Asthma

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Abstract: Asthma is the most common respiratory disorder in Canada. Despite significant improvement in the diagnosis and management of this disorder, the majority of Canadians with asthma remain poorly controlled. In most patients, however, control can be achieved through the use of avoidance measures and appropriate pharmacological interventions. Inhaled corticosteroids (ICSs) represent the standard of care for the majority of patients. Combination ICS/long-acting beta2-agonists (LABA) inhalers are preferred for most adults who fail to achieve control with ICS therapy. Allergen-specific immunotherapy represents a potentially disease-modifying therapy for many patients with asthma, but should only be prescribed by physicians with appropriate training in allergy. Regular monitoring of asthma control, adherence to therapy and inhaler technique are also essential components of asthma management. This article provides a review of current literature and guidelines for the appropriate diagnosis and management of asthma.

KEYWORDS: Pathology, Diagnosis, Treatment

I. INTRODUCTION

Asthma remains the most common chronic respiratory disease in Canada, affecting approximately 10% of the population. Although asthma is often believed to be a disorder localized to the lungs, current evidence indicates that it may represent an component of systemic airway disease involving the entire respiratory tract, and this is supported by the fact that asthma frequently coexists with other atopic disorders, particularly allergic rhinitis. Asthma Control (TRAC) in Canada study suggest that over 50% of Canadians with asthma have uncontrolled disease. Poor asthma control contributes to unnecessary morbidity, limitations to daily activities and impairments in overall quality of life.

This article provides an overview of diagnostic and therapeutic guideline recommendations from the Global Initiative for Asthma (GINA) and the Canadian Thoracic Society and as well as a review of current literature related to the path physiology, diagnosis, and appropriate treatment of asthma.

Definition

Asthma is defined as a chronic inflammatory disease of the airways. The chronic inflammation is associated with airway hyperresponsiveness (an exaggerated airway- narrowing response to triggers, such as allergens and exercise), that leadsto recurrent symptoms such as wheezing, dyspnea (shortness of breath), chest tightness and coughing. Symptom episodes are generally associated with widespread, but variable, airflow obstruction within the lungs that is usually reversible either spontaneously or with appropriate asthma treatment [4].

PATHOPHYSIOLOGY

Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-allergic (e.g., infections, tobacco smoke, cold air, exercise) triggers produce a cascade of immune-mediated events leading to chronic airway...
inflammation. hyperreactivity Evidence suggests that there may be a genetic predisposition for the development of asthma.

A number of chromosomal regions associated with asthma susceptibility have been identified, such as those related to the production of IgE antibodies, expression of airway hyperreactiveness, and the production of inflammatory mediators. However, further study is required to determine specific genes involved in asthma as well as the gene-environment interactions that may lead to expression of the disease.

**DIAGNOSIS**

The diagnosis of asthma involves a thorough medical history, physical examination, and objective assessments of lung function (spirometry preferred) to confirm the diagnosis. Bronchoprovocation challenge testing and assessing for markers of airway inflammation may also be helpful for diagnosing the disease, particularly when objective measurements of lung function are normal despite the presence of asthma symptoms.

**MEDICAL HISTORY**

The diagnosis of asthma should be suspected in patients with recurrent cough, wheeze, chest tightness and shortness of breath. Symptoms that are variable, occur upon exposure to allergens or irritants, that worsen at night, and that respond to appropriate asthma therapy are strongly suggestive of asthma. Alternative causes of suspected asthma symptoms should be excluded, such as chronic obstructive pulmonary disease (COPD), bronchitis, chronic sinusitis, gastroesophageal reflux disease, recurrent respiratory infections, and heart disease.

A positive family history of asthma or other atopic diseases and/or a personal history of atopic disorders, particularly allergic rhinitis, can also be helpful in identifying patients with asthma. During the history, it is also important to examine for possible triggers of asthma symptoms, such as dust mites, cockroaches, animal dander, moulds, pollens, exercise, and exposure to tobacco smoke or cold air. Exposure to agents encountered in the work environment can also cause asthma. If work-related asthma is suspected, details of work exposures and improvements in asthma symptoms during holidays should be explored.

