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AN OVERVIEW OF ASTHMA

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Abstract:

These are those drug which are used in the treatment of Asthma (Bronchial Asthma).Chronic obstructive lung diseases (COLD) include bronchial asthma, chronic bronchitis and emphysema. These three disorders differ in their aetiology but have one common characteristic, ie., airway obstruction which blocks effective pulmonary ventilation. Coughing, wheezing and dyspnoea are the symptoms, and become progressively worse, leading to acidosis and electrolyte imbalances. Proneness to frequent respiratory infections can precipitate acute pulmonary failure, congestive heart failure, and even cardiac arrest. The bronchodilator drugs are the mainstay in the drug management. The other drugs employed are the expectorants and mucolytic agents, anti-inflammatory agents and antitussives. antibacterials,The tone of the bronchial muscle is controlled by humoral factors and by the autonomic nervous system. In health the bronchial calibre is mainly controlled by the balance) between the parasympathetic and sympathetic nervous system Control of the bronchial smooth muscle The parasympathetic system mediated by acetylcholine. The mediated by noradrenaline caus blood flow, bronchodilatation, and pulmonary circulation. The hum operative in diseased states.

Keywords: BronchialAsthma,chronicbronchitis,AntitussivAsthma

. **Introduction:** Asthma is the most common inflammatory disease of the lungs. The prevalence of asthma is increasing in many parts of the world that have adopted aspects of the Western lifestyle, and the disease poses a substantial global health and economic burden. Asthma involves both the large-conducting and the small-conducting airways, and is characterized by a combination of inflammation and structural remodelling that might begin in utero. Disease progression occurs in the context of a developmental background in which the postnatal acquisition of asthma is strongly linked with allergic sensitization. Most asthma cases follow a variable course, involving viral-induced wheezing and allergen sensitization, that is associated with various underlying mechanisms (or endotypes) that can differ between individuals. Each set of endotypes, in turn, produces specific asthma characteristics that evolve across the lifecourse 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 or begin de novo in adulthood, and the factors that lead to the emergence and regression of asthma, irrespective of age, are poorly understood. Nonetheless, there is mounting evidence that supports a primary role for structural changes in the airways with asthma acquisition, on which altered innate immune mechanisms and microbiota interactions are superimposed. On the basis of the identification of new causative pathways, the subphenotyping of asthma across the lifecourse of patients is paving the way for more-personalized and precise specific approaches for the prevention and treatment of asthma, creating the real possibility of total prevention and cure for this chronic inflammatory disease.

Types of Asthma:

In both adults and children, asthma has been tradi-tionally classified by either symptom severity or the extent of disease control achieved using a stepwise management process, in which patients are grouped into one of four or five categories that are used to determine treatment requirements with controller drugs. These drugs include inhaled corticosteroids (ICSs), long-acting β2-adrenergic receptor agonists (LABAs), long-acting muscarinic antagonists, leukotriene receptor antagonists (LTRAs) In both adults and children, asthma has been traditionally classified by either symptom severity or the extent of disease control achieved using a stepwise management process, in which patients are grouped into one of four or five categories that are used to determine treatment requirements with controller drugs. These drugs include inhaled corticosteroids (ICSs), long-acting β2adrenergic receptor agonists (LABAs), long-acting muscarinic antagonists, leukotriene receptor antagonists (LTRAs)

1. Extrinsic Asthma (Allergic asthma)
2. Intrinsic Asthma
3. Adult-onset Asthma
4. Status Asthmaticus
5. Exerise induce Asthma
6. Occupational Asthma
7. Nocturnal Asthma
8. Aspirin -induced Asthma
9. Cough – variant Asthma
10. Eosinophilic Asthma

Epidemiology:

There are >300 million people in the world who are affected by asthma, making it one of the most common chronic diseases13. Although the prevalence of asthma is greatest in countries with a high gross domestic product, the disease is recognized worldwide. In the lowest income and most rural countries14, the prevalence of asthma tends to be ≤1%, far lower than the 10% usually seen in
developed western countries (FIG. 2). Within populations of a given gross domestic product, the prevalence of asthma follows an urban–rural gradient and a weak latitudinal gradient, that is, there is greater disease prevalence with greater distance from the equator and asthma is more common in urban areas14. Despite the low prevalence of asthma in low-income and middle-income countries, underdiagnosis and misdiagnosis together with inadequate treatment in these regions leads to considerable, and potentially avoidable, disease morbidity and mortality.The prevalence of asthma has increased in many parts of the world over the past few decades, and, until recently, asthma prevalence was increasing on a year by year basis in developed western countries The cause of the epidemic that began in the late 1970s is unclear, but the rise in asthma prevalence is consistent with a rise in other immune-mediated diseases .

