Migration Letters

Volume: 21, No: S6 (2024), pp. 406-429

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)

www.migrationletters.com

The Impact Of Changing Seasons: Seasonal Allergy Prevalence And Management

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Abstract

The allergic reactions can manifest in a variety of organs and are thought to be multifactorial, heterogeneous disorders brought on by the interaction of environmental and genetic factors. The aim of the research work is to evaluate current understanding on the environmental factors that affect the prevalence and progression of allergic illnesses such asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis. The local temperature may have an immediate impact on each patient, but it also shapes the flora and fauna in certain geographic areas, which impacts the sources of airborne and food allergies. According to epidemiological research, air pollution is strongly associated with the onset and progression of asthma and other allergic illnesses. Airborne allergens, such as dust mites, pollen, fungus, and animal dander, are among the environmental elements that have been the subject of the most research. Particulate matter (PM) and gaseous pollutants produced by industry and automobile traffic, such as ozone (O3) and nitrogen dioxide (NO2), have received the majority of attention. Diesel exhaust particle (DEP) can bind proteins and act as a possible allergy carrier by reaching the respiratory tract deeply. Foods can cause both real IgE-mediated allergies as well as a variety of non-immunological reactions linked to the immediate release of mediators or hazardous activities. More than 85,000 chemicals have been identified as being present in the human environment, and they may behave as contact allergens or irritants, resulting in allergic or non-allergic contact dermatitis. Infections may contribute to the worsening of the course of allergic disorders, which have historically been linked to their etiopathogenesis.

Key words: *Allergy, Seasonal allergy, Allergic Rhinitis, Pollen grain, Pathogenesis* **.**

Introduction

The term "allergic diseases" is often used to describe conditions like asthma, eczema, allergic rhinitis, and food allergies. Over the past 50 years, statistics from throughout the world have shown a steady rise in the prevalence of allergy illnesses worldwide [1]. A third of the population in the United States (roughly 100 million people) are affected by allergic diseases like asthma, hay fever, rhinitis, and atopic dermatitis. These conditions are linked to significant health care costs and lost productivity due to overtreatment and significant use of

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medical system resources. These consist of visits to the emergency room, urgent care centres, and hospital stays [2]. A rise in the quantity and allergenicity of airborne allergenic pollen may
possibly be responsible for these phenomena, in addition to air pollution and alterations in lifestyle [3]. Because of global climate change, more people are now experiencing allergy disorders brought on by pollen. Additionally, changes have been made to seasonal and geographic variations in pollens in the Asia-Pacific region as well as in Europe and America [4]. Allergies are made worse by the rapid growth of weeds and trees, air pollution from greenhouse gases brought on by increased traffic, the building of new companies, and modern structures, as well as by these factors. Staying in urban or rural settings won't protect anyone from allergenic plants. Allergic plants proliferate in great numbers in locations where people are harming the environment with their homes, roads, highways, and agricultural operations [5]. Depending on the exposure level, allergic reactions might range in severity. Rainfall, ambient temperature, humidity, wind speed and direction, as well as other weather factors, may change the concentrations of plant pollens and other allergens, which in turn may affect the development of allergy illnesses. Most research on the effects of climate change on aeroallergens may be broken down into a number of various categories, including the impact on pollen quantity, allergenicity, season, and dispersion [6]. The beginning, length, and severity of the pollen season change every year. One of the primary factors influencing plant phenology and pollen production is CO2, together with changes in the weather [7]. In addition, there is an urgent need for allergy risk alerts and person-centered environmental medicine services as a result of ongoing climate change. These challenges include newly introduced allergenic pollen, changing environmental parameters that have unpredictable changing health effects, and newly introduced allergenic pollen. This research paper's goal is to give a thorough summary of seasonal allergies, including its causes, warning signs, symptoms, diagnosis, treatments, and preventative measures. This research seeks to deepen our knowledge of seasonal allergies and aid medical practitioners in the efficient management of this condition.

Allergies:

Rhinitis, conjunctivitis, sinusitis, asthma, urticaria, atopic and contact dermatitis, and gastrointestinal disorders like food allergy, as well as insect sting hypersensitivity, are examples of allergic diseases that are caused by an interaction between the immune system and the interaction between genetics and environment, primarily at the mucosal surfaces.

Seasonal Allergies:

Seasonal allergies, commonly known as hay fever or allergic rhinitis, are allergic reactions that happen at particular periods of the year when certain allergens are prevalent in the environment. Depending on the particular allergens triggering the allergic reactions, different seasonal allergy types may exist.

Classification of Seasonal Allergies:

Here are some prevalent seasonal allergy kinds and how they are categorised:

Pollen Allergy:

The pollen emitted by trees, grasses, and weeds causes allergic reactions known as pollen allergies, commonly referred to as hay fever or allergic rhinitis. When these microscopic pollen grains are inhaled, come into touch with the eyes, or come in contact with the skin, they might produce symptoms. Sneezing, itchy nose, rhinorrhea, and nasal congestion are the allergens that most frequently cause these symptoms in people with pollen allergies.

Causes

Pollen allergies happen when the immune system wrongly views pollen as a dangerous substance and creates antibodies to combat it. Typical causes include:

Tree pollen
Springtime sees the release of pollen from trees like oak, birch, cedar, and pine.

Grass pollen:
Several grass species, such as Kentucky bluegrass, Bermuda grass, and Timothy grass, release pollen in the late spring and summer.

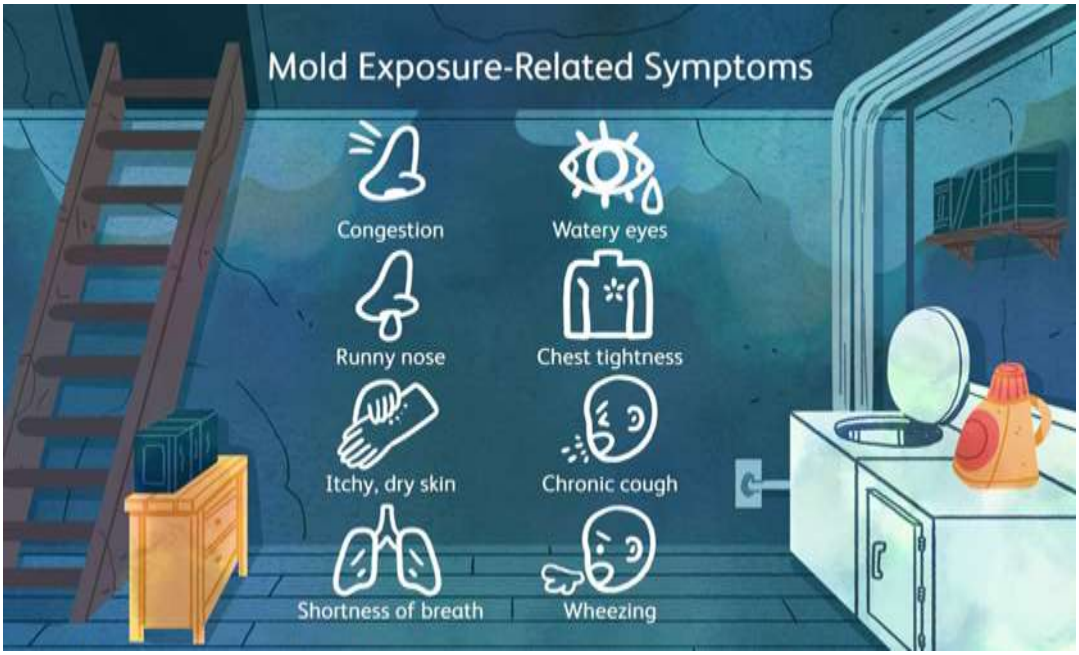
Weed Pollen :
Some plants that produce pollen in the late summer and autumn include ragweed, sagebrush, pigweed and lamb's quarters.

