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WHEEZING WISDOM: AN IN- DEPTH LOOK AT ASTHMA

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ABSTRACT

Asthma is a chronic inflammatory disease of the airways characterized by hyperresponsiveness and variable airflow obstruction. This review provides a comprehensive overview of asthma, encompassing its definition, epidemiology, pathophysiology, diagnosis, and treatment, drawing from both the Global Initiative for Asthma (GINA) and Canadian Thoracic Society guidelines. The various types of asthma, including child-onset, adult-onset, exercise-induced, cough- induced, occupational, nocturnal, and steroid-resistant asthma, are discussed. Key triggers such as allergies, tobacco smoke, environmental factors, obesity, stress, and genetic predisposition are highlighted. Diagnostic approaches, including symptom assessment, physical examination, and lung function tests, are outlined. Management strategies, emphasizing a stepwise approach with controller medications (inhaled corticosteroids, leukotriene receptor antagonists, theophylline), reliever medications (short-acting beta-agonists), and add-on therapies (long- acting beta-agonists, long-acting muscarinic antagonists, biologic therapies), are detailed. Allergen-specific immunotherapy and bronchial thermoplasty are also considered as potential treatment options. Additionally, the review explores the complex mechanisms underlying airway inflammation, including the roles of T helper 2 cells, cytokines, eosinophils, mast cells, and airway remodeling. Understanding the multifaceted nature of asthma is crucial for optimizing patient care and improving outcomes.

KEYWORDS: Asthma, long-acting, Allergic, Pathophysiology.

1. INTRODUCTION

Asthma: Asthma is one of the most common major non-communicable diseases and for many, has a substantial impact on quality of life. Globally, asthma is ranked 16th among the leading causes of years lived with disability and 28th among the leading causes of burden of disease, as measured by disability-adjusted life years. Around 300 million people have asthma worldwide, and it is likely that by 2025 a further 100 million may be affected.[1] Asthma is a heterogeneous chronic inflammatory disease of the airways that affects approximately 300 million people worldwide, and number is likely to rise to 400 million by 2025.[2] The Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis in Adults (INSEARCH) estimated the national burden of asthma at 17.23million with an overall prevalence of 2.05%. The probable estimates have indicated that around 2.05 % Indian population suffers from asthma. In addition, asthma too has attributed 13.2 thousand deaths.[3] One of our era's greatest scourges is air pollution, on account not only of its impact on climate change but also its impact on public and individual health due to increasing morbidity and mortality. There are many pollutants like Air pollution, dust, and pollen etc. that are major factors in disease in humans.[4] Although asthma is very common, affecting 5–10%of the population, the diagnosis of asthma in adults remains a challenge in the real world which results in both over- and under-diagnosis.[5] Asthma can affect people of all ages, but data were obtained from the Global Burden of Disease [GBD] study, which was conducted from 1990 to 2019 in 204 countries. Childhood asthma is a chronic lung disease caused by allergic or hypersensitivity reactions and characterized by bronchospasms and dyspnea.[6] On the whole, India has three times higher mortality and more than two times higher DALYs compared to the global proportion of asthma burden.[7] The global epidemic of asthma that has been observed in both children and adults is still continuing, especially in low to middle income countries, although it has subsided in some developed countries.[8] It is most common noncommunicable disease in children, and among the most common in adults. The great majority of people with asthma live in Low- and Middle-income countries which have disproportionately high asthma related morbidity and mortality.[9] According to the American Thoracic Society/European Respiratory Society (ATS/ERS) Task Force, asthma is defined as severe when it ‘‘requires treatment with high dose inhaled corticosteroids (ICSs) plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains uncontrolled despite this therapy.[10] The incidence and prevalence of asthma are increasing,

though regular use of inhaled corticosteroids (ICS) reduces mortality.8,9 New therapies and therapeutic targets are required for better control of symptoms and exacerbations in severe asthma patients and for avoiding adverse reactions caused by the administration of oral corticosteroids (OCS**)**.[10]