**DURING ASTHMA ATTACK THE FOLLOWING CHANGES TAKES PLACE**

The muscles around the airways tighten up, narrowing the airway. Less air is able to flow through the airway. Inflammation of the airways increases, further narrowing the airway. More mucus is produced in the airways, undermining the flow of air even more. In some asthma attacks, the airways are blocked such that oxygen fails to enter the lungs. This also prevents oxygen from entering the blood stream and traveling to the body’s vital organs. Asthma attacks of this type can be fatal, and the patient may require urgent hospitalization. At the same time carbon dioxide deposition in the lungs leads to carbon dioxide poisoning.

**TYPES OF ASTHMA**

**Child-Onset Asthma**

Asthma that begins during childhood is called child-onset asthma. This type of asthma happens because a child becomes sensitized to common allergens in the environment - most likely due to genetic reasons. The child is atopic - a genetically determined state of hypersensitivity to environmental allergens. Allergens are any substances that the body will treat as a foreign body, triggering an immune response. These vary widely between individuals and often include animal proteins, fungi, pollen, house-dust mites and some kind of dust. The airway cells are sensitive to particular materials making an asthmatic response more likely if the child is exposed to a certain amount of an allergen.
ADULT-ONSET ASTHMA

This term is used when a person develops asthma after reaching 20 years of age. Adult-onset asthma affects women more than men, and it is also much less common than child-onset asthma. It can also be triggered by some allergic material or an allergy. It is estimated that up to perhaps 50% of adult-onset asthmatics are linked to allergies. However, a substantial proportion of adult-onset asthma does not seem to be triggered by exposure to allergen(s); this is called non-allergic adult-onset asthma. This non-allergic type of adult onset asthma is also known as intrinsic asthma.

EXERCISE-INDUCED ASTHMA

Coughing, wheezing or feeling out of breath during or after exercise is called exercise-induced asthma. Level of fitness also matters a lot. A person who is unfit and runs fast for ten minutes is going to be out of breath asthma.

As with other types of asthma, a person with exercise-induced asthma will experience difficulty in getting air in and out of the lungs because of inflammation of the bronchial tubes (airways) and extra mucus.

COUGH-INDUCED ASTHMA

Cough-induced asthma is one of the most difficult asthmas to diagnose. The doctor has to eliminate other possibilities, such as chronic bronchitis, post nasal drip due to hay fever, or sinus disease. In this case the coughing can occur alone, without other asthma-type symptoms being present. The coughing can happen at any time of day or night. If it happens at night it can disrupt sleep.

OCCUPATIONAL ASTHMA

This type of asthma is triggered by something in the patient's place of work. Factors such as chemicals, vapors, gases, smoke, dust, fumes, or other particles can trigger asthma. It can also be caused by a virus (flu), molds, animal products, pollen, humidity and temperature. Another trigger may be stress.

NOCTURNAL ASTHMA

Nocturnal asthma occurs between midnight and 8 AM. It is triggered by allergens in the home such as dust and pet dander or is caused by sinus conditions. Nocturnal or nighttime asthma may occur without any daytimesymptoms recognized by the patient. The patient may have wheezing or short breath when lying down and may not notice these symptoms until awoken by them in the middle of the night - usually between 2 and 4 AM. Nocturnal asthma may occur only once in a while or frequently during the week. However, when there are no daytime symptoms to suggest asthma is an underlying cause of the nighttime cough, this type of asthma will be more difficult to recognize - usually delaying proper therapy.

STEROID-RESISTANT ASTHMA (SEVERE ASTHMA)

While the majority of patients respond to regular inhaled glucocorticoid (steroid) therapy, some are steroid resistant. Airway inflammation and immune activation play an important role in chronic asthma. Current guidelines of asthma therapy have therefore focused on the use of anti-inflammatory therapy, particularly inhaled glucocorticoids (GCs). By reducing airway inflammation and immune activation, glucocorticoids are used to treat asthma. However, patients with steroid resistant asthma have higher levels of immune activation in their airways than do patients with steroid sensitive (SS) asthma.

CAUSES OF ASTHMA

Allergies

Common sources of indoor allergens include animal proteins (mostly cat and dog allergens), dust mites, cockroaches, and fungi. It is possible that the push towards energy-efficient homes has increased exposure to these causes of asthma. Allergic reactions triggered by antibodies in the blood often lead to the airway inflammation that is associated with asthma.

