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Cytokines Involved In Asthma

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ABSTRACT: Asthma frequently includes allergic inflammation, which has the potential to both cause and worsen the condition(19). Early life's limited exposure to germs is what causes the immune system's Th1/Th2 balance, which favours a proallergenic Th2 response. Asthma or allergies manifest clinically as a result of this Th1/Th2 imbalance(23). Antigen-presenting cells (APC) and sensitised helper T lymphocytes (TC), which produce Th2 cytokines, combine to cause inflammation(19). In mild to moderate allergic asthma, type 2 CD+4 cells (Th2) and their cytokines predominate, whereas severe steroid-resistant asthma has a more mixed Th1/Th2 phenotype with a Th17 component(22). Allergy illnesses are characterised by tissue eosinophilia and Th2 type cytokines, which include interleukin IL-4 and IL-5(26). Although it has been shown that APC and TC are recruited to the lung during allergic reactions, there haven't been many functional studies on humans(19).

Objectives: To investigate how cytokinins are involved in asthma.

I. INTRODUCTION

Asthma is primarily caused by cytokines.Cytokines are proteins that are produced by several cell types involved in the host immune response and are crucial components in the regulation of intercellular signalling. With the involvement of various mediators, asthma is distinguished by inflammatory changes to the airway that result in distinctive physiopathological abnormalities.Lymphokines (cytokines produced by lymphocytes) and cytokines in general are additional names for cytokines.[1]

Cytokines in general, other names include:

- Lymphokines [Cytokines made by Lymphocytes],
- Monokine [Cytokines made by monocytes],
- Chemokine [Cytokines that have chemotactic functions],and
- Interleukin [Leukocytes that act on other leukocytes via producing cytokines][1]

Monocyte-derived cytokines, chemotactic cytokines, and interleukin-derived cytokines that act on other leukocytes are all examples of cytokines. These may have an effect on the cells that release them (autocrine action), nearby cells (paracrine action), distant cells (endocrine action), or all three[2].

Numerous physiological processes, including cell differentiation and maturation, inflammation, systemic and local immunological responses, and tissue repair, are regulated by cytokines. Cytokines undermine a real signalling system that has many connections between the various components, pleiotrophy, and redundancy, similar to a neural network. The current review discusses many cytokines connected to asthma[3].

There are two subcategories of asthma: Th2 low and Th2 high. In individuals with asthma, the levels of gene expression for Th2 cell cytokines or for the activation of epithelial cells by Th2 cell cytokines are observed[4].

Specific clinical, pathological, and treatment response traits are present in asthmatics who have expression levels above those of healthy controls.Asthmatics who are over and below this threshold and exhibiting symptoms can be identified by biomarkers of type 2 inflammation in their blood and exhaled breath[5].

PATHOPHYSIOLOGY OF TYPE 2 INFLAMMATION

Both the innate and adaptive immune systems may contribute to Th2 cell-mediated asthma. Th2 cells and innate lymphoid cells (ILCS), which produce type 2 cytokines including interleukins IL 4, IL 5 and IL 13, and other inflammatory mediators, are responsible for type 2 inflammation[6].

