the presence of a high concentration of white blood cells called eosinophils.

Symptoms tend to be more severe at night, early in the morning, or in response to triggers such as exercise or exposure to cold air. While some individuals with asthma experience symptoms only occasionally, typically in response to specific triggers, others may have frequent reactions and persistent symptoms.

Associated Conditions

Several health conditions are more common in individuals with asthma, including gastroesophageal reflux disease (GERD), rhinosinusitis, and obstructive sleep apnea. Psychological conditions are also frequently observed, with anxiety disorders affecting 16-52% of individuals and mood disorders impacting 14-41%. It remains unclear whether asthma contributes to psychological issues or vice versa.

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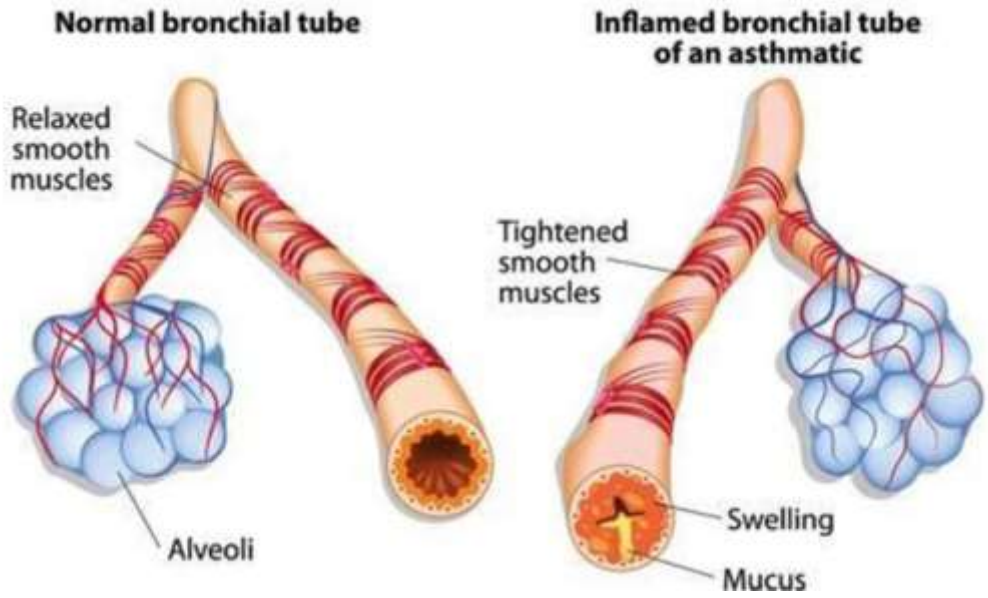
Current asthma (as opposed to former asthma) is linked to higher rates of all-cause mortality, heart disease mortality, and chronic lower respiratory tract disease mortality. Severe asthma, in particular, is strongly associated with the development of chronic obstructive pulmonary disease (COPD). Additionally, those with asthma, especially if poorly controlled, have an increased risk of adverse reactions to radiocontrast agents.



PATHOPHYSIOLOGY

Asthma is linked to immune responses driven by T helper cell type-2 (Th2) activity, a hallmark of other allergic (atopic) conditions.

Various triggers, both allergic (e.g., dust mites, cockroach droppings, pet dander, mold, and pollen) and non-allergic (e.g., respiratory infections, tobacco smoke, cold air, and physical exertion), initiate a series of immune reactions that result in chronic airway inflammation.

Increased levels of Th2 cells in the airways release specific cytokines, such as interleukin (IL)-4, IL-5, IL-9, and IL-13. These cytokines promote eosinophilic inflammation and stimulate mast cells to produce immunoglobulin E (IgE).

IgE, in turn, activates the release of inflammatory substances like histamine and cysteinyl leukotrienes. These mediators cause bronchospasm (airway smooth muscle contraction), swelling (edema), and excessive mucus production (mucus hypersecretion), leading to the classic symptoms of asthma.

The inflammatory mediators and cytokines released during the initial immune response to a triggering allergen further amplify inflammation in a late-phase response. This exacerbates airway inflammation and increases bronchial sensitivity (hyperreactivity).

Research suggests a genetic predisposition to asthma. Certain chromosomal regions have been associated with asthma-related traits, such as IgE antibody production, airway hyperresponsiveness, and inflammatory mediator activity.