TOBACCO SMOKE

Tobacco smoke has been linked to a higher risk of asthma as well as a higher risk of death due to asthma, wheezing, and respiratory infections. In addition, children of mothers who smoke - and other people exposed to second-hand smoke - have a higher risk of asthma prevalence. Adolescent smoking has also been associated with increases in asthma risk.
ENVIRONMENTAL FACTORS

Allergic reactions and asthma symptoms are often the result of indoor air pollution from mold or noxious fumes from household cleaners and paints. Other indoor environmental factors associated with asthma include nitrogen oxide from gas stoves. In fact, people who cook with gas are more likely to have symptoms such as wheezing, breathlessness, asthma attacks, and hay fever. Pollution, sulfur dioxide, nitrogen oxide, ozone, cold temperatures, and high humidity have all been shown to trigger asthma in some individuals. Weather changes have also been known to stimulate asthma attacks.

OBESITY

Overweight adults - those with a body mass index (BMI) between 25 and 30 - are 38% more likely to have asthma compared to adults who are not overweight. Obese adults - those with a BMI of 30 or greater - have twice the risk of asthma. According to some researchers, the risk may be greater for nonallergic asthma than allergic asthma.

STRESS

People who undergo stress have higher asthma rates. Part of this may be explained by increases in asthma-related behaviors such as smoking that are encouraged by stress. However, recent research has suggested that the immune system is modified by stress as well.

GENES

It is possible that some 100 genes are linked to asthma - Genes linked to asthma also play roles in managing the immune system and inflammation. There have not, however, been consistent results from genetic studies across populations - so further investigations are required to figure out the complex interactions that cause asthma. Three-fifths of all asthma cases are hereditary. The Centers for Disease Control (USA) say that having a parent with asthma increases a person's risk by three to six times. Genetics may also be interacting with environmental factors. For example, exposure to the bacterial product endotoxin and having the genetic trait CD14 (single nucleotide polymorphism (SNP) C-159T) have remained a well-replicated example of a gene-environment interaction that is associated with asthma.

AIRWAY HYPERREACTIVITY

Researchers are not sure why airway hyperreactivity is another risk factor for asthma, but allergens or cold air may trigger hyperreactive airways to become inflamed. Some people do not develop asthma from airway hyperreactivity, but hyperreactivity still appears to increase the risk of asthma.

DIAGNOSING ASTHMA

Common symptoms and signs include:

Wheezing
Coughing
Breathing difficulty
Tightness in the chest
Worsening symptoms at night
Worsening symptoms due to cold air.

PHYSICAL EXAM

A physical examination will generally focus on the upper respiratory tract, chest, and skin. A doctor will use a stethoscope to listen for signs of asthma in your lungs as you breathe. Physicians will also check for a runny nose, swollen nasal passages, and nasal polyps. Skin will be examined for conditions such as eczema and hives, which have been linked to asthma. Physical symptoms are not always present in asthma sufferers, and it is possible to have asthma without presenting any physical maladies during an examination.
ASTHMA TESTS

Lung function tests, or pulmonary function tests, are the third component of an asthma diagnosis. Spirometry is a noninvasive test that requires taking deep breaths and forcefully exhaling into a hose connected to a machine called a spirometer. The spirometer then displays two key measurements:

Forced vital capacity (FVC) - the maximum amount of air one can inhale and exhale Forced expiratory volume (FEV-1) - the maximum amount of air exhaled in one second

The measurements are compared against standards developed for a person's age, and measurements below normal may indicate obstructed airways. It is common for a doctor to administer a bronchodilator drug to open air passages before retesting with the spirometer. If results improve after the drug, there is a higher likelihood of receiving an asthma diagnosis. Children younger than 5 years of age are difficult to test using spirometry, so asthma diagnoses will rely mostly on symptoms, medical histories, and other parts of the physical examination. It is common for doctors to prescribe asthma medicines for 4 to 6 weeks to see how a young child responds.

OTHER TESTS

A "Challenge Test" (or bronchoprovocation test) is when a physician administers an airway-constricting substance (or something as simple as cold air) to deliberately trigger airway obstruction and asthma symptoms. Similarly, a challenge test for exercise-induced asthma would consist of vigorous exercise to trigger symptoms. A spirometry test is then administered, and if measurements are still normal, an asthma diagnosis is unlikely.

TREATMENT

Asthma medications are generally considered to fall into two classes: bronchodilators, which stop asthma attacks after they've started and help in preventing the attacks, and anti-inflammatories, which control the airway inflammation and prevent asthma attacks from starting.

