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To Review The Key Aspects Of Asthma, Including its Mechanisms, Diagnosis, And Therapies

Mr. Shivam Sharma[1], Ms. Harshali Thakare[2], Dr. Sonali Uppalwar[3].

Ideal institute of pharmacy Posheri Wada.
Affiliation:- Mumbai University

ABSTRACT :

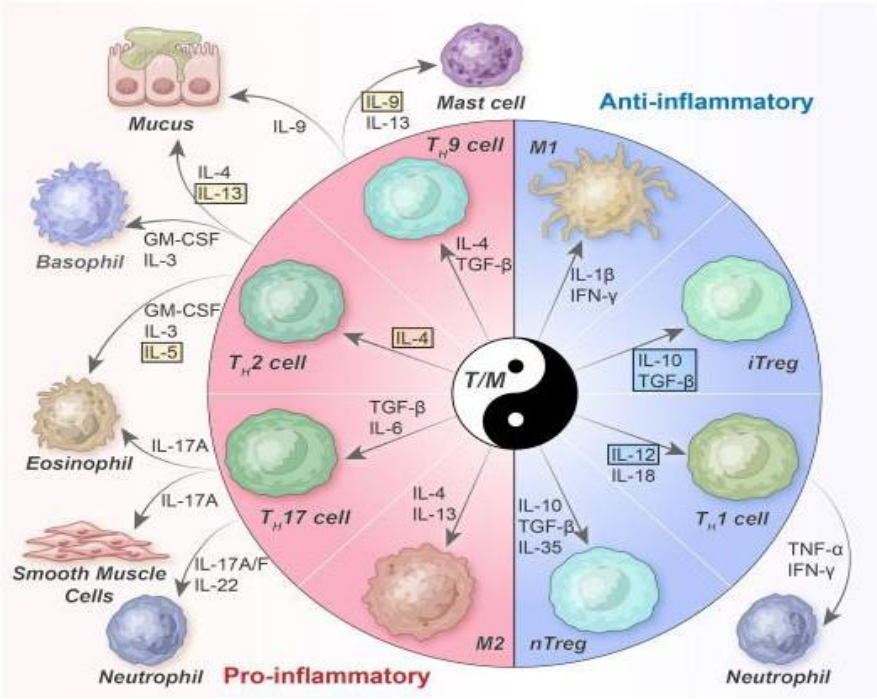
A complex interplay of immunological, environmental, and genetic variables contributes to the development and progression of asthma, a chronic inflammatory illness that affects the airways. Recent studies have demonstrated the important part exosomal microRNAs (miRNAs) play in the etiology and progression of asthma. Little extracellular vesicles called exosomes carry a variety of bioactive substances, including miRNAs, and are crucial for cell communication. In the inflammatory processes linked to asthma, these molecules play a critical role in controlling immunological responses and gene expression. Because exosomal miRNAs are involved in a number of facets of asthma, including tissue remodeling, airway hyperresponsiveness, and inflammatory regulation, they have become recognized as significant contributors to the illness. They are interesting possibilities for both prospective therapeutic targets and diagnostic indicators due to their ability to influence the behavior of target cells. The goal of this study is to present a thorough analysis of exosome formation, exosomal miRNAs' functional involvement in asthma, and their clinical consequences. It will look at how these miRNAs affect the pathophysiology of asthma, assess how well they work for diagnosing and tracking the condition, and highlight current studies that try to take advantage of their therapeutic potential.

Keyword: Ferroptosis, asthma, exosomes, miRNA, biomarkers, treatment, TCM, natural products, respiratory disorders, mechanism

Introduction

The ultimate goal is to identify asthma endotypes, but we haven't reached this stage yet. The remarkable accomplishments highlight the value of endotyping. when the endotypes and gene- class-specific sub-endotypes of cystic fibrosis (CF) were initially distinguished from the general group of illnesses characterized by inflammation and chronic airflow infection. The specific molecular therapies (2–4) have been the outcome; if they had been tried on every child with a persistent wet cough, none of them would have reached the patient's bedside.(1) Asthma was described as "a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation" in 2007.(2) Asthma was described as a reversible or intermittent blockage of the airways. The American Thoracic Society highlighted the elevated excitability in 1962.(3) Countries and regions differ greatly in the prevalence of asthma; it is more common in metropolitan areas and among those who have certain risk factors, such as allergies, smoking, and exposure to air pollution. While the frequency of asthma seems to be levelling off after decades of sharp rise in many industrialised nations, its prevalence is sharply rising in low- and middle- income nations.(4) It is estimated that between 5 and 10% of all-comers with asthma have severe asthma, while the precise prevalence is unknown. High-intensity therapy does not alleviate the
symptoms of patients with severe illness. The majority of asthma-related morbidity and mortality occurs in this demographic, and their needs are obviously unmet.(5)
In almost every industrialised nation, asthma is the most prevalent chronic paediatric respiratory condition. Atopy is more common in kids with a family history of it, and a variety of triggers, including as virus infections, indoor and outdoor allergens, exercise, tobacco smoke, and poor air quality, can often cause symptoms and flare-ups.(6) Fractional exhaled nitric oxide (FeNO) measurements can be used to measure airway inflammation, especially eosinophil inflammation, and track how well asthma patients are responding to treatment.(7) One risk factor for wheeze with RV infection, especially in children, is allergic sensitisation. It's unclear whether the allergic inflammation that frequently accompanies sensitisation makes people more vulnerable to viral infections or strengthens their capacity to cause more inflammation.(8) From a mild, intermittent condition to a severe, chronic, and challenging-to-treat condition that can occasionally be lethal, bronchial asthma exhibits a broad range of clinical manifestations [1–4]. Even though asthma deaths are rare (one in 2000 asthmatics), they have increased in recent decades.(9)