However, more research is needed to pinpoint specific genes involved and to understand how genetic and environmental factors interact to contribute to the development of asthma.

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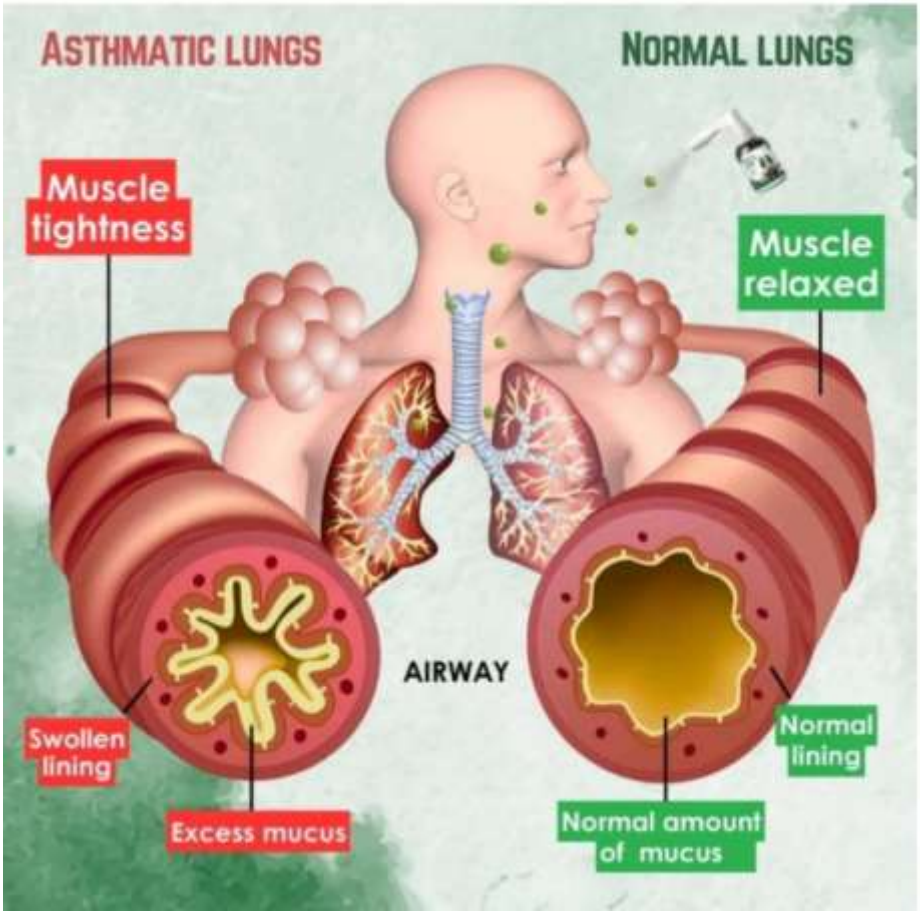

Asthma is a prevalent respiratory condition characterized by persistent inflammation of the airways, constriction of the smooth muscles in the respiratory tract, and recurrent episodes of bronchoconstriction.

According to the Centers for Disease Control and Prevention (CDC), asthma affects approximately 1 in 11 children and 1 in 12 adults in the United States.

Globally, the World Health Organization (WHO) estimates that 235 million people live with asthma. The condition can be broadly categorized into two types: allergic asthma and non-allergic asthma. This discussion will focus on allergic asthma. Regardless of the type, bronchoconstriction remains a key feature of the disease.

BRONCHIAL INFLAMMATION

The mechanisms underlying allergic asthma-caused by an immune response to inhaled allergens are among the most thoroughly studied factors contributing to the condition.

In both individuals with asthma and those without, inhaled allergens that reach the inner airways are processed by antigen-presenting cells (APCs). These cells capture and present fragments of the allergens to other immune cells.

In most individuals, these immune cells, known as naïve T helper (Tho) cells, "inspect" and typically ignore the allergen fragments. However, in people with asthma, these Tho cells differentiate into Th2 cells, a process not yet fully understood. One possible explanation is that mast cells release interleukin-4 (IL-4), which promotes the transformation of Tho cells into Th2 cells.

The newly formed Th2 cells activate the humoral branch of the immune system, leading to the production of antibodies against the allergen. When the individual is exposed to the same allergen again, these antibodies recognize it and trigger a humoral immune response.

