



REVIEW ON ASTHMA AND ITS MANAGEMENT

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ABSTRACT

Asthma is one of the common diseases. Asthma was a term used by the ancient Greeks to describe any condition that causes shortness of breath. It is a chronic inflammatory disorder of the airways associated with increased airway hyper-responsiveness, recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night/early morning.

INTRODUCTION

Asthma is one of the common diseases. Asthma was a term used by the ancient Greeks to describe any condition that causes shortness of breath. It is a chronic inflammatory disorder of the airways associated with increased airway hyper-responsiveness, recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night/early morning. Airway inflammation produces airflow limitation through acute bronchoconstriction, chronic mucus plugs formation and airway wall swelling or remodeling.^[4]

There are two general categories for classifying asthma, extrinsic and intrinsic depending upon the types of stimuli that trigger attacks.

❖ Extrinsic Asthma: It is caused by a type of immune system response to inhaled allergens such as pollen, animal dander or dust mite particles.

❖ Intrinsic Asthma: It is caused by inhalation of chemicals such as cigarette smoke or cleaning agents, taking aspirin, a chest infection, stress, laughter, exercise, cold air, food preservatives or a myriad of other factors.

Early warning signs are breathing changes, sneezing, moodiness, headache, runny/stuffy nose, coughing, chin or throat itches, feeling tired, dark circles under eyes, trouble sleeping. The diagnosis of asthma usually based on clinical history, objective measures of pulmonary function, and based on assessment of allergy. Asthma creates an extensive burden on individuals and families, as it is more often under-diagnosed and

under-treated. World Health Organization estimates that (300 million) people suffer from asthma, (2,55,000) people died of asthma in 2005 and over 80% of Asthma deaths were reported from low and lower-middle income countries. In India, an estimated (57,000) deaths were attributed to asthma in 2004 and it is one of the leading causes of morbidity and mortality in rural India. India had an estimated (15-20 million) asthmatics. It was estimated that the number of people with asthma would grow by more than (100 million) by 2025.

The prevalence of asthma had risen over the last 30 years but now appears to be stabilized, with approximately (10–12%) of adults and 15% of children affected by the disease. Occupation conditions, such as exposure to fumes, gases or dust are responsible for (11%) of asthma cases worldwide. There are different medications and available in tablets, aerosol inhalers, powder aerosols, liquids and injections. Even though many people with asthma depend on medications to prevent and relieve symptoms, some people can do several things on their own to maintain their health and lessen the possibility of asthma attacks.

By following the below suggestions and taking medications as needed, can live a healthy, active lifestyle.

- Keep home smoke free.
- Keep away from paint or strong smelling cleaning solutions such as ammonia.
- Avoid strong perfumes and hair spray.
- Keep the house well ventilated.
- Remove stuffed animals that can collect dust or wash them often or cover with plastic.
- Keep bathrooms dry and clean to prevent mold and use a dehumidifier if necessary.
- Replace filters in air conditioners because they collect dust.
- Avoid feather pillows and use synthetic materials such as Dacron.
- Avoid visits to homes with animals and do not have one in home. Select pets, such as fish, that have no dander.
- Washing hands frequently helps to prevent catching a cold.
- Avoid unnecessary exposure to colds. If likely to stir up dust, wear a mask or have someone else do the cleaning.
- Regular exercise strengthens heart and lungs, which helps relieve asthma symptoms.
- Maintain a healthy weight.
- Get plenty of sleep.
- Avoid stress.
- Vitamins and minerals will be beneficial for asthma (Vitamin- A found abundantly in carrots, pumpkin, sweet potatoes, winter squashes, cantaloupe, pink grapefruit, apricots, broccoli, and spinach. ^[1]

EPIDEMIOLOGY

The 2003 Canadian Community Health Survey found that (8.4%) of the Canadian population (≥ 12 years) of age had been diagnosed with asthma, with the prevalence being highest among teens ($> 12\%$). Between 1998 and 2001, close to (80,000) Canadians were admitted to hospital for asthma, and hospitalization rates were highest among young children and seniors. However, the survey also found that mortality due to asthma has fallen sharply since 1985. In 2001, a total of (299 deaths) were attributed to asthma. Seven of these deaths occurred in persons under 19 years of age, while the majority (62%) occurred in those over (70 years) of age. More recent epidemiological evidence suggests that the prevalence of asthma in Canada is rising, particularly in the young population. A population based cohort study conducted in Ontario found that the age- and sex- standardized asthma prevalence increased from (8.5%) in 1996 to (13.3%) in 2005, a relative increase of (55%). The age-standardized increase in prevalence was greatest in adolescents and young adults compared with other age groups, and the gender standardized increase in prevalence was greater in males compared with females. Compared with females, males experienced higher increases in prevalence in adolescence and young adulthood and lower increases at age (70 years or older). Another recent study of over (2800 school-aged) children in Toronto that assessed parental reports of asthma by questionnaire found the prevalence of asthma to be approximately (16%) in this young population. The results of these studies suggest that effective clinical and public health strategies are needed to prevent and manage asthma in the Canadian population.^[5]

ETIOLOGY AND RISK FACTORS

An extensive literature review undertaken as part of the development of the Canadian Healthy Infant Longitudinal Development (CHILD) study (an ongoing multicentre national observational study) examined risk factors for the development of allergy and asthma in early childhood. Prenatal risk factors linked to early asthma development include: maternal smoking, use of antibiotics and delivery by caesarean section. With respect to prenatal diet and nutrition, a higher intake of fish or fish oil during pregnancy, and higher prenatal vitamin E and zinc levels have been associated with a lower risk of development of wheeze in young children. Later in childhood, risk factors for asthma development include: allergic sensitization (particularly house dust mite, cat and cockroach allergens), exposure to environmental tobacco smoke, breastfeeding (which may initially protect and then increase the risk of sensitization), decreased lung function in infancy, antibiotic use and infections, and gender. Future results from CHILD may help further elucidate risk factors for asthma development.

Asthma comprises a range of heterogeneous phenotypes that Differ in presentation, etiology and pathophysiology. The risk Factors for each recognized phenotype of asthma include Genetic, environmental and host factors. Although a family History of asthma is common, it is neither sufficient nor necessary For the development of asthma. The substantial increases in the incidence of asthma over the Past few decades and the geographic variation in both base Prevalence rates and the magnitude of the increases support the Thesis that environmental changes play a Large role in the current asthma epidemic. Furthermore, environmental triggers may Affect asthma differently at different Times of a person's life, and the relevant Risk factors may change over time. Short-term studies of risk factors May suggest a lower likelihood of Asthma, whereas the same factors may Be associated with greater risk if follow- Up is more prolonged. This pattern May relate to overlap between different Wheezing phenotypes in early childhood, only some of which persist as asthma in later childhood and adulthood. Because of this phenomenon, we examine here the risk factors for persistent asthma at different ages, specifically the prenatal period, infancy, childhood and, briefly, adulthood. [5]

TYPES OF ASTHMA

There are many types of asthma :-

1. Addictive Asthma

Asthma allergy is caused by an overdose to allergens such as pollen or pet dander. If one he has asthma, allergies, and personality and / or family history of allergies, such as allergen rhinitis or hay fever, and / or eczema (skin a problem that leads to righteousness, a red rash, and sometimes small blisters). Remember that the form of asthma allergy is an annual asthma, i.e., it usually affects people in the spring or early spring in the fall. For example, a person may be diagnosed with asthma worse in spring when there is an increase in blooming flowers, and some find that their asthma is really worse in late summer or early fall due to ragweed or meld from the leaves of trees. [4]

2. Insignificant Asthma

Asthma can be caused or made worse or other underlying asthma causes, including things (annoying) in the air, like cigarettes smoke, wood smoke, perfume deodorizers, pine fragrance, new paint, house cleaning products, cooking fragrance, perfume, and outdoor air pollution. People with non-allergic asthma may have the same symptoms as those with an allergen asthma, but they are not bothered by allergens from the natural world such as pollen or fungi. Other underlying causes of asthma include respiratory diseases, such as the common cold, fever, or disease of sin, and exercise, cold air, sudden changes in air temperature, and even gastro oesophageal reflux (heartburn). [4]

3. Night Asthma

Night asthma refers to asthma symptoms that seems too bad in the middle of the night, usually between 2AM and 4AM. Interestingly, nocturnal asthma can affect anyone with any type of asthma. Factors that can cause asthma symptoms of night-time worsening may include sinus infection or postnasal drip caused by allergens such as dust worms or pet dander. A body clock is possible and play a role. The body produces adrenaline and corticosteroids, which protect against it asthma. The levels of these two items are very low between midnight and 4AM, which makes it so they are more likely to experiencesymptoms in time these times. [4]