Pro-inflammatory and antiinflammatory arms of the immune landscape in asthma Numerous inflammatory cells are drawn from the bloodstream and transported to the lungs by locally produced chemokines; these cells have functional characteristics that contribute to the development of asthma.(10) These TH17-derived cytokines, including as IL-17 and IL-22, are linked to a rise in the recruitment of neutrophils in the airways. Thus, in severe asthma, neutrophilic inflammation and TH17 polarisation are further promoted by neutrophil extracellular traps and cytoplasts. However, because IL-17 may have two regulatory functions—it may be protective during the challenge stage but exacerbate asthma in other circumstances—the exact functions of TH17 cells and IL-17 in mouse asthma models are still unclear. IL-17A stimulates fibroblast proliferation and suppresses the anti-inflammatory properties of regulatory T cells (Tregs) in models of chronic asthma.(11)



Figno:1 T-cell/macrophage networks in balance, along with their cytokine environment in asthma. Through the release of TH2 cytokines such IL-4, IL-5, IL-9, and IL-13, TH2 cells promote allergic inflammation. IFN-g is produced by TH1 cells, which are differentiated due to IL-12 and IL-18, and suppress TH2 cells. TH17 cells differentiate in a unique way when influenced by TGF-b and IL-6. Generally speaking, Tregs suppress the activity of other TH cells by releasing IL-10 and TGF-b, although asthma may impair their ability to function. GMCSF (granulocyte-macrophage colony stimulating factor), TGF (transforming growth factor), TNF (tumour necrosis factor), IFN (interferon), and Treg (naturally occurring Tregs) are examples of inducible Tregs. [11]

Risk factors

Relationships to asthma have been assessed as a function of lifestyle (e.g., living on a farm,48 diet,49 and S), environmental exposures (e.g., aeroallergens,40 pollution,41-43 and tobacco smoke), and disease onset (e.g., viral infections1,2,39). 98 LEMANSKE AND BUSSE J ALLERGY CLIN IMMUNOL FEBRUARY 2010 antibiotic use50), comorbid conditions (such as obesity and atopic dermatitis), professional exposures, and the severity of the disease (as determined by the risk domain, which is covered later; hospitalisations, frequency and severity of exacerbations, and loss of lung function, among others).(12) According to research by Borna et al., who examined the prevalence of asthma in Sweden between 2008 and 2016, it appears to be continuing to rise. The prevalence of ever having asthma, having asthma diagnosed by a doctor, using asthma medication, and having asthma now has significantly increased, according to the authors, particularly among young adults (16–25 years old). During the same time period, there was a reported rise in the prevalence of respiratory symptoms, which raises the idea that asthma is really underdiagnosed.(13) The prevalence of asthma and rhinitis as single and multimorbid conditions during puberty was analysed by gender in six MeDALL population-based birth cohorts across Europe. Multimorbid individuals with asthma and rhinitis concurrently showed the greatest "gender-shift" towards females after puberty onset and the male predominance in prevalence prior to puberty.(14)

Pathophysiology of asthma

TSLP, IL-25, and IL-33) alarmins— As a dynamic orchestrator of immune responses in T2 high asthma, the airway epithelium is the genesis of the innate immune system. The majority of asthmatics have a dysregulated epithelial barrier, with a noticeable loss of the tight junction (TJ)- mediating proteins claudin-18 and E-cadherin. In asthma aetiology, reduced barrier integrity brought on by damage to the airway epithelium is crucial because it makes it easier for allergens and microorganisms to enter the stromal tissue. Furthermore, house dust mites (HDM) and other allergens that include proteases can directly cleave epithelial TJs and interfere with barrier constructions.(15) The symptoms of asthma, a long-term inflammatory illness of the airways, include mucus production, airway oedema, remodelling of the airway walls, and severe bronchoconstriction. The symptoms of coughing, wheezing, and shortness of breath are frequent exacerbations that patients experience (Global Initiative for Asthma [GINA], 2010; National Heart, Lung, and Blood Institute/National Asthma Education and Prevention Program [NHLBI/NAEPP], 2007). An estimated 300 million people globally and 30 million in the US alone are thought to suffer with asthma, a condition whose incidence has significantly increased in recent decades (Braman, 2006). Asthma is currently one of the most prevalent chronic conditions in adult

populations, while it is the most prevalent chronic condition and a major cause of hospitalisation among children.(16) Every component stands for distinct cellular and molecular processes that define the illness process and could potentially serve as therapeutic targets. Particularly with regard to tissue remodelling and inflammatory cascades, recent developments in our understanding of these systems have highlighted significant parallels and distinctions between severe asthma and other chronic respiratory disorders.(17) Future risk is becoming more and more important as a factor to be taken into account when managing asthma1. It is necessary to quantify risk and comprehend its underlying pathophysiology in order to control it.(18)

