Childhood Asthma Epidemiology: Insights From Comparative Studies of Rural and Urban Populations

Gary W.K. Wong, MD* and Chung M. Chow, MBChB

Summary. Asthma is one of the most common chronic respiratory disorders. Many epidemiology studies have suggested an increasing trend of asthma in many different regions of the world but the exact reasons explaining such trend remain unclear. Nevertheless, changing environmental factors are most likely important in explaining the trend of asthma. Studies in the past decade have clearly shown a marked difference in the prevalence between urban and rural regions. The consistent findings of a markedly lower prevalence of asthma in children and adults who have been brought up in a farming environment clearly indicate the importance of environmental influence of asthma development. Although the exact protective environmental factors in the rural region remain to be defined, there have been many studies suggesting that early exposure to microbes or microbial products may play a role in modulating the immune system so as to reduce the future risk of asthma and allergies. Advances in the understanding of the genetic predisposition and how these genetic factors may interact with specific environment factors are of paramount importance for the future development of primary preventive strategies for asthma.


Key words: asthma; epidemiology; rural environment; risk factors.

INTRODUCTION

Asthma and related atopic conditions have become the most common chronic childhood disorders in developed countries. Numerous epidemiological studies have demonstrated an increasing trend of asthma prevalence in both developed and developing countries over the last 30 years.1–3 There have also been several recent reports showing a plateau or even a decline in the trend of asthma prevalence.4–7 These changing trends are unlikely to be explained by genetic factors while environmental factors are more likely to be important in driving these trends. In the last 10 years, many epidemiological reports have consistently documented a lower prevalence of asthma and atopy in subjects living in the rural areas when compared to those in urban areas.8–13 Increasing understanding of the ontogeny of the immune system in early life provides possible explanation of how a rural environment may protect against the development of asthma and allergies.14–18 Clear understanding of the important environmental determinants and how these determinants interact with the underlying genetic predisposition for asthma may shine light on how to develop primary preventive strategies against the development of asthma.

In this article, we review the recent data with emphasis on the studies comparing urban and rural populations and studies attempted to determine the mechanisms explaining the differences between them.

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ASTHMA EPIDEMIC IN THE DEVELOPED WORLD

Childhood asthma is the most prevalent chronic respiratory disease in the western world. Epidemiological studies performed in the last few decades showed a rapidly increasing prevalence of asthma in many countries. As documented by the International Study of Asthma and Allergies in Childhood (ISAAC), the highest prevalence of childhood asthma was found in English speaking countries such as the United Kingdom, Australia, and New Zealand. Using standardized methodologies to evaluate the secular trend of asthma prevalence, researchers have shown dramatic increase of asthma in children from the United Kingdom and Australia. In a period of 10 years from 1982 to 1992, the prevalence of wheezing within the past 12 months in schoolchildren aged 8–10 years had increased by 1.5–2.6 folds in two towns from New South Wales, Australia. In another study comparing prevalence of respiratory symptoms from two surveys done 25 years apart (1964–1989) in primary schoolchildren from Aberdeen, the prevalence of wheeze has increased from 10.4% to 19.8% while the reported diagnosis of asthma has increased from 4.1% to 10.2%. Similarly, the prevalence of asthma among children from the United States appeared to be increasingly more common.

Asthma is also now the second leading cause of hospitalization among subjects under 18 years of age in the United States. The dispensing of prescription drug for childhood asthma has increased by 2.5 times from the period of 1994–1995 to 2003–2004. There have also been many reports of increase in hospital admission as well as increase in the prevalence of objective features of asthma or atopy such as airway hyperresponsiveness and skin-prick reactivity in other western countries. The classic studies of comparing the changing trend of asthma and atopic symptoms of former East and West Germany have been most interesting. The environmental exposure and living conditions in former East and West Germany were very different. For example, the level of pollution as reflected by the concentration of sulphur dioxide and particulate matter was markedly higher in the former East Germany. However, the prevalence of wheeze, doctor diagnosed asthma and bronchial hyperreactivity was much higher in West Germany. The difference in the prevalence was most likely due to differences in environmental exposure in early life. Interestingly, rapid changes of westernization occurred in former East Germany after unification. Increasing prevalence of atopic sensitization and symptoms of hay fever were noted among children from the Eastern part of Germany. However, there were no significant changes in the prevalence of asthma or bronchial hyperresponsiveness. The authors suggested that the children were born 3 years before unification and they were exposed to western living condition only after the third birthday. Early exposure factors shortly after birth or even prenatally might have been more important in determining subsequent susceptibility to asthma. Identification of the possible environmental factors that explain the changing trend will provide insights into the etiologies of asthma and related atopic conditions.