2. Epidemiology of Asthma

Global Prevalence: Asthma affects an estimated 300 million people worldwide, with the prevalence varying by region. Developed countries report higher prevalence rates, but asthma is increasing in low- and middle-income countries as well.[11] The Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis in Adults (INSEARCH) estimated the national burden of asthma at 17.23million with an overall prevalence of 2.05%. The probable estimates have indicated that around 2.05 % Indian population suffers from asthma. In addition, asthma too has attributed 13.2 thousand death.[12] Asthma can affect people of all ages, but data were obtained from the Global Burden of Disease [GBD] study, which was conducted from 1990 to 2019 in 204 countries.[13]

Regional prevalence of Asthma: According to reports from major international respiratory groups, including the International Study of Asthma and Allergies in Childhood (ISAAC), the Global Asthma Network (GAN), and the European Community Respiratory Health Survey (ECRHS), “current wheezing” (within the past 12 months) was found to be a sensitive epidemiological definition for active asthma, while the “ever-diagnosed asthma” definition was specific for lifetime asthma.[14]

3. Pathophysiology of asthma

Asthma is associated with T helper cell type-2 (T2) immune responses, which are typical of other atopic conditions. Asthma triggers may include allergic (e.g., house dust mites, cockroach residue, animal dander, and pollens) and non-allergic (e.g., viral infections, exposure to tobacco smoke, cold air, exercise) stimuli, which produce a cascade of events leading to chronic airway inflammation. Elevated levels of T2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, and promote eosinophilic inflammation and immunoglobulin E (IgE) production.[15] IgE production, in turn, triggers the release ofinflammatory mediators, such as histamine and cysteinyl leukotrienes, that cause bronchospasm (contraction of the smooth muscle in the airways), enema, and increased mucous secretion, which lead to the characteristic symptoms of asthma.[16]

4. Classification of Asthma

A) Phenotypes of Asthma: Asthma phenotypes are defined based on various factors such as age of onset, symptom patterns, and inflammatory markers. Commonly recognized asthma phenotypes include.

- **Allergic Asthma**: Characterized by immune system activation (IgE-mediated) triggered by allergens (e.g., pollen, dust mites).[17]
- **Non-Allergic Asthma**: More common in adults, where symptoms are not triggered by allergens but by other factors like stress, exercise, or air pollution.
- **Occupational Asthma**: Occupational asthma is caused by exposure to certain irritants in the workplace. There are more than 200 substances including gases, dust particles and chemicals that are known to cause asthma in the work place.[18]

B) Severity Classification of Asthma

Asthma severity is typically classified based on the frequency of symptoms, the need for rescue medication, and the degree of lung function impairment. The classification generally includes.

C) Asthma Triggered

- **Indoor allergens:** such as dust mites, mold, and pet dander or fur.
- **Outdoor allergens:** such as pollens and mold.
- **Poor air quality:** or very cold air.[19]

5. Risk Factors

Lifestyle factors: Obesity, poor diet, and lack of physical activity can also contribute to asthma risk.[20]

Smoking: This is one of the most common triggers for asthma in adults. Smoking may also increase the severity of wheezing and coughing. If pregnant women smoke, it increases the child's risk for wheezing.

Genetics: A family history of asthma or other allergic conditions increases the risk of developing asthma.[21]

6. Clinical Features

Wheezing: A high-pitched whistling sound during exhalation, often due to narrowed airways.

Shortness of breath (dyspnea): Difficulty breathing, particularly during physical activity or at night.

Coughing: Often worse at night or early morning; it can be dry or accompanied by sputum production.

Chest tightness: A feeling of constriction or pressure in the chest, especially during exacerbations.