Asthma Attacks

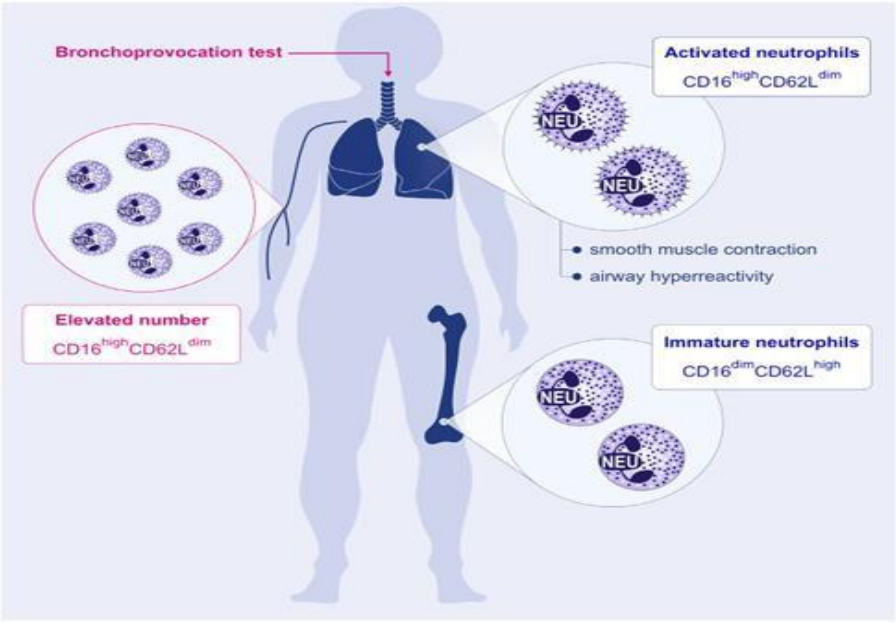
All too frequently, asthma attacks can result in fatalities, lower quality of life, a significant financial strain on healthcare, and poor respiratory and lung growth patterns. Asthma attacks are lung attacks, not "exacerbations," a meaningless term that suggests a temporary annoyance Both the UK National Review of Asthma Deaths2 and a recent meta-analysis of the risk variables for an asthma lung attack (106) pointed out that having one negative attitude associated with social aspects.(19)

MOLECUL AR MECHANISMS IN THE DEVELOPMENT OF ASTHMA

The development of asthma is caused by immune system cells migrating to the lungs and exhibiting their functional characteristics. 59. It was shown that circulating memory Th2 and Th2- resident memory T cells enter the lung parenchyma and cause perivascular inflammation, which encourages the recruitment of CD4+ T cells and eosinophils. Near airways, Th2-resident memory cells multiply and cause mucus metaplasia, AHR, and activation of airway eosinophils. According to transcriptional research, circulating memory Th2 cells and Th2-resident memory cells have different transcriptional profiles but share a core Th2 gene signature(20).

Molecular mechanisms in allergic and nonallergic asthma

A Th1/Th2 imbalance is often observed in allergic asthma, and protein S helps shift this balance back toward Th1. Protein S is a glycoprotein that acts as an anticoagulant, anti-inflammatory, and anti-apoptotic agent. It's linked to a decrease in airway hyperresponsiveness (AHR), reduced infiltration of inflammatory cells in lung tissue, lower levels of Th2 cytokines, and decreased IgE levels. Research by Asayama et al. demonstrated that protein S can help combat allergic asthma by boosting the type 1 cytokines TNF-α and IL-12 while simultaneously reducing the presence of IL-5+ Th2 cells.(21)



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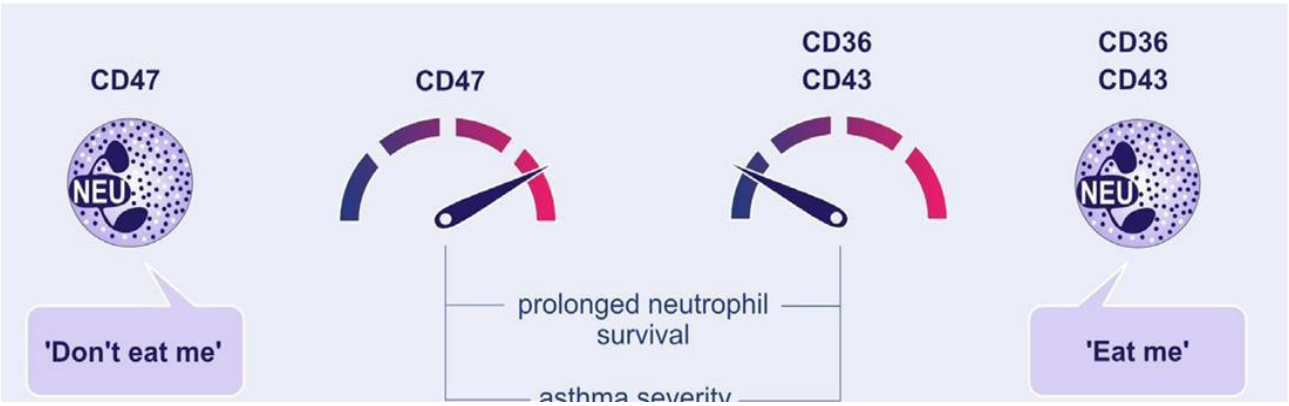


Fig no: 2 A novel neutrophil subgroup in asthma. In humans, neutrophils released from the bone marrow that express low levels of CD16 and high levels of CD62L. This CD16dimCD62Lhigh subset is considered representing immature neutrophils, whereas the CD16highCD62Ldim subset is thought to be mature and induces systemic inflammation. Also, their frequency increases in the blood after the bronchoprovocation test. In allergic asthmatics, neutrophils upregulate surface CD47 and simultaneously downregulate surface CD36 and CD43. The phagoptosis signals may play a role in prolonging neutrophil survival and asthma severity. CD62L, cluster of differentiation 62 ligand [21]