Mold Allergy

According to estimates, 10% of people have IgE antibodies to common inhalant molds [8]. It is anticipated that around half of these people (5% of the population) may experience allergy symptoms at some point as a result of exposure to fungi allergens [9]. Despite the presence of indoor fungal allergens, outdoor exposure is typically more significant in terms of sensitization and disease development. Asthma occurrence, persistence, and severity have all been associated to fungus sensitization. The other atopic manifestations, such as allergic rhinitis and, to a much lesser extent, atopic dermatitis, are sometimes thought to be caused by molds. Asthma is a recognised lower airway disease caused by allergic reactions to inhaled mold antigens.

Symptoms:

Symptoms of mold allergies are as so Sneezing,Runny or stuffy nose ,Itchy or watery eyes, Coughig, Postnasal drip ,Itchy throat or ears, skin rash or hives, Fatigue ,Headache, People with mold allergies might occasionally develop asthma symptoms, such as wheezing, shortness of breath, and tightness in the chest, especially if they already have an asthmatic condition.



Ragweed Allergy :

Asteraceae is the family name for the herb known as ragweed (Ambrosia artemisiifolia). It is a little, weedy plant with an unusual blossom. Globally, there are more than 30 species. North America is where the weed Artemisiifolia is native to. Ragweed pollen can produce severe allergic reactions. Due to the fact that the ragweed pollen season only lasts for two months in the late summer, it is a typical seasonal pollination. 8.2% of German individuals have artimisiifolia, and this frequency is rapidly increasing. Even at relatively low amounts (5–10 pollen grains per m3 of air), sensitive patients can develop allergic reactions. As a result, ragweed pollen may be a novel allergen, possibly to blame for recent asthmatic events, and is anticipated to be significantly more common than previous pollen kinds [10].

Other Plant allergies:

Birch pollen allergy : Birch trees discharge pollen into the air, usually in the spring, which can cause allergic reactions.

Oak Pollen allergy: Oak trees produce pollen into the air, usually in the spring, which can cause allergic reactions.

Grasses and other plant allergies: In addition to some grass varieties, plants including sagebrush, lamb's quarters, and pigweed can also cause allergic reactions.
Factors triggering Seasonal Allergies:

Indoor allergens

House Dust mites allergen (HDM):
HDMs are pyroglyphidae that frequently inhabit habitations. . Proteases, which are persistent in the faeces and are found in the mite's gut, are thought to cause allergic sensitization and asthma because of their ability to break down proteins. High indoor humidity and high temperatures are favourable for their spread. There are 33 groups of mite allergens. They are a significant source of allergens and can cause allergic reactions in people who are sensitive.

Here are some details regarding household dust mites:
Appearance: The size of a house dust mite ranges from 0.2 to 0.3 millimetres. They have eight legs and a translucent body, yet the naked eye cannot see them.

Habitat: Dust mites prefer warm, moist settings. They prefer air with a humidity level of at least 50% and temperatures between 68 and 77 degrees Fahrenheit (20 and 25 degrees Celsius). They can frequently be found in curtains, upholstered furniture, bedding, rugs, and other soft furnishings. In the case of unhealthy buildings, of which there are many, the structure as a whole typically has one or more flaws that cause high indoor humidity, which causes HDMs, mould multiplication, and the release of those organisms' metabolites [11].

Diet: The dead skin cells that people and animals expel are a food source for house dust mites. They are frequently discovered in locations where there is a significant buildup of dust because these skin cells are numerous in dust.

Allergens: The faeces and body parts of dust mites contain allergenic proteins. When exposed to these allergens, sensitive people may experience allergic reactions that result in symptoms including sneezing, coughing, watery eyes, nasal congestion, and asthma attacks.

Preventions

Although it is impossible to completely eradicate dust mites, there are steps you can do to minimise their number and your exposure to allergies. To lessen exposure to dust mite allergens, cover pillows, mattresses, and bedding with allergen-proof materials.

i. Regularly wash bedding in hot water (at least 130 degrees Fahrenheit or 54 degrees Celsius) to kill dust mites.

ii. Frequent vacuuming of carpets, rugs, and upholstered furniture should be done with a vacuum cleaner equipped with a high-efficiency particulate air (HEPA) filter.

iii. Use dehumidifiers or air conditioners to keep interior humidity levels below 50%.

iv. Reduce the usage of plush animals, heavy curtains, and carpets since these might harbour dust mites.

v. To prevent dust buildup, wipe off surfaces often with a moist cloth. A diverse strategy is used by programmes that have been shown to be successful, including community health workers, environmental counselling, therapeutic education, and home repair [12].

Molds:

One of the major categories of microorganisms found in all structures is microscopic fungi, or mold. Even though there are thousands of different species of mold, only about 80 of them are known to be responsible for harmful health effects in people. Molds may develop on a variety of surfaces, including natural products like wood, paper, cloth, and food. Because they need both moisture and a food supply to grow, they frequently do best in wet, humid situations. Bathrooms, kitchens, basements, and places with water damage are typical interior locations where Mold may be discovered. Molds may be problematic when they grow inside, despite the fact that the break down decaying organic materials in nature. Some people's allergic responses an respiratory problems might be exacerbated by mold exposure. Health issues brought on by mold are more likely to affect people who have allergies or asthma.

Preventions:

It's crucial to regulate moisture levels indoors to stop the spread of mold. This may be accomplished by repairing any leaks or water damage right once, utilizing dehumidifiers in humid areas, and making sure there is adequate ventilation. If mold is already there, it should be carefully removed to stop the spores from spreading. To handle significant mold development, professional mold remediation may be required in some circumstances.

Pets

According to market research data supplied by animal food providers, a pet is a member of almost 50% of families in industrialised nations. There are just as many cats as dogs, but cats are more allergicgenic [13]. Based on the clinical history, pet allergy is easily documented. Due to their tiny size, which ranges from 2 to 10 m, allergenic particles are able to remain airborne and adhere to surfaces and clothes [14]. It might be challenging to avoid cat allergies. Cat allergens are widespread, so even patients without cats at home will come into contact with them frequently. Basic avoidance techniques do not reduce cat-allergen levels while the cat is still present in the home.The so-called "hypoallergenic cats" have been promoted by a number of pet businesses, although there is no scientific proof to back up this claim [15].