Exposure to allergens causes activation of

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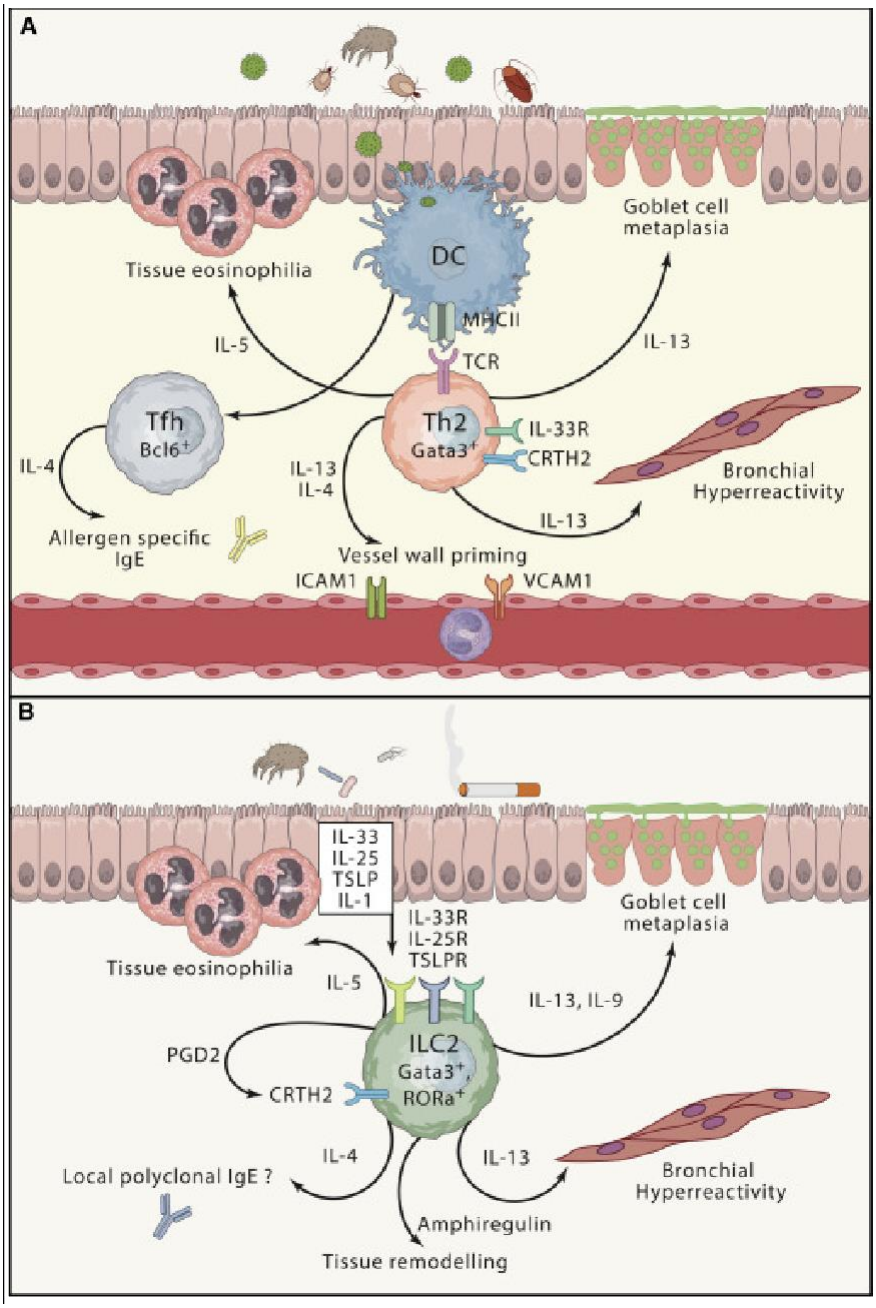
dendritic cells consists antigens (APC),these antigens are recognised by MHC class 2 known as Th2 memory cells.These cells releases certain cytokines consists interleukins. When it comes to the pathophysiology of Type 2 inflammatory airway disease, type 2 cytokines play a variety of roles.The differentiation, maturation, mobilisation, and survival of IL-5R+ alpha eosinophil progenitors in the bone marrow are all significantly influenced by IL 5.Mast cells and basophils are both developed with the aid of IL 5. Both IL 4 and IL 13 contribute to B cell class switching, IgE production, basophil and mast cell degranulation, release of proinflammatory mediators, disruption of the blood-brain barrier, and tissue remodelling.Goblet cell hyperplasia, smooth cell contactility, and mucus production are all impacted by IL13[5].



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II. Materials And Methods :

Cytokines: Types, Function and Significance.

CYTOKINES

Cytokines are a class of humoral factors in both innate and adaptive immunity. They are tiny proteins that perform signalling between cells. The affinity of cytokines for cell membrane receptors is greater.

Based on their modes of action, cytokines are categorised into three groups:

1. Proinflammatory, contributing to the inflammatory response (interferon gamma, IL-2,6,8 and TNF-alpha)
2. Anti-inflammatory, inhibiting the growth of inflammation (IL-4, 10, etc.).

3. Immune system controllers that have particular roles (cytotoxic, antiviral). Based on their respective roles, cytokines are categorised into three groups:

1. Cytokines that are cytotoxic (anti-cancer and anti-viral).

2. Th1 and Th17 cytokines, which are involved in allergic reactions.

3. Cytokines' involvement in immune-regulatory and suppressive responses[7].

Different kinds of proteins known as cytokines direct immune cells where to go and what to do in order to maintain the health of your immune system.