The ISAAC was developed to measure the prevalence of childhood asthma, allergic rhinitis, and atopic eczema for international comparison using standardized and validated methodologies. Random samples of schoolchildren from more than 150 centers in 56 countries were recruited for study in ISAAC Phase One and Phase Three. The prevalence rates of wheeze in the past year in 13–14-year-old were found to vary widely from the highest 32.6% in Wellington, New Zealand to the lowest of 1.5% in Borivali, India. The most striking feature of the ISAAC studies was that the highest rates of asthma symptoms were in western countries whose predominant language is English. The good news is that no further increase was noted among countries with high prevalence when the Phase Three data were compared to those obtained in Phase One performed approximately 7 years previously. Furthermore, children of the same ethnic background living in different cities were found to have different prevalence rates of asthma symptoms. Within the Chinese population, the prevalence rate of asthma symptoms was found to be highest in children from Hong Kong. The 12-month prevalence of wheeze in 13–14-year-old as identified by the ISAAC written questionnaire was 8.6% while it was 4.8% in children from Guangzhou which is only a 2 hr drive from Hong Kong. Given the similar genetic background of these children from different Chinese cities, environmental exposure factors are likely to be important, resulting in the observed differences of asthma prevalence within the same ethnic group.

FARMING EXPOSURE AND PREVALENCE OF ASTHMA AND ALLERGIES

Over the past decade, there have been many studies demonstrating lower prevalence of asthma and allergies in children brought up in a farming environment (Table 1). Brau-Fahrlander et al. reported a study of 1,620 Swiss children aged 6–15 years showing farming as a parental occupation was significantly associated with lower rates of symptoms of allergic rhinitis and atopic sensitization. After adjustment for covariates, farming as a parental occupation was significantly associated with lower rates of sneezing attacks during the pollen seasons (odds ratio [OR] 0.34; 95% confidence interval [CI] 0.12–0.89). In another large German study of 10,163 children aged 5–7 years, the prevalence rates of hay fever (OR 0.52; 95% CI 0.28–0.99) and wheeze in the past year (OR 0.55; 95% CI 0.36–0.86) were significantly lower in farmers’
corroborated these findings.10–12,30–33 Both the German children when compared with children not living in a rural farming environment.9 Several other studies performed in Canada, Austria, Finland, and the United States corroborated these findings.10–12,30–33 Both the German and Austrian studies revealed that exposure to livestock was an important factor associated with protection against asthma and allergies for those living in a rural environment. It should also be noted that not all farming environments are associated with protection against allergies. The results of the PARSIFAL studies suggested that exposure to sheep farming was associated with increased risk of allergies, but the explanation for this association remained to be explored.34

There have also been studies investigating the effect of farming environment in the prevalence of asthma and atopy in adults. In a cross-sectional study of adults from Southern Germany living either in rural, suburban, and urban communities, a total of 4,405 subjects aged 25–75 years were recruited. Subjects were assessed by a self-administered questionnaire asking for allergic respiratory symptoms along with measurement of serum specific IgE antibodies.35 The urban population was found to have an increased risk of allergic rhinitis (OR 1.5; 95% CI 1.2–1.9), and atopic sensitization (OR 1.2; 95% CI 1.0–1.4) in comparison to rural residents. Furthermore, exposure to farm environment in childhood has been found to be protective against subsequent development of asthma and atopic sensitization in young adulthood. In a cross-sectional questionnaire survey of 10,618 Finnish University students aged 18–25 years with a subgroup of 296 underwent skin-prick test and specific-IgE measurements, current asthma was significantly lower in subjects with exposure to farm environment than those who had not (OR 0.22; 95% CI 0.07–0.70).36 In addition, sensitization to cat was less common in subjects with childhood farm exposure that those without (1.5% vs. 13.1%; OR 0.10; 95% CI 0.02–0.47). The data from the European Community Respiratory Heath Survey (ECRHS) also found similar results of protection against allergies if the subjects have had exposure to a farming environment during childhood.37 The important research question is to find out the factors associated with a farming environment conferring the protection against asthma and allergies.

