Review Article

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Asthma: The Changing Face of Allergens

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Abstract

It is known that asthma is one of the leading serious chronic illness affecting children in the United States. It is largely accepted that gene-environment interactions are responsible for the development of asthma; allergic sensitization has been demonstrated to be one of the major risk factors. While there appears to be a rather clear relationship between allergen exposure and allergic sensitization, a dose-response relationship is mostly relevant for "susceptible" individuals. Allergic multi-sensitization has increased significantly in the last few decades with young age, family history of allergy and urban living being identified as significant risk factors for allergic sensitization. Moreover, the changes in lifestyle and environment in the recent decades have modified the specific risk factors which predispose to the development of asthma.

Collectively, this review article suggests that there is a connection between environmental changes and allergic sensitization which contributes to the risk of developing asthma. Identifying the changing patterns of allergens and understanding their predictive ability in relation to asthma and other allergic diseases is crucial for the design of personalized diagnostic tools for the management of the chronic illness.

Keywords: Asthma; Allergic Sensitization; Allergens.

Background

Asthma is known to be a chronic inflammatory disorder of the airways, associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. Variable airflow obstruction that occurs within the lung during an attack is often reversible either spontaneously or with treatment. [1] Exposure to an allergen is an important risk factor for the development of atopic sensitization to that specific allergen and re-exposure triggers the asthmatic episode.[2]

Heterogeneity of Disease Asthma

Asthma comprises a range of heterogeneous phenotypes that differ in presentation, etiology and pathophysiology. The risk factors for each recognized phenotype of asthma include genetic, environmental and host factors. Family and twin studies have indicated that genetics plays an important role in the development of asthma.[3-5] Genome-wide linkage studies and case–control studies have identified 18 genomic regions and more than 100 genes associated with asthma in different populations.[6],[7] In particular, there are consistently replicated regions on the long arms of chromosomes 2, 5, 6, 12 and 13.[8] Association studies of unrelated individuals have also identified more than 100 genes associated with asthma.[9],[10] Asthma runs strongly in families and is about half due to genetic susceptibility and about half due to environmental factors.[3],[11],[12] The strong familial clustering of asthma has encouraged an increasing volume of research into the genetic predisposition to disease. Although identification of all asthma genes is incomplete, genetic findings are already changing the prevailing view of asthma pathogenesis. Disease risk will be estimated more accurately by determining networks of gene-gene and gene-environment

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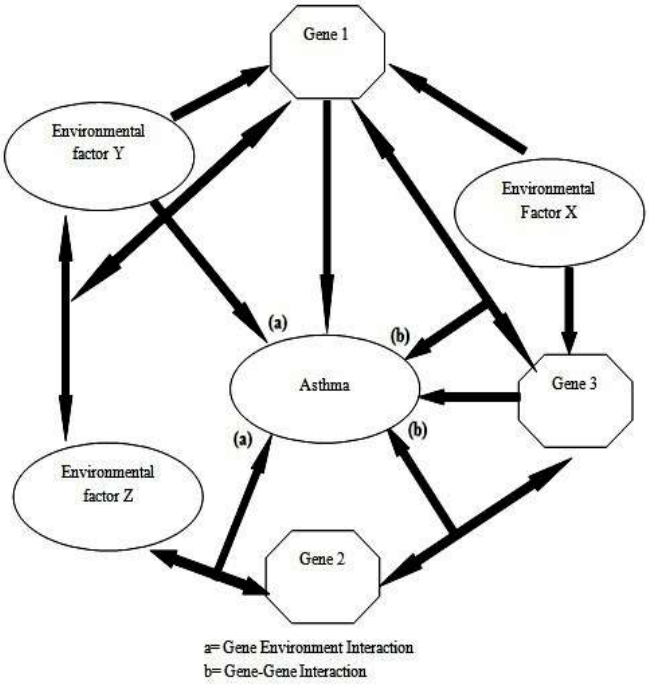


interactions and how polymorphisms contribute. (Fig 1)

Remodelling and Pathogenesis of asthma:

Asthma is a T-helper-cell 2 (Th2)-mediated chronic airway inflammation accompanied by bronchial hyperresponsiveness (BHR). The damage of epithelial cells, goblet cell hyperplasia, subepithelial fibrosis and smooth muscle hypertrophy and hyperplasia are involved in the development of BHR.[13] Activation of the epithelial–mesenchymal tropic unit in the airway, by interacting with cells which produce Th2 cytokines, is proposed to lead to the proliferation of fibroblasts and airway smooth muscle (ASM), contributing to BHR and airway remodelling.[14] Multiple genes and environmental factors play important roles in the pathogenesis of asthma. (Fig 2) emodeling is characterized by the appearance of permanent changes in the bronchial epithelium and the basement membrane as well as the underlying submucosa, capillaries, and smooth muscle. These changes permanently and irreversibly impair the correct functioning of the airways in almost all cases, and in most patients the airways are not susceptible to "restitutio ad integrum" even with long-term treatment.[15]

Asthmatic airways tissues have increased numbers of mast cells, activated eosinophils, and activated helper T lymphocytes. Helper T lymphocytes that produce proallergic, proinflammatory cytokines (e.g., IL-4, IL-5, IL-13) and chemokines (e.g., RANTES, eotaxin) arbitrate this inflammatory process. Other immune cells, named cytotoxic T lymphocytes, Natural killer (NK) cells, eosinophils, mast cells, basophils produce these proallergic, proinflammatory cytokines and chemokines as well. Airways inflammation is strongly linked to hypersensitivity of airways smooth muscle (airways hyperresponsiveness) to irritant exposures, such as cold air, dry air, strong odors, and particulate matter in smoke. (Supplementary Figure 1)

Airway inflammation causes less reversible airways changes, such as basement membrane thickening, subepithelial collagen deposition, and smooth muscle and mucus gland hypertrophy and hyperplasia. These airway "remodeling" abnormalities resemble an abnormal tissue repair process in response to continual tissue injury. Therefore, continual airway inflammation and remodeling are believed to trigger the chronic functional and pathologic abnormalities as well as the irregular and episodic clinical manifestations of asthma.

Allergic multi-sensitization and asthma

So now it is known that asthma is one of the leading serious chronic illnesses of children in the U.S. It is largely accepted that gene-environment interactions are responsible for the development of asthma; allergic sensitization has been demonstrated