4. Pregnancy Asthma

Among pregnant patients with asthma, one- Thirdly they will find improvement in their plans for asthma, one-third will remain stable, and one- Third, they will deal with asthma. Improved asthma control during pregnancy is a thing associated with lower pregnancy- related rates problems. [4]

5. Chest at Work

Asthma at work means asthma i.e., newly discovered and caused by exposure tub substance (chemicals or animal proteins, because example) at work. If one can reduce exposure to these causes, he can do reducing the symptoms of asthma. Keep that in mind Asthma doesnot refer to humans it has already been diagnosed that you have more asthma it tends to explode when exposed to irritating dust or smoke in the workplace. [4]

6. Smoking

Cigarette smoke makes asthma harder to irritate airways and make them shrink Smoking in adults with asthma is associated with a rapid decrease in lung capacity performance, increased symptoms of stiffness and stiffness of the frequency of further attacks in a non- invasive response to inhaled corticosteroids. Although the studies are limited to most people of asthma patients have not yet been performed, smoking cessation obviously has certain numbers significant health benefits that may be the most important for four patients existing respiratory disease. Appropriate counselling should therefore be given to everyone patients with asthma smoking and medical conditions such as nicotine alternative treatmentmay work. [4]

7. Immunotherapy

The definition of allergy and response is described in asthmatics, and its guidance in management can improve outcomes. Specific allergen immunotherapy, or desensitisation, Illegal administration of certain allergen releases through subcutaneous injections increasing concentration with the aim of reducing physical tolerance. The process can workby making interleukin-10 produce regulatory T-cells. This was found at it is especially useful in allergic rhinitis but has also been shown to improve symptoms as well airway response in patients with chronic asthma. All in all, the benefits that come with it humble treatment, but discriminatory treatment can be very effective, and is associated with healththreatening anaphylaxis. [4]

SIGN AND SYMPTOMS ASSOCIATED WITH ASTHMA

• Explosion:

The sound of a whistle is often heard there breathing.

• Coughing:

Coughing or hitting that may not go away and it happens often or worse at night.

• Chest tightness:

You feel like there is a cord pull tightly and tightly around the chest.

• Shortness of Breath:

You feel like someone he tries to breathe through the grass and can't get some air at all. Breathing in particular difficult. [4]

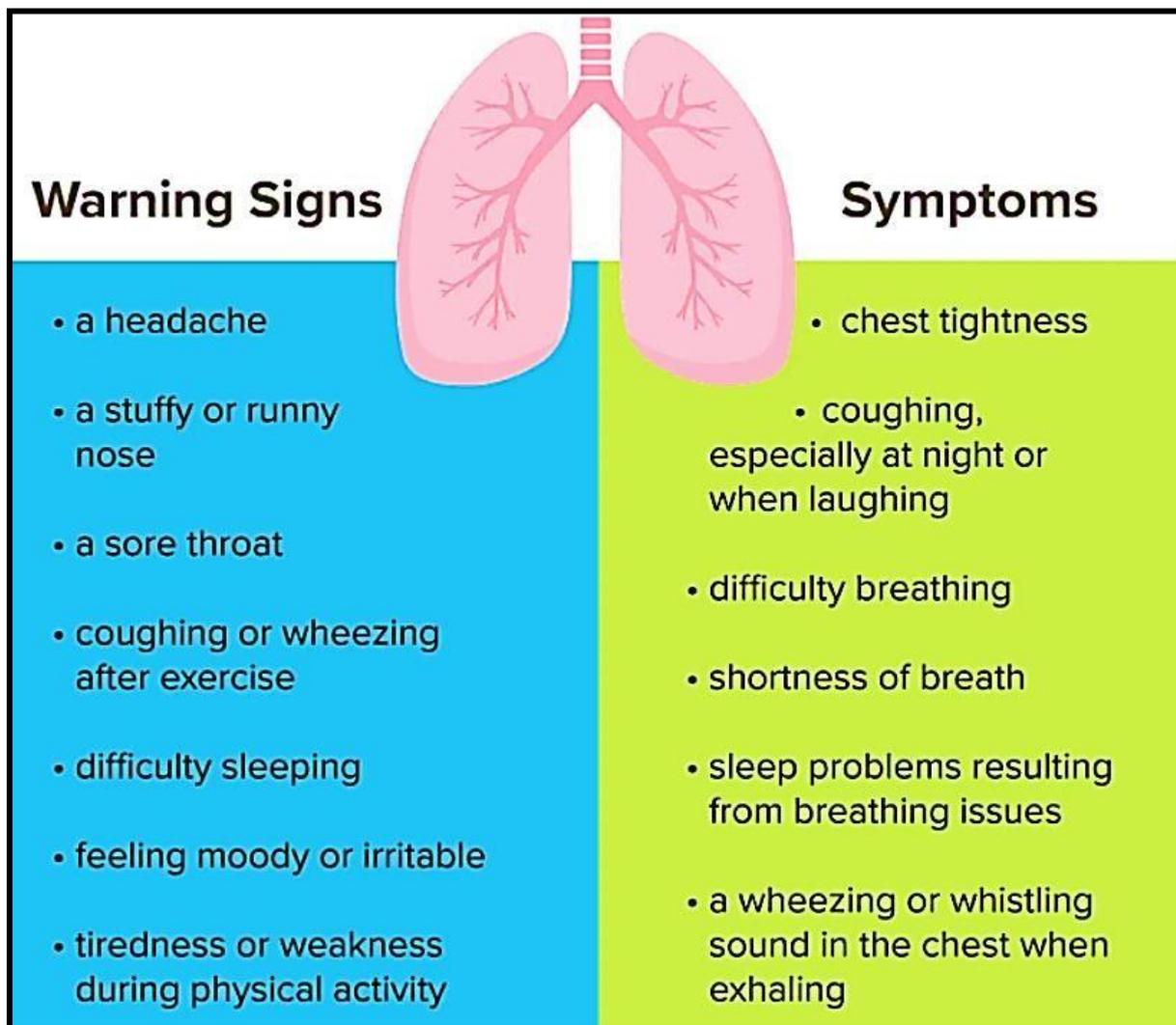


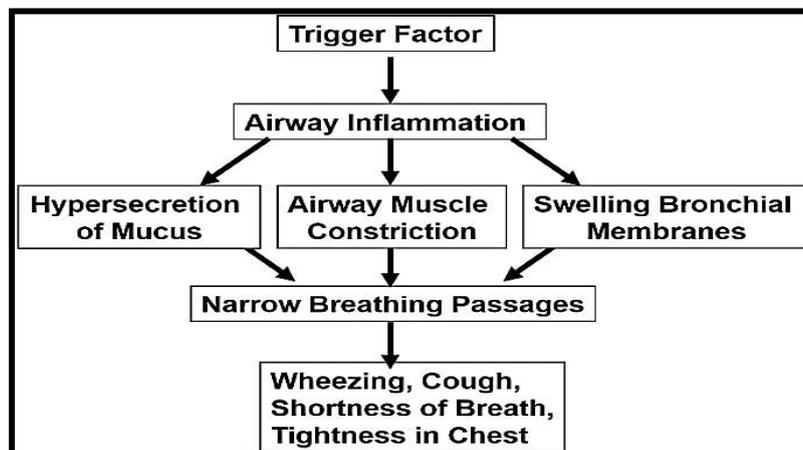
Fig.No.-01:- Warning Signs And Symptoms Associated With Asthma

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. Elevated levels Of Th2 cells in the airways release specific cytokines, Including interleukin (Il)-4, Il-5, Il-9 And Il-13, that Promote eosinophilic inflammation and immunoglobulin E (Ige) production by mast cells. Ige production, in Turn, triggers the release of inflammatory mediators, Such as histamine and cysteinyl leukotrienes, that cause bronchospasm (contraction of the smooth muscle in the airways), edema (swelling) and increased mucous secretion (mucous hypersecretion), which lead tothe characteristic symptoms of asthma. [7]

The mediators and cytokines released during the early phase of an immune response to aninciting 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 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 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. [7]

Fig.No.:- 02- Asthma Trigger Factors



SCHEMATIC REPRESENTATION OF PATHOPHYSIOLOGY OF ASTHMA.