Dog hair, skin cells that have shed, saliva, and urine all contain dog allergies. When it comes to triggering allergies, breeds are same. Compared to cats, dogs are less frequently to blame for allergic reactions. Counselling for avoiding things does not provide better results than cat allergies do.

Preventions

1. Limit Exposure: Keep your distance from dogs and cats if at all feasible. This includes avoiding their residences, such as friends' homes or pet supply businesses.

2. Pet free Zones: Create pet-free zones in particular parts of your house, such as bedrooms or rooms where you spend a lot of time. This may assist in lowering the level of allergens in the air you breathe.

3. Clean Frequently: Keep your home clean often to get rid of allergies. Pet dander may be lessened by cleaning, wiping down surfaces, and vacuuming with a HEPA filter. A hoover with a HEPA filter could be a good idea because it can successfully capture tiny particles.

4. Use of Allergen-resistant bedding: To build a barrier against pet allergies, spend money on hypoallergenic bedding covers, such as mattress and pillow covers. Regularly wash bedding in hot water to get rid of allergies.

5. Wash hands and Clothing: Ensure that you properly wash your hands with soap and water after coming into touch with cats or dogs. Prior to washing your hands, avoid touching your face or eyes. Additionally, wash your clothing right away to get rid of any allergens that may have stuck to them before changing.

6. Air purifiers and Filters: To assist in removing pet allergies from the air in your home, take into account employing air purifiers or air filters using HEPA technology. These gadgets can be very helpful in pet-free zones or situations where there are animals present.

7. Seek professional help: Consult an allergist or immunologist if your allergies are severe and are seriously affecting your quality of life. In order to aid with symptom relief, they might offer advice on available treatments, such as drugs or allergy injections (immunotherapy).

Cockroaches:

Low-income housing's kitchens are where cockroach allergens are most prevalent. The morbidity of asthma is influenced by the interaction of cockroach allergen exposure and allergic sensitization.

Strategies to reduce cockroach allergens:

There is a therapeutic advantage from methods that successfully reduce cockroach allergen levels. All goods should be stored in airtight containers, the kitchen should be kept spotless, the garbage should be emptied frequently, food shouldn't be left out, and roach traps should be placed.

Rodents:

Similar to cockroach allergies, mouse allergens are primarily prevalent in inner-city homes and are made of lost skin cells, urine, and hair follicles. While allergen levels in homes and schools may be high, there is ongoing debate on their connection to asthma morbidity [16].

Preventions

Rodents are crucial players in ecosystems because they spread seeds, serve as prey for carnivores, and in certain cases, act as disease reservoirs. Maintaining rodent populations and protecting them is essential for keeping ecosystems in balance.

Here are some common preventive measures

Taxidermy:

The activity of mounting and conserving animal specimens for exhibition is known as taxidermy. When rodents are preserved via taxidermy, the specimen is painstakingly peeled, and the skin is then cleaned, treated, and mounted on a form or mannequin that replicates the animal's natural position. Typically, the internal organs are removed, and filling materials are used to retain the specimen's form. Rodents may be preserved for a long time and shown via taxidermy at museums or other educational facilities.

Specimen collection:

In a collection, rodents can also be maintained as entire specimens. With this technique, the animal is captured, put to death humanely, and then the complete corpse is preserved. For entire specimens, the following preservation techniques are frequently used:

a. **Dry Specimens**: This approach calls for meticulous preparation and drying of the rodent. After that, it is kept in a regulated setting to guard against rot and insect damage. Dry specimens are frequently utilised in research collections and can be used for DNA analysis or morphological study.

b. **Wet Specimens**: The rat is immersed in a preservative, such as formaldehyde or alcohol, during wet preservation. By using this technique, the animal's original colour and texture are preserved. In scientific study, wet samples are frequently employed and kept in airtight containers.

c. **Skeleton and Skulls:** Preparing skeletons or skulls is another technique of conserving rodents. This entails meticulously cleaning the bones and removing the specimen's flesh and soft tissues. The cleaned bones are then preserved individually or are articulated. Anatomical study, comparative morphology, and evolutionary studies frequently make use of preserved skeletons and skulls.

Outdoor Allergens

Pollens

Pollens that trigger allergic reactions are those that are tiny enough to be carried by the wind. Most people who have a pollen allergy develop rhinoconjunctivitis. During pollination, grass-pollen allergy as well as Parietaria pollen allergy cause an increase in non-specific bronchial hyperreactivity [17].

Avoidance:
It is crucial to get a clear allergologic diagnosis since pollen avoidance is only useful when the offending pollen is airborne. Patients are advised to avoid being outdoors during this time period if at all possible since the humidity is higher and the pollen particles are more likely to cling to anthers then. Additionally, windows in both your automobile and house need to be closed. Patients may be instructed to use their air conditioner, put on a pollen mask and wraparound glasses, turn on their air conditioning, take a shower, and wash their hair after spending a lot of time outside. Even if they haven't been supported by control tests, these suggestions make reasonable.

Outdoor mold:

The species of Alternaria and Cladosporium are thought to be the main outdoor allergens that cause sensitization, the onset of rhinitis and asthma, as well as asthma attacks that can be fatal. Penicillium and Aspergillus xerophilic species, on the other hand, act as indoor allergens and contribute to allergy disorders. Regarding indoor allergens, it can be challenging to diagnose outdoor mould allergies since allergenic extracts aren't well-standardized and the majority of fungal extracts have a wide range of cross-reactivity with taxonomically unrelated fungi [18].

Non allergic Triggers:

The majority (>80%) of childhood asthma flare-ups have been linked to viral infections [19]. Due to their seasonal rhythm, these diseases are commonly referred to as the "September epidemic". Although respiratory syncytial virus, enterovirus, coronavirus, and human metapneumovirus can also be implicated, rhinoviruses are the most often seen viruses. Viruses and allergens work together to aggravate asthma and lead to hospitalization.

Preventions
There are no preventative therapies other than avoiding contact with infected people, receiving a flu shot, and receiving pharmacologic therapy in the initial few days after exposure.

Active Smoking:

Asthmatics who smoke are likely to experience a higher rate of hospitalization than asthmatics who do not smoke. Active smokers and ex-smokers had worse asthma control and more asthma exacerbations. Additionally, the most effective medication for persistent asthma currently on the market, inhaled corticosteroids, performs less well among smokers. Smokers' withdrawal symptoms and cravings for nicotine decreased with time at a slower pace among people with asthma. According to Perret et al., there are a number of approaches to enhance smoking cessation methods for smokers who have asthma, including individualised treatments, insisting on "lung age," offering long-term follow-up, and, in the case of teenagers, enlisting the help of older friends to provide asthma information.