1. **Chemokines**: Chemokines point immune cells in your body towards infection-fighting areas.
2. **Interferons**: Interferons instruct cells to erect barriers to prevent viruses from infecting your body. Interferons "interfere" with the process by which viruses reproduce, or create new viruses after invading a healthy cell.
3. **Interleukins**: The word "inter" means between, and "leukocyte" is another name for a white blood cell. These two words combine to form the name "interleukins," which means "between leucocytes." Initially, researchers believed that leukocytes were the only cells that produced interleukins and that they exclusively communicated with other leukocytes. However, we now understand that these proteins are released by cells besides leukocytes. Interleukins can also transmit information between cells other than leukocytes[8].
4. **Tumour Necrosis Factor (TNF)**: TNF helps your body control inflammation. Additionally, TNF activates immune cells that destroy tumour cells.
5. **Colony stimulating factor**: Hematopoietic stem cells are instructed by a colony-stimulating factors (CSF) to differentiate into particular cell types. White blood cells, red blood cells, and platelets are all produced by hematopoietic stem cells (HSC), which are precursor cells. Hematopoiesis, a process, is when these adjustments happen. For instance, granulocyte- colony stimulating factor (G- CSF) instructs an HSC to develop into a neutrophil, a kind of white blood cell. Neutrophils aid in infection prevention[8].

Some cytokines are named by the kind of cell that produces them, such as:

- Lymphokines: Made by a specific kind of white blood cell called a lymphokine.

- Monocytes, a type of white blood cell, create monokines[8].

INTERLEUKIN 2

It was first identified as T-cell growth factor (TCGF), a powerful mitogen and growth regulator of T cells. IL-2 is a glycosylated globular protein. A significant source of IL 2 is

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activated T cells, notably Th0 and TH1 cells, whereas IL 2 can also be secreted in vitro by B lymphocytes when certain conditions are met. Following activation, antigen-activated T cells release IL-2, which is later followed by a change in the high-affinity IL 2 receptors on the same cells[9].

Following immunological activation, CD+4 alpha/beta T cells differentiate to form discrete effector subpopulations that may be identified by their cytokine production, expression of transcriptional master regulators specific to particular lineages, and cytokine needs. Additionally crucial to CD+8 effector cells is IL 2. In response to infection, navie antigen-specific CD8+ T cells multiply and develop into effector cytotoxic T lymphocytes, which produce proinflammatory cytokines like IFN-gamma and develop the capacity to destroy infected cells[10].

ROLE IN ASTHMA

IL 2 levels are elevated in the bronchoalveolar lavage fluid of asthmatic patients. Patients with acute severe asthma have higher levels of IL 2R-bearing T-lymphocytes in their blood, and asthmaticus cells recovered from bronchoalveolar lavage following allergen exposure had higher levels as well.

Cyclosporine A inhibits allergic airway eosinophilia but not bronchial hyperresponsiveness because it interferes with the transcription factors AP-1 and NF-AT and IL 2 gene transcription in activated T-lymphocytes. These effects of cyclosporine A may result from a reduction in the expression of IL 2, as well as GM-CSF and IL 5 and other cytokines[11].

INTERLEUKIN 3

The primary sources of IL 3 are mast cells and activated helper T cells[12]. By increasing T regulatory cell responsiveness and suppressing the growth of type 2 innate lymphoid cells, the pro-inflammatory protein IL 3 seemed to control the severity of allergic asthma[13].

Asthma that has been controlled by steroids has been linked to IL 3. Additionally, the rIL 3 therapy improved the eosinophilia and mucus production in the airways[14]. Important eosinophil modulators are IL3, IL5, and GM-CSF. IL3 and IL5 can all affect eosinophils, while GM-CSF can also affect eosinophils[15].

The activation of inflammatory innate lymphoid type 2 cells was also reduced by IL 3. These immune cells release chemicals that can contribute to the onset of allergic illness. When IL 3 was injected, they displayed decreased cell surface expression of the pro-inflammatory binding receptor ST -2, which is crucial for activating this cell type. IL 3 has immunoregulatory qualities that can lessen bronchial asthma symptoms.

INTERLEUKIN 4

Th2 derived T lymphocytes, specific lymphocyte subpopulations, eosinophils, basophilic cells, and mast cell lineage cells are all sources of IL 4. Human CD4+ T cells from healthy, non-allergic people who have their CD40 ligand crosslinked provide a co-stimulatory signal that boosts the production of IL 4. Antigen receptor activation on T lymphocytes and IgE Fc receptor crosslinking on mast cells and basophils are other ways to activate synthesis[16].

Important pro-inflammatory functions of IL 4 in asthma include inducing the switch from IgE to VCAM-1 expression, promoting eosinophil transformation across endothelium, promoting mucus secretion, and differentiating T-helper type 2 lymphocytes that release cytokines[14].