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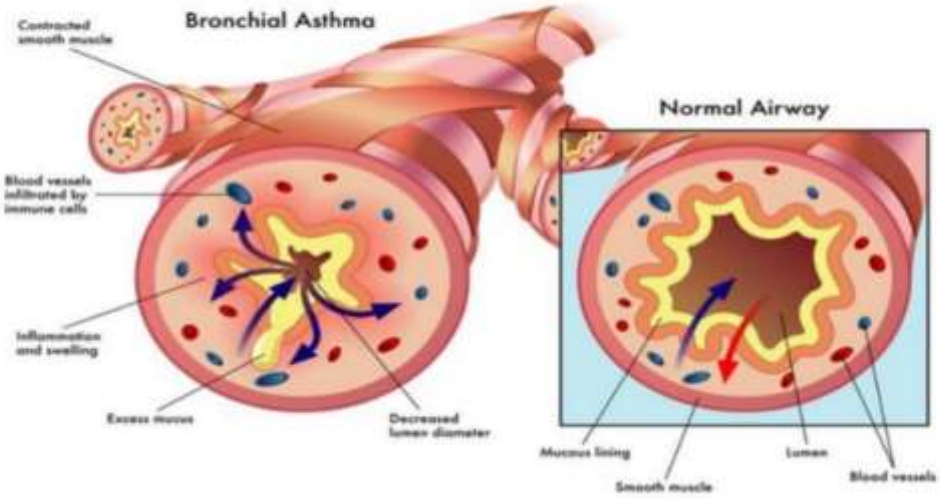
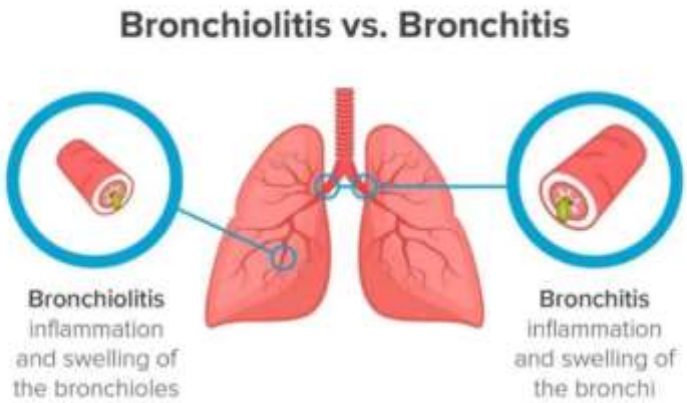


INFLAMMATION RESULTS

chemicals are produced that cause the wall of the airway to thicken, cells which produce scarring to proliferate and contribute to further 'airway remodeling', causes mucus producing cells to grow larger and produce more and thicker mucus, and the cell-mediated arm of the immune system is activated. Inflamed airways are more hyper-reactive, and will be more prone to bronchospasm.

The "hygiene hypothesis" postulates that an imbalance in the regulation of these Ta cell types in early life leads to a long-term domination of the cells involved in allergic responses over those involved in fighting infection. The suggestion is that for a child being exposed to microbes carly in life, taking fewer antibiotics, living in a large family, and growing up in the country stimulate the TH1 response and reduce the odds of developing asthma. Asthma is associated with a procoagulant state in the bronchoalveolar space



Exposure to indoor volatile organic compounds (VOCs) can act as a trigger for asthma. For instance, formaldehyde exposure has been positively linked to the condition.

While phthalates found in some types of PVC are associated with asthma in both children and adults, most evidence does not establish a causal relationship between asthma and acetaminophen (paracetamol) or antibiotic use. A 2014 systematic review revealed that the observed link between acetaminophen use and asthma disappeared when respiratory infections were considered. However, maternal use of acetaminophen during pregnancy is associated with an increased risk of asthma in children. Similarly, maternal psychological stress during pregnancy is a recognized risk factor for childhood asthma.

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Asthma is also linked to exposure to common indoor allergens, including dust mites, cockroach droppings, animal dander (skin, fur, or feathers), and mold. Efforts to reduce dust mites have not shown significant improvements in symptoms among sensitized individuals. On the other hand, weak evidence suggests that repairing buildings to reduce mold exposure may alleviate asthma symptoms in adults.