Air Pollution

In addition to affecting plant development, pollen and flower output, and the length of the entire pollen season, air pollution and climate change can have more immediate health impacts by raising the number of allergenic proteins in pollen. According to Zhao et al. (2016), high concentrations of some pollutants, such as nitrogen dioxide (NO2), which is linked to traffic and therefore more common in urban areas, enhance total pollen allergenicity, raising the relevant allergy risk for people with sensitised immune systems.

Daily asthmatic symptoms and a decline in lung function are linked to variations in outside gaseous and particle air pollution.[20] Because there is no practical means to minimize exposure, it is difficult to avoid outdoor air pollution. Asthmatic patients shouldn't stay indoors during times of high air pollution, according to national officials, because indoor air pollution might be even more dangerous. Cigarette smoke is the leading source of indoor air pollution. By avoiding cooking-related pollutants, avoiding the use of sprays and other cleaning products that release volatile organic compounds (VOCs), selecting furniture and building materials with low VOC emissions, and routine air exchange by natural or mechanical ventilation, indoor chemical air pollution can be reduced. The broader public now has access to these recommendations.[21]

Drugs:

Nevertheless, some drugs may cause unwanted consequences that resemble the signs and symptoms of seasonal allergies.For instance, antihistamine and decongestant drugs like pseudoephedrine can cause nasal dryness and congestion, which may resemble the symptoms of seasonal allergies.

Stress and Emotional Distrubances:

By altering immune cell function through neurological and hormonal mechanisms, stress may worsen airway inflammation. Exacerbations and emergency treatments have repeatedly been linked to psychological causes[22] High trigger scores were linked to negative life events, perceived stress, and carer depression among Puerto Rican children.[23].

Food Reaction:

The condition known as a food allergy, which is an immune reaction that is unfavourable to food proteins, is becoming more and more prevalent. Food intolerance is a non-immune reaction that involves metabolic, toxic, pharmacologic, and unknown pathways, whereas food allergy is completely different from that.[24] Atopic dermatitis, eosinophilic gastrointestinal disease, allergic contact dermatitis, acute urticaria/angioedema, oral allergy syndrome, atopic dermatitis, food protein-induced enteropathy/enterocolitis syndrome, and atopic dermatitis are all illnesses linked to immune-mediated food allergy. The two broad kinds of food allergies are IgE-mediated and non-IgE-mediated. IgE-mediated responses typically manifest quickly, with clinical symptoms beginning anywhere from a few minutes to many hours after intake. The majority of non-IgE-mediated diseases are chronic, and therefore may be more challenging to manage with food avoidance alone than IgE-mediated diseases. When it comes to shellfish, peanut, tree nuts, and IgE-mediated food allergies, deadly anaphylaxis is a common occurrence. Many foods, including pickled foods, dried fruits, and beverages including beer, wine, and soft drinks, contain sulfites, which are employed as preservatives and antioxidants. When taken by those who already have asthma or allergic rhinitis, they might cause allergy-like symptoms such wheezing, tightness, and coughing.[25] Fear for those who are affected by food allergies has increased as a result of the possibility for this disastrous outcome and the extensive media

coverage of this disease. In contrast to prevalence statistics based on doctor diagnoses, more people think they have food allergies. Despite the prevalence being 5% of adults and 8% of children, up to one-third of the population feels they have a food allergy[26].

Allergic Rhinitis:

The prevalence of allergic rhinitis (AR) has rapidly increased in recent years, raising concerns about the condition on a global scale. Over the past three decades in Europe, the prevalence of AR among Danish people has climbed from 19% to 32%.[27] In a similar vein, over the past six years, the standardised prevalence of adult AR in China has climbed by 6.5% in Asia.[28] In China's northern grassland area, where significant seasonal pollen concentrations are found, the incidence of self-reported pollen-induced AR (PiAR) has reached an extraordinarily high proportion of 32.4%.[29] A consistent rise in rhino-conjunctivitis was also seen in three national cross-sectional surveys of Japanese youngsters done between 2005 and 2015.[30] Children who are impacted by AR often experience sleep issues as well as lost time at work and school, decreased involvement in outdoor activities, and other issues. Asthma risk is considerably increased with AR. Asthma is present in more than 40% of AR patients.[31] Due to type 2 helper T (Th2) cell-induced mucosal inflammation and IgE-mediated reactions to inhaled allergens, AR is characterised by sneezing, nasal irritation, airflow restriction, and watery rhinorrhea.[32] It shares a tight relationship with other inflammatory conditions that affect the mucous membranes of the respiratory tract, including asthma and allergic conjunctivitis. A complicated immune reaction to allergens causes AR.[33] An allergen is first taken up by antigen-presenting cells at a mucosal location, which causes the activation of T lymphocytes that are specific to the allergen in draining lymph nodes. Epithelial cytokines including IL-25, IL-33, and thymic stromal lymphopoietin are then released as a result of the simultaneous activation of epithelial cells. Th2 innate lymphoid cells and basophils produce cytokines including IL-13 and IL-4 as a result of this mechanism, which impacts a Th2 cell response that is targeted at dendritic cells. When Th2 cells are produced as a result of such a release, they can convert B-cells into plasma cells and subsequently create IgE antibodies that are specific to allergens. A second encounter causes the allergen to bind to IgE on the surface of mast cells and circulating basophils, activating those cells and causing the release of histamine and leukotrienes. The usual AR symptoms can be brought on by these mediators.[34] Additionally, local Th2 lymphocyte activation causes the production of cytokines that direct the entrance of inflammatory cells into the mucosa, increasing the sensitivity of the nasal mucosa to allergens. Leukotrienes produce vasodilation, but histamine generated by mast cells can activate blood vessels to enhance vascular permeability. The stimulation of sensory neurons results in the activation of many central reflexes, including a motor reflex that induces sneeze and parasympathetic reflexes that result in nasal discharge and vasodilation. Additionally, the sympathetic nerve to the venous sinusoids is suppressed, causing vascular congestion and nasal blockage.[35].