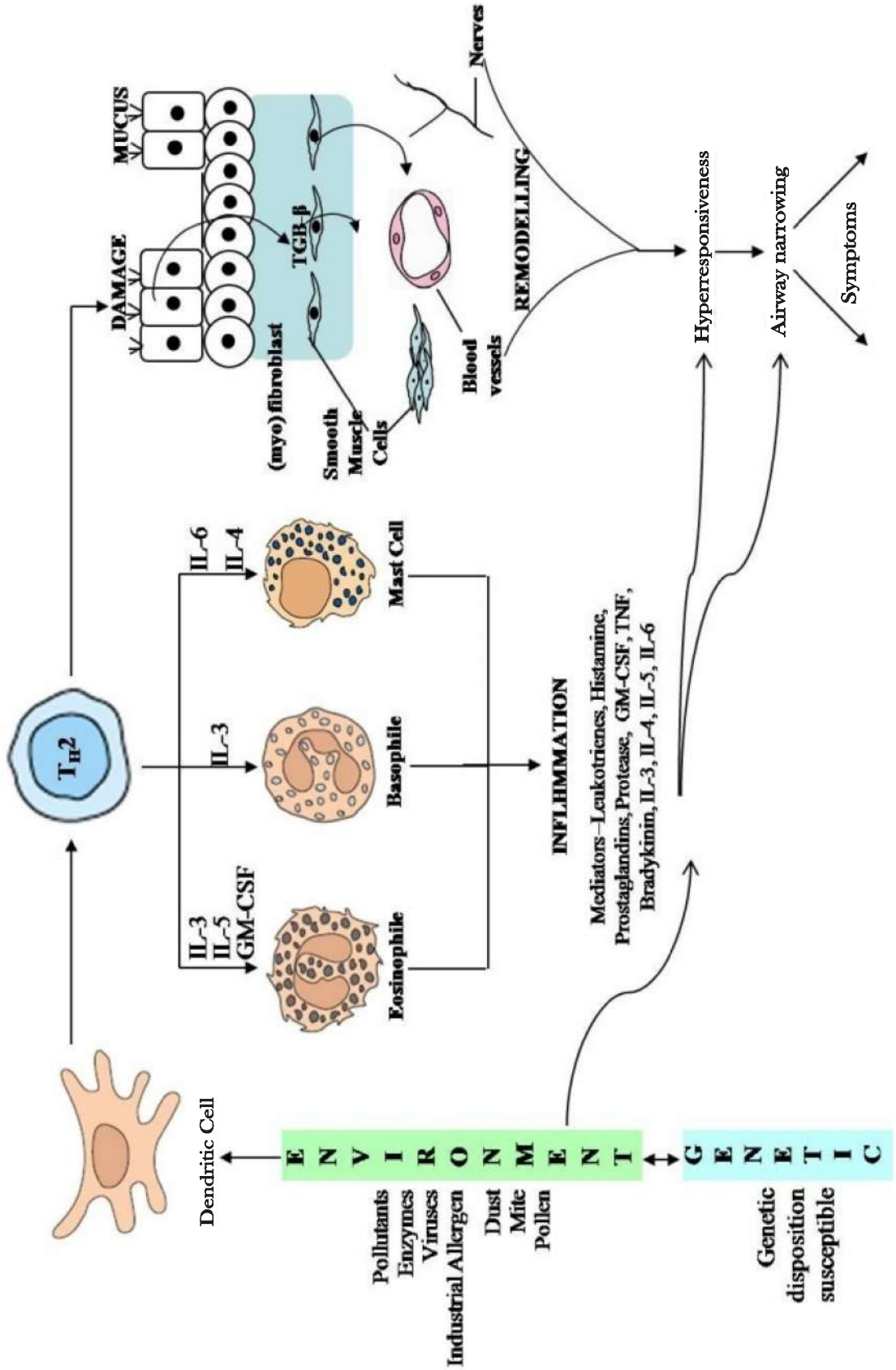
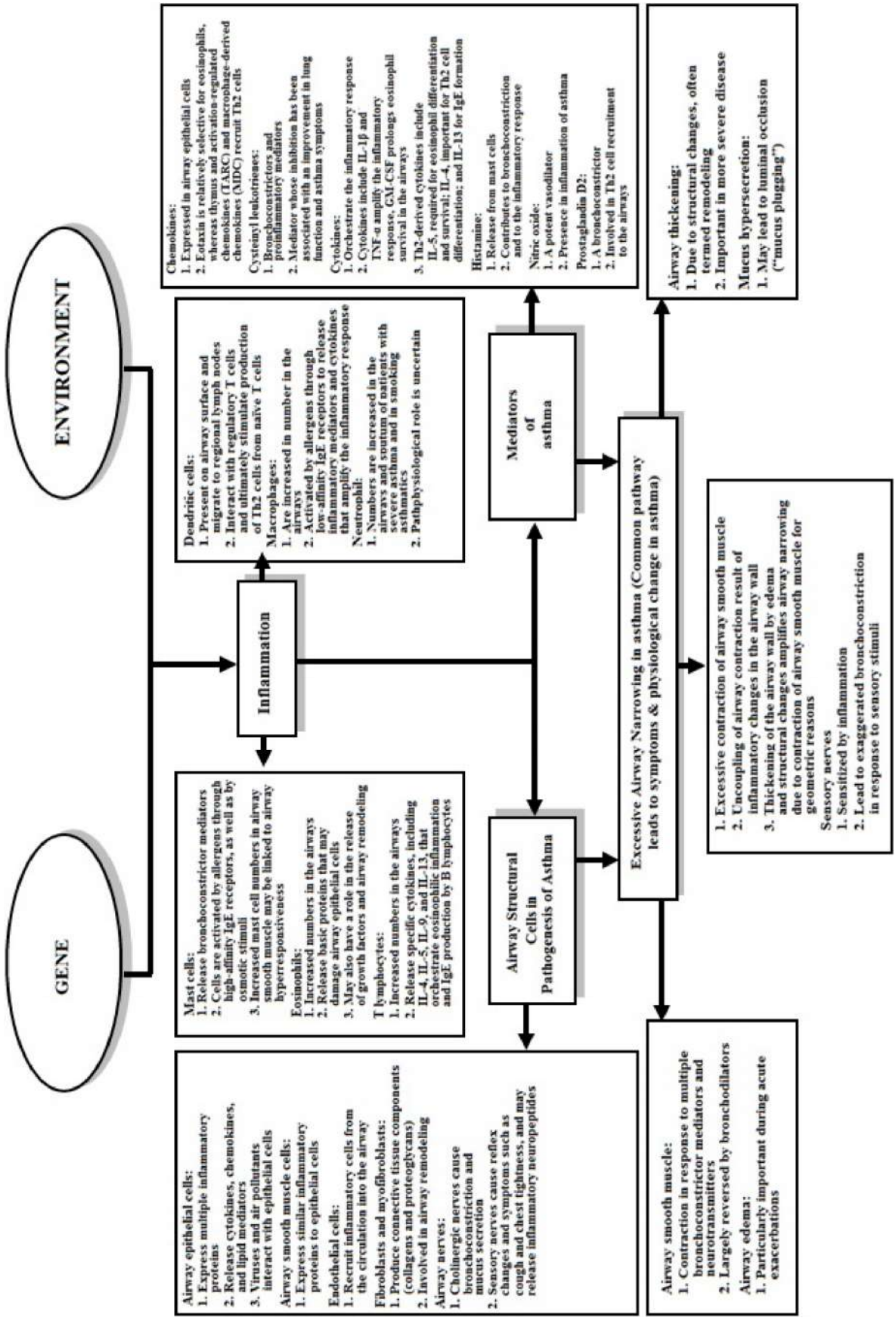