Certain viral respiratory infections, such as respiratory syncytial virus (RSV) and rhinovirus, acquired during early childhood, may increase the likelihood of developing asthma. However, some infections might reduce the risk of asthma, highlighting the complex relationship between infection and immune system development.

HYGIENE HYPOTHESIS

The hygiene hypothesis suggests that the rising prevalence of asthma worldwide may be an unintended consequence of reduced exposure to non-pathogenic bacteria and viruses during early childhood.

This reduced exposure is thought to result, in part, from increased hygiene practices and smaller family sizes commonly seen in modern societies. These factors may limit the development of a balanced immune system, potentially increasing the risk of asthma and other allergic conditions.

Exposure to bacterial endotoxin in early childhood may prevent the development of asthma, but exposure at an older age may provoke bronchoconstriction. [67] Evidence supporting the hygiene hypothesis includes lower rates of asthma on farms and in households with pets.

Use of antibiotics in early life has been linked to the development of asthma.

Also, delivery via caesarean section is associated with an increased risk (estimated at 20-80%) of asthma this increased risk is attributed to the lack of healthy bacterial colonization that the newborn would have acquired from passage through the birth canal.

There is a link between asthma and the degree of affluence which may be related to the hygiene hypothesis as less affluent individuals often have more exposure to bacteria and viruses

There is also a correlation between asthma and socioeconomic status. Individuals from less affluent backgrounds often experience greater exposure to bacteria and viruses, which may support the hygiene hypothesis and explain the lower asthma prevalence in these populations.

GENETIC

A family history of asthma is a significant risk factor, with numerous genes implicated in the condition. If one identical twin has asthma, the likelihood of the other being affected is approximately 25%.

By the end of 2005, at least 25 genes had been associated with asthma across six or more populations, including SPINK5, LTC4S, IL4R, ADAM33, and others like GSTM1, IL10, and CTLA-4. Many of these genes are involved in immune system regulation or inflammation. However, even for well-replicated genes, findings have not been consistent across all populations studied.

In 2006, a single genetic association study identified over 100 genes linked to asthma, and new associations continue to emerge.

Some genetic variants may increase the risk of asthma only when combined with specific environmental factors. For instance, a single nucleotide polymorphism (SNP) in the CD14 region has been linked to asthma in individuals exposed to endotoxins, which are bacterial products commonly found in the environment.

MEDICAL CONDITIONS

The combination of atopic eczema, allergic rhinitis, and asthma is referred to as atopy. A history of atopic diseases is the strongest risk factor for developing asthma, with significantly higher rates observed in individuals with eczema or hay fever.

Asthma has also been linked to eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome), an autoimmune disorder characterized by vasculitis. Additionally, some individuals with specific forms of urticaria may experience asthma symptoms.

There is a noted correlation between obesity and an increased risk of asthma, with the prevalence of both conditions rising in recent years. Contributing factors may include reduced lung function due to excess fat and the pro-inflammatory state caused by adipose tissue.

EXACERBATION

Some individuals will have stable asthma for weeks or months and then suddenly develop an episode of acute asthma. Different individuals react to various factors in different ways, 571 Most individuals can develop severe exacerbation from a number of triggering agents.

Several home factors can trigger asthma exacerbations, including dust, animal dander (particularly from cats and dogs), cockroach allergens, and mold. Perfumes are also a common cause of acute attacks, especially in women and children.

Both viral and bacterial infections of the upper respiratory tract can aggravate asthma symptoms. Additionally, psychological stress may worsen asthma, as it is believed to alter the immune system and increase the airway inflammatory response to allergens and irritants.

Asthma flare-ups in school-aged children tend to peak in the autumn, shortly after they return to school. This may be due to a combination of factors, including poor adherence to treatment, increased exposure to allergens and viruses, and changes in immune tolerance. While there is limited evidence