ROLE IN ASTHMA

Along with other cytokines including IL 5, IL 9, and IL 13, the gene responsible for producing IL 4 is produced by mast cells and Th2 cells. When TH0 type cells are indirectly differentiated into Th2 type cells, IL 4 is a key factor. It contributes to the presentation of VCAM-1 on the surface of endothelial cells and the production of IgE from B cells in chemotaxis. These VCAM-1 aid in the firmly adhering of eosinophils, basophils, monocytes, and T-lymphocytes to blood vessels, which is followed by the diapediasis of the blood artery into the tissues[17].

The release of IL 8 and TNF-alpha, both of which raise the number of neutrophils in lung tissue, is thought to be triggered by IL 4. As a result, eosinophils gather inside and close to airways. Additionally, increased mucus secretion causes a worsening of airway blockage. By preventing T cells and eosinophils from apoptosizing, IL 4 indirectly keeps the acute allergic reaction in check. Asthma persistence is correlated with eosinophil presence[17]

INTERLEUKIN 5

In addition to mast cells and eosinophils, activated CD+4 T-cells of the Th2 subset also produce and secrete IL-5[18].

Th2 lymphocytes are the main source of IL 5, however airway mast cells are also a source[19]. Since IL 5 encourages eosinophil development,

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differentiation, and activation, it plays a critical role in the pathophysiology of allergic illness[20].IL-5, along with IL-4 and
IL-13, has been identified as important cytokines underlying the pathophysiology of Th2 asthma due to its crucial function in eosinophil production, release, and recruitment to tissues[21].

INTERLEUKIN 10

A cytokine called interleukin 10 was initially classified as a cytokine production inhibitor. T helper 2 cells, B cells, macrophages, keratinocytes, mast cells, and some tumour cells all produce this protein[22]. By lowering inflammatory cytokine and chemokine production as well as by restricting class 2 CD80-CD86 expression on antigen-presenting cells, IL 10 can suppress airway inflammation.

It can also inhibit antigen presentation to T cells.In fact, the lack of IL 10 causes severe allergen-induced airway inflammation with excessive IL-4, IL-5, and IFN- Gamma production compared with that of wild type mice[23].

Further research revealed that II-10 reduces both Th1 and Th2 mediated inflammation in people and is generated by both Th1 and Th2 cells. Other peripheral blood cells have shown IL-10 to have the same cytokine-inhibitory properties. The reduction of IL-2 synthesis, cell proliferation, and CD28 tyrosine phosphorylation in signalling appear to be the main causes of IL-10's direct impacts on Th1 and Th2 states[24]. Mammals have a range of particular cells that can make IL 10, but the main lymphocyte sources are macrophages, monocytes, mast cells, and B cells. Although IL-10 boosts the growth of some types of immune cells, such as B cells and mast cells, and can promote the synthesis of immunoglobulins, as was mentioned above, its most pronounced and strong effects are related to the functional suppression of inflammatory cells[24].

According to its recognised immunologic roles, IL 10 RNA has been discovered in mast cells, conventional B cells, and activated Th2 lymphocytes of CD+4 cell lines. Furthermore, it has been demonstrated that IL 10 reduces the synthesis of TNF-Alpha in mast cells generated from human cord blood, potentially further closing the knowledge loop regarding IL 10 message induction, protein expression, and cell signalling response[24]. The presence of an IL 10 mechanism in those cells to reduce histamine and pro-inflammatory cytokine production would seem to be of some importance given the significance of the mast cell associated with the human lung allergic mechanism and as a part of the resolution of the airway inflammatory response[24].

INTERLEUKIN 13

Th2 polarised CD4+ T cells are the main producers of IL-13, although it is also produced by a wide range of other cell types, including both Th1 CD4+ T cells and CD8+ T cells. The ligand studies also suggest that IL-13 is produced by numerous non-T-cell populations that are of particular importance to the allergic response, such as mast cells, basophils, and eosinophils. However, the natural killer Tcells may be an important source of IL-13 early in the allergic response[25].

