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"ACOMPREHENSIVE OUTLOOK, ASTHMA"

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Abstract

Asthma is the most common inflammatory disease of the lungs. The prevalenceof asthma is increasing in many parts of the world that have adopted aspects of Western lifestyle, and the disease poses a substantial global health and economic burden. Asthma involves both the large-conducting and the small-conducting air ways, and is characterized by a combination of inflammation andstructural remodeling that might begin in utero. Disease progression occurs in thecontext of a developmental background in which the postnatal acquisition of asthma is strongly linked with allergic sensitization. Most asthma cases follow avariable course, involving viral- induced wheezing and allergen sensitization, that is associated with various underlying mechanisms (or endotypes) that can differ between individuals. Each set ofendotypes, in turn, produces specific asthma characteristics that evolve across the life course of the patient. Strong genetic and environmental drivers of asthma interconnect through novel epigenetic mechanisms that operate prenatally and throughout childhood. Asthma can spontaneously remit orbegin de novo in adulthood, and the factors that lead to the emergence and regression of asthma, irrespective of age, are poorly understood. None the less, thereis mounting evidence that supports a primary role for structural changes in theairways with asthma acquisition, on which altered innate immune mechanisms andmicrobiota interactions are superimposed. On the basis of the identification of newcausative pathways, the sub phenotyping of asthma acrossthe life course of patients is paving the way for more-personalized and precise pathway- specific approaches for the prevention and treatment of asthma, creating the realpossibility of total prevention and cure for this chronic inflammatory disease.

Introduction

Asthma remains the most common chronic respiratory disease in Canada, affecting approximately 10% of the population. Although asthma is often believedto be a disorder localized to the lungs, current evidence indicates that it mayrepresent a component of systemic air- way disease involving the entire respiratorytract, and this is supported by the fact that asthma frequently coexists with otheratopic disorders, particularly allergic rhinitis. Despite significant improvements inthe diagnosis and management

of asthma over the past decade, as well as the availability of comprehensive and widely-accepted national and international clinical practice guidelines for the disease, asthma control in Canada are mains sub optimal. Results from the recent Reality of Asthma Control (TRAC) in Canada study suggestthat over 50% of Canadians with asthma have uncontrolled disease. Poor asthmacontrol 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 ofcurrent literature related to the pathophysiology, 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 hyper responsiveness (anexagge rated air way-narrowing response to triggers, such as allergens and exercise), that leads to recurrentsymptoms such as wheezing, dyspnea (shortness of breath), chest tightness and coughing. Symptom episodes are generally associated with wide spread, but variable, air flow obstruction with in the lungs that is usually reversible either spontaneously or with appropriate asthma treatment .

WHO Definition :

Asthma is a chronic disease characterized by recurrent attacks of breath lessness and wheez sleeplessness, daytime fatigue reduced activity Which vary in severity and frequency from person-to-person symptoms may occur several times in a day or week in affected individuals, and for some people become worse during physical activity or at night. During an asthma attack, the lining of bronchial tubes well, causing he air ways to narrow and reducing the flow of air into and out of the lungs. Recurrent asthma symptoms frequently cause Level sand school and work absenteeism.

Epidemiology

Asthma is significantly more prevalent in women (10.4%) than in men(6.2%), those below the poverty line (11.8%), and in those who report being anethnic or racial minority, especially black race (10.2%) and Puerto Rican Hispanicethnicity(14.9%). Geographic prevalence also ranges widely, from 4.9% to 12.7%by state. Despite a wide array of treatment options, almost half of adults withasthma report having one or more attacks in the previous year, highlighting the importance of symptom management and disease control. Asthma is classically thought of asa disease that begins in youth. Although it is true that asthma is most commonly first diagnosed in childhood, it can become clinically apparent at any age. Indeed, a national survey suggests that the rate of first asthmadiagnosis for those older than 65 (3.1% per year) is not substantially different thanthose between 18 and 34 (4.0% per year). The estimated prevalence of asthmaamong adults over 65 years of age is 7%, which is similar to the overall prevalence.History of prematurity, early lung infections, rhinitis, smoking, and obesity are all risk factors for adult-onset asthma Therefore, the onset ofchronic cough in an older patient should not dissuade the clinician from considering asthma.

Morbidity

About 60% of all asthmatics visit their physician at least once a year regarding their condition. Office visits doubled from1975-1994(see table below). Emergency department (ED) visits and hospitalizations are also increasing, with 466,000 hospitalizations in1993and 1.9million ED visits in 1995. Office Visits (1980-1994) and ED Visits (1992-1995) and Hospitalizations (1980- 1994) Due to Asthma Data unavailable for 1980.