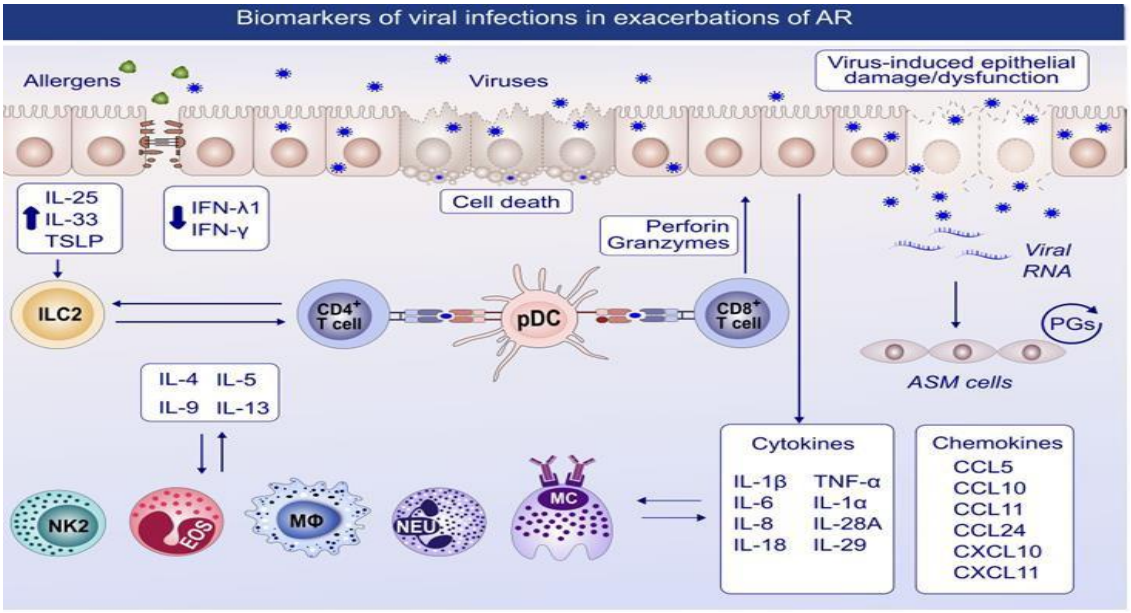
Molecular mechanisms in asthma due to obesity

Felix and Kuschnir78 added to a recent article by Meurs et al. by pointing out that arginase inhibitors may help obese asthma patients by increasing the L-arginine/asymmetric dimethylarginine ratio. 79. Meurs et al.'s response concurred and proposed an even stronger connection, stating that obese asthma patients have higher levels of arginase expression and activity. But the mechanism underlying this is still unclear, providing opportunities for further study.(22)

Classification of Asthma[23]

BIOMARKERS IN CHRONIC RHINOSINUSITIS

CRS is classified into various endotypes and phenotypes. While many different phenotypes and endotypes are known, the most commonly utilized phenotype is the distinction into CRS with and without nasal polyps (CRSwNP and CRSsNP). 28,140 But in recent years, the biological treatment options have focused more on Th2 disease signs, regardless of whether nasal polyps are present. For CRSwNP patients, the first Type 2 has hit the market: duplilumab, a biologic anti-IL4Rα. Other Type 2s, such as anti-IgE, anti-IL5, and anti-IL5Rα, may follow soon. (141–143) The results of CRS cluster analysis have demonstrated that CRSsNP and CRSwNP are not mutually exclusive but rather share overlapping inflammatory signatures, with Type 2 inflammation being the most common endotype in both CRSsNP and CRSwNP, particularly in western.



Figno:3 Biomarkers of viral infections in the exacerbation of AR. After the epithelial cells are infected with viruses, the replicating virus can cause cell lysis and direct damage to the epithelium, which causes deficiency in the production of antiviral interferon (IFN)-β and IFN-λ1. Together with the allergen-induced cytokines IL-25, IL-33 and TSLP, ILC2s are activated and produce more Type 2 cytokines. Subepithelial plasmacytoid dendritic cells (pDCs) recognize virus antigens and present them to CD4+ T cells and CD8+ T cells through MHC class II or I and drive them toward a more Type 2 centric response. Excessive release of chemokines and cytokines can be triggered by infections such as respiratory–syncytial virus (RSV). Together with Type 2 cytokines, they could further promote the function of Type 2 macrophages, a small fraction of IL-4-secreting NK cells, IL-4-secreting NK-T cells, neutrophils, eosinophils and mast cells and augment Type 2 responses in chronically inflamed airways. With the production of perforin and granzymes, CD8+ T cells can show cytotoxicity to virus-infected epithelial cells and induce apoptosis. (24)

ChildhoodAsthma

When preschoolers exhibit persistent wheezing, coughing, chest tightness, and dyspnea, the phrase "not all that wheezes is asthma" applies, making it more difficult to identify asthma in school-aged children (6 years and older). A common history of recurrent wheezing, coughing, chest tightness, and dyspnea is typically used to suspect the diagnosis in younger children. Certainly, these symptoms do not indicate the presence of asthma. The majority

of other respiratory problems that exhibit these same recurrent symptoms are uncommon, though and it is customary to start asthma treatment without first ruling out these other respiratory disorders Of school-aged children with asthma, between 60 and 75 percent have an allergy.(25)