Airway inflammation. Airway inflammation is a prominent feature of asthma (FIG. 4). T2-type inflammation occurs in >80% of children and in the majority of adults with asthma in association with sensitization to environmental allergens, such as those from dust mites, fungi, pets and pollens24–26. This sensitization is often associated with other clinical manifestations of atopy such as atopic dermatitis (eczema), allergic rhinoconjunctivitis and food allergy. The inflammatory infiltrate that accompanies T helper 2 (TH2) lymphocyte responses is mainly composed of eosinophils but also includes mast cells, basophils, neutrophils, monocytes and macrophages27. Cellular activation and release of inflammatory mediators in asthma is evidenced by mast cell degranulation
and eosinophil vacuolation.

Allergen sensitization also requires an interaction between specialized antigen-presenting airway den-
dritic cells (DCs) and T cells. This mechanism involves processing of allergen into small peptides and the selective major histocompatibility complex (MHC) class II presentation of these processed peptides to the T cell receptors of naive T cells31 (FIG. 6). Effective allergen signalling also requires co-stimulatory interactions between DCs and T cells38 that take place in local lymphoid collections39, resulting in T cell differentiation into TH2-type T cells. These TH2-type T cells secrete the pro-allergic cytokines, IL-3, IL-4, IL-5, IL-9, IL-13 and granulocyte–macrophage colony-stimulating factor (GM-CSF), Although much of the focus in asthma pathophysiology has been on positive drivers of inflammation, the defective resolution of inflammation is emerging as a mechanism that might also be involved in asthma. The failure to adequately downregulate the inflammatory response could result in the prolonged survival of mast cells and eosinophils as a result of the cytokine milieu of the asthmatic airway. In addition, an important new paradigm in asthma pathophysiology is the potential role of lipoxins and resolvins as mediators of the endogenous resolution of inflammation .

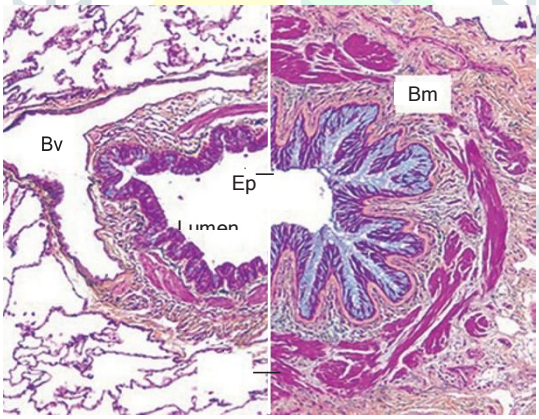
Airway remodelling

In asthma, the airway wall thickens in proportion to disease severity and duration50,51. This remodelling involves an increase in airway smooth muscle, thickening of the subepithelial reticular lamina, matrix deposition throughout the airway wall, angiogenesis, neuronal proliferation and epithelial mucous metaplasia a process that involves the appearance of mucous cells in new areas of the airways and increased production of mucus. Epithelial damage results from the separation of columnar cells from basal cells. This can be detected by staining of sputum from patients with asthma, showing detached columnar cells as Creola bodies. Thickening of the subepithelial basement membrane is confined to the reticular lamina and results from deposition of 'repair-type' collagens I, III, V and VI together with periostin, tenascin, osteopontin and fibronectin54–56. Subepithelial collagen is produced by a sheath of myofibroblasts that lie beneath the epithelium. An epithelial–mesenchymal trophic unit, located between the epithelial and smooth muscle layers of the airway.

Disease onset

Prenatal and postnatal risk factors. Prenatal risk fac- tors for the development of asthma include ethnicity, low socioeconomic status, stress, caesarean section and maternal tobacco smoking, whereas postnatal risk factors include the levels of endotoxins and allergens within the home, viral and bacterial infection, air pollu-tion, antibiotic use, paracetamol exposure and obesity[84].For example, prematurity confers a fourfold increase inthe risk of developing asthma[85], representing the larg- est effect of any known epidemiological risk factor for this disease[86]. In addition, increased airway responsive-ness is present at birth. Given that this phenotype is known to be associated with prematurity and low birth weight, this physiological marker of asthma suscepti- bility is thus present in at-risk babies before any viral illness

Childhood viral illness and lung function. A key trigger for the onset of asthma in children is severe wheezing in early life in response to viral infections, especially respir- atory infection with syncytial virus (RSV) or rhinovirus. A second trigger is the emergence and then persistence of a T2-type allergic immune response in the airways (FIG. 8). In the first 2 years of life, all children become infected with RSV and rhinovirus68, so the question is not whether infection is a causal factor in the onset of asthma, but whether there is an underlying develop- mental defect of the lungs and/or the innate immune system that confers asthma susceptibility.