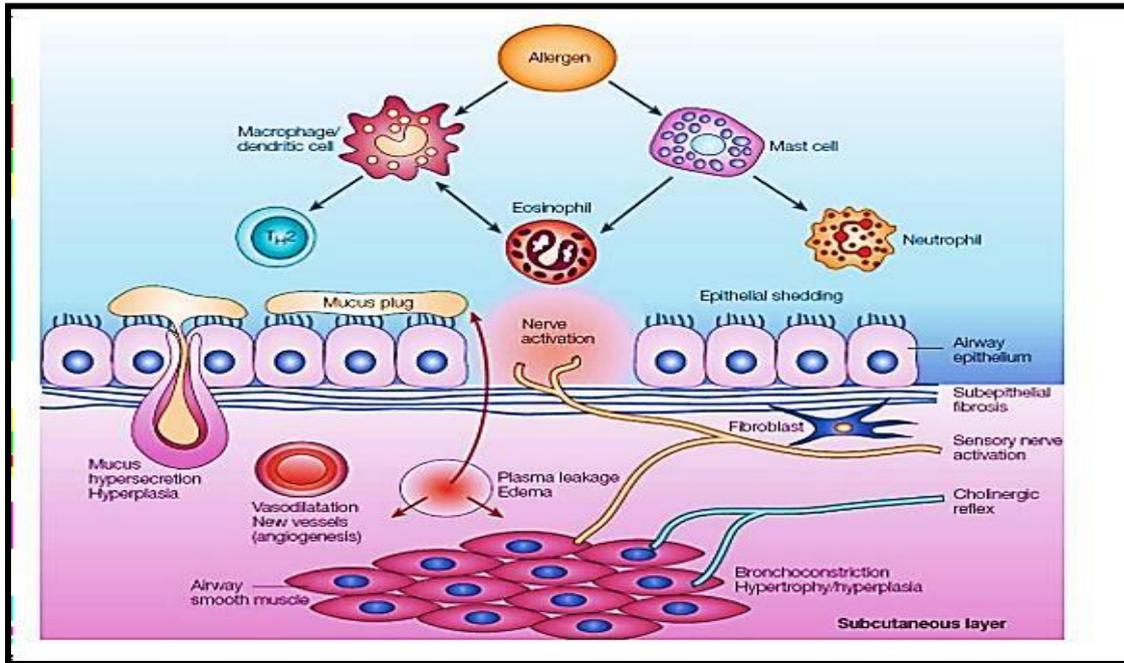


Fig.No. :- 03 – Pathophysiology Of Asthma (Schematic Representation) [8]

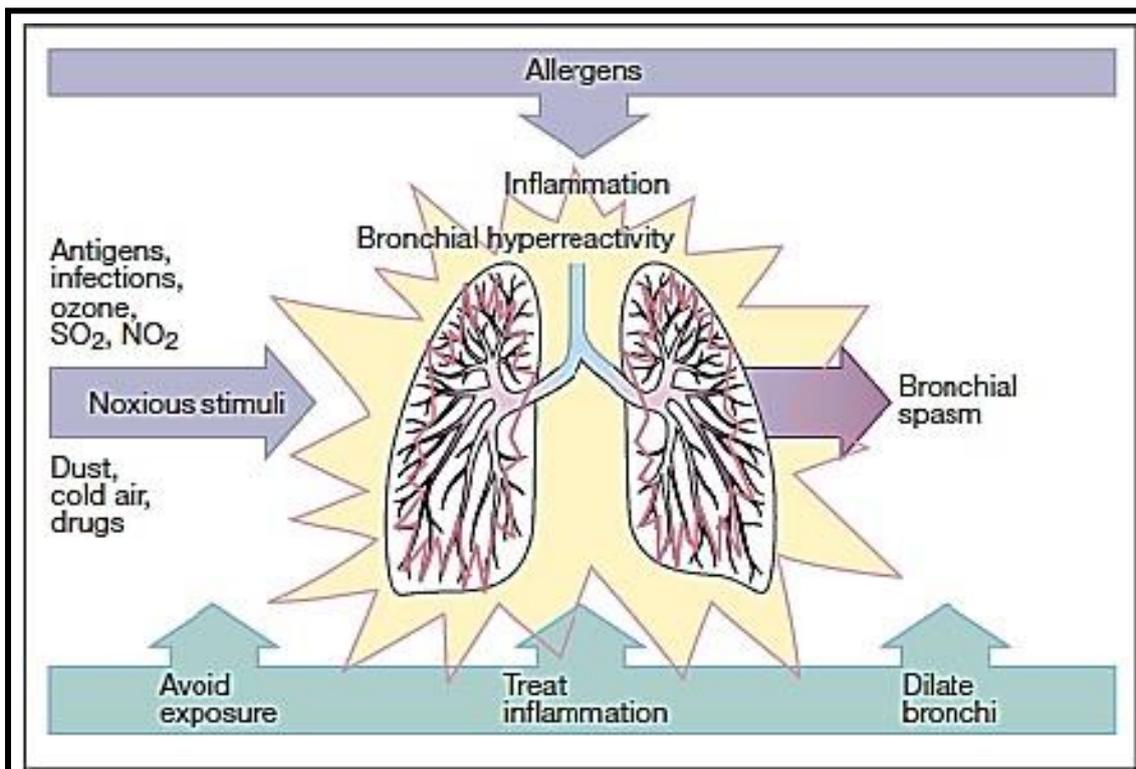


Fig.No.:- 04- Asthma Pathophysiology And Therapeutic Approach [8]

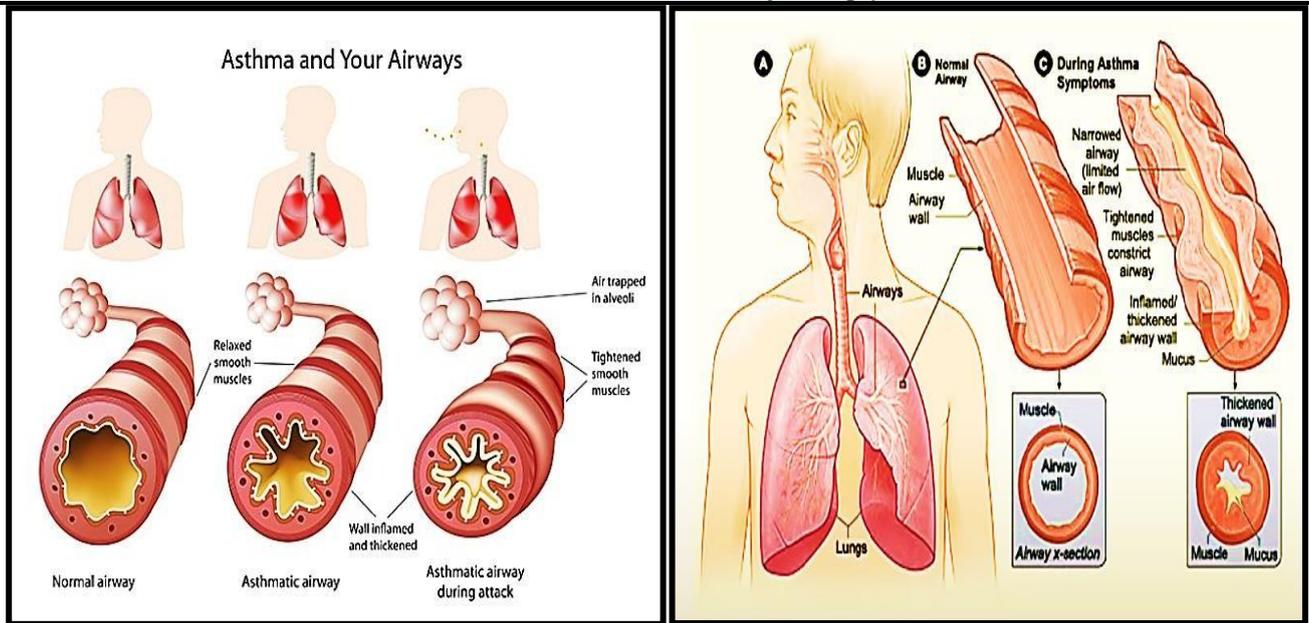


Fig.No.:- 05- Normal Airways Vs Asthmatic Airways^[8]