The Burden of Childhood Asthma

Asthma in children is prevalent in the West and often undiagnosed in minority groups in the US and Europe. Asthmamorbidity significantly burdens minority communities, which also experience greater rates of hospitalization, ED visits, and even fatalities. Children's quality of life (QoL) is impacted by asthma control. The better the quality of life, the better the asthma control. Uncontrolled asthma is linked to decreased lung function, poor activity performance, and a lower quality of life. The majority of asthma attacks happen at night. Nearly 50% of children with asthma who visited an outpatient clinic at a university hospital experienced symptoms at night.(26)

Asthma Control

The existence of symptoms throughout the day, activity limitations, nocturnal symptoms and awakenings, the requirement for asthma medication, and an evaluation of lung function in children starting at age six are all indicators of asthma control. Complete control is achievable, but inadequate adherence and breathing technique frequently compromise the medication's best effects. In addition to these variables, other illnesses like obesity, mental illness, allergic rhinitis, and respiratory dysfunction may make it more difficult to achieve ideal control. Clinical experience demonstrates that many kids lack self-control. Only 18% of children in the latter (Swiss) trial had good asthma control [81], 33% had satisfactory asthma control, and 49% had unsatisfactory asthma control with disturbed sleep, limited activities, and absences from school.(27)

Diagnosis

Symptoms and signs and diagnostic criteria

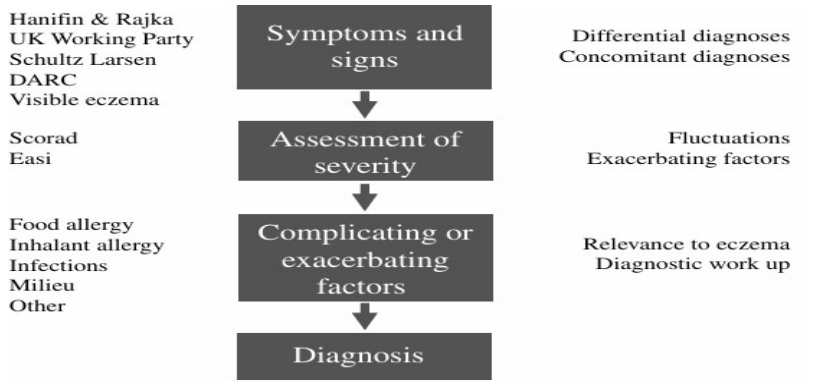
The diagnostic criteria created by Hanifin and Rajka are generally accepted, and their usage is crucial in the diagnosis of AD, particularly for patients who do not exhibit the disease's usual phenotype (Fig. 3) (100). Although using solely visible eczema as a criterion could result in an overdiagnosis of the condition, other criteria have been proposed (101) that correlate well with those of Hanifin and Rajka. Although skin biopsies are not necessary for the diagnosis, they may be necessary to rule out alternative diagnoses, especially in adults.(28)

In vivo testing for allergies

The skin prick test is easy to use, reasonably priced, and yields results fast. Standardized procedures, controls, and allergen extracts should all be used while conducting tests. The child's age and personal medical history will determine the panel of allergens tested, which should also change based on allergens unique to the local area. Testing should ideally be performed by trained and experienced medical professionals, such as doctors or nurses. The potency of the extract, the child's recent usage of H1-antihistamine, the operator's expertise, and the instrument used to prick or puncture the skin are some of the factors that affect the results of skin prick tests. It is recommended that a skilled clinician interpret the results and determine their clinical significance.(29)

Differential diagnosis

When severe skin erythema is present together with exudation or blistering, for instance, the differential diagnosis of acute AD is distinct from that of chronic lichenified forms. In children, genodermatoses like Netherton syndrome, which includes the recently reported immune dysregulation polyendocrinopathy enteropathy X-linked syndrome should be suspected, as should other, more uncommon diseases, particularly in cases that are resistant. In both children and adults, vitamin deficiencies and cancers, particularly cutaneous T cell lymphoma/mycosis fungoides, should be taken into consideration



Figno:4 Diagnostic approach to patients presenting with symptoms and signs of atopic dermatitis[30]

IgE-mediated allergy

The primary risk factor for both the onset of asthma and its severity and duration is allergic sensitization (10, 15, 18). Furthermore, atopic dermatitis and/or food-specific IgE raise the chance of being sensitized to allergens in the air and may be indicators of the onset of asthma. Consequently, all children should have allergy testing as part of their diagnostic evaluation. Evaluation of symptoms, case histories, and in vivo and in vitro testing are the foundations for allergy diagnosis.(31)

Exacerbating factors

Allergens.

Exposure to allergens has a significant role in host allergic sensitization and is frequently the cause of asthma symptoms in both adults and children. It typically takes two to three years of life for the generation of antigen-specific IgE antibody to aeroallergens (such as mites, trees, grasses, and animal dander) to take place. This leads to allergy sensitization but is not always the result of allergic illness. As a result, asthma brought on by aeroallergens is rare in the first year of life, starts to become more common in later childhood and adolescents, and peaks in the second decade. These varied results suggest that these connections are in fact intricate and may entail interactions between genes and the environment. It has been shown that pollen immunotherapy dramatically lowers the likelihood of developing asthma and airway hyperresponsiveness in school-aged children who initially have merely allergic rhinitis.

Infections.