A number of other cytokines and mediators, such as IL-9, IL-25, histamine, adenosine, and endothelin-1, have also been linked to the regulation of IL-13 production. Much of the allergic phenotype is recapitulated in the murine lung by overexpression of either IL-9 or IL-25; however, the fact that neutralisation of IL-13
completely abolishes the phenotype in both of these scenarios suggests that these two cytokines may actually function by inducing the production of IL-1[25].
Human airway smooth muscle responds to Ca2+ responses in vitro via a
STAT6/JAK-independent mechanism when IL-13 is present. Some have hypothesised that STAT6-dependent pathways may be relevant in acute AHR, but STAT6-independent AHR
and airway remodelling mechanisms may be important in chronic models. It signals through MAP kinases ERK and JNK, affecting the smooth muscle of the airways. IL-13 overexpression causes inflammation, remodelling, and AHR, all of which are characteristics of asthma. Allergen-induced AHR is eliminated when the soluble receptor-Fc fusion protein inhibits IL-13[26].

Additionally supporting its role in the pathophysiology of AHR, IL-13 is overexpressed in asthmatics' sputum, bronchial submucosa, peripheral blood, and mast cells in the airway
smooth muscle bundle. In bronchial biopsy homogenates, both atopic and nonatopic asthmatics had elevated levels of human IL-13 mRNA[26].

INTERLEUKIN 17

It was initially discovered that activated CD4+ T lymphocytes generate IL-17. Later, after

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studying IL-23-mediated immunological pathogenesis, a unique CD4+ T helper cell subset known as the TH17 cell lineage was identified. Tumour necrosis factor (TNF), IL-6, and, to a lesser extent, IL-17, IL-17F, and IL-22 are all produced by TH17 cells. Later research identified the main transcription factor regulating the TH17 cell lineage as the retinoid acid-related orphan receptor (RORyt). Although the significance of TH17 cells in inflammatory autoimmune illnesses was first noted, mounting evidence now contends that TH17 cells and the cytokines they produce are also important in the pathogenesis of allergic asthma. The expression of IL-17 is elevated in the sputum, bronchoalveolar lavage fluid, and the

lung.IL-17 and IL-17F can cause lung structural cells to secrete proinflammatory cytokines (such as TNF, IL-18, G-CSF, and IL-6) and chemokines (such as CXCL1/Gro-a, CXCL2, and CXCL8/IL-8), leading to neutrophil infiltration. In patients with asthma, the severity of AHR is positively correlated with IL-17 expression levels[27].

Although the majority of individuals with mild asthma are able to control their symptoms with current treatments, about 10% of people with severe asthma are still poorly controlled even with high-dose inhaled medication. This subgroup of asthma patients had elevated levels of the IL-17 protein in their airways, which was associated with enhanced neutrophil infiltration, the production of the chemokine IL-8, and the degree of airway hyperresponsiveness. An immunohistochemistry method was used in a recent study to further show that patients with severe asthma had a much higher number of

IL-17-producing cells in their lung tissue than do patients in other asthma patient groups. Notably, in the subepithelial tissues, these immunoreactive IL-17+ cells were exclusively mononuclear cells that were grouped with inflammatory cells.These findings show a favourable correlation between the presence of IL-17A+ cells and the severity of human asthma. However, it is still unknown which IL-17-producing cell type causes acute exacerbations of asthma in humans in response to different airway injuries[27].

TNF-ALPHA

Mast cells and macrophages are the main sources of TNF-a, but other cells can also produce it. TNF-a is known to be secreted by eosinophils, neutrophils, smooth muscle cells, fibroblasts, and epithelial cells. CD4+ cells release TNF-a, whereas CD8+ cells secrete little to no TNF-a. TNF can cause the generation of TNF. Mast cells produce TNF-a and react to it, demonstrating a beneficial autocrine loop that increases mast cell activation[28].

Asthmatics airways appear to express TNF-a more than those of healthy patients, according to data. TNF-a, which is released in response to allergen exposure, has been found to be present in mast cell granules. TNF-a production by human lung mast cells can reach 150 pg/106 cells/24 hours, and it is induced by IgE-dependent activation and stem cell factor

(c-kit ligand), a growth and survival factor for must-cells. Within minutes, preformed TNF-a is released from sensitised mast cells' IgE that has been crosslinked by allergens. Nuclear factor KB (NF-kB) is a mediator of TNF-a that allows human mast cells to increase their own secretion. Eosinophils, epithelial cells, and airway macrophages are some other airway cells that have the ability to produce TNF-a[28].