Pathogenesis of Allergic Rhinitis

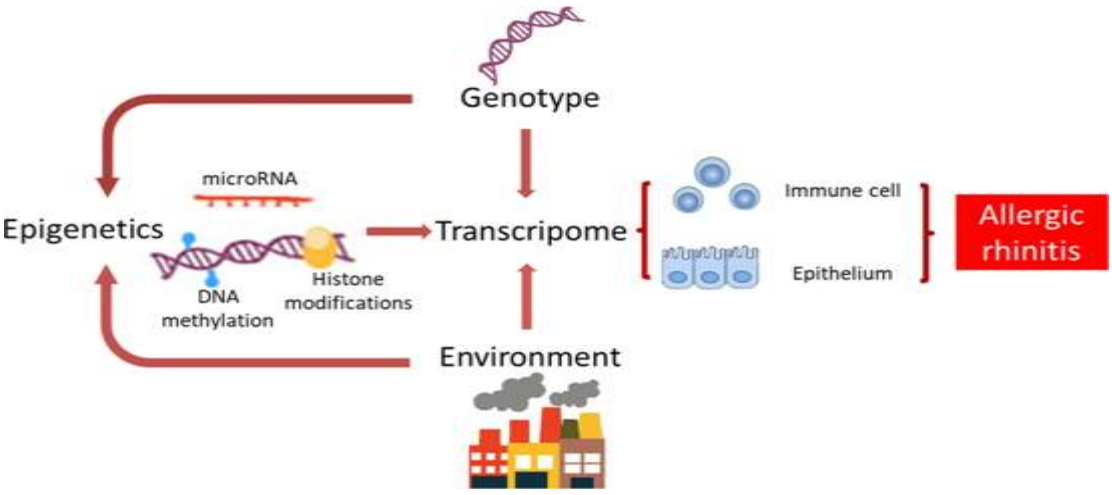
AR and other allergy disorders have a convoluted pathophysiology. It is recognised that associations between genetic and environmental variables have a role in certain immunologic circumstances. Many of the factors contributing to the rise in AR prevalence may be environmental, including exposure to allergens, air pollution, climate change, ozone, smoking, virus infections, and environmental toxicants. Furthermore, certain epigenetic alterations brought on by environmental exposure may support cellular homeostasis and the emergence of allergy disorders. 1. The relevance of epigenetics has been highlighted in several recent research.[36] It is now well acknowledged that the pathophysiology of many illnesses is significantly influenced by changes in gene activities rather than changes in DNA sequences.[37] Studies have clarified the significance of epigenetics in the pathophysiology of

AR, including changes in DNA methylation, histone acetylation, and miRNA levels.[38] Several modifications to DNA methylation and histone acetylation occur in host cells.[39] Recent information on allergic rhinitis suggests that the degree of DNA methylation in the SLFN12 gene in response to grass pollen can predict the severity of allergic reactions.[40] Patients with AR have been shown to have variable levels of histone modification and altered mRNA in potential genes.

Environmental Factors

It is believed that exposure of atopic persons to external environmental variables is a key element in the aetiology of AR. Ambient air pollutants, aeroallergens (such as pollen, mould, and house dust mites [HDM]), and climate make up the majority of the external environmental exposome. According to a recent study, air pollution may be a factor in the increased occurrence of AR. Exhaust gases (such as nitrogen dioxide [NO2], sulphur dioxide [SO2], and ozone [O3]) and particulate matter (PM) are the two primary categories for chemical air pollutants produced by both manmade and natural sources. The size and content of PM vary. Increased prenatal PM2.5 exposure throughout the middle of pregnancy (16–25 weeks) is important for the development of asthma by age 6, particularly in boys.32 Airway oxidative stress, which causes inflammation, structural remodelling, and a higher risk of sensitization, of related pathways.

The main inhaled particles and causes of aeroallergy (AR) include aeroallergens (pollens, moulds, and HDM). According to Wang and colleagues, 32.4% and 18.5%, respectively, of all cases of acute respiratory syndrome (AR) in Northern China are caused by pollen. According to several research, pollen allergen levels in ambient air across many different nations and areas are strongly connected with the prevalence or severity of AR.[41] According to a recent research, Europe's increasing exposure to birch pollen and concentration levels have led to a rise in the prevalence of birch pollen sensitivity. The BAMSE cohort's data show that exposure to moulds or moisture from infancy raises the risk of asthma and rhinitis up to the age of 16, especially for rhinitis and persistent asthma into adolescence.[42] HDM is a substantial allergen for ongoing AR and a considerable risk factor for the development of allergic respiratory conditions. Even before the start of clinical symptoms, HDM nasal provocation tests in children with mite monosensitivity raise both upper and lower airway eosinophilic inflammation.[43] Innate and adaptive immune cells participate in the pathophysiologic mechanism of allergic rhinitis (AR), which causes specific immunoglobulin E (IgE) production, activation of eosinophils, and degranulation of mast cells and basophils with the consequent clinical symptoms of AR. Inciting allergens include pollen and dust mites.



Cellular and Molecular Factor:

A malignant memory When it comes to the pathogenesis of allergy illnesses like AR, T helper (Th) 2 cells are crucial. The function of IL-17A, often known as IL-17, in AR has been documented in a number of studies. In AR patients, serum IL-17 levels are regarded as a measure of allergy severity since they are strongly correlated with allergy intensity throughout the pollen season.[44] Patients with grass pollen allergies have peripheral blood myeloid DCs that are more likely to stimulate T cell IL-17 production in a lab setting. TSLP production is regulated by IL-17A and IL-25 in opposition to one another, but IL-25 outweighs IL-17A's inhibitory effect, suggesting that in individuals with AR, TSLP and IL-17 are upregulated in response to stimuli. This data implies that IL-17 might play a significant role in the emergence of AR.[45].

Treatment:

There are currently a variety of treatment options available for AR, including patient education, strategies to avoid irritants and allergens, medication, allergen immunotherapy (AIT), nose irrigation, and less conventional treatments like acupuncture and surgery.

Patient Education:

To track the disease's symptoms, medication use, and quality of life more effectively and promptly, mobile applications have been created.[46] In this context, a sizable, cross-sectional, multicenter, and real-world study has shown that MASK Diary, a mobile phone app customised for use in various nations and freely available on Google Play and Apple stores, can gather information on daily visual analogue scale (VAS) scores for (a) overall allergic symptoms, (b) nasal, ocular, and asthma symptoms, (c) work, and (d) medication. In addition, the study showed that MASK diary, regardless of geographic, cultural, or linguistic variables, is helpful in assessing daily AR management in a vast population.[47].

Pharmacotherapy:

Currently, pharmacotherapy includes leukotriene receptor antagonists, antihistamines, mast cell stabilisers, nasal/oral corticosteroids, and short-term nasal decongestants. Fluticasone propionate and azelastine, a new topical combination of a nasal corticosteroid and an intranasal antihistamine, have been shown to be beneficial in reducing AR symptoms. Another possibility for treating AR is resveratrol, a naturally occurring nonflavonoid polyphenol with anti-

inflammatory characteristics. Clinical investigations have demonstrated its effectiveness in treating both adult and paediatric patients.

Acupuncture and traditional Chinese medicine have also shown effective treatments for AR. In this regard, acupuncture has been found to be a viable and secure therapeutic choice for AR patients after a clinical investigation including 238 participants who received both active and sham treatment.[48]

The significant impact of sphenopalatine ganglion acupuncture in the treatment of AR has been underlined in more recent investigations. A more recent randomised controlled trial by Mi et al revealed that active sphenopalatine ganglion acupuncture is secure and noticeably more effective than passive sphenopalatine ganglion acupuncture, which Wang et al had previously shown to improve nasal ventilation and modulate autonomic nervous activity in healthy participants.[49].

Immunotherapy:

The sole etiological therapy for AR to far is AIT. SCIT and SLIT are two examples of conventional AIT for AR. Numerous randomised controlled studies, meta-analyses, and systematic reviews have shown that AIT is effective[50]. AIT has reportedly been shown to be both safe and well-tolerated in addition to being effective. Recombinant allergens, allergoids, and allergen peptides, among other modified allergens, have recently been created for use in AIT.