7. Diagnosis

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. The high-pitched whistling sound while you exhale - or wheezing - is a key sign of both an obstructed airway and asthma. 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.[22]

Asthma Tests: Lung function tests, or pulmonary function tests, are the third component of an asthma diagnosis. Spirometry is a non-invasive 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 inhales 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.[23]

8. Management of Asthma

The primary goal of asthma management is to achieve and maintain control of the disease in order to prevent exacerbations (abrupt and/or progressive worsening of asthma symptoms that often require immediate medical attention and/or the use of oral steroid therapy) and reduce the risk of morbidity and mortality. Other goals of therapy are to minimize the frequency and severity of asthma symptoms, decrease the need for reliever medications, normalize physical

activity, and improve lung function as well as overall quality of life. The level of asthma control should be assessed at each visit using the criteria in Table 1.[24]

Managing asthma

Identifying and avoiding asthma triggers will help you to maintain an active and healthy lifestyle with asthma. The following list discusses common triggers and suggests ways to handle them.[25]

- Tobacco smoke - avoid inside and outside of the home
- Air pollution - try antihistamine medications and staying indoors
- Pollen - try antihistamine medications and staying indoors
- Animal dander - keep pets outside, wash them often, find them a new home
- Viral infections - see a physician
- Heavy exercise - lower the impact of your exercise routine and consult a doctor
- Stress - many methods of stress reduction exist, including breathing, meditation, progressive relaxation, and exercise.
- Dry or cold air - wear a scarf over your mouth and nose during winter months
- Dust mites - keep sheets, blankets, pillows, and stuffed toys clean
- Sulfites in dried food and wine - avoid foods with allergens.[26]

Treatment of Asthma: Inhaled corticosteroids (ICSs)

ICSs are the most effective anti-inflammatory medications which are available for the treatment of asthma and they represent the centre point of therapy for most patients.[27] Lowdose ICS monotherapy is recommended as first-line maintenance therapy for most children and adults with asthma.[28]

Combination ICS/LABA inhalers

LABA monotherapy is not recommended in patients with asthma as it does not impact airway inflammation and is associated with an increased risk of morbidity and mortality. LABAs are only recommended when used in combination with ICS therapy.[29] The combination of a LABA and ICS has been shown to be highly effective in reducing asthma symptoms and exacerbations, and is the preferred treatment option in adolescents or adults whose asthma is inadequately controlled on low-dose ICS therapy, or in children over 6 years of age who are uncontrolled on moderate ICS doses.[30] Although there is no apparent difference in efficacy between ICSs and LABAs given in the same or in separate inhalers, combination ICS/LABA inhalers are preferred because they preclude use of the LABA without an ICS, are more

convenient and may enhance patient adherence. Four combination ICS/LABA inhalers are available in Canada: fluticasone propionate/salmeterol, budesonide/formoterol, mometasone/formoterol and fluticasone furoate/vilanterol (see Table 7).[31] Combination budesonide/formoterol has been approved for use 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-dose ICS who warrant treatment with combination therapy.[32]

Leukotriene modifiers can help you

- Breathe more easily.
- Exercise despite a breathing condition.
- Keep your airway open.
- Lessen mucous in your chest and throat.
- Prevent breathing trouble, such as allergic reactions and asthma attacks.
- Reduce the number and severity of reactions and attacks.[33].

9. Asthma in special population: Asthma in Pregnancy

Pregnant women with asthma require special attention because asthma symptoms can worsen or improve during pregnancy. Proper asthma control is essential for the health of both the mother and fetus. ICS and rescue medications (e.g., albuterol) are considered safe during pregnancy, while oral corticosteroids and leukotriene modifiers are used cautiously due to potential risks to fetal development. Regular monitoring is recommended, and an asthma action plan should be adjusted as necessary**.**[34]

Asthma in the Elderly

Asthma in older adults presents unique challenges, as the condition may be complicated by comorbidities such as chronic obstructive pulmonary disease (COPD), heart disease, and osteoporosis. Additionally, elderly patients may have a reduced response to medications or may experience more side effects. Proper medication management, including the use of ICS and bronchodilators, is essential, but there is a need to monitor for drug interactions and adjust doses accordingly.[35]

10. Advances in asthma research and therapy

Digital Health and Asthma Monitoring: The use of wearable devices and mobile health applications has improved asthma management. These technologies allow for real-time

monitoring of symptoms and medication adherence, enabling timely interventions and more personalized care (Alessa et al., 2020).[36]