First, certain viruses have been suggested to be in charge of the onset of the asthmatic phenotype in premature children. In this context, rhinovirus and respiratory syncytial virus (RSV) have been the viruses most convincingly shown. 1, 2, Different responses to these infections may be caused by abnormalities in innate immune responses, changes in the epithelial cell barrier that facilitate viral replication, and possibly increased virulence of pathogenic virus strains in individuals who are predisposed to asthma. Second, upper respiratory tract virus infections are a major cause of acute exacerbations of airway obstruction in patients with established asthma, especially in children, which may lead to recurrent hospital stays or outpatient visits.The common cold virus,
rhinovirus, is the most common cause of exacerbations; however, other viruses, including as parainfluenza, RSV, influenza, and coronavirus, have also been involved, albeit to a lower degree.

Exercise

One of the more frequent causes of airway blockage in asthmatic individuals is exercise. 79 Wheezing, coughing, shortness of breath, and, in children, chest pain or discomfort are some or all of the symptoms of exercise-induced bronchospasm (EIB). After stopping exercise, the symptoms often subside within 15 to 30 minutes, with the most intense episodes lasting 5 to 10 minutes. The majority of the time, bronchoconstriction is not severe enough to be fatal, and when it is, it nearly always indicates either advanced, untreated disease, confusing triggers (such as concurrent allergen or irritant exposure), or both.(32)

Types of Allergies

Atopic Dermatitis

Immune dysregulation, compromised skin barrier function, and genetic risk all play a part in the illness. The function of epidermal barrier proteins like filaggrin and the effect of environmental exposures on disease severity have been emphasized by recent studies. 21 Histopathological analysis of AD usually shows a thick perivascular infiltration of lymphocytes and eosinophils, spongiosis (edema between epidermal cells), and epidermal hyperplasia. These characteristics mirror the long-term inflammation and compromised integrity of the epidermal barrier seen in AD. 22 Increased amounts of mast cells and eosinophils can be detected by cytological analysis of blood or skin samples, especially during acute flare-ups. By highlighting the existence of these cells and their level of activation, immunocytochemistry and cytospin preparations can shed light on the inflammatory mechanism that underlies AD. 23

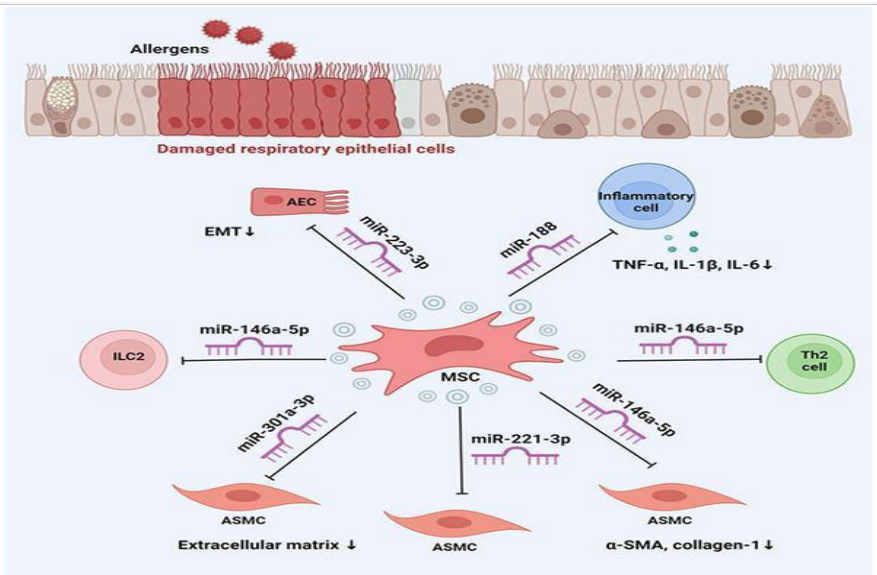
Allergic Rhinitis

The symptoms of allergic rhinitis include rhinorrhea, sneezing, and congestion of the nose. Airborne allergens like pollen, dust mites, mold, and allergen exposure frequently cause it. Sneezing, nasal congestion, and itching are among the symptoms. Similar to asthma, the pathogenesis involves the activation of mast cells and eosinophils in the nasal mucosa by IgE. The effects of allergic rhinitis on quality of life and the effectiveness of new treatments have been investigated in recent research. 28 Histopathological analysis of the nasal mucosa in allergic rhinitis shows mast cell and eosinophil infiltration in the lamina propria, edema, and hyperplasia of the epithelial layer. The inflammatory reaction to allergens is reflected in these alterations.(33)

Food Allergy

The symptoms of food allergies, which are immune-mediated responses to particular food proteins, can range from minor gastrointestinal distress to life-threatening anaphylaxis. The gastrointestinal tract is frequently affected by histopathological alterations in food allergies; biopsies may reveal epithelial destruction and eosinophilic infiltration in the lamina propria. These alterations are a reflection of the local inflammatory reaction to allergens. When gastrointestinal biopsies or aspirates are examined cytologically, more mast cells and eosinophils may be seen. These cells' degranulation and role in the allergic reaction can be evaluated using immunocytochemistry.(34)