Allergic Conjunctivitis:

A set of disorders known as allergic conjunctivitis are brought on by the eyes' reaction to environmental allergens. They affect 10–20% of the population, making them widespread.[51] Currently, 20% of the world's population suffers from some kind of allergy, and allergy rates are rising. Ocular symptoms might occur in up to 40–60% of allergy sufferers.[52] Though allergic conjunctivitis often does not impair vision, it does cause substantial symptomatology and considerably worse quality of life for those who are affected, particularly children and adolescents because certain of the disease's manifestations are more frequently experienced by them. But occasionally, severe types might impair vision if they have a convoluted course and damage the cornea, since this could lead to corneal scarring and pannus. In order to enhance patients' quality of life, reduce the likelihood of relapses, and prevent potential consequences, it is crucial that these disorders are identified early and correctly treated.

Common eye symptoms and indicators of allergic conjunctivitis, which is often bilateral, including Itching, the hallmark of allergic eye disease, Foreign body sensation, Serous or mucous discharge,Conjunctival hyperemia and Tarsal papillary reaction. It is possible to distinguish between symptoms that appear more frequently in the early or late stages of the disease. The acronym TIRED, initially proposed by Fauquert, describes the early symptoms, which are generated by histamine coupling with its receptors and include tears, itching, redness, and edoema (either conjunctival or palpebral edoema).[53] and then Hours later, late indications manifest as epithelial infiltration with a range of cells, including lymphocytes, neutrophils, basophils, and eosinophils. The abbreviation POVD stands for photophobia, ocular pain, visual impairment, and discharge, which are symptoms of the later phase that causes chronic inflammation.[54]

Pathogenesis:

The result of a type 1 allergic response is allergic conjunctivitis. When an allergen contacts the conjunctiva in someone who is sensitive, they have the following reaction: B-cells generate

immunoglobulin E (IgE) as a result of cytokines produced by Th2-cells. The allergen and the mast cell membranes may bind to the secreted IgE, causing the release of inflammatory mediators. When this happens, an inflammatory response is triggered, and within 30 minutes, there is an acute symptomatic reaction. This is then followed by a second, delayed phase, during which more mast cells, eosinophils, and inflammatory cells are recruited to the conjunctiva, causing the symptoms to persist.

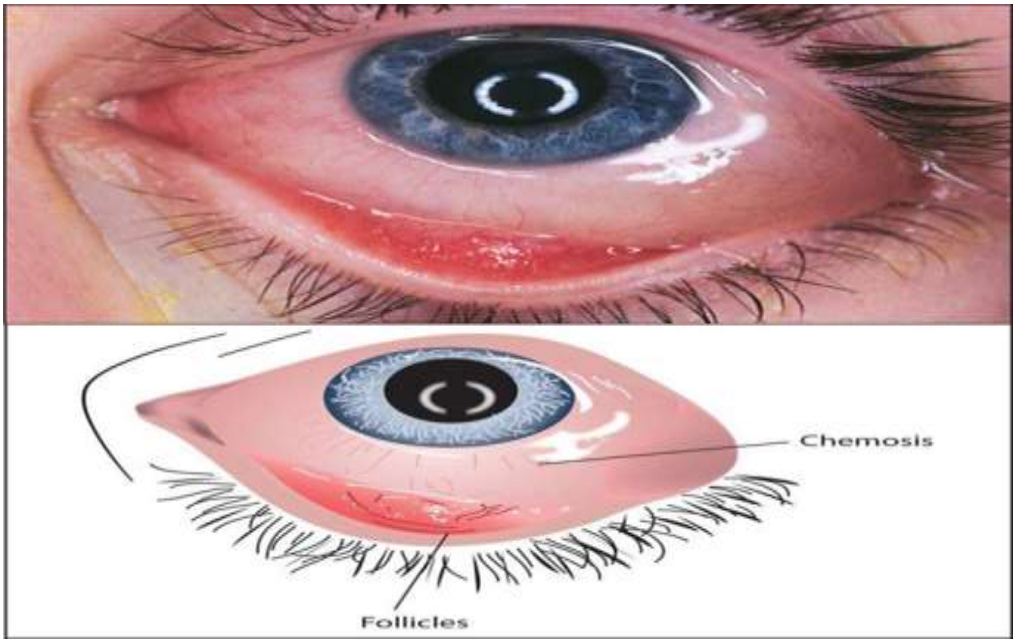
Classification:

The European Academy of Allergy and Clinical Immunology's (EAACI) Ocular Allergy group has changed the categorization of allergic conjunctivitis to distinguish between two forms of ocular surface hypersensitivity disorders: ocular allergy or ocular nonallergic hypersensitivity. Both IgE-mediated and non-IgE-mediated pathways may contribute to the first kind, ocular allergy.[55] Seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal keratoconjunctivitis (VKC), and atopic keratoconjunctivitis (AKC) are all examples of ocular allergies that are IgE-mediated. Contact blepharoconjunctivitis (CBC), VKC, and AKC are non-IgE-mediated types. Giant papillary conjunctivitis (GPC), irritative conjunctivitis, irritative blepharitis, and other ambiguous or mixed forms are examples of the second kind, ocular non-allergic hypersensitivity. Both IgE-mediated and non-IgE-mediated processes are thought to contribute to the development of VKC and AKC. The many varieties of allergic conjunctivitis**,** however, are occasionally connected because people who have one type of the condition may subsequently develop another form of ocular hypersensitivity.

Seasonal and Perennial Allergic Conjunctivitis:

More than 95% of ocular allergy cases in the United States are attributed to SAC and perennial acute conjunctivitis (PAC), making it the most common kind of allergic conjunctivitis. Seasonal or perpetual describe the progression of the illness, which is seen in both sexes and affects 15% to 40% of the general population.[56] SAC referred to as hay fever conjunctivitis, is a bilateral acute condition that typically results from outdoor allergens such grass pollens. As a result, it only manifests itself at specific times of the year that may change depending on seasons and climate. The cause of PAC, which is likewise bilateral but chronic with phases of aggravation and remission, is typically indoor airborne antigens such dust mites or pet hair. The only difference between the two disorders is the frequency of the symptoms; PAC occurs throughout the year and is often less severe than SAC, which tends to be worse from spring through autumn and lessens in the winter months. Both kinds can also range in severity from mild to severe, depending on how severe the symptoms are and how they affect quality of life.But more than 50% of patients report having daily symptoms, and almost 75% believe they are severe.[57] Mast cells in sensitised individuals have allergen-specific IgE bound to their surfaces; as a result, when an antigen binds to these mast cells' membrane receptors, histamine and other already-formed inflammatory mediators like leukotrienes and prostaglandins are released. In virtually all instances, it is possible to prove the existence of certain IgE antibodies to airborne allergens. When this happens, an inflammatory response is triggered, and within 30 minutes, there is an acute symptomatic reaction. This is then followed by a second, delayed phase, during which more mast cells, eosinophils, and inflammatory cells are recruited to the conjunctiva, causing the symptoms to persist. When exposed to the allergen, patients endure brief episodes of acute or subacute symptoms, which totally disappear between attacks. The primary symptoms are TIREd (tearing, itching, redness, and edoema), although other symptoms include photophobia, a moderate papillary response, chemosis, and palpebral edoema. Itching and chemosis are the main symptoms of this kind of conjunctivitis, and they are completely out of proportion to the degree of hyperemia.[58]. The nasal portion of the conjunctiva usually experiences more itching, and the watery discharge may contain some

mucus, which can be deceiving. Despite the possibility, severe types of SAC and PAC seldom cause corneal involvement.[59].