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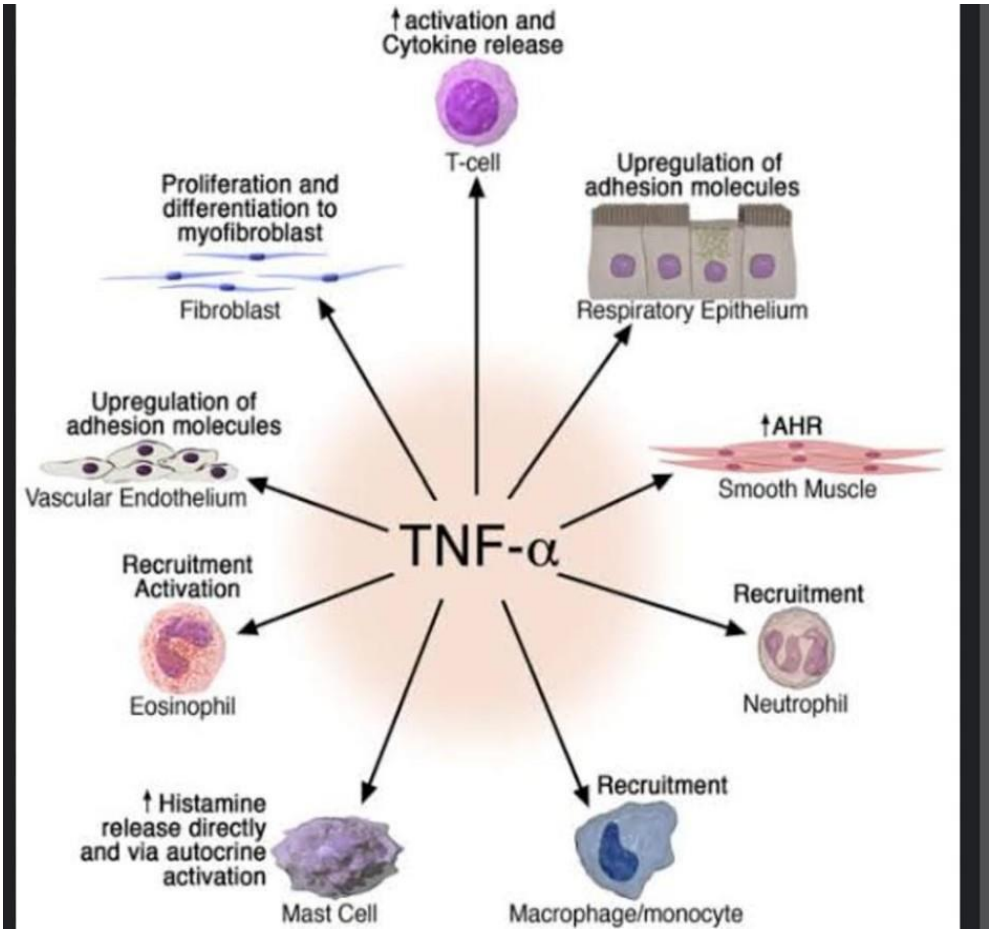

TNF-a has a significant amplifying effect on the inflammation associated with asthma because it stimulates neutrophil transepithelial migration via IL-8 and encourages chemotaxis ofeosinophils and monocytes, and it participates in the activation of T cells. The more severe forms of asthma are related with airway neutrophilia, and TNF-a injection into rats' airways induces active airway neutrophilia. In contrast to normal participants, the peripheral blood mononuclear cells from asthmatic subjects produced more TNF-a, IL-8, and GM-CSF after being activated with LPS[28].

In comparison to leukocyte cultures from healthy participants, asthmatic subjects' leukocyte cultures that had been treated with phytohemagglutinin plus phorbol myristate acetate (PHA+PMA) BAL produced considerably more TNF-a and IFN-g. TNF-a's potent ability to promote fibroblast proliferation provides evidence that it plays a part in tissue remodelling[28].

Cytokine expression:

It was investigated whether the expression of cytokine product coincided with allergen-induced increases in IL-4 and IL-5 cytokine mRNA expression.

Immunohistochemistry was used in biopsies where significant numbers of cytokine mRNA-producing cells had been seen to determine whether cells were expressing IL-4 and

IL-5 protein. The median/mm2(interquartile range) of IL-4 positive cells in the five biopsies under investigation was 28 (2.5,200). Due to insufficient sections, double immunohistochemistry was not done to determine the cell source of immune-reactive IL-4 protein, while the majority of IL-14 protein positive cells showed the typical morphology of eosinophils (Fig. 1b). In any of the five examined samples, there was no sign of the IL-5 protein at 6 hours[29].