The effect asthma has on an individual's quality of life and the extent to which it may restrict daily activities is often overlooked. Yet, it is an important partof understanding this condition and the benefits that effective treatment can bring. Results from a 1998 survey conducted by the American Lung Association (ALA)highlight these quality-of-life issues.

	Office Visits		ED Visits		Hospitalizations	
Age (years)	1994	Increase from 1980 (%)	1995	Increase from 1992* (%)	1994	Increase from 1980 (%)
0-4	1,024,000	98	248,000	-14	97,000	73
5-14	2,004,000	23	322,000	11	67,000	20
15-34	1,876,000	65	566,000	29	78,000	15
35-64	3,982,000	164	630,000	75	139,000	9
>65	1,488,000	119	101,000	13	85,000	8
Total	10,374,000	90	1,867,000	27	466,000	21

Asthma etiology

The cause of asthma is not known, but risk factors have been identified and gene-environment interactions are important. Genetics are known to play a role, with asthma with heritability ranging between 35% and 95%. Large genetic studieshave identified hundreds of genetic variants associated with an increased risk ofasthma. Epigenetic variations in how the genetic code is translated have also beenshown to have a role in the development of asthma. Respiratory infections, especially viral infections early in life, increase the risk of developing asthma,particularly if the symptoms are severe. Airborne environmental expo- sures increase the risk of asthma, including tobacco smoke, pollutants, and ozone. Atopicconditions and sensitization to inhalant allergens are also associated with developing asthma. Other factors have been theorized to play a role in asthma development, including effectsof the microbiome, vitamin D, chemical exposure, dietary changes, stress, and metabolites Current asthma understanding entails a broad amount of genetic diversity, which is variably translated and environmentally influenced via epigenetic and transcriptional factors, leading to less diverse features with resulting cardinal asthmatic symptoms.

Pathology:

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. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9and IL-13,that promote eosinophilic inflammation and immunoglobulin E (IgE) production by mast cells. IgE production, inturn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that cause broncho spasm (contraction of the smooth muscle in the airways), edema (swelling) and increased mucous secretion (mucous hypersecretion), which lead to the characteristic symptoms of asthma. The mediators and cytokines released during the early phase of an immune response to an inciting allergen, trigger a further inflammatory response (late-phase asthmatic response) that leads to further airway inflammation and bronchial hyperreactivity. Evidence suggests that there may be a genetic Redis- position 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 hyperresponsiveness, 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

Classification :

The initial classification is based on the presence of certain clinical Features before treatment. The presence of one of the features of severity is sufficient to place a patient in that category. A patient should be assigned to the most severe grade in which any feature occurs. The characteristics noted in this classification is general and may overlap because asthma is highly variable. Furthermore, a patient's classification may change overtime

Mild Persistent Asthma:

Symptoms of cough, wheeze, chest tightness or difficulty breathing three to six times a week
• Flare-ups-may affect activity level
• Night time symptoms three to four times a month
• LungfunctiontestFEV1equaltoorabove80percentofnormalvalues
• Peakflowlessthan20 to30percentvariability.

Moderate Persistent Asthma :

- Symptoms of cough, wheeze, chest tightness or difficulty breathing
  Daily Flare-ups-may affect activity level
- Night time symptoms 5 or more times a month
- Lung function test FEV 1 above 60 percent but below 80 percent of normal
- Peak flow more than 30 percent variability.

Severe Persistent Asthma

- Symptoms of cough, wheeze, chest tightness or difficulty
- Breathing continual
- Night time symptoms frequently
- Lung function test FEV1 less than or equal to 60 percent of normal values
- Peak flow more than 30 percent variability.
- The level of asthma severity will determine the types of medicine required to Get asthma under control.

Another type of classification commonly seen is

1) Chronic asthma
2) Acute severe asthma
3) Allergic asthma
4) Exercise induced asthma.
5) Nocturnal asthma