Diagnosis:
It is crucial to look into and determine which allergens the patient is allergic to since the treatment of allergic conjunctivitis frequently rely on evidence of an allergy. To identify the allergens that trigger the reaction, a complete anamnesis must be performed as the first step. There is no need for additional testing once the reason has been identified. Skin prick or patch testing are the next step if more research is required, even if no clearly identifiable allergies have been discovered. Skin prick tests are utilised for the other disorders, but patch testing are favoured for CBC. These tests are conducted with a regular battery of allergens and occasionally with others that are not typically evaluated but are thought to be the allergen's source. Serum specific IgE measurements for the aeroallergens can be taken into consideration if skin testing is necessary but not advised (for example, if the patient is taking antihistaminic systemic medications), if results are unclear (for example, if dermatographism is present), or simply to supplement the findings of prior SPT.

After systemic allergy assessment testing, a conjunctival allergen provocation test (CAPT) may be used to clarify the cause if there is any uncertainty.[60]

Treatment

It is thought that a third of people go undiagnosed and untreated despite allergic conjunctivitis interfering with their ability to work, go about their everyday lives, and enjoy life. There are more studies and clinical trials being done on the topic as a result of the fact that allergic disorders are becoming more common, having a greater impact on productivity, and costing more to treat. Significant progress has recently been achieved in the treatment of severe or ocular allergies, especially in immunomodulators and immunotherapy, the only existing disease-modifying therapies that have the potential to produce long-lasting benefits.

Avoid Contact with Allergens:

Nonpharmacologic therapies should always be used as a first line of therapy together with topical therapies. Although it is usually difficult to enforce, complete allergen avoidance is the best option. This is particularly crucial in PAC and SAC as well as in VKC or AKC where there is a known sensitivity. It is a problem in GPC as well, and the signs and symptoms can be reduced by shortening the time spent wearing contacts, switching the cleaning solution, or fitting the patient with a new kind of contact lens, particularly one that is disposable every day.

Decongestant:
One of the earliest topical therapies for treating allergy symptomatology was the use of alpha-adrenergic agonists, particularly those that bind to alpha-1 receptors, such as naphazoline, tetrahydrozoline, oxymetazoline, or brimonidine tartrate. They are available over-the-counter and are used to treat hyperemia, however teenagers and young children should not use them. They can be used in situations of sporadic itching and redness and have a quick beginning of effect, but there is a chance that patients will use them inappropriately. They are short-lived and come with a number of adverse effects, including hypersensitivity, eye discomfort, and tachyphylaxis. They should only be used sparingly and as a temporary fix in our clinical practise.

Antihistamines:

Although clinical studies favour the use of dual action drugs (antihistamine + mast cell stabilisers), especially if preservative free, there are several antihistamine medications available on the market that may be used topically, but none has demonstrated a clear benefit over the others. Levocabastine, pheniramine maleate, and azelastine are the drugs used the most commonly.[61]

In situations of allergic rhino-conjunctivitis, oral antihistamines such loratadine, desloratadine, and fexofenadine are highly helpful. However, compared to topical antihistamines, they are more frequently associated with systemic adverse effects such drowsiness. Additionally, they reduce tear production, which may worsen the conjunctivitis symptoms by causing dry eye symptoms.

Mast Cell Stabilizers:

Mast cell stabilisers have a loading duration of around two weeks and are used as prophylaxis because they prevent mast cell degranulation. Cromolyn sodium was the first medication of this kind to be created, and other medications like nedocromil sodium, lodoxamide, and pemirolast were more efficient and started working faster.

NSAIDS:
Non-Steroidal Anti-Inflammatory Agents can lessen the symptoms of allergic conjunctivitis, but because they can cause burning or stinging when administered, few people take them. Topical NSAIDs are typically added to a topical antihistamine or dual-action drug for short-term usage.

Leukotriene inhibitor:

Oral administration of the leukotriene inhibitor montelukast reduces PAC and SAC symptoms, however it is less efficient than oral antihistamines. Oral aspirin and montelukast have also been utilised in VKC.[62]

Immunotherapy:

Immunotherapy aims to reduce the rhinitis and conjunctivitis symptoms and indications brought on by recognised allergens and to stop them from recurring. If first-line therapies are unsuccessful, allergy-specific immunotherapy may be attempted. It may also be used to alter the course of the disease naturally. On the same rationale as in rhinoconjunctivitis, allergen immunotherapy may be explored for isolated allergic conjunctivitis (both IgE- and non-IgE-mediated).

Surgery:

Eye surgery can be required in situations of VKC and AKC that are extremely resistant. In the treatment of severe types of VKC with corneal ulcers, papillae removal, in some cases with grafting of autologous conjunctiva, amniotic membrane, or mucous membrane is beneficial.[63] Subepithelial deposits in VKC can call for plaque excision. Surgery could be required in AKC to treat eyelid and conjunctival scarring. Subcapsular cataracts and/or severe ocular surface disease may aggravate atopic illness and AKC and necessitate extensive surgery, such as superficial keratectomy, limbal transplantation, or keratoprosthesis implantation.

Eczema and Atopic Dermatitis:

Atopic dermatitis, also known as atopic eczema, is a complicated, diverse inflammatory skin disorder that, in the majority of instances, has a well-known distribution pattern. Extensors frequently become implicated when it settles across the cheek area in infancy, and by the time a child is two years old, flexural distribution predominates. Although seldom found in youngsters, the acral pattern is primarily observed in the adult population. The diagnosis of atopic dermatitis is mostly reliant on clinical symptoms because there isn't a reliable, conclusive biomarker. Hanifin and Rajka listed the diagnostic characteristics of atopic dermatitis in 1980; they provided four basic and 23 minor criteria, and a definite diagnosis required the presence of at least three basic and three minor criteria.[64] The morphologies and locations of AD lesions vary, including extensor, head/neck, hand/foot, and prurigo nodules, lichenoid papules, and follicular eczema. Skin discomfort is one of several symptoms that increase the burden of the disease, even though itching is the most common and troublesome sign of AD.[65] The incidence, chronicity, and duration of AD do not follow a uniform path across time. The physical, emotional, and psychological strain caused by this intricate arrangement of characteristics lowers quality of life (QOL).[66]

It is possible that genetics and environment have a role in the disease's heterogeneity because the clinical presentation of AD varies greatly among geographic locations, age groups, ethnic groups, and the underlying immunopathogenesis.[67].

symptoms:

The burden of AD is substantially impacted by symptoms. Itch is the most common, troublesome, and detrimental to QOL symptom of AD.[68] The sign of skin soreness, which was previously ignored, is crucial in AD. In AD, pain is a discrete symptom that only sporadically correlates with itch. Pain affects quality of life and mental health, varies in frequency and intensity with the severity of AD. Without excoriation, pain can still develop as a result of red, swollen skin (particularly on the face), skin fissures (especially on the hands and digits), and, less frequently, stinging from topical treatments. Many AD patients use terminology like "pinprick," "electric shock," and "stinging" to describe their skin discomfort, which are similar to neuropathic pain. In AD, sleep disturbances are frequent, particularly when the condition is more advanced. AD is linked to weariness that makes it difficult to carry out daily tasks, frequent daytime drowsiness, insomnia, feeling exhausted, less time spent sleeping,

difficulty falling asleep, early morning awakenings, and a rise in reports of sleep disruptions to medical professionals.[69]

Although frequently undetected, mental health problems, particularly anxiety and sadness, are also widespread among AD patients. These symptoms appear to be significantly influenced by the severity of AD, which in turn adds to the total disease burden.[70] In comparison to other chronic immune-mediated disorders such psoriasis, urticaria, asthma, and autoimmune disease, AD has greater levels of psychosocial distress. Patients' perceptions of the severity of their AD are predicted by itch, pain, sleep disruption, anxiety, and sadness taken together [71].

Comorbidities:

Hanifin-Rajka and the United Kingdom Working Party both include atopic comorbidities, such as food allergies and hay fever, as they are closely related to AD. These disorders are caused by type 2 immune skewing and shared epidermal-barrier defects.[72] Although asthma (e.g., younger age, lower household income) and hay fever (e.g., older age, greater household income) have additional special relationships, AD severity is the best predictor of atopic comorbidities.

Food allergies caused by IgE are more prevalent in newborns and young children with moderate-severe AD. Food allergy testing is a crucial consideration for kids with refractory AD, especially to identify those at risk of anaphylaxis, even if diet restrictions are unlikely to cure AD [73] Atopic keratoconjunctivitis is linked to numerous visual symptoms, including the possibility of blindness, and may be more frequent in AD patients than previously thought. Due to a combination of skin barrier failure, frequent topical drug use, and increased immunological responsiveness to transcutaneous irritants and contact allergens, AD is linked to a greater risk of allergic contact dermatitis. Anxiety, sadness, suicidality, and attention deficit (hyperactivity disorder) disorder (ADD/ADHD) may be more prevalent in AD patients as a result of AD symptoms, patient burden, and neuro-inflammation.[74]

Increased cutaneous (bacterial, viral, and fungal) and extracutaneous (otitis media, sepsis, endocarditis, and bone and joint infections) infections may occur more frequently in AD patients as a result of skin-barrier dysfunction, decreased antimicrobial peptides, immune dysregulation, bacterial dysbiosis (with increased colonisation by pathogenic bacteria), and chronic immunosuppressive medication use.[75]

Treatment:

According to AD treatment recommendations, therapy should be escalated based on AD severity and should include both non-pharmacologic and pharmacologic therapies. Depending on the practise recommendations, several severity evaluation methods for therapy stratification are used [76]

In terms of normal clinical practise, the American Academy of Dermatology (AAD) advises against utilising the severity measures for AD that are currently available and instead promotes broad inquiries regarding the signs, symptoms, course, and QOL effects of AD.[77] The foundational approach to managing AD across all severity levels relies on non-pharmacologic treatments that fall into three broad categories: optimised bathing, consistent moisturising, and trigger avoidance (i.e., altering the environment to remove known allergies, irritants, etc.). Topical corticosteroids (TCS) of low to moderate strength should be used once or twice daily to active eczema lesions in mild AD, frequently for up to one week after clearing. Other options include topical janus kinase (JAK) inhibitors like ruxolitinib, phosphodiesterase-4 inhibitors like crisaborole, and topical calcineurin inhibitors (TCI). TCS potency should be raised to medium-high in mild AD, but non-steroid options should also be taken into account. These patients may benefit from maintenance (or "proactive") treatment, which is using topical

anti-inflammatories on a regular basis, 1-3 times per week, to flare-prone regions to avoid flares.

In moderate and severe AD, specialist referral (e.g., dermatologist) is critical for consideration of advanced therapies, which include phototherapy, systemic immunosuppressants (e.g., cyclosporine A, methotrexate, mycophenolate mofetil, azathioprine), biologics (e.g., dupilumab, tralokinumab), oral JAK inhibitors (e.g., abrocitinib, baricitinib, upadacitinib), and in certain cases, wet-wrap therapy or inpatient hospitalisation. Systemic corticosteroids are discouraged as a chronic therapy due to their widespread systemic side-effects associated with chronic usage and risk of rebound flares, despite their common use for the management of moderate-severe AD. Systemic corticosteroids may be used as a stopgap measure until better long-term treatment is found or as a quick fix for acute, severe flares. There is evidence to support the use of some adjunct medicines to treat AD comorbidities at all levels of severity (e.g., oral antihistamines for allergy diseases, antibiotics for infections), whereas well-controlled trials are lacking for other interventions (e.g., complementary and alternative medicine, probiotics, specialty diets)[78].

Asthma:

In different nations, 1–18% of the population suffers from asthma, which is a chronic airway inflammation characterised by a number of respiratory symptoms as wheezing, chest tightness, coughing, and reversible expiratory airflow restriction [79] One of the most prevalent forms of asthma, known as seasonal allergic asthma, has some connections to respiratory allergic illnesses brought on by pollen. John Bostock, a doctor at Guy's Hospital in London in 1819, made the first mention of pollen allergies. In the 20th century, allergic asthma and seasonal rhinitis were identified in millions of people.

Conclusion:

Since the last 200 years, the prevalence of allergy disorders has increased. Before that time, hay fever, a condition that is simple and straightforward to diagnose, was practically unknown in Europe and North America. Genetic reasons are improbable to account for this quick growth. Exposure to ambient air pollution is one of the possible environmental causes that has been hotly contested. The evidence to suggest that outdoor pollution to sulphur dioxide, particulate matter, diesel exhaust, and ozone is causally related with the onset of allergic diseases is weak, aside from passive smoking, which has convincingly been shown to increase the risk for asthma and bronchial hyperresponsiveness among exposed children. Instead, characteristics including socioeconomic status, allergy exposure, early childhood illnesses, dietary habits, and growing up in anthroposophic homes or a farming setting may show to be more significant when determining sibship number in communities or families. There is scant evidence to support the hypothesis that exposure to air pollutants such ozone, sulphur dioxide, particulate matter, or road exhaust causes the development of new cases of atopy or asthma. Asthma and allergies are examples of multifactorial illnesses that will eventually benefit from a greater knowledge of the complicated interplay between environmental influences and genetic determinants, which will lead to better prevention efforts.

Conflict of Interest:

The authors have no conflict of interest.

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