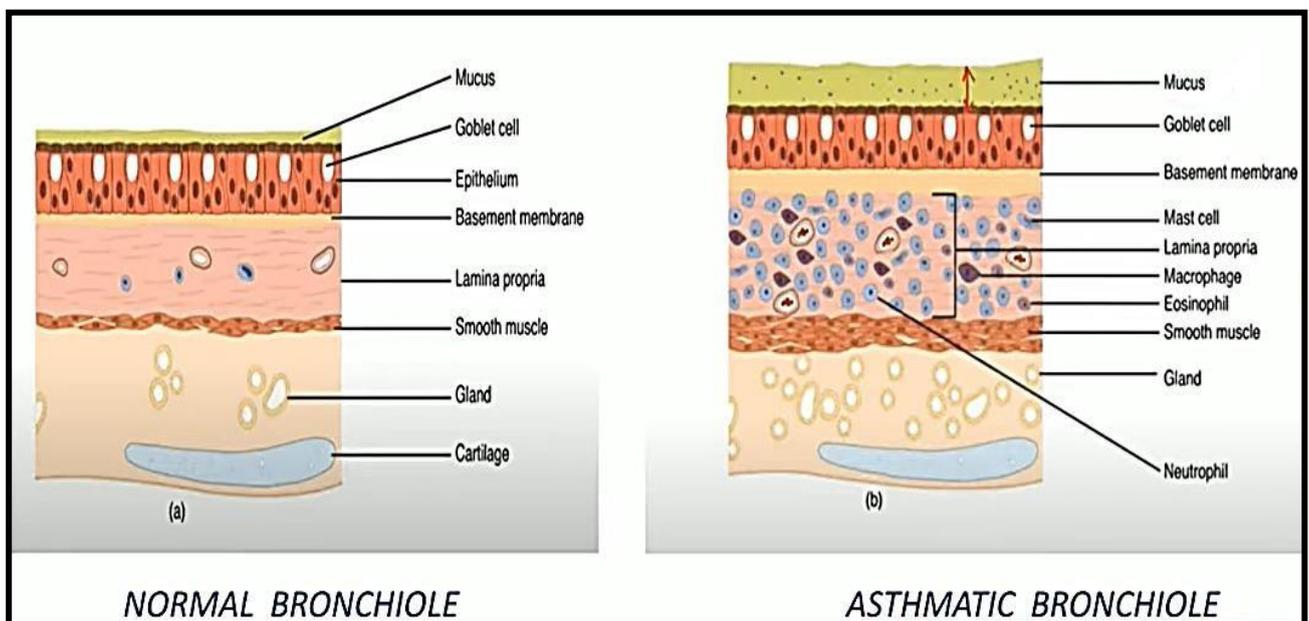


Fig.No.:- 06- Normal Bronchiole Vs Asthmatic Bronchiole^[8]

DIAGNOSIS OF ASTHMA

Table No:- 01-Diagnosis of asthma based on medical history, physical examination and objective measurements. [10][1]

MEDICAL HISTORY
<ul style="list-style-type: none"> • Assess For Classic Symptoms Of Asthma:- <ul style="list-style-type: none"> – Wheezing – Breathlessness – Chest Tightness – Cough (With Or Without Sputum) • Assess For Symptom Patterns Suggestive Of Asthma:- <ul style="list-style-type: none"> – Recurrent/Episodic – Occur/Worsen At Night Or Early In The Morning – Occur/Worsen Upon Exposure To Allergens (E.G., Animal Dander, Pollen, Dust Mites) Or Irritants(E.G., Exercise, Cold Air, Tobacco Smoke, Infections) – Respond To Appropriate Asthma Therap • Assess For Family Or Personal History Of Atopic Disease (Particularly Allergic Rhinitis)
PHYSICAL EXAMINATION:-
<ul style="list-style-type: none"> –Examine For Wheezing On Auscultation –Examine Upper Respiratory Tract And Skin For Signs Of Other Atopic Conditions
OBJECTIVE MEASUREMENTS:-
<ul style="list-style-type: none"> • Perform Spirometry (Preferred) To Confirm The Diagnosis <ul style="list-style-type: none"> – Diagnostic Criteria: <ul style="list-style-type: none"> ■ FEV₁ ↑ (After Bronchodilator): ≥ 12% And ≥ 200 MI • Consider PEF As An Alternative If Spirometry Is Unavailable <ul style="list-style-type: none"> – Diagnostic Criteria: <ul style="list-style-type: none"> ■ PEF ↑ (After Bronchodilator): ≥ 20% And 60 L/Min ■ Diurnal Variation: >20% • If Spirometry (Or PEF) Is Normal, But Symptoms Are Present Consider:- <ul style="list-style-type: none"> – Challenge Testing (E.G., Methacholine, Histamine, Mannitol, Exercise) – Non-Invasive Markers Of Airway Inflammation (Exhaled Nitric Oxide, Sputum Eosinophilia) – Trial Of Appropriate Asthma Therapy
ALLERGY TESTING:-
<ul style="list-style-type: none"> • Perform Skin Tests To Assess Allergic Status And Identify Possible Triggers.

DIAGNOSIS

The diagnosis of asthma involves a thorough medical history, physical examination, and objective assessments of lung function (spirometry preferred) to confirm the diagnosis (See Table No. 01). Bronchoprovocation challenge testing and assessing for markers of airwayinflammation may also be helpful for diagnosing the disease, particularly when objective measurements of lung function are normal despite the presence of asthma symptoms. [10][1]

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. It is also important to assess for comorbidities that can aggravate asthma symptoms, such as allergic rhinitis, sinusitis, obstructive sleep Apnea and gastroesophageal reflux disease. The diagnosis of asthma in young children is often more difficult since episodic wheezing and cough are common in this patient population and spirometry is unreliable in patients under 6 years of age. A useful method of confirming the diagnosis in young children is a trial of treatment with short-acting bronchodilators and inhaled corticosteroids (ICSs). [10][1]

PHYSICAL EXAMINATION

Given the variability of asthma symptoms, the physical examination of patients with suspected asthma is often unremarkable. Physical findings are usually only evident if the patient is symptomatic. Therefore, the absence of physical findings does not rule out a diagnosis of asthma. The most common abnormal physical finding is wheezing on auscultation, which confirms the presence of airflow limitation. Physicians should also examine the upper respiratory tract and skin for signs of concurrent atopic conditions such as allergic rhinitis or dermatitis. [10][1]

OBJECTIVE MEASUREMENTS OF LUNG FUNCTION

Spirometry is the preferred objective measure to assess for reversible airway obstruction (i.e., rapid improvement in lung function after inhalation of a rapid-acting bronchodilator) and to confirm a diagnosis of asthma. It is recommended for all patients over 6 years of age who are able to undergo lung function testing. Spirometry must be performed according to proper protocols. It is commonly performed in pulmonary function laboratories, but can also be performed in primary-care offices. During spirometry, the patient is instructed to take the deepest breath possible and then to exhale as hard and as fully as possible into the mouthpiece of the spirometer.

Spirometry measures the forced vital capacity (FVC, the maximum volume of air that can be exhaled) and the forced expiratory volume in 1 second (FEV1). The ratio of FEV1 to FVC provides a measure of airflow obstruction. A diagnosis of asthma is confirmed when there is: (1) an improvement in FEV1 of at least 12% and at least 200 ml 15–20 minutes after administration of an inhaled rapid-acting bronchodilator, or (2) an improvement in FEV1 of at least 20% and at least 200 ml after 2 weeks of treatment with an anti-inflammatory agent. In the general population, the FEV1/FVC ratio is usually greater than 0.80 (and possibly greater than 0.90 in children) and, therefore, any values less than these suggest airflow limitation and also support a diagnosis of asthma. Because of the variability of asthma symptoms, patients will not exhibit reversible airway obstruction at every visit.

Therefore, to increase sensitivity, spirometry should be repeated, particularly when patients are symptomatic. Peak expiratory flow (PEF) monitoring is an acceptable alternative when spirometry is not available, and can also be useful for diagnosing occupational asthma and/or monitoring response to asthma treatments. PEF is usually measured in the morning and in the evening. A diurnal variation in PEF of more than 20% or an improvement of at least 60 L/min or at least 20% after inhalation of a rapid-acting bronchodilator suggests asthma. Although simpler to perform than spirometry, PEF is not as reliable. Therefore, as mentioned earlier, spirometry is the preferred method of documenting airflow limitation and confirming the diagnosis of asthma. [10][1]

CHALLENGE TESTING

When lung function tests are normal, but symptoms suggest asthma, measurements of airway responsiveness using direct airway challenges to inhaled bronchoconstrictor stimuli (e.g., methacholine or histamine) or indirect challenges with mannitol or exercise may help confirm a diagnosis of asthma. Challenge testing should be conducted in accordance with strict protocols in a laboratory or other facility equipped to manage acute bronchospasms. Testing involves the patient inhaling increasing doses or concentrations of a stimulus until a given level of bronchoconstriction is achieved, typically a 20% fall in FEV1. An inhaled rapid-acting bronchodilator is then provided to reverse the obstruction. Test results are usually expressed as the dose or concentration of the provoking agent that causes the FEV1 to drop by 20% (the PD20 or PC20, respectively). For methacholine, a PC20 value less than 8 mg/ml is considered a positive result indicative of airway hyperreactivity, and supports a diagnosis of asthma. However, positive challenge tests are not specific to asthma and may occur with other conditions such as allergic rhinitis and COPD. Therefore, challenge testing may be most useful for ruling out asthma. A negative test result in a symptomatic patient not receiving anti-inflammatory therapy is highly sensitive for ruling out the disease.