BRONCHODILATORS

Bronchodilators provide relief during an asthma attack. They relax muscles in the air tubes, forcing them to open up and allowing the patient to breathe. Bronchodilators also may help to clear mucus from the lungs, allowing it to move more freely and be more easily coughed out. Some examples of bronchodilators include short-acting beta-agonists used to prevent exercise-induced asthma, anticholinergics used in addition to or as an alternative to short-acting beta-agonists and theophylline a long-acting drug used to treat severe asthma.

ANTI-INFLAMMATORIES

Anti-inflammatories prevent asthma attacks by keeping air tubes open all of the time. They are designed to reduce swelling in the air tubes and decrease the amount of mucus. Cromolyn and nedocromil are two examples of anti-inflammatory medicines. Corticosteroids are the most popular class of anti-inflammatories and are the drug of choice for persistent asthma. Other anti-inflammatories include mast cell stabilizers.

SIDE EFFECTS

There is always a risk of side effects associated with taking medicine. These may include sore throat, nervousness, nausea, rapid heartbeat, loss of appetite, or staying awake. A doctor will modify the treatment plans if side effects become severe.

OVER-THE-COUNTER

Over-the-counter asthma drugs such as "Primatene Mist" and "Bronkaid" are widely available bronchodilators that provide short-term relief. These medicines, however, do not control long-term asthma and should not be used every day to relieve asthma symptoms. Check with a physician before using over-the-counter medicines.
The most common device used to deliver medicine to the lungs of asthmatics is the metered-dose inhaler. Inhalers have two parts: 1) a canister consisting of a propellant, the medicine, and stabilizers, and 2) an actuator or mouthpiece consisting of a discharge nozzle and a dust cap. Inhalers are easily used by pressing down the top of the canister and inhaling the gas that is released. Usually the medicine administered by metered-dose inhalers is a bronchodilator, corticosteroid, or a mast cell stabilizer.

As an alternative to the aerosol-based metered-dose inhalers, dry powder inhalers deliver medicine from a capsule in powder form. These devices require the device into the lungs and can be more complicated to use than metered-dose inhalers.

Medication may also be administered using a nebulizer, providing a larger, continuous dose. Nebulizers vaporize a dose of medication in a saline solution into a steady stream of foggy vapor that is inhaled by the patient. Nebulizers are more common in hospital settings for patients who have difficulty using a metered-dose inhaler.

Asthma spacers are attachments that can be added to metered-dose inhalers. The spacer goes between the patient's mouth and the mouthpiece of the inhaler and it acts as a reservoir that briefly holds the medication. Spacers allow a patient to inhale the medicine without having to coordinate the breathing and mechanical actions needed to use an inhaler. Spacers also help patients deliver the medication directly to the lungs, avoiding medicine on the side of the mouth and the condition known as "thrush".

Asthma is the most common respiratory disorder in Canada, and contributes to significant morbidity and mortality. A diagnosis of asthma should be suspected in patients with recurrent cough, wheeze, chest tightness and dyspnea, and should be confirmed using objective measures of lung function (spirometry preferred). Allergy testing is also recommended to identify possible triggers of asthma symptoms.

In most patients, asthma control can be achieved through the use of avoidance measures and appropriate pharmacological interventions. ICSs represent the standard of care for the majority of asthma patients. For those who fail to achieve control with low-to-moderate ICS doses, combination therapy with a LABA and ICS is the preferred treatment choice in most adults. LTRAs can also be used as add-on therapy if asthma is uncontrolled despite the use of low-to-moderate dose ICS therapy, particularly in patients with concurrent allergic rhinitis. Anti-IgE therapy may be useful in select cases of difficult to control asthma. Allergen-specific immunotherapy is a potentially disease-modifying therapy, but should only be prescribed by physicians with appropriate training in allergy. All patients with asthma should have regular follow-up visits during which criteria for asthma control, adherence to therapy and proper inhaler technique should be reviewed.

A clinical diagnosis of asthma should be suspected in patients with intermittent symptoms of wheezing, coughing, chest tightness and breathlessness. Objective measurements of lung function, preferably using spirometry, are needed to confirm the diagnosis. All asthma patients should be prescribed a rapid-acting bronchodilator to be used as needed for relief of acute symptoms. ICS therapy is the standard of care for most patients with asthma.
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