Therapeutic Potential of Mesenchymal stem cells (MSCs) Derived Exosomal miRNAs since of their malleable qualities, MSCs are potential prospects for therapeutic applications since they can develop into osteoblasts, adipocytes, and chondroblasts under the right circumstances. 99,100 The therapeutic actions of MSCs are mediated in large part by exosomes generated from MSCs. Through the transmission of growth factors and miRNAs that stimulate cell proliferation and differentiation, MSC exosomes aid in tissue repair and regeneration. 101, 102 Exosomal miRNAs generated from MSCs have immunomodulatory effects in asthma that slow the course of the condition. For instance, it has been confirmed that exosomal miR-146a-5p suppresses the overactivation of the immune system by downregulating the production of plasminogen activator inhibitor-2, hence inhibiting Th2 cell development. TNF-α, IL-1β, and IL-6 in ASMCs treated with platelet-derived growth factor, as well as inhibited ASMC migration and proliferation, hence reducing airway inflammation and remodeling in the mouse model of OVA-induced asthma. 108 These results demonstrate the important potential of exosomes produced from MSCs in reducing asthmatic airway inflammation. Additionally, exosomal miR-221-3p derived from human bone marrow MSCs has been shown to limit the proliferation, migration, and extracellular matrix deposition of ASMCs by targeting fibroblast growth factor 2 and thereby blocking the ERK1/2 signaling pathway. This reduces the histopathological damage and airway hyperresponsiveness in an OVA-induced asthmatic mouse model.(35)



ALLEVIATINGAIRWAYINFLAMMATIONANDMODELLING

FIG NO 5: The therapeutic potential of MSC-derived exosomal miRNAs in asthma. MSC-derived exosomal miRNAs, including miR-146a-5p, miR-223-3p, miR-188, miR-221- 3p, and miR-301a- 3p, mitigate airway inflammation and remodeling via inhibiting the secretion of inflammatory cytokines, the proliferation of ILC2, Th2 cells and ASMC, as well as the production of extracellular matrix, α-SMA, and collagen-1. AECs, airway epithelial cells; ASMC, airway smooth muscle cell; α-SMA, α-smooth muscle actin; EMT, epithelial-mesenchymal transition; IL, interleukin; miRNAs, microRNAs; Th, T-helper. indicates an inhibitory effect and ↓ indicates downregulation.(36)

Treatment Strategy for CLC

Targeted Therapies

Targeted treatments, which promise more accurate and efficient interventions that directly target particular molecular changes causing tumor development and survival, have become an essential treatment option for colorectal cancer. Utilizing the distinct genetic and molecular properties of cancer cells, these treatments enable individualized treatment plans that seek to enhance results and reduce side effects.

(1) The most and oldest known targeted medications are inhibitors of the epidermal growth factor receptor (EGFR). 68,69 One of the most common oncogenic factors in CLC, especially non-small cell lung cancer (NSCLC), is EGFR mutations. Targeted treatments such EGFR tyrosine kinase inhibitors (TKIs), which selectively block the activity of the mutated EGFR protein, may be helpful for patients with EGFR-mutant CLC.

(2) Anaplastic Lymphoma Kinase (ALK) Inhibitors: ALK gene rearrangements are a significant oncogenic factor in lung cancer, particularly colorectal cancer (CLC), which accounts for a portion of non-small cell lung cancer incidences. According to some reports, ALK inhibitors—

such as crizotinib, ceritinib, alectinib, brigatinib, and lorlatinib—have completely changed the way that ALK-positive NSCLC is treated. They are more effective than conventional chemotherapy and greatly increase both overall and progression-free survival.(37)

Surgery

Some researches have indicated that surgery is still the mainstay of treatment for resectable CLC, as it achieves total tumor excision with curative purpose. 87, 88 A number of parameters, such as the size, location, and extension of the CLC, influence whether the tumor is resectable. By removing the tumor and maintaining lung function, surgery gives patients the best chance of long- term survival. As surgery cannot contribute to the treatment of allergic disease itself, it may only be used in certain precise conditions such as turbinate hypertrophy, cartilaginous or bony obstruction of the nasal airways or secondary and independent sinus disease.(38)