HYGIENE HYPOTHESIS AND ASTHMA

Over the past two decades, there have been many epidemiological studies aiming at testing the so-called “hygiene hypothesis.” In 1989, Strachan38 proposed that infection in early childhood transmitted by unhygienic contact with older siblings or acquired prenatally from other by contact with older children, may have a protective effect on the subsequent development of asthma and allergies. His original observation of the inverse relationship of household size and self-reported prevalence of allergic rhinitis was further supported by several other studies using objective markers of atopy such as skin-prick tests.39,40 Several large cross-sectional and longitudinal studies have also found that attendance of day care in early childhood was protective against the development of asthma in later life.41,42 In the longitudinal study of the Tucson cohort, children have been followed carefully for the development of wheezing illness since birth.42 Subjects with one or more older siblings at home or attended day care centers during the first 6 months of life were found to have a lower risk (OR 0.3) of wheezing from the age of 6 years onwards. In general, family sizes are usually larger in those living in rural area and this may be one of the contributing factors to lower prevalence of asthma and allergies in children living in the rural environment. Over the past decade, the hygiene hypothesis has led to many research studies aiming at determining the role of infections and microbial exposure in modulating the immune system in a way which affects the subsequent risk of asthma and allergies.

TABLE 1— Major Comparative Studies of Children From Farming and Non-Farming Environments

<table>
<thead>
<tr>
<th>References</th>
<th>Location of study</th>
<th>n</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Germany</td>
<td>10,163</td>
<td>Farmers’ children was found to have lower prevalences of hay fever (OR = 0.52), asthma (0.65) and wheeze (0.55). Exposure to livestock was a significant protective factor</td>
</tr>
<tr>
<td>10</td>
<td>Switzerland</td>
<td>1,620</td>
<td>Atopic sensitization was lower in children from full-time farmers (OR = 0.24)</td>
</tr>
<tr>
<td>11</td>
<td>Austria</td>
<td>2,283</td>
<td>The prevalence of asthma, hay fever and positive skin-prick reactivity was significantly lower in children from a farming background</td>
</tr>
<tr>
<td>13</td>
<td>Canada</td>
<td>1,199</td>
<td>Adolescents raised on a farm had a lower risk of asthma (0.59) as defined as having wheeze and BHR</td>
</tr>
<tr>
<td>50,51</td>
<td>Austria, Germany, Switzerland</td>
<td>2,618</td>
<td>Exposure to stables before 1 year and consumption of farm milk were associated with protection against allergies. Endotoxin level in mattress’s dust was inversely related to atopic asthma</td>
</tr>
<tr>
<td>34</td>
<td>Austria, Germany, Netherlands, Sweden, Switzerland</td>
<td>8,263</td>
<td>Pig keeping, farm milk consumption, frequent stay in animal sheds, child’s involvement in haying were associated with lower risk of asthma. These factors were also associated with higher expression levels of genes of the innate immunity (CD14 and Toll-like receptor)</td>
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INFECTION AND DEVELOPMENT OF ASTHMA AND ATOPY

The hygiene hypothesis has opened up a whole new paradigm for research into the possible pathogenetic mechanisms for asthma and allergies. Shaheen et al. performed a study in African young adults from Guinea-Bissau showing an inverse association of measles infection and atopy. The history of measles infection in childhood was associated with a significant reduction in the risk of skin-prick test positivity to *Dermatophagoides pteronyssinus* (OR 0.2; 95% CI 0.05–0.81) and *D. farinae* (OR 0.2; 95% CI 0.06–0.71). In a large cross-sectional study of Italian military cadets, the prevalence rate of atopy, asthma, and allergic rhinitis were significantly lower in hepatitis A seropositive individuals.

Past exposure to hepatitis A most likely represent a marker of poor hygienic condition rather than a specific protection against asthma due to hepatitis A infection. The investigators subsequently determined the prevalence of positive serology to *Toxoplasmosis gondii* and *Helicobacter pylori* in atopic and non-atopic individuals. The results confirmed that atopy, asthma and hay fever were inversely associated with exposure to these food born infections in a dose-dependent way. In addition, there have also been studies suggesting the possible protective role of tuberculosis in the development of asthma and allergies.

The possible immunological mechanisms underlying the observed epidemiological associations between infections and asthma have been extensively studied. The current understanding is that exposure to microbes or microbial products in early life may prime the immune system resulting in an up regulation of T-helper 1 cells (Th-1) and a down regulation of T-helper 2 lymphocyte through the enhanced production of interleukin-12 (IL-12) and interferon-gamma (IFN-γ), while the production of Th-2 cytokines is diminished thereby reducing the propensity to develop IgE mediated atopic disorders.