Challenge testing is contraindicated in patients with FEV1 values less than 60-70% of the normal predicted value (since bronchoprovocation could cause significant bronchospasms), in patients with uncontrolled hypertension or in those who recently experienced a stroke or myocardial infarction. [10][1]

NON-INVASIVE MARKERS OF AIRWAY INFLAMMATION

The measurement of inflammatory markers such as sputum eosinophilia (amount of eosinophils in the sputum) or levels of exhaled nitric oxide (a gaseous molecule produced by some cells during an inflammatory response) can also be useful for diagnosing asthma. Evidence suggests that exhaled nitric oxide levels may be better able to identify asthmatic patients than basic lung function testing, and may also be useful for monitoring patient response to asthma therapy. Although these tests have been studied in the diagnosis and monitoring of asthma, they are not yet widely used in Canada. With further clinical evidence and use, these markers of airway inflammation will likely become more commonly available. [10][1]

ALLERGY SKIN TESTING

Allergy skin testing is also recommended to determine the allergic status of the patient and to identify possible asthma triggers. Testing is typically performed using the allergens relevant to the patient's geographic region. Although allergen-specific ige tests that provide an in vitro measure of a patient's specific (IgE) levels against particular allergens have been suggested as an alternative to skin tests, these tests are less sensitive and more expensive than skin tests. [10][1]

DIFERENTIAL DIAGNOSIS

Conditions that should be considered in the differential diagnosis of adults with suspected asthma may include: COPD, bronchitis, gastrointestinal reflux disease, recurrent respiratory infections, heart disease, and vocal cord dysfunction. Distinguishing asthma from COPD can be particularly difficult as some patients have features of both disorders. The term asthma COPD overlap syndrome (ACOS), though not a single disease entity, has been adopted to describe these patients. A recent population-based cohort study conducted in Ontario suggests that the prevalence of concurrent asthma and COPD is increasing, particularly in women and young adults.

The differential diagnosis of asthma is unique for infants and young children and includes anatomic defects (laryngo- or tracheomalacia, congenital heart defects), physiological defects (primary ciliary dyskinesia) and genetic conditions such as cystic fibrosis and primary immunodeficiency, to name just a few conditions. A chest X-ray may be considered in the work-up of a child with suspected asthma, particularly if the diagnosis is unclear or if the child is not responding as expected to treatment. Table 02 lists conditions to consider in the differential diagnosis of recurrent respiratory symptoms in children. [10][1]

Table No :- 02- Diferential Diagnosis Of Recurrent Respiratory Symptoms In Children^[1]

INFECTIONS	CONGENITAL PROBLEMS
<ul style="list-style-type: none"> • Recurrent Respiratory Tract Infections • Chronic Rhino-Sinusitis • Tuberculosis 	<ul style="list-style-type: none"> • Tracheomalacia • Tracheo-Esophageal Fistula • Cystic Fibrosis • Bronchopulmonary Dysplasia
MECHANICAL PROBLEMS	<ul style="list-style-type: none"> • Congenital Malformation Causing Narrowing Of The Intrathoracic Airways • Primary Ciliary Dyskinesia Syndrome • Immune Deficiency • Congenital Heart Disease
<ul style="list-style-type: none"> • Foreign Body Aspiration • Gastroesophageal Reflux • Vocal Cord Dysfunction 	

MANAGEMENT OF ASTHMA (TREATMENT)

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 No.03 and treatment should be tailored to achieve control. In most asthma patients, control can be achieved using both trigger avoidance measures and pharmacological interventions. ^{[2][1]}

The pharmacologic agents commonly used for the treatment of asthma can be classified as controllers (medications taken daily on a long-term basis that achieve control primarily through anti-inflammatory effects) and relievers (medications used on an as-needed basis for quick relief of bronchoconstriction and symptoms). Controller medications include ICSS, leukotriene receptor antagonists (LTRAS), LABAS in combination with an ICS, long-acting muscarinic receptor antagonists (LAMAS), and biologic agents

including anti-IGE therapy and anti-IL-5 therapy. Reliever medications include rapid-acting inhaled beta2-agonists and inhaled anticholinergics. Allergen-specific immunotherapy may also be considered in most patients with allergic asthma, but must be prescribed by physicians who are adequately trained in the treatment of allergies. Systemic corticosteroid therapy may also be required for the management of acute asthma exacerbations. A simplified, stepwise algorithm for the treatment of asthma is provided in Fig.No.07. [2][1]

Table.No.:- 03- Criteria For Assessing Ashtma Control. [2][1]

No exacerbations
Fewer than 3 doses/week of a rapid-acting beta2-agonist bronchodilator
Daytime symptoms < 3 days/week
No nighttime symptoms
Normal physical activity
No absenteeism from work or school
FEV1 or PEF at least 90% of personal best

FEV1 forced expiratory volume in 1 s, PEF peak expiratory flow

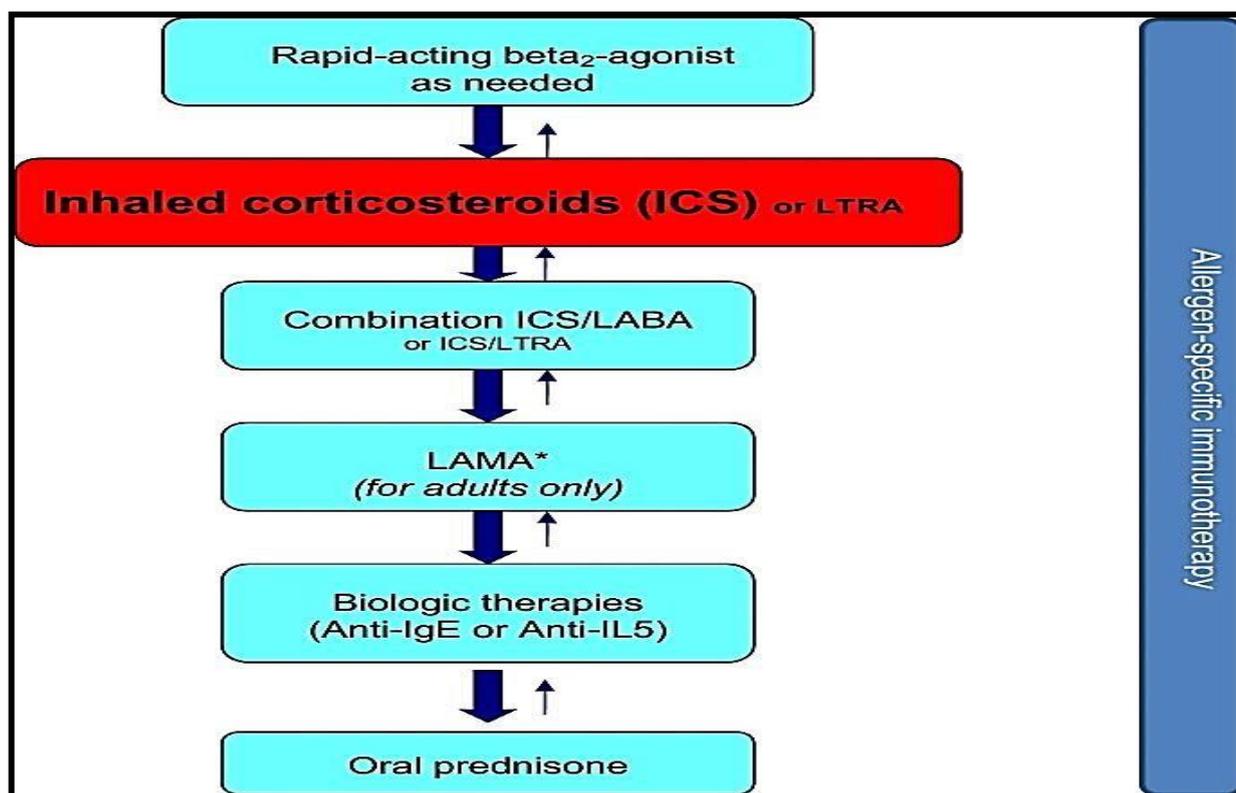


Fig.No.:-07:- A Simplified, Stepwise Algorithm For The Treatment Of Asthma. [2][1]

AVOIDANCE MEASURES

Avoidance of exposure to tobacco smoke is important for all patients with asthma. Avoidance of other relevant allergens/irritants is also an important component of asthma management. Patients allergic to house dust mites should be instructed to use allergen- impermeable covers for bedding and to keep the relative humidity in the home below 50% (to inhibit mite growth). Pollen exposure can be reduced by keeping windows closed, using an air conditioner, and limiting the amount of time spent outdoors during peak pollen seasons. For patients allergic to animal dander, removal of the animal from the home is recommended and usually results in a significant reduction in symptoms within 4-6 months. However, compliance with this recommendation is poor and, therefore, the use of high- efficiency particulate air (HEPA) filters and restricting the animal from the bedroom or to the outdoors may be needed to help decrease allergen levels. Measures for reducing exposure to mould allergens include cleaning with fungicides, de-humidification to less than 50%, and HEPA filtration.