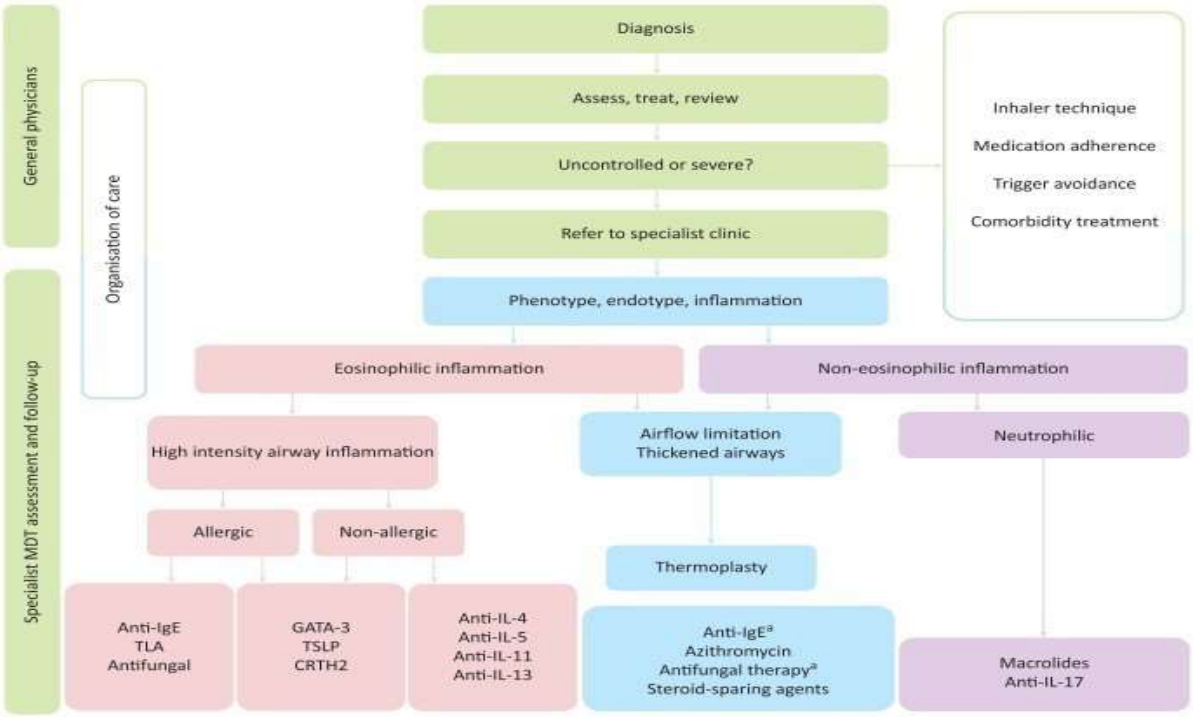
Diagnosis:

Primary care doctors will diagnose asthma based on medical history, a Physical exam, & results from tests. He or she also will determine the level of Asthma severity—that is, whether it's intermittent, mild, moderate, or severe. Severity level will determine what treatment is started.
A Veteran may need to see an asthma specialist if:
Special tests are needed to be sure you have asthma.?
If a life-threatening Asthma attack has occurred.? If the Veteran needs more than one kind of medicine or higher doses of medicine to control your asthma, or if you have overall Difficulty getting your asthma well controlled. If the Veteran is thinking about getting allergy treatment.

Medical History:
The doctor may ask about family history of asthma and allergies. He or she Also, may ask about the presence of asthma symptoms, and when and how often They occur. The doctor will also want to know if the symptoms seem to happen Only during certain times of the year or in certain places, or if they get worse at night The doctor also may want to know what factors seem to set off symptoms Or worsen them. The doctor may ask about related health conditions that can Interfere with asthma management. These conditions include a runny nose, sinus infections, reflux disease, psychological stress, and sleep aponia.

Physical Exam:
The doctor will listen to the Veteran's breathing and look for signs of asthma or allergies. These signs include wheezing, a runny nose or swollen nasal passages, and allergic skin conditions such as eczema. Keep in mind that someone can still have asthma even if theses ignsaren't present on the day of the examination.

Diagnostic Tests:
Lung Function Test: The doctor will use a test called spirometry to check how the lungs are working. This test measures how much air a patient can breathe in and out. It also measures how fast the patient can blow air out. The doctor also May give the patient medicines and then test again to see whether the results Have improved. If the starting results are lower than normal and improve with the medicine, and if your medical history shows a pattern of asthma symptoms, your diagnosis will likely be asthma.



Other Tests:

Your doctor may order other tests if he or she needs more information to make a diagnosis. Other tests may include: Allergy testing to find out which allergens may be involved, if any? A test to measure how sensitive the airways are. This is called a bronchoprovocation test. Using spirometry, this test repeatedly measures lung function during physical activity or after receiving increasing doses of cold air or a special chemical to breathe in? A test to show whether another disease with the same symptoms as asthma, such as reflux disease, vocal cord dysfunction, or sleep apnoea may be present. A chest x-ray Oran ECG (electrocardiogram). These tests will help find out whether a foreign objector other disease may be causing asthma symptoms.

Signs and Symptoms of Asthma:

Common asthma symptoms include:

- Coughing. Coughing from asthma is often worse at night or early in the morning, making it hard to sleep.
- Wheezing. Wheezing is a whistling or squeaky so und that occurs when breathing.
- Chest tightness. This may feel like something is squeezing or sitting on Your chest.
- Shortnessof breath. Some people who have asthma say they can't catch their breath or they feel out of breath. They may feel like they can't get air out of their lungs.
- Not all people who have asthma have these symptoms. Likewise, having
- These symptoms don’t always mean that someone has asthma. A lung functions test, done along with a medical history (including type and frequency of symptoms) and physical exam, is the best way to diagnose asthma for certain.