Histopathology of the asthmatic airway Cross section of a severe asthmatic airway (right) compared with a normal airway (left). Asthma involves mucosal inflammation that most frequently consists of activated eosinophils, mast cells and T lymphocytes within the context of a remodelled airway with mucous metaplasia, an increase in smooth muscle (Sm), fibrosis and angiogenesis. Bm, basement membrane; Bv, blood vessel; Ep, epithelium. Republished with permission of Dove Medical Press, from Clinical update on the use of biomarkers of airway inflammation in the management of asthma

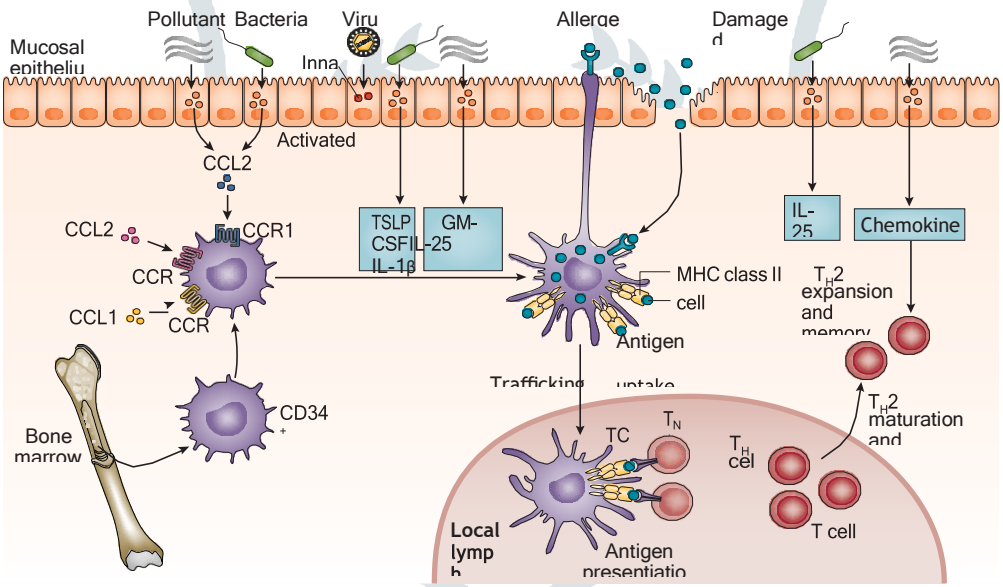
Bacterial pathogens. Along with a potential involve- ment of the intestinal microbiota in asthma, there is also increasing recognition that the presence of micro- organisms in the respiratory tract, including the upper airways, and the way that the immune system responds to these, is likely to have an effect on respiratory health[95] (FIG. 8). The presence of bacterial pathogens per se is not necessarily associated with disease risk, suggesting that an effective mechanism must normally operate to pro- tect against *trans*-epithelial invasion in situations where local homeostasis is disturbed and barrier function is compromised

Microbiota and the 'hygiene hypothesis'. Epidemiologists have also had difficulty in integrating knowledge about putative risk factors into a comprehensive theory about the developmental origins of the disease and the rela-tionship of asthma to patient susceptibility to infection. One such attempt is the 'hygiene hypothesis', which was developed almost 25 years

ago. This hypothesis posited that respiratory infections 'protected' against asthma and allergies by 'educating' the immature infant immune sys- tem influence developmental asthma susceptibility and immune function through epigenetic mechanisms . Evidence that supports a role for the maternal gastro- intestinal microbiota in asthma development is also emerging. The maternal microbiota might affect the developing fetal immune system during pregnancy and influence respiratory health during infancy[94]. The infant gastrointestinal microbiota develops postnatally and is influenced by factors linked to asthma risk, such as mode of delivery, infant feeding practices, antibiotic exposure and exposure to siblings and pets. Whether the infant gastrointestinal microbiota is the 'missing link' between early-life environmental exposures and asthmarisk is yet to be determined