Furthermore, microbial exposure may also enhance the activity of T regulatory cells resulting in immune suppression and a subsequent down-regulation of both Th-2 and Th-1 immunity. Further research into the underlying immunological mechanisms are necessary in order to have a full understanding how infections in early life may be beneficial in protecting against asthma and allergies.

THE RURAL ENVIRONMENT AND ASTHMA

As discussed in the previous sections, there are ample of evidence confirming the protective effect of a farming environment against the development of asthma and allergies. One important factor of the rural environment associated with reduction of allergies is exposure to livestock. In a study of the children of German farmers, frequent contact with livestock was associated with the lowest prevalence of atopy (OR 0.41; 95% CI: 0.23–0.74). Similarly, in an Austrian study of farmers’ children, the protection of the farming environment against atopic sensitization was lost after adjustment for contact with livestock or poultry. Subsequently, a large collaborative study was performed in rural areas of Germany, Switzerland and Austria on 2,618 primary school children. The results revealed that early exposure to stables and consumption of unpasteurized farm milk was associated with the lowest frequencies of asthma, hay fever and atopic sensitization. The relation of exposure to stables and the protection against asthma and allergies may be related to the high levels of both viable and nonviable microbes that are usually found in the farming environment especially in livestock farming. In addition, the investigators collected dust samples from the bed mattress to determine the concentration of endotoxin levels. The levels of endotoxin was inversely related to the prevalence of hay fever, atopic asthma, and atopic sensitization. Furthermore, stimulated cytokines production of peripheral blood lymphocytes including tumor-necrosis factor α and interleukin-10 showed an inverse relationship with endotoxin level in the dust sample from mattress suggesting a down-regulation of the immune response in children exposed to high level of endotoxin.

As endotoxin is only one component of the cell wall of Gram negative bacteria, it may only be one marker of possible load of microbial exposure. The researchers also examined the relationship of allergies and the level of *N*-acetyl-muramic acid in the dust samples. *N*-Acetyl-muramic acid is a major component of bacterial peptidoglycan, found in bacterial cell wall. As the cell wall of Gram-positive bacteria is thicker, the measurement of muramic acid should reflect more of the burden of environmental exposure to Gram positive bacteria. The results showed an inverse relationship of mattress dust muramic acid and prevalence of asthma even after adjustment for the endotoxin concentration. However, there was no association with atopy as defined by the presence of specific IgE. Therefore, the protection against asthma associated with exposure to Gram positive bacteria may be due to modulation of the immune system independent of the pathway leading to the production of IgE.

In addition to human epidemiological studies, inhalation of stable dust extract was also found to suppress the development of airway hyperresponsiveness and airway eosinophilia in an experimental model of ova-albumin sensitized mice. Clear understanding of the underlying immune mechanisms of the protection associated with exposure to bacterial components will help to explain why the rural farming environment is associated with lower prevalence of asthma.

Other than the exposure to livestock, there are many differences among the other lifestyle factors between the

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rural farming families and non-farming families. In a study of 765 children from Finland, consumption of raw vegetables was more frequent in farming families and frequent consumption of raw vegetables was inversely associated with atopy.\(^5^4\) In another large cross-sectional study of more than 10,000 Chinese schoolchildren recruited from Hong Kong, Beijing, and Guangzhou, the prevalence of asthma and wheeze was two times higher in Hong Kong than in the other two cities from Mainland.\(^5^5\) Frequent consumption of raw vegetables was one of the factors explaining the disparity of asthma prevalence between Hong Kong and Mainland China.\(^5^6\)

Consumption of unpasteurized farm milk has been consistently found to be inversely associated with a variety of allergic manifestations. In a study of German schoolchildren, consumption of unpasteurized farm milk was found to higher among farmers' children.\(^5^0\) Riedler et al.\(^5^0\) showed that consumption of farm milk in the first year of life was one of the strongest protective factors against the development of asthma and atopic sensitization in schoolchildren. Furthermore, in a study of 293 New Zealand schoolchildren, consumption of unpasteurized milk in the first 2 years of life was inversely associated with eczema (OR = 0.4; 95% CI: 0.2–0.8) and allergic rhinitis (OR = 0.3; 95% CI: 0.1–0.7).\(^5^7\) Perkin and Strachan reported in a large study of 4,767 primary schoolchildren from rural England, current unpasteurized milk consumption was associated with less current eczema symptoms (OR = 0.59; 95% CI: 0.40–0.87) and a lower rate of atopy as measured by positive response to skin-prick test (OR = 0.24; 95% CI: 0.10–0.53).\(^5^8\) Furthermore, unpasteurized milk consumption was associated with a reduction in total IgE level and higher production of whole blood stimulated interferon-\(\gamma\) which is a Th1 cytokine.