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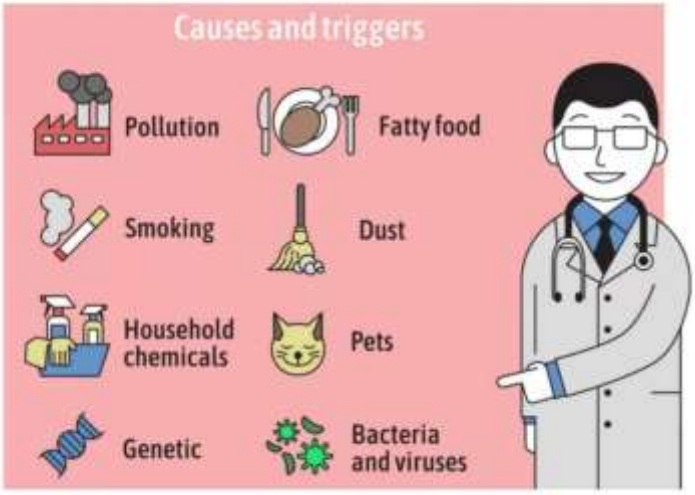
on how to prevent autumn exacerbations, seasonal treatment with omalizumab (starting four to six weeks before school resumes) may help reduce asthma flare-ups, although it is a costly option.



DIAGNOSIS

The diagnosis of asthma requires a comprehensive approach, including a detailed medical history, physical examination, and objective lung function assessments, with spirometry being the preferred method for confirmation. Additional tests, such as bronchoprovocation challenge testing and evaluation of airway inflammation markers, can aid in diagnosis, especially when lung function appears normal despite asthma symptoms.

Medical History

Asthma should be considered in individuals who experience recurrent symptoms such as cough, wheezing, chest tightness, and shortness of breath. Symptoms that are variable, triggered by allergens or irritants, worsen at night, or improve with appropriate asthma treatment strongly indicate the condition.

It is essential to rule out alternative causes for these symptoms, such as chronic obstructive pulmonary disease (COPD), bronchitis, chronic sinusitis, gastroesophageal reflux disease (GERD), recurrent respiratory infections, and heart disease.

A family history of asthma or atopic conditions, along with a personal history of allergic disorders like allergic rhinitis, can support the diagnosis. Identifying triggers such as dust mites, cockroaches, pet dander, mold, pollen, physical activity, exposure to tobacco smoke, or cold air-is crucial.

Work-Related Asthma

If occupational asthma is suspected, a detailed review of workplace exposures and symptom changes during holidays or time away from work should be conducted.

Comorbidities

Evaluating for comorbid conditions, including allergic rhinitis, sinusitis, obstructive sleep apnea, and GERD, is critical, as these can exacerbate asthma symptoms.

Diagnosing asthma in young children can be challenging because episodic wheezing and coughing are common in this age group, and spirometry is unreliable for children under six years of age.

Diagnosis in Young Children

A practical approach to confirm asthma in young children is a trial of treatment with short-acting bronchodilators and inhaled corticosteroids (ICSs). Significant clinical improvement during therapy, followed by symptom recurrence when treatment is stopped, strongly suggests asthma.

Physical Examination

Asthma symptoms are often variable, so the physical examination of suspected cases is frequently normal, especially if the patient is asymptomatic during the evaluation. The absence of abnormal findings does not exclude asthma. When present, wheezing heard during auscultation is the most common abnormal finding and indicates airflow limitation.

Physicians should also check the upper respiratory tract and skin for signs of atopic conditions, such as allergic rhinitis or dermatitis, which may coexist with asthma.

Objective Lung Function Measurements

Spirometry is the preferred test to evaluate reversible airway obstruction (demonstrated by rapid improvement in lung function after using a short-acting bronchodilator) and confirm asthma. It is recommended for all patients over six years old who can perform lung function tests.

The ratio of FEV1 to FVC is a key indicator of airflow obstruction. Asthma is confirmed when there is either:

An improvement in FEV1 of at least 12% and at least 200 mL within 15-20 minutes after administering an inhaled rapid-acting bronchodilator, or

An improvement in FEV1 of at least 20% and at least 200 ml. after two weeks of treatment with an anti-inflammatory agent.

In the general population, the FEV1/FVC ratio is typically greater than 0.80 (and possibly above 0.90 in children). Values below these thresholds indicate airflow limitation, supporting a diagnosis of asthma.

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Repeated Spirometry
Due to the variability of asthma symptoms, patients may not always show reversible airway obstruction during a single visit. Repeating spirometry, especially when the patient is symptomatic, enhances diagnostic accuracy.

Peak Expiratory Flow (PEF) Monitoring

When spirometry is unavailable, PEF monitoring is a suitable alternative. PEF is measured twice daily, usually in the morning and evening.