Allergen sensitization of the airways during the induction of allergic-type asthma. Infection (bacterial and viral) and pollutants perturb the airway epithelium, which leads to initial danger signaling and activation of innate signaling receptors. This signaling causes airway epithelial cells (ECs) to secrete chemokines and leads to trafficking of immature dendritic cells (DCs) to the mucosal epithelium. These DCs respond to danger signals through pattern recognition receptors (PRRs), which leads to their maturation into competent antigen-presenting myeloid-type DCs. Allergen detection and processing by these activated DCs is mediated by the extension of cellular processes into the airways or by the capture of allergens that have breached the epithelium. Allergen-loaded DCs then drive T cell differentiation by migrating to local lymph nodes where they interact with naive T cells (TN) via the T cell receptor (TCR), major histocompatibility complex (MHC) class II and co-stimulatory molecules. DC activation and T helper 2 (TH2) cell maturation and migration into the mucosa are influenced by additional epithelial-derived cytokines and chemokines, including IL-25, IL-33, CC-chemokine ligand 17 (CCL17) and CCL22. CCR, CC-chemokine receptor

Diagnosis, screening and prevention



Diagnosis

The diagnosis of asthma involves a thorough medical history, physical examination, and objective assessments of lung function in those ≥ 6 years of age (spirometry preferred, both before and after bronchodilator) to document variable expiratory airflow limitation and confirm the diagnosis (see Table 1). Bronchoprovocation challenge testing and assessing for markers of airway inflammation may also be helpful for diagnosing the disease, particularly when objective measurements of lung function are normal despite the presence of asthma symptoms

Medical history

• **Assess for classic symptoms of asthma**:

- Wheezing
- Breathlessness
- Chest tightness
- Cough (with our without sputum)

• **Assess for symptom patterns suggestive of asthma:**

- 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 therapy Assess for family or personal history of atopic disease (particularly allergic rhinitis)

Physical examination

- Examine for wheezing on auscultation
- Examine upper respiratory tract and skin for signs of other atopic conditions
- Objective measures for confirming variable expiratory airflow limitation (spirometer preferred)
- Documented airflow limitation:
- Diagnostic criteria: at least once during diagnostic process when FEV1 is low, confirm that FEV1/FVC is reduced (normally > 0.75–0.80 in adults, > 0.90 in children)

Management

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, and treatment should be tailored to achieve control. In most asthma patients, control can be achieved using both trigger avoidance measures and pharmacological interventions. 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 anticholinergic 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 (see Allergen-specific immunotherapy article in this supplement)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

Controller medications

Inhaled corticosteroids (ICSs)

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 mono therapy 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. Children who fail to achieve control on a moderate ICS dose should be referred to an asthma specialist, such a respirologist, an allergist, an immunologist or a paediatrician. It is also recommended that children receiving daily ICS therapy do not increase their daily ICS dose with the onset of a viral illness

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 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 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

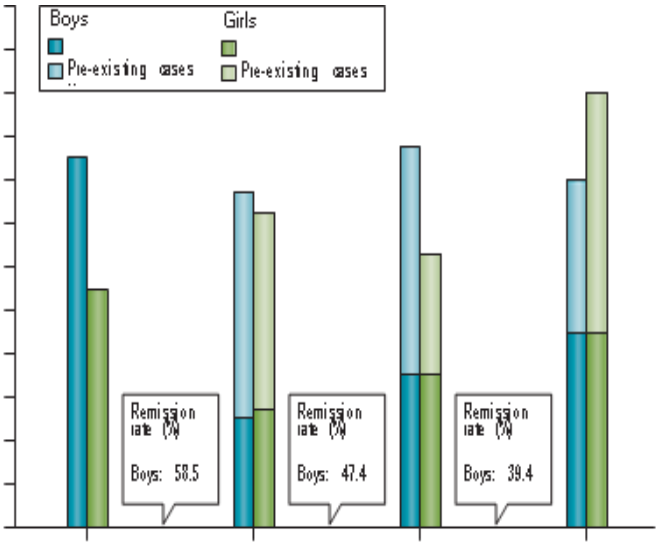
Bronchial thermoplasty

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

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 theray

Proportions of children and adolescents with asthma in the Isle of Wight birth cohort



Asthma triggers

Wherever possible, avoidance of triggers should be part of every patient's written asthma action plan. Common triggers include253:

Inflammatory factors

- Allergens
- Respiratory infections
- Work

Irritants

- Exercise
- Cold air
- Temperature change
- Strong odours
- Stress and emotions

Others

- Tobacco
- Medication
- Food additives
- Pollutants
- Gastric reflux

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.

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