The types of asthma symptoms, how often they occur, and how severe they are may vary over time. Sometimes symptoms may just be annoying. Other times they may be troublesome enough to limit activities of daily living. Severe symptoms can threaten one’s life. It's vital to treat symptoms when they Are first noticed them so they don't become severe with proper treatment, most people who have asthma can expect to have few, If any, symptoms either during the day or at night.

Medicines:

Doctors will consider many things when deciding which asthma medicines are best for the patient. Doctors usually use a stepwise approach to prescribing medicines. Asthma medicines can be taken in pill form, but most are taken using a device called an inhaler. An inhaler allows the medicine to go right to the lungs. Not all inhalers are used the same way. Ask the doctor and other clinicians on the Healthcare team can show the patient the right way to use an inhaler.

Long-Term Control Medicines:

Most people who have asthma need to take long-term control medicines daily to help prevent symptoms. The most effective long-term medicines reduce Airway inflammation. These medicines are taken over the long term to prevent Symptoms from starting. They don't give you quick relief from symptoms Inhaled Corticosteroids. Inhaled corticosteroids are the preferred medicines for long-term control of asthma. These medicines are the most effective long term control medicine to relieve airway inflammation and swelling that makes the airways sensitive to certain substances that are breathed in. Reducing inflammation helps prevent the chain reaction that causes asthma symptoms. Most people who take these medicines daily find they greatly reduce how severe symptoms are and how often they occur Inhaled corticosteroids are generally safe when taken as prescribed. They're Very different from the illegal an a bolic steroids taken by some athletes. Inhaled corticosteroids aren't habit-forming, even if taken every day for many years. But, like many other medicines, inhaled corticosteroids can have side effects. Most doctors agree that the benefits of taking inhaled corticosteroids and preventing asthma attacks far outweigh the risks of side effects. One common side effect from inhaled corticosteroids is a mouth infection Called thrush. Often patients can use as pacer or holding chamber to avoid thrush. A spacer or holding chamber is attached to the inhaler when taking medicine to Keep the medicine from landing in the mouth or on the back of the throat. Rinsing The mouth out with water after taking inhaled corticosteroids also can lower the risk of thrush with severe asthma, patients may have to take corticosteroid pills or liquid for short periods to get asthma under control. If taken for long periods, these medicines may increase the chance of cataracts and osteoporosis.

Medicines Other Long-term Control. Medicines include:

Inhaledlong-actingbeta2-agonists. These medicines open the airways and may be added to low dose inhaled corticosteroids to improve asthma control. Aninhaledlong-actingbeta2-
agonist shouldn't be used alone. Leukotriene modifiers. These medicines are taken by mouth. They help block the chain reaction that increases inflammation in the airways. Cromolyn and nedocromil. These inhaled medicines also help prevent inflammation and can be used to treat asthma of mild severity. Theophylline. This medicine is taken by mouth and helps open the airways. If the doctor prescribes a long-term control medicine, it should be taken every Day to control asthma. Asthma symptoms will likely return or get worse if the medication is
stopped.

Quick-Relief Medicines:

All people who have asthma need a quick-relief medicine to help relieve Asthma symptoms that may flare up. Inhaled short-acting beta2-agonists are the first Choice for quick relief. These medicines act quickly to relax tight muscles around the airways during a flare-up. This allows the airways to open up so air can Flow through them. Quick-relief medication is taken when asthma symptoms are first noticed. If patients are using this medicine more than 2 days a week, they should talk with their doctor about how well controlled the asthma really is. You shouldn't use quick relief medicines in place of prescribed long-term control medicines.

Conclusion:

Asthma is a heterogenic and complex disease originating from a variety of gene environment interactions. Most asthma exhibits type 2inflammation, which is often seen in allergic conditions and also as an immune response to parasites. Type 2inflammation is mediated by respiratory epithelium and type 2 The per lymphocytes. Inflammation of the bronchi leads to increased mucus production, increased bronchoconstriction, and collagen deposition narrowing the airways. Asthma is often episodic, with a variety of environmental triggers that vary among asthmatics. Triggers include viruses, allergens, irritants (smoke), exercise, and temperature changes. The inflammation causes obstruction primarily of the bronchial airways with symptoms of shortness of breath, wheezing, chest tightness, and cough. The bronchoconstriction in asthma is Often reversible with an inhaled β2 agonist. Reversibility often helps differentiate asthma from

other pulmonary conditions. There are proven methods to diagnose and treat most asthmatics, making knowledge of asthma important for Physicians who treat inflammatory disorders of the upper or lower airways.

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