Targeted Drug Delivery Systems

Nanoparticle-based drug delivery systems are being developed to target the lungs more efficiently. These systems improve drug bioavailability at the site of action and may allow for lower doses with fewer systemic side effects. For instance, liposomal formulations can encapsulate corticosteroids, delivering them directly to inflamed lung tissue, thus enhancing their anti-inflammatory effects.[37]

11. Challenges in Asthma Care

Barriers to Adherence

- **Cost of Medication:** The cost of asthma medications, especially controller medications like inhaled corticosteroids, can be prohibitively high for many individuals. High costs, even with insurance, can lead to medication non-adherence, where patients may reduce or stop treatment to save money (Adams et al., 2019).[38]
- **Psychosocial Factors**: Mental health issues such as anxiety, depression, or stress can affect adherence. Patients may feel overwhelmed or not motivated to follow treatment plans, especially if they do not perceive an immediate benefit (Fitzgerald et al., 2021).[39]

2. Barriers to Access to Care

- **Socioeconomic Factors:** Individuals from lower-income backgrounds often face significant barriers to accessing healthcare. This includes limited access to primary care providers, lack of health insurance, and living in areas with few healthcare resources (Kapur et al., 2019). These factors can delay diagnosis and treatment, leading to poorer asthma management.[40]
- **Geographic Barriers:** People living in rural or underserved areas often struggle to access specialized asthma care due to a lack of healthcare facilities or specialists nearby. This geographic disparity leads to delayed or inadequate asthma management.[41]

12. Future Direction

Innovations in Asthma Prevention and Control Environmental and Lifestyle Interventions

- **Direction**: As research into asthma's environmental triggers continues, there will be increasing focus on preventing asthma through environmental control. Technologies like

air purifiers, wearable sensors to track allergens and pollution exposure, and smarter urban planning can reduce environmental triggers. Public health initiatives will encourage asthma-friendly lifestyles, such as reducing tobacco smoke exposure, dietary interventions, and regular physical activity.[42]

- Example: Air pollution reduction strategies (like reducing traffic emissions or improving indoor air quality) will become integral to asthma control, especially in urban environments.[43]

Global Efforts for Asthma Awareness and Education Global Collaboration for Asthma Guidelines

- **Direction**: Continued collaboration among global organizations like the Global Initiative for Asthma (GINA) will lead to the development of unified asthma management guidelines that emphasize a comprehensive, patient centered approach. These guidelines will incorporate cutting-edge research and treatments, ensuring that all healthcare providers, regardless of location, have access to evidence-based care recommendations.[44]

Example: International bodies will work to harmonize asthma management strategies across different regions, particularly in low-income countries, ensuring that all patients receive appropriate care regardless of geographic location.[45]

School-Based Asthma Education

- **Direction:** Schools will play a more prominent role in asthma education, with programs designed to educate children, teachers, and school nurses about asthma management. This approach will ensure that children with asthma are better supported in their school environment, leading to fewer missed school days and improved quality of life.
- **Example:** School-based asthma programs will include training for teachers to recognize asthma symptoms and take appropriate action in emergencies.[46]

13. CONCLUSION

Asthma is a complex, chronic inflammatory disease affecting millions worldwide, causing symptoms such as wheezing, coughing, shortness of breath, and chest tightness Its impact is substantial, causing significant morbidity, mortality, and economic burden. While a cure remains elusive, effective management strategies exist to achieve and maintain control, significantly improving patients' quality of life. This review emphasizes the importance of understanding the various types of asthma, recognizing triggers, and adhering to

comprehensive treatment plans outlined in clinical practice guidelines. Continued research and personalized approaches offer hope for further advancements in asthma management, ultimately minimizing the impact of this pervasive condition. It is important for those with asthma to work closely with healthcare providers to develop personalized treatment plans and monitor symptoms to prevent flare-ups and manage the condition effectively. Early diagnosis and consistent management are key to improving quality of life for asthma patients.

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