Indicators of asthma from PEF monitoring include:

A diurnal variation of more than 20%, or

An improvement of at least 60 L/min or 20% following inhalation of a rapid-acting bronchodilator.

CHALLENGE TESTING
When lung function tests are normal but symptoms suggest asthma, airway responsiveness can be evaluated through challenge testing. This involves exposing the patient to bronchoconstrictor stimuli (e.g., methacholine or histamine) or indirect challenges such as mannitol or exercise.

Challenge testing should be conducted under strict protocols in a controlled environment equipped to manage acute bronchospasms. The test measures the dose or concentration of a stimulus required to induce a significant bronchoconstriction, typically defined as a 20% reduction in FEV1.

NON-INVASIVE MARKERS OF AIRWAY INFLAMMATION
The measurement of inflammatory markers, such as sputum eosinophilia (the concentration of eosinophils in sputum) or exhaled nitric oxide levels (a gas produced by certain cells during inflammation), can aid in diagnosing asthma.

Exhaled nitric oxide levels may be more effective at identifying asthma than basic lung function tests and can also help monitor a patient's response to therapy.

Although these tests have been studied for asthma diagnosis and management, they are not yet widely used in Canada. As more clinical evidence emerges and their availability increases, these tools will likely become more commonly utilized.

ALLERGY SKIN TESTING
Allergy skin testing is recommended to assess the patient's allergic status and identify potential asthma triggers. This testing typically uses allergens relevant to the patient's geographic region.

TREATMENT
The primary objective of asthma management is to achieve and maintain control of the condition to prevent exacerbations-sudden or progressive worsening of symptoms requiring immediate medical attention or oral steroid therapy-and to reduce the risk of complications and mortality.

Assessing and Tailoring Treatment
Asthma control should be evaluated at each visit using established criteria, and treatment should be adjusted accordingly. Most patients can achieve control through a combination of avoidance strategies and pharmacological treatments.

Pharmacological Treatments
Asthma medications are categorized as:
Controllers: Taken daily for long-term management, primarily targeting inflammation

These include:
Inhaled corticosteroids (ICSS)
Leukotriene receptor antagonists (LTRAS)
Long-acting beta2-agonists (LABAs) combined with ICS
Anti-IgE therapy
Relievers: Used as needed for rapid symptom relief and bronchodilation. These includ
Rapid-acting inhaled beta2-agonists
Inhaled anticholinergics

AVOIDANCE MEASURES
Avoiding relevant allergens and irritants is a crucial aspect of asthma management.

Allergen Avoidance Strategies
House Dust Mites: Patients allergic to dust mites should use allergen-proof covers for bedding and maintain indoor humidity levels below 50% to prevent mite growth.

Pollen: To minimize pollen exposure, patients should keep windows closed, use air conditioning, and limit outdoor activities during peak pollen seasons.

Animal Dander: Removing pets from the home is the most effective strategy, often leading to symptom improvement within 4-6 months. However, as compliance is often low, using high-efficiency particulate air (HEPA) filters and keeping pets out of bedrooms or outdoors may help reduce allergen levels.

Mould Allergens: Exposure can be minimized through cleaning with fungicides, using dehumidifiers to maintain humidity below 50%, and installing HEPA filters.

Tobacco Smoke: Patients should avoid smoking and exposure to second-hand smoke.

Challenges and Adherence
Implementing these avoidance strategies can be demanding, and patient adherence is often suboptimal. To encourage adherence, physicians should provide regular reassessments, guidance, and motivation.

Combining Strategies
For optimal asthma control, patients should be advised to implement multiple avoidance measures simultaneously, as

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single interventions have shown limited effectiveness in improving asthma outcomes.

RELIEVER MEDICATIONS

Inhaled rapid-acting beta2-agonists are the preferred medications for relieving acute asthma symptoms and should be prescribed to all individuals with asthma.

In Canada, several short-acting beta2-agonists (SABAs), such as salbutamol and terbutaline, as well as one long-acting beta2-agonist (LABA), formoterol, are approved for this purpose. SABAS should only be used as needed to relieve symptoms. Frequent use (three or more times per week) suggests worsening asthma control and necessitates a reassessment of treatment to better manage symptoms.