Since these avoidance strategies can be labour-intensive, patient adherence is usually suboptimal. Frequent reassessments, encouragement and empowerment by the treating physician are often required to help promote adherence to these strategies. Furthermore, patients should be advised to use a combination of avoidance measures for optimal results, since single-strategy interventions have demonstrated no measurable benefits in asthma control. [2][1]

INHALED MEDICATION DELIVERY DEVICES

Inhaled asthma medications come in a variety of forms including pressurized metered-dose inhalers (pMDIs) and dry powder inhalers (DPIs) (Turbuhaler, Diskus, Twisthaler, Ellipta). Not all medications are available in the same delivery devices. Also, some devices have dose counters included and others, such as pMDIs, do not. The most important factor in selecting a medication delivery device is to ensure that the patient uses it properly.

In children, it is recommended that (pMDIs) always be used with a spacer device since they are as effective as nebulizers; a pMDI with spacer is also preferred over nebulizers. A spacer with face mask is recommended for children 2–4 years of age, while a spacer with mouthpiece is recommended for children 4–6 years of age. To transition to a spacer with mouthpiece, children must be able to form a seal around the mouthpiece and breathe through their mouths. For children 6 years of age or over, a pMDI plus spacer with mouthpiece or DPI is recommended. Since children must have sufficient inspiratory force to use a DPI, these devices are generally not recommended for children under 6 years of age. [1]

RELIEVER MEDICATIONS

Inhaled rapid-acting beta₂-agonists are the preferred reliever medications for the treatment of acute symptoms, and should be prescribed to all patients with asthma. In Canada, several short-acting beta₂-agonists (SABAs; e.g., salbutamol, terbutaline) and one LABA (formoterol) are approved for this indication. SABAs should only be taken on an as-needed basis for symptom relief. Use of an as-needed SABA in the absence of a controller therapy should be reserved for patients with symptoms less than twice per month, without nocturnal awakening in the past month, or an exacerbation within the past year. In children with well-controlled asthma, a SABA should be used less than three times per week. [1]

Unlike other LABAs, formoterol has a rapid onset of action and, therefore, can be used for acute symptom relief. Given that LABA monotherapy has been associated with an increased risk of asthma-related morbidity and mortality, formoterol should only be used as a reliever in patients 12 years of age or older who are on regular controller therapy with an ICS.

Short-acting anticholinergic bronchodilators, such as ipratropium bromide, may also be used as reliever therapy. These agents appear to be less effective than inhaled rapid-acting beta₂-agonists and, therefore, should be reserved as second-line therapy for patients who are unable to use SABAs. They may also be used in addition to SABAs in patients experiencing moderate to severe asthma exacerbations. Short-acting anticholinergic bronchodilator therapy is not recommended for use in children. [1]

CONTROLLER MEDICATIONS

INHALED CORTICOSTEROIDS (ICs)

ICSs are the most effective anti-inflammatory medications available for the treatment of asthma and represent the mainstay of therapy for most patients with the disease. Low-dose ICS monotherapy is recommended as first-line maintenance therapy for most children and adults with asthma. Regular ICS use has been shown to reduce symptoms and exacerbations, and improve lung function and quality of life. ICSs do not, however, “cure” asthma, and symptoms tend to recur within weeks to months of ICS discontinuation. Most patients will require long-term, if not life-long, ICS treatment.

Since ICSs are highly effective when used optimally, factors other than treatment efficacy need to be considered if ICS therapy is unsuccessful in achieving asthma control. These factors include: misdiagnosis of the disease, poor adherence to ICS therapy, improper inhaler technique, continued trigger exposure or the presence of other comorbidities. If, after addressing such factors, patients fail to achieve control with low-to-moderate ICS doses, then treatment should be modified. For most children, ICS dose escalation (to a moderate dose) is the preferred approach to achieve control, while the addition of another class of medications (usually a LABA) is recommended for patients over 12 years of age. Low, medium and high doses of ICS therapy varies by age and are summarized in Table 04. Children who fail to achieve control on a moderate ICS dose should be referred to an asthma specialist, such as a respirologist, an allergist, an

immunologist or a pediatrician. It is also recommended that children receiving daily ICS therapy do not increase their daily ICS dose with the onset of a viral illness^[1]

SIDE EFFECTS

The most common local adverse events associated with ICS therapy are oropharyngeal candidiasis (also known as oral thrush) and dysphonia (hoarseness, difficulty speaking). Rinsing and expectorating (spitting) after each treatment and the use of a spacer with pmd devices can help reduce the risk of these side effects. Systemic adverse effects with ICS therapy are rare, but may occur at high doses, such as > 500 µg of fluticasone propionate equivalent, and include changes in bone density, cataracts, glaucoma and growth retardation. Patients using high ICS doses should also be monitored for adrenal suppression. It is important to note that the potential for side effects with ICS therapy needs to be considered in the context of other steroids (i.e., systemic, intranasal and topical) that may be prescribed for other atopic conditions such as allergic rhinitis or atopic dermatitis. ^[1]

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. 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. Although there is no apparent difference in efficacy between ICS 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 04). 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. ^[1]

LEUKOTRIENE RECEPTOR ANTAGONISTS

The LTRAs, montelukast and zafirlukast, are also effective for the treatment of asthma and are generally considered to be safe and well tolerated. Because these agents are less effective than ICS treatment when used as monotherapy, they are usually reserved for patients who are unwilling or unable to use ICSs. LTRAs can also be used as add-on therapy if asthma is uncontrolled despite the use of low-to-moderate dose ICS therapy or combination ICS/LABA therapy. It is important to note, however, that LTRAs are considered to be less effective than LABAs as add-on therapy in adults. In children, if medium-dose ICS

therapy is ineffective, LTRAs are considered the next-line treatment option. If, however, the child has persistent airway obstruction, the addition of a LABA may be preferred. [1]

LONG – ACTING MUSCARINIC RECEPTOR ANTAGONISTS

The LAMA, tiotropium, administered by mist inhaler can be used as add-on therapy for patients with a history of exacerbations despite treatment with ICS/LABA combination therapy. It is only indicated for patients 12 years of age and older. [1]

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 over 12 years of age who are intolerant to or continue to be symptomatic despite other add-on therapies. [1]

BIOLOGIC THERAPIES

The anti-IgE monoclonal antibody, omalizumab, has been shown to reduce the frequency of asthma exacerbations by approximately 50%. The drug is administered subcutaneously once every 2–4 weeks and is approved in Canada for the treatment of moderate to severe, persistent allergic asthma in patients 6 years of age or older. At present, omalizumab is reserved for patients with difficult to control asthma who have documented allergies, an elevated serum IgE level, and whose asthma symptoms remain uncontrolled despite ICS therapy in combination with a second controller medication. [1]

Two monoclonal antibodies to IL-5 have been approved in Canada for patients aged 18 years or older with severe Eosinophilia: Mepolizumab and Reslizumab. These are given every 4 weeks by subcutaneous injection and intravenous infusion, respectively, and are indicated in patients who are uncontrolled despite treatment with high-dose ICS therapy and an additional controller therapy, such as a LABA, and who have elevated blood Eosinophils. Recently, Benralizumab, a monoclonal antibody against the IL-5 receptor has also been approved in Canada for the treatment of adult patients with severe Eosinophilic asthma. [1]

(Table 04) provides a list of the commonly used controller therapies and their recommended dosing regimens. It is important to note that long-term compliance with controller therapy is poor because patients tend to stop therapy when their symptoms subside. Therefore, regular follow-up visits are important to help promote treatment adherence. [1]

Table.No.04 – Overview of the main controller therapies used for the treatment of asthma. [1]