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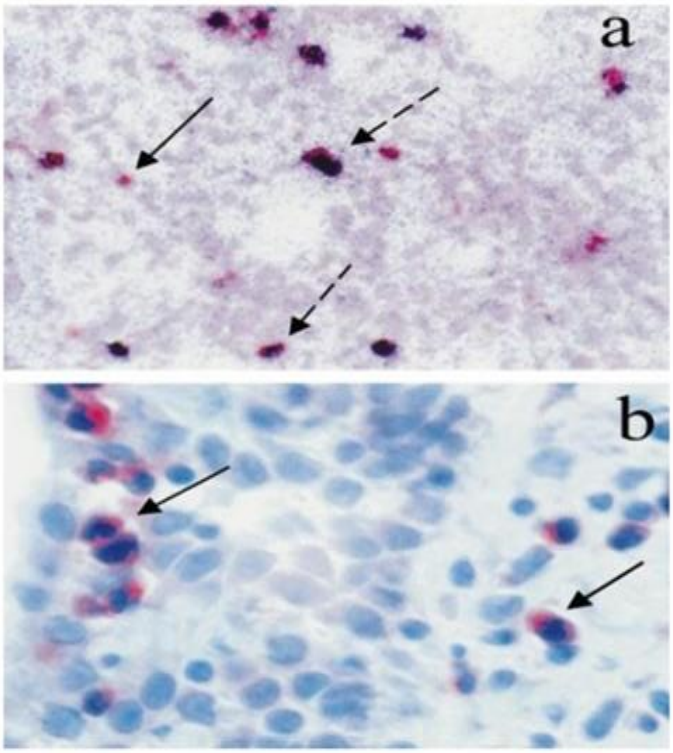

Figure 1. (a) In situ co-localization of IL-4 mRNA to eosinophilshybridization/immunohistochemistry. Broken arrows indicate the presence of IL-4 mRNA in EG21 eosinophils. An EG21 eosinophil without IL 4 mRNA expression is depicted by the solid arrow.
(b) IL-4 protein immunostaining in a nasal sample taken six hours after an allergen exposure. IL-4-positive cells are indicated by solid arrows.

A prior study that shown that grass pollen allergen provocation caused late symptoms and rasal obstruction in 50% of patients between 3 and 10 h led to the selection of the 6 h time point. Additionally, earlier research in the skin and nose revealed a surge in eosinophils 6 hours after challenge. The current results at 6 hours are in contrast to earlier results in the nasal mucosa at 24 hours, when CD31 T-cells (about 70%) were the main cell sources of IL-4 and IL-5 with less significant contributions from mast cells (15-20%) and eosinophils (0+5%

IL-5 and nil IL-4 expression). Eosinophils may therefore be the predominant cytokine-producing cells in the nasal mucosa at 6 h as opposed to 24 h[29].

In contrast to IL-5, which did not express IL-4 protein, immunohistochemistry employing monoclonal antibodies specific for cytokines demonstrated that the increase in IL-4mRNA identified at 6 h after allergen challenge was followed by IL-4 protein production. A quicker time course for IL-4's mRNA translation than IL-5's could be one factor. For instance, the peak time for IL-4 protein detection in the supernatant fluids of completely differentiated human T-cell clones is 4+6 h, whereas the peak time for IL-5 protein is 18+24 h[29].

THERAPEUTIC STRATEGIES OF ASTHMA:

Three stages of allergy development can be distinguished based on how the disease manifests: (1) the epithelial environment stage, (2) the Th2 polarisation stage, and (3) the tissue damage stage.

Air exposure to allergens triggers the release of proinflammatory cytokines (Group 1) in the airway epithelium for the epithelial environment stage of asthma (allergic sensitization stage), including TSLP, IL-6, IL-8, TNF-a, IL-25, IL-33, and GM-CSF. Therapeutic approaches at this point concentrate on reducing inflammation. A Th2 environment is induced by the cytokine TSLP, which is Th2-prone.It activates DCs, and the TSLP-activated DCS create a microenvironment that is Th2-prone.Professional antigen-presenting cells known as DCs use a variety of surface chemicals and cytokines, such as IL-12, TGF-B, IL-6, IL-23, and IL-1, to influence the polarisation of T helper

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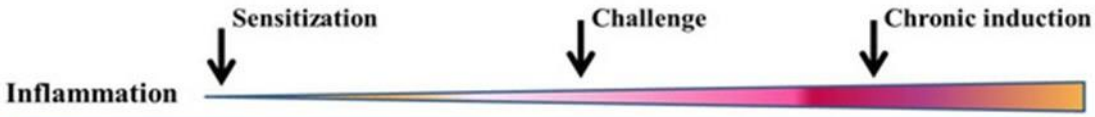
cells[30].