The inverse relationship of atopic diseases and consumption of unpasteurized farm milk is intriguing. Unpasteurized milk is known to contain a variety of Gram negative bacteria, many of them are known human pathogens.\(^5^9,6^0\) Exposure to these micro-organisms or their byproducts may affect the development of the immune system particularly in early life. In addition, unpasteurized milk is rich in Lactobacilli and the use of their byproducts may affect the development of the skin-prick test (OR\(^\approx\)0.24; 95% CI: 0.10–0.53). Furthermore, unpasteurized milk consumption was associated with a reduction in total IgE level and higher production of whole blood stimulated interferon-\(\gamma\) which is a Th1 cytokine.

As discussed earlier, helminth infections are associated with a polarized Th2 type of immune response. Several mechanisms have been proposed to explain the possible protection of helminth infection against asthma and atopy.\(^7^4\) There may be competition between helminth-induced polyclonal IgE and aero-allergen specific IgE for the high affinity IgE receptor on mast cells. The helminth specific IgG4 may also cross react and compete with antigen-specific IgE thereby inhibiting the IgE mediated response. A study in Gabonese children provided further insight in explaining the inverse relationship of helminth infection and atopy.\(^7^5\) The investigator showed that there was no relationship between total serum IgE and SPT reactivity to specific allergens (mite, cat, grass, dog). The inability to react to challenge with specific allergen was associated with higher level production of anti-inflammatory cytokine interleukin-10 by peripheral blood mononuclear cells stimulated by parasite antigen. These results suggest that increase production of this cytokine may be an important component in conferring protection against allergies in helminth infected subjects.

The role of a novel subset of CD4\(^+\) T cells, T-regulatory cells, has also been intensively studied in recent years. These T-regulatory cells are capable of producing high levels of IL-10 and transforming growth factor \(\beta\).\(^7^6\) These cells are likely to play an important role in explaining the protective effect of helminth infection against asthma.

**HELMINTH INFECTIONS AND ASTHMA**

Parasitic infections are common diseases affecting the rural population in tropical regions, while asthma is rather uncommon in these regions.\(^5^4\) There have been many studies suggesting that helminth infection may protect against asthma and allergies.\(^6^5–6^8\) Such a relationship seems paradoxical as helminth infections are characterized by a strong Th2-type of host immune response such as elevation of IgE and eosinophilia.\(^6^9\) An interesting study performed in Venezuela revealed a low prevalence of positive SPT to aeroallergens in subjects from an endemic area of Ascaris infection.\(^7^0\) Treatment with anthelmintic medication resulted in increase in the prevalence of positive SPT. In another recent study of 2,865 children aged 5–19 years from Ecuador, active infections with helminth and the presence of chronic infection were associated with protection against skin-test reactivity.\(^7^1\) However, there are also a few studies showing helminth infections and increased risk of asthma.\(^7^2,7^3\) The discrepancy among the reported studies could be attributable to the variation of the intensity and chronicity of helminth infections. It should be noted that the development of the immune system is also affected by other infections such as tuberculosis, salmonellosis as well as other fecal-oral infections. Altering one component of the total burden may not have a strong effect in affecting the development of atopy or asthma in some populations.

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and allergies. The relationship of helminth infection and asthma has a very important implication. With the improvement of sanitation in tropical rural areas, the burden of helminth infection will decrease and this may be associated with increase in the prevalence or severity of asthma.

**ASTHMA IN DEVELOPING COUNTRIES**

Epidemiological studies have clearly shown that asthma is more common in developed nations than in developing countries. The data from the Phase 3 studies of the ISAAC revealed that the highest prevalence of asthma were from English speaking countries such as New Zealand and the UK. However, latest epidemiological studies have also shown a plateau or even a decline in prevalence in some of these developed nations. On the other hand, the prevalence was relatively lower in developing countries such as India, Ethiopia, and Indonesia. With the process of economic development and urbanization, the prevalence of asthma and related atopic conditions has been found to be increasing. A recent study of Ghanaian children has demonstrated a twofold increase of the prevalence of exercise induced bronchospasm and sensitization over a 10-year period. Indeed, ISAAC Phase 3 data from Africa showed that the prevalence of wheeze in the past year in several countries such as Congo, and Republic of Guinea were approaching the prevalence rates found in western European countries. Nevertheless, in some other developing countries such as Malaysia, the prevalence of asthma in schoolchildren has remained unchanged over a period of 7 years.