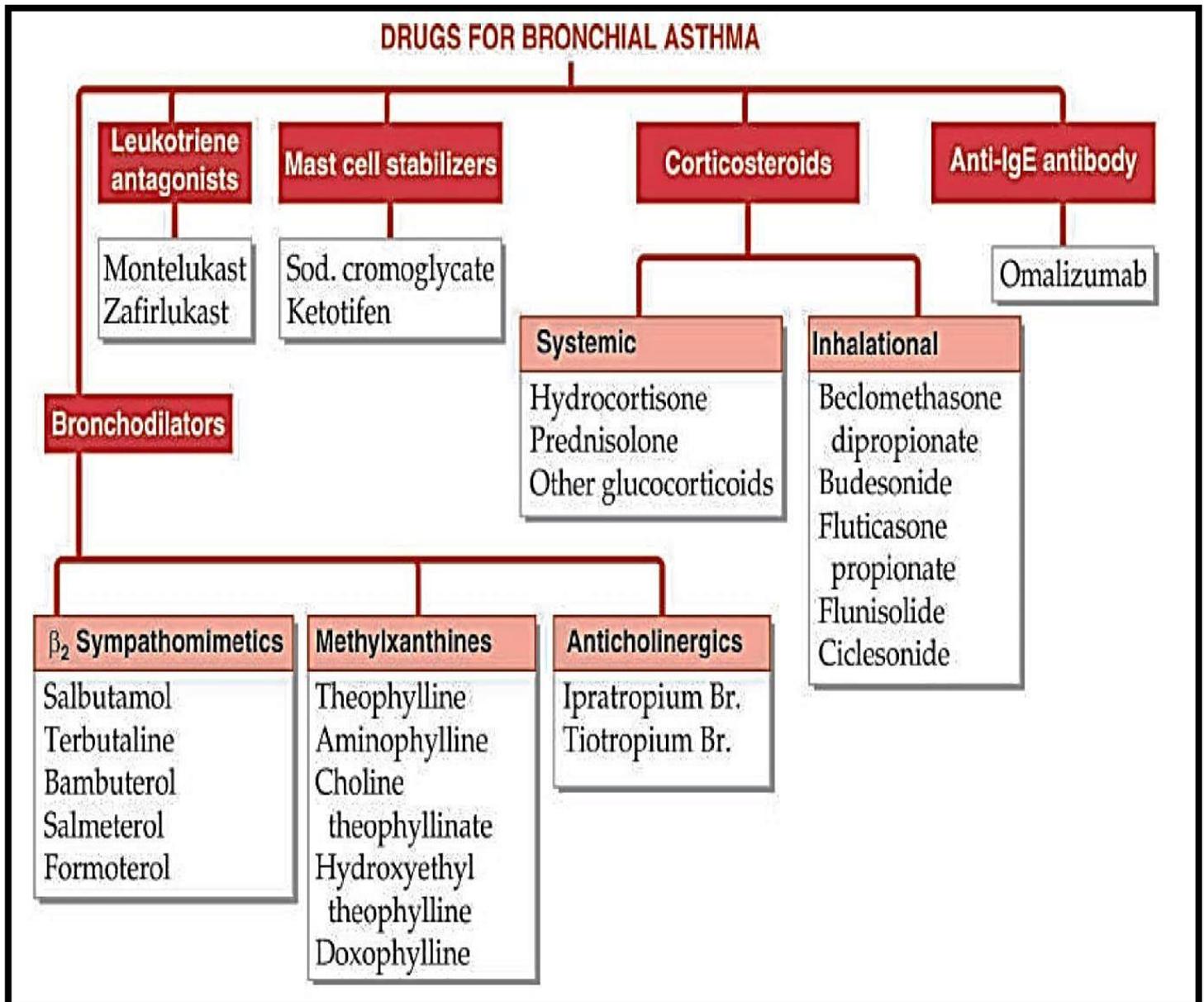
ICSs	Usual adult dose	Pediatric dose information	
		< 6 years of age	6–18 years of age
Beclomethasone (Qvar, generics)	pMDI: 100–800 µg/day, divided bid	pMDI <ul style="list-style-type: none"> • Low 50 µg bid • Med 100 µg bid • High refer to specialist <i>Approved age by Health Canada</i> ≥ 5 years 	pMDI <ul style="list-style-type: none"> • Low 50–100 µg bid • Med > 100 µg bid • High > 200 µg bid
Budesonide (Pulmicort)	DPI: 400–2400 µg/day, divided bid Nebules: 1–2 mg bid	DPI not recommended for children < 6 years	DPI <ul style="list-style-type: none"> • Low 100 µg bid • Med 200–400 µg bid • High > 400 µg bid <i>Approved age by Health Canada</i> ≥ 6 years
		Nebules: 0.25–0.5 mg bid (for children 3 months to 12 years)	
Ciclesonide (Alvesco)	pMDI: 100–800 µg/day	pMDI: <ul style="list-style-type: none"> • Low 100 µg once daily • Med 200 µg daily • High refer to specialist 	pMDI: <ul style="list-style-type: none"> • Low 100 µg once daily • Med 200–400 µg daily • High > 400 µg daily <i>Approved age by Health Canada</i> ≥ 6 years
Fluticasone propionate (Flovent HFA, Flovent Diskus)	pMDI/DPI: 100–500 µg bid	pMDI/DPI <ul style="list-style-type: none"> • Low 50 µg bid • Med 100–125 µg bid • High refer to specialist <i>Approved age by Health Canada</i> ≥ 1 year for pMDI, ≥ 4 years for Diskus (DPI) 	pMDI/DPI <ul style="list-style-type: none"> • Low ≤ 100 µg bid • Med > 100–200 µg bid • High ≥ 200 µg bid
Mometasone (Asmanex)	DPI: 200–400 µg/day	DPI not recommended for children < 6 years	DPI <ul style="list-style-type: none"> • Low ≤ 200 µg daily • Med > 100–200 µg bid • High > 200 µg bid • <i>Approved age by Health Canada</i> ≥ 12 years

ICSs	Usual adult dose	Pediatric dose information	
		< 6 years of age	6–18 years of age
Fluticasone furoate (Arnuity Ellipta)	DPI: 100–200 µg/day	Not indicated for children < 12 years	
Combination ICS/LABA inhalers			
Budesonide/formoterol (Symbicort)	DPI (maintenance): 100/6 µg or 200/6 µg, 1–2 puffs od or bid; max 4 puffs/day DPI (maintenance and reliever): 100/6 µg or 200/6 µg, 1–2 puffs bid or 2 puffs od; plus 1 puff prn for relief of symptoms (no more than 6 puffs on any single occasion); max 8 puffs/day	Refer to specialist	DPI <ul style="list-style-type: none"> • Low 100/6 µg 1 dose bid • Med 100/6 µg 2 doses bid, 200/6 µg 1–2 doses bid • High > 200/6 µg 2 doses bid <i>Approved age by Health Canada ≥ 12 years</i>
Fluticasone furoate/salmeterol (Advair pMDI, AdvairDiskus)	pMDI: 125/25 µg or 250/25 µg, 2 puffs bid Diskus: 100/50 µg, 250/50 µg or 500/50 µg: 1 puff bid	Refer to specialist <i>Approved age by Health Canada ≥ 4 years for Diskus (DPI)</i>	DPI/pMDI <ul style="list-style-type: none"> • Low 100/50 µg bid • Med > 100–200 µg bid • High ≥ 250/50 µg bid <i>Approved age by Health Canada ≥ 12 years for pMDI</i>
Mometasone/formoterol (Zenhale)	For patients previously treated with Low-dose ICS: 50/5 µg, 2 puffs bid Medium-dose ICS: 100/5 µg, 2 puffs bid High-dose ICS: 200/5 µg, 2 puffs bid	Refer to specialist	pMDI <ul style="list-style-type: none"> • Low 50/5–100/5 µg 1 dose bid • Med 100/5 µg 2 doses bid, 200/5 µg 1–2 doses bid • High > 200/5 µg <i>Approved age by Health Canada ≥ 12 years</i>
Fluticasone furoate/vilanterol (Breo Ellipta)	DPI: 100/25 µg/day or 200/25 µg/day	Not indicated for children < 18 years of age	
LTRAs			
Montelukast (Singulair)	10 mg tablet od (taken in the evenings)	4 mg po daily <i>Approved age by</i>	5 mg po daily (6–14 years) 10 mg po daily (≥ 15 years)

ICSs	Usual adult dose	Pediatric dose information	
		< 6 years of age	6–18 years of age
		<i>Health Canada</i> ≥2 years	
Zafirlukast (Accolate)	20 mg tablet bid, at least 1 h before or 2 h after meals	Refer to specialist	20 mg tablet bid, at least 1 h before or 2 h after meals <i>Approved age by Health Canada</i> ≥ 12 years
LAMAs			
Tiotropium (Spiriva Respimat)	1.25 µg, 2 puffs od	Not indicated for children < 18 years	
Anti-IgE therapy			
Omalizumab (Xolair)	150–375 mg sc every 2–4 weeks (based on patient's weight and pre-treatment serum IgE level)	Not indicated for children < 6 years	75–375 mg sc every 2–4 weeks (based on patient's weight and pre-treatment serum IgE level)
Anti-IL5 therapy			
Mepolizumab (Nucala)	100 mg sc every 4 weeks	Not indicated for children < 18 years	
Reslizumab (Cinqair)	3 mg/kg IV every 4 weeks	Not indicated for children < 18 years	
Benralizumab (Fasenra)	30 mg sc every 4 weeks for the first 3 doses, then every 8 weeks thereafter	Not indicated for children < 18 years	

Pediatric dose information adapted from BCGuidelines.ca Guidelines & Protocols Advisory Committee, 2015^[1]

CLASSIFICATION OF DRUGS FOR ASTHMA

Fig.No.-08- Classification Of Drugs For Asthma.^[6]

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 routine or long-term use should be avoided if at all possible, particularly in children. 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 necrosis of the hip. ^[1]

BRONCHIAL THERMOPLASTY

Bronchial thermoplasty involves the treatment of airways with a series of radiofrequency pulses. This treatment may be considered for adult patients with severe asthma despite pharmacotherapy. [1]

ALLERGEN SPECIFIC IMMUNOTHERAPY

Allergen-specific immunotherapy involves the subcutaneous or sublingual 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. Although it has been widely used to treat allergic asthma, it is not universally accepted by all clinical practice guideline committees due to the potential for serious anaphylactic reactions with this form of therapy.