Unlike other LABAS, formoterol has a rapid onset of action, making it suitable for relieving acute symptoms. However, due to the increased risk of asthma-related morbidity and mortality associated with LABA monotherapy, formoterol should only be used as a reliever in individuals aged 12 years or older who are also on regular inhaled corticosteroid (ICS) therapy.

Short-acting anticholinergic bronchodilators, such as ipratropium bromide, may also be used for symptom relief. However, these medications are generally less effective than inhaled rapid-acting beta2-agonists and should be considered second-line options for patients who cannot use SABAS.

In cases of moderate to severe asthma exacerbations, short-acting anticholinergics may be used in combination with SABAS. However, regular use of short-acting anticholinergic therapy is not recommended for children.

CONTROLLER MEDICATIONS

Inhaled corticosteroids (ICSs)

Inhaled corticosteroids (ICSs) are the most effective anti-inflammatory medications available for asthma treatment and are considered the cornerstone of therapy for most individuals with the condition.

Low-dose ICS monotherapy is the recommended first-line maintenance treatment for most children and adults with asthma. Regular use of ICSs has been shown to reduce symptoms, prevent exacerbations, and improve lung function and quality of life.

However, ICSs do not "cure" asthma. Symptoms often return within weeks to months after discontinuing treatment, meaning most patients will require long-term, and in some cases lifelong, ICS therapy.

If asthma remains uncontrolled despite ICS treatment, factors other than medication effectiveness should be considered. These include:

Misdiagnosis of asthma
Poor adherence to ICS therapy
Incorrect inhaler technique
Coexisting medical conditions

If these issues are addressed and asthma control is still not achieved with low to moderate doses of ICS, treatment adjustments are necessary. For most children, increasing the ICS dose to a moderate level is preferred. For patients aged 12 years and older, adding another class of medication, typically a long-acting beta2-agonist (LABA), is recommended.

Common local side effects of ICS therapy include oropharyngeal candidiasis (oral thrush) and dysphonia (hoarseness or difficulty speaking). These side effects can be minimized by rinsing the mouth and spitting after each inhalation or using a spacer device.

Systemic side effects with ICS therapy are rare but may include adrenal suppression, changes in bone density, cataracts, glaucoma, and growth suppression.

LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRAS)

Leukotriene receptor antagonists (LTRAS), such as montelukast and zafirlukast, are effective and generally well-tolerated options for asthma treatment. However, because they are less effective than inhaled corticosteroids (ICSs) as monotherapy, they are typically reserved for patients who cannot or choose not to use ICSs.

LTRAS may also be used as an add-on treatment for patients whose asthma is uncontrolled despite low-to-moderate dose ICS therapy. It is important to note that in adults, LTRAS are considered less effective than long-acting beta2-agonists (LABAS) as add-on therapy.

In children, the evidence is less clear, and treatment decisions should consider the child's symptoms and any comorbid conditions. For example:
If a child with asthma also has allergic rhinitis, adding montelukast may be beneficial.

If the child has persistent airway obstruction, adding a LABA may be more appropriate.

Combination ICS/LABA Inhalers

LABA monotherapy is not recommended for asthma treatment because it does not address airway inflammation and is linked to an increased risk of asthma-related morbidity and mortality. LABAs should only be used in combination with ICS therapy.

The combination of a LABA with an ICS has proven to be highly effective in reducing asthma symptoms and preventing exacerbations. It is the preferred treatment for adolescents and adults whose asthma is not adequately controlled with low-dose ICS therapy, or for children over six years of age whose asthma is uncontrolled with moderate-dose ICS therapy.

Although ICS and LABAs can be delivered through separate inhalers with similar effectiveness, combination ICS/LABA inhalers are preferred. They prevent LABA use without an ICS, are more convenient, and may improve patient adherence.

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Three combination ICS/LABA inhalers are available in Canada: salmeterol/ fluticasone (Advair), budesonide/formoterol (Symbicort) and mometasone/formoterol (Zenhale). Combination budesonide/formoterol has recently been approved for use in Canada as a single inhaler for both daily maintenance (controller) and reliever therapy in individuals 12 years of age and older.

It should only be used in patients whose asthma is not adequately controlled with low-to moderate ICS doses or whose disease severity warrants treatment with combination therapy.