The increase in asthma in developing countries is most likely related to the change of lifestyle and environmental exposure. This process of development has frequently been termed “westernization.” However, what particular factors of westernized life style contribute to the development of asthma and allergies are not clear. A combination of factors is likely to be responsible and we have discussed many of these possible factors such as exposure in the rural environment, level of hygiene, exposure to infections and microbial components, dietary changes, and parasitic infections. Accurate documentation of changes in these factors along with careful monitoring of asthma prevalence in developing countries will enable us to evaluate the potential role of these factors in the development of asthma.

**GENE-ENVIRONMENT INTERACTIONS IN ASTHMA**

We have discussed many factors that may be operating in the rural areas resulting in the disparity of asthma prevalence between rural and urban areas. We should not ignore the vast amount of literature on the genetic contribution to the development of asthma and allergies. Although genetic factors alone cannot explain the increase in asthma prevalence over the past few decades or the disparity of asthma prevalence between urban and rural populations, the understanding of how various genes may interact with specific environmental factors is important for the future development of primary prevention of asthma.

As asthma is an inflammatory disease of the airways characterized by a Th2 type of immune response, many genes involved in various inflammatory pathways have been studied extensively. It is beyond the scope of this review to examine the literature related to genetic influences of asthma development and there have been several excellent reviews written on this topic. However, we should understand the patterns of variation of allelic frequencies in genes related to T-helper immune response of various populations and how these variations may affect the future trend of asthma in these population when the environment changes with time.

It has been observed that the frequency of alleles that promote Th2 activities is higher in populations with ancestry in the tropics. Such enhanced Th2 response may have a protective role against helminth infections in the tropics. With the improvement of hygienic condition and reduction of parasitic infection, such enhanced Th2 activities will no longer provide any survival advantage. Instead, such relatively enhanced Th2 response may predispose the population to higher prevalence or increased severity of allergic diseases such as asthma. One of the most widely studied asthma genes is CD14. The studies of this gene clearly illustrate the complexities of interaction between genes and the environment. CD14 is a specific receptor for lipopolysaccharides (LPS) and other bacterial cell wall components. Baldini et al. first reported that a single nucleotide polymorphism (SNP) of CD14 at position-159 was associated with the development of asthma. Furthermore, the T allele for CD14/-159 was found to be associated with higher level of serum soluble CD14 receptor. Subsequently, our group has also found that atopic homozygotes for T allele in Chinese children had higher serum IgE than carriers of the other two genotypes. However, there have been several large studies showing no association. In contrast, Kedda et al. reported that the T allele was over-transmitted within atopic subjects. The story became clear when Eder et al. studied the relationship of atopy and endotoxin exposure after stratifying the subjects by their CD14 genotypes. At low level of endotoxin exposure, homozygotes for C allele have the highest risk for allergic disease. However, these subjects are at the lowest risk at high levels of endotoxin exposure. Two other studies corroborated this finding. The exact biological mechanisms for this pattern are still not clearly understood. Complex diseases like asthma are likely the result of interaction of genetic predisposition and exposure to
environment factors at critical time. As our lifestyle changes from a primarily rural environment to a modern westernized urban surrounding, many of our previously “protective” genotypes may be partly responsible for diseases that are usually associated with a modern lifestyle. Clear understanding of how these genes interact with various environmental factors leading to the development of asthma will shine light on how to develop primary preventive measure for asthma.

CONCLUSION

The epidemiology studies comparing asthma in urban and rural areas have provided us directions of research to define the important environmental factors modulating the immune system towards the development of asthma and related atopic diseases. It is likely that the lower prevalence of asthma in the rural environment is a result of exposure to a “package” of factors which collectively influences the developing immune system. The process of urbanization results in many changes such as dietary factors, alteration of the pattern of infections, reduction of family size, reduction of exposure to microbes, increase in the use of antibiotics and immunization. Advances in the understanding of the interaction between genetic factors and environmental determinants enable to have a better understanding of the pathogenesis of asthma. When we have a clear understanding of how various genes may interact with various protective environmental factors in the rural setting resulting in protection against the development of asthma, we will be able to devise possible primary preventative strategies against the development of asthma in the future.

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