Fig. 2: Remodeling and Pathogenesis of asthma.

Supplementary Fig. 1: Detailed graphic presentation of mechanism of asthma



to be one of the major risk factors for the development of asthma.[16],[17] While there appears to be a rather clear relationship between allergen exposure and allergen sensitization, a dose-response relationship is mostly relevant for "susceptible" individuals. Allergic multi-sensitization has increased significantly in the last few decades with young age, family history of allergy and urban living being identified as significant risk factors for allergic sensitization. Moreover, the changes in lifestyle and environment in the recent decades have modified the specific risk factors in asthma even for well recognized risks such as occupational exposures, as is the case with adult onset asthma. [18-23]

Lifestyle changes have affected the prevalence of asthma as more and more cultures have adopted the western ways of life. Four features have been shown to be associated with such a lifestyle. First, the increased time spent indoors leading to increased exposure to allergens such as house dust mites. Second, the exposure to micro-organisms has changed due to improved hygiene and the increased use of antibiotics. Third, with the decline in the level of physical activity that the children get these days, the prevalence of obesity has increased remarkably. Last but not the least, the drastic change in the diet, with the shift from the consumption of fresh foods such as vegetables and fruits to the increasing demand and consumption of manufactured and processed food articles.[16]

Data suggest that house dust mites, pets, moulds, cockroaches, houseflies, rice grain dust, house mice, rats and other indoor allergens are the common allergens which are associated with asthma and other atopic disorders.[24-29] In low resource settings, exposure to indoor pollution such as smoke and fumes, use of biomass fuels and poor housing, are important risk factors for developing asthma . A study also suggested that acculturation and lifestyles played an important role in the incidence of asthma in which an increased risk of allergic asthma was observed with crop exposure, pesticide use and early life on a farm.[30] Pollen also is a well known allergen and recent studies have shown that environmental changes, seasonal variations and sudden occurrences such as thunderstorms and dust storms may increase the allergenic cloud of pollen and lead to acute exacervbations of the disease.[31-37] Allergic sensitization to cannabis sativa is rarely reported, but the increasing consumption of marijuana in the recent times has contributed to some reports of it triggering asthma.[38] Exposure to traffic, particularly to diesel exhaust, may exacerbate preexisting allergic conditions but does not necessarily induce the development of new cases of asthma and atopy. Diesel particles have also been shown to absorb allergens from grass pollen onto their surface and may therefore act as potential carriers to increase deposition of pollen allergens in the lung. In this way, both the allergen dose and the antigenicity of the pollen allergen may be enhanced by automobile-related pollution.[39-45]

Cleaning sprays, bleach, ammonia, disinfectants, mixing products, and specific job tasks, PVC have been identified as specific causes and/or triggers of asthma.[46] Epidemiological studies suggest that maternal exposure to environmental hazards, such as particulate matter, is associated with increased incidence of asthma in childhood. [47-48]

Conclusion

Collectively, these studies suggest that there is a connection between environmental changes and allergen sensitization which contributes to the risk of asthma and/or the severity of asthma.

Identifying the changing patterns of allergens and understanding their predictive ability in relation to asthma and other allergic diseases is crucial for the design of personalized diagnostic tools. The recent developments in the field of diagnosis and monitoring of asthma have been very promising. With the advent of neonatal screening of immunodeficiencies and asthma biomarkers, we can expect changes in the rate of diagnosis of this chronic disease and this also gives way to development of newer and a better protocols for management of the disease.

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