1.3 Other Treatment Regimens

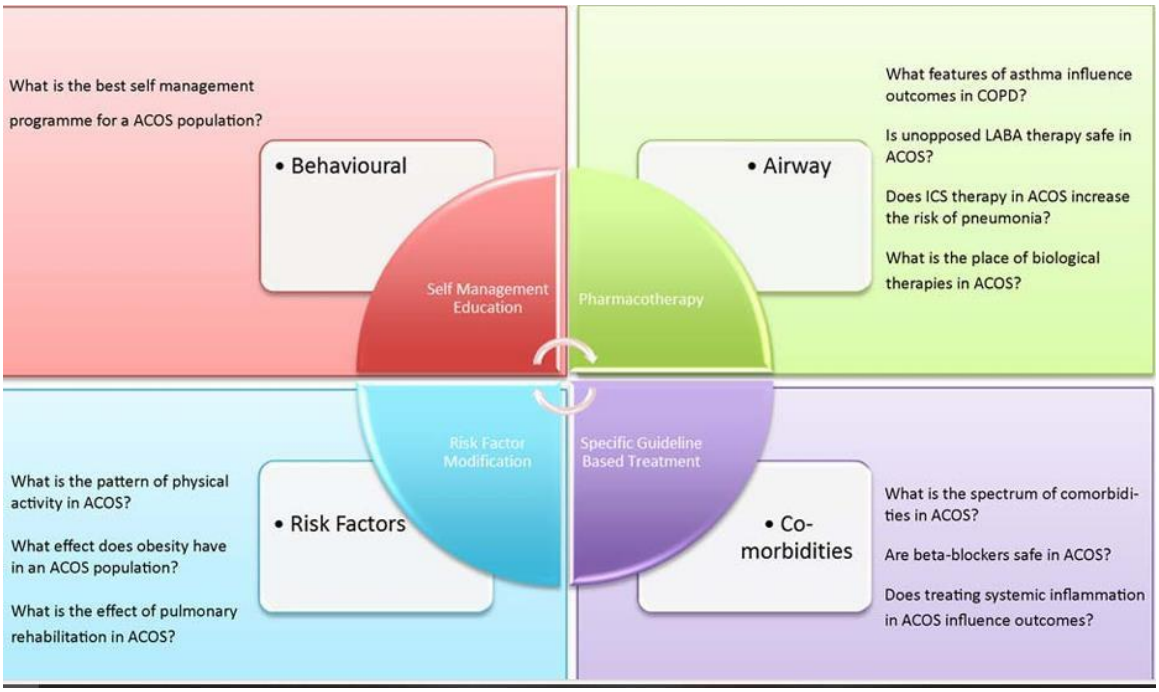
Drugs are used in chemotherapy, a systemic treatment, to kill cancer cells all over the body. Chemotherapy can either be administered alone for unresectable tumors in CLC or in conjunction with other treatments to improve treatment results. 93. For the treatment of CLC, platinum-based chemotherapy regimens, which include medications like carboplatin or cisplatin, are frequently used. Chemotherapy regimens are also frequently incorporated into multimodal treatment techniques, such as adjuvant or neoadjuvant therapy in conjunction with surgical resection, or in conjunction with immunotherapies and targeted therapies. Radiation therapy is used with curative aim as a last treatment for locally advanced disease or as adjuvant therapy after surgical resection, and it is a crucial part of local-regional treatment.(39) A cheap and easy remedy that has been demonstrated to have some effectiveness is saline douche (228, 1760–1762). Methods that are physico-chemical have been suggested. Rhinoscopy is successful (1763), but more research with less complicated tools is required. Pollen-blocker creams (1765) or nasal filters (1764) might lessen nasal symptoms when exposed to grass and ragweed pollen naturally. The UK has been selling inert cellulose powder since 1994 as a treatment for hay fever and as a way to lessen the symptoms of pollenrhinitis (1766).(40)

FUTURE RESEARCH

There are numerous research topics that need to be looked into, which is not surprising considering the lack of evidence to support treatment decisions in cases when asthma and COPD overlap. Airway-related questions, comorbidity, risk factors, and self-management are the four domains in which the scientific inquiry can be divided.

Airways

The characterization of the overlap between asthma and COPD has to be improved. As has been the case with other diseases, a risk-based strategy is probably going to be most helpful. Long- acting bronchodilator therapy should be started to manage symptoms of COPD, and ICS should be added when the FEV1 drops below 50% expected or patients have frequent exacerbations.



FIGNO:6 Asthma–COPD overlap syndrome (ACOS) research directions. ICS, inhaled corticosteroid; LABA, long-acting β2 agonist. Adapted with permission from 'The Lancet'.[41]

COMORBIDITY

In COPD, omorbidities are prevalent and significantly affect patient outcomes. The prevalence and range of overlap comorbidities between asthma and COPD, as well as their effects, are not well understood. Furthermore, very little is understood about the mechanisms underlying the overlap between asthma and COPD and comorbidities. Research examining the overlap of asthma and COPD comorbidities will yield much-needed information.

RISK FACTORS

It is well known that physical activity is important for people with COPD, and compared to their healthier older counterparts, patients with COPD are less active and more sedentary. 89 Characterizing physical activity in an asthmatic population has been the subject of much less research. Research on the features, effects, and treatment options of physical inactivity and sedentary behavior in a population with asthma and COPD overlap is constantly developing.

SELF-MANAGEMENT

Which techniques for self-management are effective when asthma and COPD coexist? Both asthma and COPD self-management programs have shown promise; however, asthma self- management programs cannot be immediately applied to COPD patients,94 and cautious patient selection is necessary to prevent injury. 95. Since asthma and COPD patients may need a different approach, it is reasonable to presume that this needs to be tested in an overlap population.(42)

Discussion

Although roptosis, a distinct type of cell death, is linked to a number of illnesses, its molecular details are still somewhat unclear, underscoring the need for additional study. Basic research, such as in vitro and in vivo studies, has provided the majority of the insights to date. Natural compounds' varying effects, metabolism, and absorption in various species provide difficulties for their clinical development as medications. The conversion of natural materials into medicinal medicines is made much more difficult by the lengthy time needed to get research funding and carry out clinical studies.(43) In addition to behavioral, toxicological, molecular biology, and genomic testing, modern drug research necessitates the use of advanced techniques like liquid chromatography-mass spectrometry, metabolomics, pharmacokinetics, and data mining [198–200]. These methods present both opportunities and challenges in moving natural products from the lab to the clinic.(44)

Conclusion

Enhancing clinical practice and promoting future research in asthma treatment and management are the goals of the review, which links clinical presentations with underlying molecular causes and highlights the significance of individualized medication Lifestyle changes and pharmaceutical therapies are both necessary for the effective management of allergies. Treatment options for patients with severe or refractory allergies have increased due to recent advancements in new therapies, such as precision medicine and biologics. Furthermore, self-management techniques and patient education are essential for enhancing quality of life and maximizing therapy results. In asthma, exosomal miRNAs play a key role in controlling the remodeling and inflammatory processes, providing important insights into the disease's causes and opening up new avenues for diagnostics and treatment.

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