A Cochrane review of 88 randomized controlled trials examining the use of allergen-specific immunotherapy in asthma management confirmed its efficacy in reducing asthma symptoms and the use of asthma medications, and improving airway hyperresponsiveness. Similar benefits have been noted with sublingual immunotherapy, which is now available for use in Canada for grass and ragweed allergies, as well as house dust mite-induced allergic rhinitis. Evidence also suggests that allergen-specific immunotherapy may prevent the onset of asthma in atopic individuals.

At present, allergen-specific immunotherapy should be considered on a case-by-case basis. Allergen-specific subcutaneous immunotherapy may be considered as add-on therapy in patients using ICS monotherapy, combination ICS/LABA inhalers, ICS/ltras and/or omalizumab if asthma symptoms are controlled. It should not be initiated in patients with uncontrolled asthma or an FEV₁ < 70% of predicted. For subcutaneous immunotherapy, asthma must be controlled at the time of each injection, and it must be administered in clinics that are equipped to manage possible life-threatening anaphylaxis where a physician is present. Since allergen-specific immunotherapy carries the risk of anaphylactic reactions, it should only be prescribed by physicians who are specialists in allergy. [1]

INDICATIONS FOR REFERRAL

In older children, adolescents and adults, referral to a specialist in asthma care (e.g., respirologist, allergist) is recommended when:

- Atypical asthma symptoms are present or the diagnosis of asthma is in question;
- The patient has poor asthma control (poor lung function, persistent asthma symptoms) or severe asthma exacerbations (≥ 1 course of systemic steroids per year or hospitalization) despite moderate doses of ICS (with proper technique and good compliance);
- The patient requires a detailed assessment for and management of potential environmental triggers;
- The patient has been admitted to the intensive care unit (ICU) for asthma.

In young children 1–5 years of age, referral to an asthma specialist is recommended when there is diagnostic

uncertainty or suspicion of comorbidity; poor symptom and exacerbation control despite ICS at daily doses of 200–250 µg; a life-threatening event (requiring ICU admission and/or intubation); and/or for allergy testing to assess the possible role of environmental allergens. [1][2]

REMEDIES FOR ASTHMA

GINGER

Ginger is a well-known natural remedy for a variety of ailments, including asthma. Researchers have found that it can help reduce inflammation and prevent airway obstruction. Also, studies show that it contains nutrients that can increase the muscle-relaxing effects of certain asthma medications. [4]

MUSTARD OIL

When you have asthma, massage with mustard oil can help. Clarifies breathing and retrieves normal breathing. [4]

FIGS

The nutritional properties of figs promote respiratory health and help release phlegm as well as reducing respiratory difficulty. [4]

GARLIC

The following garlic solution can help clear lung congestion for the first time asthma. • Boil two or three cloves in one quarter cup of milk. • Let it cool to room temperature and drink. [4]

COFFEE

Regular caffeine in coffee can help control asthma attacks because it acts as a bronchodilator. Hot coffee helps to relax and clear airways to help you breathe more easily. The stronger the coffee, the better the result. But try not to drink more than three cups of tea or black coffee a day. If you do not like coffee, you can choose a cup of hot black tea. Don't use caffeine as a standard treatment however. [4]

EUCALYPTUS OIL

Pure eucalyptus oil is an effective treatment for asthma symptoms. The most potent properties Research has shown that it contains a chemical called eucalyptol which can help to isolate mucus. [4]

BELOVED HONEY

Honey is one of the oldest treatments for asthma. Alcohol and ethereal oil in honey help reduce asthma symptoms. Just inhaling the scent of bees produces good results to other people. You can also add one teaspoon of honey to a glass of hot water and drink it at least three times a day. [4]

CONCLUSION

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 using 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. Lamas or biologic therapies targeting ige or IL-5 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.

Most people find that allergies to food or medications cause their asthma symptoms. If one has been plagued by flare-ups, lo and behold what he eats and drinks, and whatever medications you may be taking. Asthma affects 3– 5% of the U.S. population and most frequently children rather than adults. Flight ban is possible be due to the smooth muscles in the walls of bronchi and small bronchioles, enema of mucosa of airways, mucus enlarged fluid, and / or damage to the epithelium of the way of the spirit.

REFERENCES

1. Review On Practical Guide For Allergy Asthma And Immunology In Canada 2018, Vol.14, Issue 2018.
2. Review On Management Of Asthma Role Of Clinical Pharmacist, ISSN-2347- 7881, Vol.2, Issue 2, PG.No.- 124-133.
3. Allergy, Asthma And Clinical Immunology , Kim And Mazza, Vol.7, Issue 2011,
4. Asthma A Comprehensive Outlook, Vol.08, Issue- 3, ISSN-2349-6002, Pg.No 70-74.
5. Asthma: Epidemiology, Etiology And Risk Factors, Vol.9, Issue-2009. Pg.No-181-190.
6. Essentials Of Medical Pharmacology, Edition -8TH , New Delhi., Issue -2019, Drugs For Bronchial Asthma , Pg.No.- 237-254.
7. Pathophysiology Of Ashtma , Issue – 2007, Pg.No -11-71.
8. Color Atlas Of Pharmacology 2nd Edition, Revised And Expanded, Issue-2000. Pg.No.- 328-330.
9. Wechsler, M.E., Managing Asthma In Primary Care: Putting New Guideline Recommendations Into Context , Vol. 84, Issue-2009, Pg.No- 707-717.
10. Kaplan AG, Balter MS, Bell AD, Kim H, Mcivora RA: Diagnosis Of Asthma In Adults. CMAJ. 2009, Pg.No.-210-220.
11. Abramson MJ, Puy RM, Weiner JM: Allergen Immunotherapy For Asthma. Cochrane Database, Vol – 04, Issue 2003.

12. Grembiale RD, Camporota L, Naty S, Tranfa CM, Djukanovic R, Marsico SA: Effects Of Specific Immunotherapy In Allergic Rhinitic Individuals With Bronchial Hyperresponsiveness. *Am J Respir Crit Care Med*, Vol. 06, Issue – 2000.
13. *Drug Today* , Vol. 02, Issue – 2012, Pg.No.- 893-913.
14. Ober C, Hoffjan S. *Asthma Genetics*, Vol.07, Issue-2006., Pg.No- 95-100.
15. Schaub B, Lauener R, Von Mutius E. The Many Faces Of The Hygiene Hypothesis. *Jallergy Clin Immunology*, Issue-2006,Pg.No-969-977.
16. Lin RY, Rehman A. Clinical Characteristics Of Adult Asthmatics Requiring Intubation, Issue 1995, Pg.No.261-277.
17. Boulet LP, Becker A, Berube D, Beveridge R, Ernst P, Canadian Asthma Consensus Group Canadian Asthma Consensus Report, Issue- 1999.
18. Lugogo, N., Que, L.G., Fertel, D., Kraft, Issue-2010, Pg.No.-258-267, 5TH Edition.
19. Magnetic Resonance Imaging Techniques For Pre-Clinical Lung Imaging, Issue-2014,Pg.No- 1-183.
20. Agertoft L, Pedersen S. Effects Of Long-Term Treatment With An Inhaled Corticosteroid On Growth And Pulmonary Function In Asthmatic Children, Issue- 1994., Vol.05, Pg.No. 373-381.
21. American Thoracic Society. What Constitutes An Adverse Health Effect Of Air Pollution? Official Statement Of The American Thoracic Society. *Am J Respir Crit Care Med*, Issue-2000, Vol.1, Pg.No.- 665-673.
22. Zielen S, Kardos P, Madonini E: Steroid-Sparing Effects With Allergenspecific Immunotherapy In Children With Asthma: A Randomized Controlled Trial, Issue- 2010, Vol . 1 , Pg.No- 942-949.
23. Ducharme Fm, Dell Sd, Radhakrishnan D, Grad Rm, Watson Wt, Yang Cl, Zelman M. Diagnosis And Management Of Asthma In Preschoolers: A Canadian Thoracic Society And Canadian Paediatric Society Position Paper, Vol.03, Issue-2015, Pg.No-135-143.
24. Abramson MJ, Puy RM, Weiner JM. Injection Allergen Immunotherapy For Asthma. *Cochrane Database Syst Review*, Issue-2010, Vol.8,
25. Statistics Canada. *Asthma. Health Reports*, Vol. 16, Issue-20