THEOPHYLLINE

Theophylline is an oral bronchodilator with modest anti-inflammatory effects. Given its narrow therapeutic window and frequent adverse events (e.g., gastrointestinal symptoms, loose stools, seizures, cardiac arrhythmias, nausea and vomiting), its use is generally reserved for patients whose asthma is uncontrolled despite an adequate trial of ICS, LABAS and/or LTRAS.

Anti-IgE Therapy

Omalizumab, an anti-IgE monoclonal antibody, has been shown to reduce asthma exacerbations by approximately 50%. It is administered via subcutaneous injection every 2 to 4 weeks and is approved in Canada for patients aged 12 years and older with moderate to severe persistent allergic asthma.

Currently, omalizumab is typically reserved for individuals with difficult-to-control asthma who have confirmed allergies and whose symptoms remain uncontrolled despite treatment with inhaled corticosteroids (ICSs).

Long-term adherence to controller therapy is often poor, as many patients stop treatment once their symptoms improve. Regular follow-up appointments are crucial to encourage adherence and ensure effective asthma management.

SYSTEMIC CORTICOSTEROIDS

Systemic corticosteroids, such as oral prednisone, are generally used for the acute treatment of moderate to severe asthma exacerbations. While chronic systemic corticosteroid therapy may also be effective for the management of difficult to control asthma, prolonged use of oral steroids are associated with well-known and potentially serious adverse effects and, therefore, their long-term use should be avoided if at all possible.

Adverse events with short-term, high-dose oral prednisone are uncommon, but may include: reversible abnormalities in glucose metabolism, increased appetite, edema, weight gain, rounding of the face, mood alterations, hypertension, peptic ulcers and avascular

Allergen-specific immunotherapy

Allergen-specific immunotherapy involves the subcutaneous administration of gradually increasing quantities of the patient's relevant allergens until a dose is reached that is effective in inducing immunologic tolerance to the allergen

Allergen-specific immunotherapy has been widely used to treat allergic asthma, but it is not universally endorsed by all clinical practice guidelines due to the potential risk of serious anaphylactic reactions.

A Cochrane review of 75 randomized controlled trials demonstrated that allergen-specific immunotherapy is effective in reducing asthma symptoms, lowering medication requirements, and improving airway hyperresponsiveness. Similar benefits have been observed with sublingual immunotherapy, which which is expecte expected to gain approval in Canada soon. Additionally, evidence evidence su suggests that allergen-specific immunotherapy may help prevent the development of asthma in atopic individuals.

Currently, allergen-specific immunotherapy should be considered on a case-by-case basis. It may be used:

As a trial before starting ICS therapy in patients with very mild allergic asthma and coexisting allergic rhinitis.

As an add-on therapy for patients already using ICSs alone.

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For patients on combination treatments, such as ICS/LTRAS, ICS/LABAS, or omalizumab, provided their asthma is well-controlled.

Due to the risk of anaphylaxis, allergen-specific immunotherapy should only be prescribed by physicians with specialized training in allergy management. Injections must be administered in clinics equipped to handle life-threatening anaphylactic reactions, with a physician present. To minimize risks, asthma must be well-controlled, and the patient's FEV1 should be above 70% of the predicted value at the time of each injection.

CONCLUSION

Asthma is the most common respiratory condition in Canada and is a major contributor to illness and death. It should be suspected in individuals experiencing recurrent episodes of cough, wheezing, chest tightness, or shortness of breath, and confirmed using objective lung function tests, preferably spirometry. Allergy testing is also recommended to identify potential triggers of asthma symptoms.In most cases, asthma can be effectively managed with avoidance strategies and appropriate medications.

Inhaled corticosteroids (ICSs) are the standard treatment for most patients. For those whose asthma remains uncontrolled with low-to-moderate ICS doses, combination therapy with an ICS and a long-acting beta2-agonist (LABA) is the preferred option for most adults. Leukotriene receptor antagonists (LTRAS) may also be considered as an add-on therapy, especially in patients with coexisting allergic rhinitis.

Anti-IgE therapy, such as omalizumab, may be beneficial for certain patients with difficult-to-control asthma. Allergen-specific immunotherapy is another potential option that may modify the course of the disease. However, it should only be prescribed by specialists trained in allergy management.

All individuals with asthma should have regular follow-up visits to assess asthma control, ensure adherence to treatment, and review proper inhaler technique.

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