T cell stimulation and allergen restimulation are the main concerns in asthma stage 2. after polarising the airway environment to a Th2-promoting state.Naive T cells may be made to differentiate into Th2 cells by DCs, which eventually causes B cells to produce IgE. Tho cells may differentiate into Th2 cells, Th9 cells, or Th17 cells after being restimulated with a new antigen and release various Group 2 cytokines, such as IL-4, IL-5, IL-9, IL-13, or IL- 17, to activate eosinophils, basophil mast cells, or goblet cells. This step of eosinophil and mast cell degranulation is critical for airway hypersensitivity[30].

In Stage 3 of asthma, Group 3 cytokines including TGF-Band IL-10 cause local inflammation in the bronchi and lung, which triggers the beginning of tissue repair. TGF-B aids in tissue fibrosis and healing. TGF-B and IL-10 also aid in the growth of regulatory cells (Figure 2)[30].



Group	1	2	3
Stage/cell	Epithelial environment	Th2 polarization	Tissue damage
	DCs	Th, B cells	Tr, SMCs, Fibroblasts
Signal pathway	ER stress signal pathway, NF-κB	GATA3, JAK/STAT	Smad 2/3, Foxp3
Cytokines	TSLP, TNF-α, GM-CSF IL-6, IL-25, IL-33	IL-4, IL-5, IL-9, IL-13, IL-17	TGF-β, IL-10, ADAM 33 VEGF, MMP, CTGF

Figure 2 : It shows the three steps of an asthma treatment plan using cytokines.

III. CONCLUSION

As a result, the chronic inflammatory respiratory disease known as asthma is greatly influenced by cytokines. Our review includes an examination of how cytokines are involved in asthma. This article specifically focuses on a group of cytokines expressed and secreted by white blood cells known as interleukins and their role in asthma.The course of physiology of asthma is influenced by a number of cytokines, which contribute to airway inflammation, hyperresponsiveness, and remodelling.The symptoms and characteristics of asthma are brought on by an imbalance of the cytokines that cause inflammation (pro-inflammatory and anti-inflammatory).

Interleukin 5 and IL 13, as well as other pro-inflammatory cytokines, are mediators of allergic asthma. They encourage the eosinophil recruitment of immunoglobulin E (IgE), as well as the hyperresponsiveness of the airways. These pro-inflammatory cytokines are produced by Th2 cells, which are differentiated from naive T cells by IL -4.

TNF-alpha, also known as tumour necrosis factor, is a crucial cytokine in asthma. By encouraging the synthesis of collagen and the growth of smooth muscles, it encourages inflammation and aids in the remodelling of the airways. Other cytokines and chemokines are also produced as a result of Tnf Alpha, which intensifies the inflammatory response.

Inflammation of neutrophils and severe asthma are linked by interleukin 17 (IL-17).The recruitment and activation of neutrophils are encouraged by IL-17, which results in airway information and resistance to corticosteroid therapy. Th 17 cells, a subset of t cells, are responsible for its production.

On the other side, asthma is defended by anti-inflammatory cytokines like interleukin 10 (IL-10) and transforming growth factor-beta (TGF-beta). They decrease t cell activation, promote regulatory t cell activity, and suppress the generation of pro-inflammatory cytokines. These inflammatory cytokines prevent excessive inflammation and support immunological homeostasis. Targeted biologic medicines have been created as a result of our growing understanding of the role cytokines play in asthma.

In certain patient subgroups, monoclonal antibodies that selectively target cytokines including IL-4, IL-5, IL-13, and IL-17 have demonstrated benefit in lowering asthma exacerbations and improving lung function.

In conclusion, the development and severity of asthma are influenced by the complex interactions between pro-inflammatory and anti-inflammatory cytokines. In order to find new treatment targets and improve the management of this complex respiratory condition, additional research in this field is crucial.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVATIONS

Th2:T-helper 2; APC:Antigen Presenting Cell; ILCS:Innate Lymphoid Cells; TNF:Tumour Necrosis Factor; IFN-g: Interferon-gamma; CSF:Colony Stimulating Factor;HSC:Hemato poietic Stem Cell; GM-CSF:Granulocyte Macrophage Colony Stimulating Factor; VCAM:Vascular Cell Adhesion Molecule; MAPK:Mitogen Activated Protein Kinase; ERK:Extracellular Signal-Regulated Kinase; JNK:Jun N-Terminal Kinase; AHR: Airway Hyperresponsiveness; STAT 6: Signal Transducer and Activator of Transcription 6.

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